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Eleven years ago, as a neuromuscular fellow, Aiesha Ahmed, MD, was encouraged by her mentors to attend the AANEM Annual Meeting. It was an educational experience Dr. Ahmed will never forget and she’s been a member of AANEM ever since!

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HODGKIN LYMPHOMA RADIOTHERAPY NEUROMUSCULAR MORBIDITY: A LARGE TERTIARY CARE CENTER EXPERIENCE
Tatsuya Oishi (Rochester, MN), Cory Kogelschatz (Murray, UT), E. Matthew Hoffman (Rochester, MN), Kogulavadanan Arumaithurai (Rochester, MN), Sue Visscher (Rochester, MN), Bijan Borah (Rochester, MN), Nathan Young (Rochester, MN), Stephen Ansell (Rochester, MN), William Krauss (Rochester, MN), Christopher Klein (Rochester, MN)

INTRODUCTION: Hodgkin lymphoma (HL) is a hematologic malignancy treated with chemoradiation and has a favorable longterm prognosis. Delayed neuromuscular complications from radiation are under-recognized.

OBJECTIVE: To quantitate neuromuscular complications from radiotherapy in HL.

METHODS: Medical records from Mayo Health Care system were electronically retrieved, identifying pre-specified neuromuscular complications among radiation-treated HL patients between January 1, 1994 to December 31, 2016. Diagnostic trends, clinical visits and morbidity were reviewed.

RESULTS: Of an estimated 4,100 post-radiotherapy HL patients, 192 (4.7%) were identified with neuromuscular complications. Mean latency to physician visit for symptoms was 23.9 years (range: 1-50). Most commonly identified complications included myopathy (73), plexopathy (54), myelopathy (53), and polyradiculopathy (25). Other notable findings included benign and malignant nerve sheath tumors (9), mononeuropathies (phrenic and long thoracic, 14), and compressive spinal meningioma (4). Patients frequently had multiple coexisting complications (single=147, double=33, triple=8, quadruple=4). Cardiac (55) and pulmonary (29) complications were also seen. History of HL was occasionally overlooked by neurologists (50/347 clinical notes, or 14.4%). Hospital and outpatient visits for complications were frequent: neuromuscular (77/413 visits) versus cardiopulmonary (127/413 visits). Head drop and plexopathies were the most readily recognized complications. Testing was largely exclusionary, except when imaging identified secondary malignancy. Estimated modified Rankin Score at diagnosis varied: 0-1 (55.6%), 2-3 (6.5%), and 4-5 (38.0%).

SUMMARY/CONCLUSION: Neuromuscular complications among post-radiation HL are diverse, not uncommon, with delayed morbidity, and often difficult to diagnose. Survivorship recommendations should acknowledge awareness of neurological complications, in addition to more recognized cardiac/pulmonary/gastrointestinal sequelae.

Tatsuya Oishi, MD
Best Abstract Award Recipient

Disclosures:
Christopher Klein - Honorarium from Akcea Therapeutics.
HEPATITIS SPASTIC PARAPLEGIA: CLINICAL AND GENETIC SPECTRUM IN A SELECTED ARGENTINEAN GROUP
Facundo Heredia (Capital Federal, Argentina), Cintia Marchesoni (Buenos Aires, Argentina), Andres Berardo (Capital Federal, Argentina), Luciana León Cejas (Buenos Aires, Argentina), Lucía Schottlaender (London, United Kingdom), Ricardo Reisin (Buenos Aires, Argentina), Henry Houlden (London, United Kingdom), Stephanie Efthymiou (London, United Kingdom), Jana Vandrovcova (London, United Kingdom), Marcelo Ruggiero (Buenos Aires, Argentina), Emanuel Silva (Posadas, Argentina), Javier Rolle (Buenos Aires, Argentina), Gisella Gargiulo (Buenos Aires, Argentina), Marta Mednia (Buenos Aires, Argentina), Cecilia Vas (Buenos Aires, Argentina)

INTRODUCTION: Hereditary spastic paraplegia (HSP) refers to a heterogeneous group of disorders characterized clinically by progressive lower limb spasticity and weakness. Based on the presence or absence of additional neurological or systemic abnormalities, HSP is classified as complicated (cHSP) or uncomplicated (uHSP). Diagnosis of HSP is challenging due to the lack of a clear genotype-phenotype correlation as well the many genes implicated.

OBJECTIVE: To determine the clinical and molecular characteristics of a cohort of Argentinean patients with idiopathic spastic paraplegia.

METHODS: We performed clinical, neurophysiological, laboratory, radiological, and genetic studies in 42 consecutive patients with HSP (66% female; mean age: 48 years, range: 22-76). A 62 gene panel was performed using TruSight™ One and Agilent SureSelect Focused Exome.

RESULTS: In our group 52% met the criteria of uHSP. In the cHSP cohort, the most frequently associated symptom was dysarthria, followed by hearing loss and ataxia. NCSs showed symptomatic axonal sensory/motor neuropathy in 2 cHSP patients, and asymptomatic axonal sensory neuropathy in 8 patients (5 uHSP/3 cHSP). Brain MRI showed corpus callosum atrophy in 1 cHSP patient and cerebellar atrophy in another cHSP patient. Laboratory workup was unremarkable in all patients. Pathogenic mutations were identified in 13/42 (30.9%) patients: SPG4 (3), SPG6 (3), SPG7 (3), SPG11 (2), SPG10 (1), and ALS2 (1). Variants of unknown significance were detected in the following genes in 5 additional patients (EEF2, PRKN, KCNC3, WSHC5, and MARS).

SUMMARY/CONCLUSION: A third of our patients with HSP presented a pathogenic mutation. We found a similar frequency of SPAST, SPG6, and SPG7 mutations in our population.

Facundo Heredia, MD
Best Abstract Award Recipient-Runner Up

MORPHOMETRIC ANALYSIS OF PERIPHERAL MYELINATED NERVE FIBERS THROUGH DEEP LEARNING
Jun Li (Detroit, MI), Bo Hu (Detroit, MI), Daniil Moiseev (Detroit, MI)

INTRODUCTION: Most neurological diseases produce one of two key pathological changes—axonal loss or demyelination, or a combination of the two. Traditional manual quantification of the pathologies is time-consuming and may suffer from inter-observer variation. Deep machine learning in artificial intelligence may be used through a convolutional neural network (CNN)-based approach to segment images of peripheral nerve.

OBJECTIVE: To automate quantification of nerve morphometrics.

METHODS: We used Keras, a deep-learning library, to create a CNN based on U-net architecture for improved localization of image features. Training data included 280 microscopic images of mouse sciatic nerve cross-sections paired with their respective segmentation masks accumulated from our previous studies.

RESULTS: After training, accuracy plateaued at 0.91 dice coefficient, and the validation dice coefficient varied between 0.81 and 0.85. Compared to the manual method, the CNN-based automated method exhibited a 2.5% decrease of nerve fiber density, 4.2% lower axonal diameter, 2.0% larger myelin thickness, and 2.6% lower g-ratio. Distribution of myelinated fiber diameters was similar between the two methods. After training, segmentation of each image was instantaneous.

SUMMARY/CONCLUSION: We have developed a CNN-based method to analyze nerve morphometrics. Previously acquired nerve images were used to train the computational model to recognize pathological changes. The trained model decreased analysis time with excellent accuracy in axonal density and g-ratio with minimal manual refinements required. Overall, greatly increased efficiency in the automation outweighs minor limitations, thus justifying our confidence in its prospects, including applications in human skin biopsies and sural nerve biopsies.

Jun Li, MD, PhD
President’s Research Initiative Award Recipient
THE SURFACE POTENTIAL QUANTIFICATION ENGINE INTEGRATES ACTIVE VOLUNTARY IDENTIFICATION TO ENHANCE FASCICULATION ANALYSIS IN AMYOTROPHIC LATERAL SCLEROSIS

James Bashford (London, United Kingdom), Aidan Wickham (London, United Kingdom), Raquel Iniesta (London, United Kingdom), Emmanuelle Drakakis (London, United Kingdom), Martyn Boutelle (London, United Kingdom), Kerry Mills (London, United Kingdom), Christopher Shaw (London, United Kingdom)

INTRODUCTION: Fasciculations are a clinical hallmark of ALS. The Surface Potential Quantification Engine (SPiQE) is a novel analytical tool to identify fasciculation potentials (FPs) from high-density surface EMG (HDSEMG) in ALS. The method is accurate on relaxed recordings amidst fluctuating noise levels. However, a third of sampled recordings required time-consuming manual exclusion of voluntary activity.

OBJECTIVE: To develop an automated procedure capable of rapidly excluding voluntary potentials (VPs) and integrating with the established SPiQE pipeline.

METHODS: Six ALS patients and 2 control subjects (benign fasciculation syndrome and multifocal motor neuropathy) underwent monthly 30-minute HDSEMG recorded from the biceps and gastrocnemius over 6 months. In MATLAB, we developed and compared the performance of 4 active voluntary identification (AVID) strategies, producing a decision aid for optimal selection. Fasciculation frequency (FF) was calculated for each recording.

RESULTS: Assessment of 601 1-minute recording samples demonstrated the specific temporal pattern of voluntary activity, permitting the development of sensitive (AVID-1A), specific (AVID-2), and screening (AVID-0/AVID-1B) strategies for VP exclusion. For 97/165 (58.8%) 30-minute recordings, AVID-0 confirmed the absence of voluntary activity. For the remaining recordings, the median exclusion times (13.1, 2.3, 3.4; minutes), processing times (36.1, 16.3, 49.5; seconds), and FFs (27.4, 38.8, 38.8; number per minute) of 3 AVID strategies (1A, 1B, 2) were compared. The overall median FF was 40.5 per minute (10.6-79.4 interquartile range).

SUMMARY/CONCLUSION: AVID is a flexible, targeted approach to exclude voluntary activity from HDSEMG recordings. SPiQE provides systematic and reliable FP analysis from raw 30-minute recordings in ALS.

James Bashford, MA, MRCP
President’s Research Initiative Award Recipient

CUTANEOUS SILENT PERIODS IN PATIENTS WITH EARLY STAGE AMYOTROPHIC LATERAL SCLEROSIS

Rachel Pérez-Lalana (La Habana, Cuba), Tatiana Zaldivar (La Habana, Cuba) Gloria Lara (La Habana, Cuba), Asdrúbal Arias (La Habana, Cuba), Yodeisy Ferrer (La Habana, Cuba), Orla Hardiman (Dublin, Ireland), Joel Gutiérrez (La Habana, Cuba)

INTRODUCTION: The cutaneous silent period (CSP) is an electrophysiological response equivalent to the withdrawal reflex. It is mediated by inhibitory circuits at the spinal cord. The CSP could be useful to evaluate spinal cord inhibitory responses in ALS.

OBJECTIVE: To determine whether CSP can be elicited in early stage ALS and to characterize its electrophysiological features.

METHODS: CSP responses were evaluated in 23 patients with early stage ALS (age: 59.3±10.9 years) and 15 control subjects (age: 62.1±10.4 years). Needle EMG activity was recorded from the thenar muscles while the subjects performed a mild voluntary contraction. CSPs were induced with electrical stimulation, delivered to the middle finger, with 3 levels of intensity of electrical stimulation (25, 50, and 75 mA). The onset latency and the total duration of CSP responses were quantified and compared across groups and levels of intensity of stimulation.

RESULTS: All ALS subjects displayed identifiable CSP responses at high intensities of stimulation (75-100 mA). The CSP durations were increased in ALS patients for all levels of stimulation (25 mA: 62.1±24.0 versus 37.2 ±7.1, p=0.000; 50 mA: 73.3±33.9 versus 44.4±7.6, p=0.003; 75 mA: 88.1± 42.7 versus 45.7±6.6, p=0.000). ALS patients showed similar onset latencies to control subjects.

SUMMARY/CONCLUSION: The increased mean CSP durations observed in the ALS patients could indicate increased inhibition of spinal motor neurons. It is also possible that a reduced number of spinal motor neurons could contribute to these results. CSP could be a useful probe to explore the balance between inhibition and excitability of spinal motor neurons.

Rachel Pérez-Lalana, MSc
President’s Research Initiative Award Recipient
REFERENCE VALUES FOR MOTOR UNIT NUMBER INDEX BASED ON STUDY OF 120 HEALTHY INDIVIDUALS

Bei Cao (Chengdu, China), Yongping Chen (Chengdu, China), Qianqian Wei (Chengdu, China), Lingyu Zhang (Chengdu, China), Huifang Shang (Chengdu, China)

INTRODUCTION: Motor unit number index (MUNIX) is a novel and noninvasive electrophysiological index measuring the number of functioning motor neurons in a given muscle. Previous studies have found that MUNIX can be used to assess the disease progression of ALS. However, few studies have reported reference values for MUNIX.

OBJECTIVE: To investigate the features of MUNIX in healthy individuals and establish reference value ranges in 5 muscles, including the right abductor pollicis brevis (APB), abductor digiti minimi (ADM), biceps brachii (BB), tibialis anterior (TA), and trapezius (TR).

METHODS: We included in 120 healthy individuals and measured the MUNIX in the right APB, ADM, BB, TA, and TR muscles in every participant. Taking into account that the loss of motor neurons is associated with aging, the subjects were stratified by an interval of 10 years (participants were separated into 6 different age groups ranging 20-79), and we established reference values for each age group.

RESULTS: The study enrolled 120 healthy subjects (60 male, 60 female; mean age: 49.6±17.4 years, range 20-79, median age: 50). The mean MUNIX of the APB, ADM, BB, TA, and TR were 181.2±46.9, 159.4±39.0, 166.3±39.5, 147.4±41.2, and 163.8±41.5, respectively. Age was inversely correlated with the MUNIX of the APB, ADM, BB, TA, and TR.

SUMMARY/CONCLUSION: We established MUNIX reference values in the APB, ADM, BB, TA, and TR in different age groups, which may help in monitoring disease progression of neuromuscular diseases, such as ALS.

Bei Cao, MD
President’s Research Initiative Award Recipient

ELECTROMYOGRAPHY-BASED PHONE CURSOR CONTROL USING DEEP NEURAL NETWORKS

Ronald Cotton (Chicago, IL)

INTRODUCTION: Accessing a smartphone is an important part of modern life, but for many people with quadriplegia the only option is using a stick grasped in the mouth. Decoding neural data is a promising approach, but not ready for routine use. Surface EMG from residual muscle is less invasive but has its own challenges—often requiring burdensome calibration and unnatural control schemes while tethered to research equipment.

OBJECTIVE: To develop a wireless EMG-based cursor control system requiring only a phone.

METHODS: A Bluetooth-enabled 8-channel differential EMG system was developed with accompanying Android application for data acquisition and was used to record from muscles available in many quadriplegic patients (trapezoids, rhomboids, deltoids, and sternocleidomastoid). EMG signals were decoded using a deep neural network. The first stage was a variational autoencoder to learn a latent space representation, and the second stage mapped this to 2D cursor control. The variational autoencoder was trained from natural movement, and the second stage used supervised learning while the user attempts to chase a cursor during a training game.

RESULTS: The hardware produced high quality EMG recording. The variational autoencoder rapidly learned a latent space representation of the muscle activation patterns. The training game allows the user to self-select movement patterns for control and the network rapidly learned this mapping, allowing accurate cursor control.

SUMMARY/CONCLUSION: This addresses some challenges for quadriplegic patients to control a phone via EMG: it uses wireless and portable hardware with a training approach that allows more natural movements and can be rapidly trained.

Ronald Cotton, MD, PhD
President’s Research Initiative Award Recipient
MEASURING UPPER MOTOR NEURON DYSFUNCTION IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

INTRODUCTION: Objective identification of cortical motor neuron disease in ALS remains an area of need in the clinic and research settings. Transcranial magnetic stimulation (TMS) can objectively disclose corticospinal tract involvement in ALS. Brain MRI quantitative susceptibility mapping (QSM) analysis also identifies degenerating neurons in the motor cortex because of abnormal iron deposition. The relative value of each method in identifying corticospinal tract disease is not certain.

OBJECTIVE: To assess the diagnostic value of using both TMS triple stimulation technique (TST) and MRI/QSM protocols in ALS patients in clinical practice.

METHODS: In this retrospective study, all patients with suspected ALS seen in Neurology at the Hospital for Special Surgery during 2015-2018 having undergone TST and MRI/QSM were reviewed. We identified 13 patients; 4 did not have ALS and were excluded, 9 had El Escorial defined probable or definite ALS.

RESULTS: In 7/9 patients (77.77%), both TST and MRI/QSM showed abnormal cortical responses. In 1 patient, TST showed the motor cortex to be unresponsive but QSM was normal. In another patient, TST was normal and QSM showed abnormal iron deposition. TST showed a non-responsive motor cortex in all ALS patients.

SUMMARY/CONCLUSION: QSM and TST studies seem to be useful objective markers to identify motor neuron dysfunction in ALS patients consistent with clinical findings and disease severity. In clinical practice, both tests should be performed since in some patients, one test could be negative.

Armin Maghsoudlou, MD
President's Research Initiative Award Recipient
Resident and Fellow Member Award Recipient

THE DIAGNOSTIC YIELD OF REPETITIVE NERVE STIMULATION
Tingting Hua (Columbia, MO), Emily Bailey (Kirksville, MO), Raghav Govindarajan (Columbia, MO)

INTRODUCTION: Low frequency repetitive nerve stimulation (RNS) is commonly used in the diagnosis of myasthenia gravis (MG). The effect of various clinical factors on its diagnostic yield is unknown.

OBJECTIVE: To assess the impact of clinical, serological, and demographic factors on the diagnostic yield of RNS.

METHODS: Patients with an established MG diagnosis and at least 1 year followup at the hospital were retrospectively analyzed. Fishers t-test was used to test the association between various clinical factors and RNS yield.

RESULTS: Thirty-two (49.2%) patients were in Myasthenia Gravis Foundation of America (MGFA) Class I, 14 (21.5%) were in MGFA class IIa, 13 (20.0%) were in MGFA class IIb, and the remaining 6 (9.2%) were in MGFA classes IIIa-V. Thirty-two patients were seropositive for MG antibodies, 20 were seronegative. Eleven patients underwent RNS in the inpatient setting; 54 were tested in the outpatient setting. Acetylcholine receptor (AChR) binding antibody titer ranged from 0.12 nmol/L to 118 nmol/L (Mayo Clinic). Diagnostic yield was higher for seropositive patients as compared to seronegative (p<0.05). Patients with MGFA class III or higher also had higher diagnostic yield as compared to lower classes (p<0.05). Diagnostic yield was the highest for patients with MGFA class III or higher tested in an inpatient setting (p<0.05).

SUMMARY/CONCLUSION: Testing conducted in an inpatient setting, seropositive status, MGFA class III or higher are predictors of a positive RNS in the diagnosis of MG.

Tingting Hua, BS
Medical Student Research Award Recipient
10  DIAGNOSTIC ERRORS AND THE IMPLICATIONS FOR AMYOTROPHIC LATERAL SCLEROSIS PATIENTS  
Catherine Rodriguez (Columbia, MO), Emily Bailey (Kirksville, MO), Raghav Govindarajan (Columbia, MO)  
INTRODUCTION: ALS is a fatal degenerative motor neuron disease that can be difficult to diagnose due to a variety of initial presenting symptoms. A diagnostic error may result in medical or surgical interventions that are not efficacious and may harm the patient, as surgery has been shown to hasten the progression of ALS.  
OBJECTIVE: To identify clinical factors and types of cognitive errors that can result in misdiagnosis of ALS.  
METHODS: Electronic medical records of 88 ALS patients receiving treatment at the University of Missouri Hospital from 2011-2017 with at least 1 year followup were analyzed to collect demographic information and clinical characteristics of their ALS. If the patient received an incorrect diagnosis, the number of physicians seen, incorrect diagnosis, treatment, type of diagnostic error, clinical factors contributing to the misdiagnosis, and type of physician who gave the incorrect diagnosis were recorded. Diagnostic errors were categorized according to Patient Safety Network's 4 categories of cognitive bias. Statistical analysis of data was done using a Fisher's exact test.  
RESULTS: Veterans were misdiagnosed due to availability heuristic, while non-veterans were misdiagnosed due to anchoring heuristic (p<0.05). Lower limb onset was most commonly misdiagnosed due to anchoring heuristic (p<0.05). Bulbar onset was most commonly misdiagnosed due to availability heuristic (p<0.05). Surgical intervention was the most common treatment for an incorrect diagnosis (p<0.05).  
SUMMARY/CONCLUSION: Absence of upper motor neuron signs on examination, presence of sensory symptoms, and absence of tongue fasciculations are common causes of ALS misdiagnosis.  
  
Catherine Rodriguez, BS  
Medical Student Research Award Recipient  

11  AUTOIMMUNE STATIN-ASSOCIATED MYOPATHY: AN UNUSUAL CASE  
Nikita Chhabra (Scottsdale, AZ), William Peppo (Glendale, AZ), Christina Chrisman (Phoenix, AZ)  
INTRODUCTION/BACKGROUND: HMGCR antibody-positive necrotizing myopathy is a lesser known possible side effect of statins. This condition typically presents with symmetrical, proximal muscle weakness. However, our patient had an unusual presentation with asymmetric weakness and dysphagia.  
CASE REPORT: We describe a case of a 57-year-old male who presented with 5 months of worsening pain and weakness of the proximal thigh and shoulder muscles, with more severe weakness on the left side. He also endorsed significant dysphagia, resulting in a 10-kg weight loss. He had a history of hyperlipidemia, treated with atorvastatin for the last 4 years. The patient initially presented to his family physician, who conducted laboratory tests and instructed him to discontinue atorvastatin, suspecting myalgia, but this did not relieve his symptoms. The patient's creatine phosphokinase was elevated at 7085 u/L. He was instructed to go to the ER due to concern of rhabdomyolysis. The patient underwent muscle biopsy which revealed mild necrotizing myopathy. A standard myositis panel was negative. However, the HMGCR antibody returned as positive, which allowed diagnosis of autoimmune statin-associated necrotizing myopathy. The patient was discharged and started on 30 mg prednisone and 150 mg azathioprine, but his symptoms continued to worsen. He was then admitted and started on IVIg, which resulted in significant improvement. He was discharged home after 3 days of treatment.  
SUMMARY/CONCLUSION: Due to the ubiquitous use of statins, being able to recognize the various types of myopathy with which they are associated is crucial as they demand distinct management and have variable prognoses.  
Nikita Chhabra, MSIII, H.BSc.  
Medical Student Research Award Recipient
OUTCOMES IN SPINAL MUSCULAR ATROPHY INFANTS ON NUSINERSEN THERAPY
Joshua Kaltman (Decatur, GA), Sumit Verma (Johns Creek, GA)

INTRODUCTION: Intrathecal nusinersen was approved for spinal muscular atrophy (SMA) in 2016. However, post-approval therapy outcome studies amongst infants are limited.

OBJECTIVE: To evaluate outcomes of SMA infants on nusinersen.

METHODS: Retrospective study of SMA infants (SMN2 copy number ≤ 2) on nusinersen therapy between 2017-2019 was performed. Baseline and followup weight, Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP- INTEND) scores, right abductor digiti minimi (ADM) and abductor pollicis brevis (APB) compound muscle action potentials (CMAPs), duration of bilevel positive airway pressure (BiPAP), gastrostomy tube, tracheostomy, and death were recorded. Descriptive statistics were used.

RESULTS: Nine infants (5 girls) with symptom onset at mean age of 2.33±1.67 months (range: 1-5) and genetic confirmation at 3.67±1.92 months (range: 1-6) were included. Nusinersen therapy was started at mean age 5.17±2.06 months (range: 2.5-8.0; mean delay from age of diagnosis: 1.44±0.62). Median followup was 6.5 months (range: 2.5-17.0). Mean baseline and followup results: weight 6.39±1.26 (3.60-7.96) and 8.6±2.0 (6.3-11.7) kg, CHOP-INTEND 26.6±8.40 (14-40) and 40.4±6.66 (38-52; max 64), right APB CMAP 0.68±0.33 (0.3-1.3) and 1.37±0.40 (0.9-2.1) mV, and right ADM CMAP 0.46±0.25 (0.2-0.8) and 0.38±0.15 (0.2-0.6) mV. All infants failed swallow study and 6 (67%) underwent gastrostomy. Seven (78%) required BiPAP, 2 (22%) tracheostomy, and 1 (11%) died of respiratory failure.

SUMMARY/CONCLUSION: SMA infants on nusinersen improved in weight, CHOP-INTEND scores, and CMAP amplitudes. However, swallow dysfunction and respiratory insufficiency remained the leading cause of morbidity and mortality even among treated subjects.

Joshua Kaltman, BS
Medical Student Research Award Recipient

DIAGNOSTIC AND CODING ACCURACY OF IDIOPATHIC INFLAMMATORY MYOPATHIES AT THOMAS JEFFERSON UNIVERSITY: A RETROSPECTIVE STUDY
Andrew Sinensky (Philadelphia, PA), Connie Tang (Philadelphia, PA), Goran Rakocevic (Philadelphia, PA)

INTRODUCTION: Idiopathic inflammatory myopathies (IIMs) are a heterogenous group of disorders most commonly diagnosed by rheumatologists and neurologists. The clinicopathological criteria for more distinct forms of inflammatory myopathies such as dermatomyositis (DM), inclusion body myositis (IBM), and polymyositis (PM) are well established and confirmed by muscle biopsy.

OBJECTIVE: To investigate the diagnostic criteria and correlated ICD-10 coding practices in patients with myositis, with a particular interest in the characterization of IIMs, in order to identify areas for improvement.

METHODS: We conducted a retrospective search of electronic records of myopathies during the past 5 years. We identified and reviewed 376 unique patients with myositis using the ICD-10 codes M33 and G72. Muscle biopsy was used as a gold standard for diagnosis. For patients who did not have a muscle biopsy, the clinical diagnosis of myositis was queried and reviewed.

RESULTS: In our cohort of 376 patients, we identified 128 with an ICD-10 code for a distinct IIM: 28 with IBM, 13 with DM, and 87 with PM. An additional 248 patients had drug-induced, systemic illness-associated, or other unspecified myopathies. Of the 128 patients with a distinct IIM, 70 (54.7%) had a diagnostic muscle biopsy and 30 (23.4%) others were previously misdiagnosed in the ICD-10.

SUMMARY/CONCLUSION: Inflammatory myopathies without a muscle biopsy for diagnostic classification remain a diagnostic challenge, therefore leaving in a large group of IIMs inadequately characterized, coded, and managed. Improving diagnostic and coding practices at the onset of the disease is essential for appropriate management and better outcomes of patients with myositis.

Andrew Sinensky, BS
Medical Student Research Award Recipient
ASSOCIATIONS BETWEEN NEUROMUSCULAR DISEASES AND OBSTETRICS AND GYNECOLOGY COMPLICATIONS
Zahra Haider (Columbia, MO), Raghav Govindarajan (Columbia, MO)

INTRODUCTION: Few studies have been performed on the complications and outcomes of pregnancy in women diagnosed with a neuromuscular disease. Similarly, limited information is available about their risk of developing a gynecologic issue.

OBJECTIVE: To analyze whether there is an association between a certain neuromuscular disease (i.e., myasthenia gravis, ALS, muscular dystrophy, Charcot–Marie–Tooth disease, spinal muscular atrophy) and developing obstetrics and gynecology (OB/GYN) complications. This information can help improve care for patients who are concerned about their reproductive health risks.

METHODS: Ninety-five female patients with a diagnosis of a neuromuscular disease were examined. Using retrospective chart analysis, we collected data on demographics, neuromuscular disease, and OB/GYN complications. The data were coded and analyzed in Microsoft Excel. P-values were calculated to determine any statically significant association between OB/GYN complication and neuromuscular disease.

RESULTS: With a p-value of 0.9160, we conclude that there is no statistical evidence from the available data to support an association between OB complications and type of neuromuscular disease. Additionally, with a p-value of 0.3348, we conclude that there is no statistical evidence from the available data to support an association between GYN complications and type of neuromuscular disease.

SUMMARY/CONCLUSION: Analysis of our data shows that there is no statistically significant association between these neuromuscular diseases and the OB/GYN complications we examined. These patients frequently have concerns about their reproductive health. Currently, only few studies address these questions. Additional studies must be performed to set appropriate guidelines for the management of reproductive health issues in these patients.

Zahra Haider, BS
Medical Student Research Award Recipient

RETROSPECTIVE ANALYSIS OF COMORBIDITIES ASSOCIATED WITH MYASTHENIA GRAVIS
Brian Blankenship (Columbia, MO), Raghav Govindarajan (Columbia, MO)

INTRODUCTION: Myasthenia gravis (MG) is a chronic condition requiring longterm immunosuppressive therapy. The development of comorbid conditions can impact MG treatment and prognosis.

OBJECTIVE: To assess the development of comorbidities in newly diagnosed MG within the first 12 months.

METHODS: This is a retrospective chart review of all adult MG patients whose data was acquired from 2011-2015 and had at least a year followup in our clinic. The breakdown of 70 patients included (39 men, 31 women; mean age: 62 years, range: 20-97) is 67 Caucasian, 3 African American, 47 seropositive, 6 thymectomy, 3 Myasthenia Gravis Foundation of America (MGFA) class 1, 29 MGFA class 2a, 11 MGFA class 2b, 20 MGFA class 3a, 6 MGFA class 3b, 1 MGFA class 4a, 43 on prednisone, 4 on prednisone and steroid-sparing agent, 15 on steroid-sparing agent alone, 5 on maintenance IVIg, and 10 on pyridostigmine alone.

RESULTS: Of those 70 patients, 35 comorbid events were experienced. Steroid and immunosuppressive related events were the most frequent comprising 31.4%, of which osteoporosis was most common (p=0.0030). Infections and neurological events each comprised 28.6% with pulmonary infections and peripheral neuropathy being the most common, respectively. Other comorbid events accounted for 14%, which included chronic obstructive pulmonary disease, stroke, acute kidney injury, gastrointestinal bleed, and hypothyroidism. Older patients tended to have significantly more comorbid events (p=0.0594).

SUMMARY/CONCLUSION: In conclusion, many patients diagnosed with MG experience comorbid events within the first 12 months, most frequently including steroid and immunosuppressive related complications followed closely by infections and other neurological conditions.

Brian Blankenship, BS
Medical Student Research Award Recipient
INFLUENZA VACCINATION OF PATIENTS WITH AUTOIMMUNE NEUROMUSCULAR DISORDERS: A WEB-BASED SURVEY OF CURRENT PRACTICES AND PERCEPTIONS
Tess Litchman (New Haven, CT), Richard Nowak (New Haven, CT), Bhaskar Ray (New Haven, CT)

INTRODUCTION: Influenza vaccination of patients with autoimmune neuromuscular disorders such as myasthenia gravis (MG), chronic inflammatory demyelinating polyneuropathy (CIDP), or Guillain–Barré syndrome (GBS) is controversial, and no clear guideline exists.

METHODS: We performed a web-based survey among neurologists across the United States to explore current practices regarding the recommendation of flu shot for patients with MG, CIDP, and GBS.

RESULTS: There were 181 responses with highest numbers from California (8.8%), Connecticut (8.8%), and Texas (8.3%). Respondents were further characterized as being in practice on average 15.5±11.2 (SD) years and self-reported the following specialty practice: neuromuscular medicine (50%), general neurology (20%), mixed (20%), and other (10%). A total of 6448 MG, 2310 CIDP, and 1907 GBS patients were followed across practice settings. Respondents reported recommending a flu shot either for all or for >50% of patients in 95%, 84%, and 67% of their MG, CIDP, and GBS patients, respectively. Temporal association of disease relapse with flu shot was reported in 1.6%, 4%, and 9% of MG, CIDP, and GBS patients, respectively. Recurrent relapses occurred in 87% (26/30), 92% (23/25), and 74% (26/35) of patients with MG, CIDP, and GBS, respectively, who received another flu shot.

SUMMARY/CONCLUSION: Influenza vaccination was perceived to be safe in the majority of patients with autoimmune neuromuscular disorders. Neurologists appeared to be more conservative in recommending immunization for patients with a history of GBS. Temporally associated disease relapses appeared to be a risk factor for relapse with subsequent immunization.

THE LESION OF ANTERIOR INTEROSSEOUS NERVE SYNDROME IS NOT IN THE FOREARM
Esther Zusstone (Cincinnati, OH), Zsuzsanna Arányi (Budapest, Hungary), Scott Wolfe (New York, NY), Joseph Feinberg (New York, NY), Ogonna Nwawka (New York, NY), Steve Lee (New York, NY), Darryl Sneag (Plainview, NY)

INTRODUCTION: Anterior interosseous nerve syndrome (AINS) is a peripheral neuropathy often characterized by a severe pain prodrome and palsy of its innervated muscle(s), sometimes attributed to Parsonage–Turner syndrome or compression neuropathy.

OBJECTIVE: To test the hypothesis that (1) hourglass constrictions (HGCs) are present within the AIN fascicular group of the median nerve near the level of the humeral medial epicondyle (ME) and (2) there is no compression of the median nerve or AIN in the forearm.

METHODS: A radiologist and neurologist at 2 sites analyzed high-resolution MRI (n=22) and ultrasounds (US, n=23) to evaluate the median nerve and AIN within the arm and forearm in patients with EDX- and/or clinically-confirmed AINS.

RESULTS: HGCs were identified in all MRI cases, and constrictions and/or swelling in 87% of US cases. On MRI, HGCs were located an average of 2.4 cm proximal to the ME, at posterior/posteromedial (68%, avg=1.7 cm, expected location of the AIN fascicle), anterior/anteromedial (19%, avg=5.3 cm, expected location of pronator teres [PT]/flexor carpi radialis [FCR] fascicle), posterolateral (5%, avg=1.0 cm), and anterolateral (8%, avg=9.4 cm) locations. On US, HGCs were located an average of 4.5 cm proximal to the ME, at posterior/posteromedial (55%, avg=4.3 cm), medial (36%, avg=5.0 cm), and posterolateral (9%, avg=4.0 cm) locations. No extrinsic compressive lesions of the median or AIN within the arm or forearm were identified.

SUMMARY/CONCLUSION: HGCs of the AIN fascicle of the median nerve are hallmark imaging findings in AINS, often concomitantly involving the PT/FCR fascicle.
UTILIZATION OF LEG MAGNETIC RESONANCE IMAGING AS AN ADDITIONAL DIAGNOSTIC TOOL IN THE ASSESSMENT OF FOOT DROP

Tara Torabi (New Haven, CT), Sukanthi Kovvuru (New Haven, CT), Richard J Nowak (New Haven, CT), Bhaskar Roy (New Haven, CT)

INTRODUCTION/BACKGROUND: Needle EMG/NCSs are often the preferred diagnostic methods to evaluate foot drop. Sampling of different leg muscles with needle EMG, looking for neurogenic changes, is required to assess the underlying etiology. MRI of the leg can identify neurogenic changes in different muscles and thus provide further supportive information.

CASE REPORT: Seven cases of foot drop (4 right, 3 left) were reviewed. Two patients had known underlying neuropathy and 3 also had milder or chronic dorsiflexion weakness in the other leg. In 3 cases, where needle EMG was suggestive of possible peroneal neuropathy across the fibular head without significant denervation changes on needle EMG, MRI of the leg did not show any preferential edema in peroneal-innervated muscles. In all these cases, recovery was rapid and complete. Two cases of peroneal neuropathy with significant axon loss had edema only in the peroneal-innervated muscles on MRI. In both cases recovery was limited. In 1 case with clinical suspicion of peroneal neuropathy, needle EMG was suggestive of more diffuse changes and MRI reflected muscle edema in all leg muscles. In the last case, the patient had isolated peroneus longus atrophy on clinical examination, however MRI reflected edema in L5-innervated muscle groups; needle EMG confirmed this finding.

SUMMARY/CONCLUSION: MRI of the leg can be a useful diagnostic tool in selected cases of foot drop. Further study can help to better understand the potential of MRI in such cases.

Tara Torabi, MSc
Medical Student Research Award Recipient

DESIGNING EDUCATION TO IMPROVE CLINICIAN PERFORMANCE IN TREATING UPPER LIMB SPASTICITY: A CONTINUING MEDICAL EDUCATION CASE REPORT

Annette Schwind (Orangeburg, NY)

INTRODUCTION/BACKGROUND: Patients with upper limb spasticity (ULS) can benefit from treatment with injectable botulinum neurotoxin-A (BoNT-A), but clinicians exhibit gaps in knowledge, competence, and performance regarding its optimal use. Nine regional workshops were implemented combining expert-led discussions, patient narratives, and small group hands-on exercises to address learning needs of clinicians using BoNT-A injections to treat ULS.

CASE REPORT: In the workshops, participants reviewed evidence-based best practices, uncovered their personal learning needs, and practiced using recommended techniques. Observational assessments of skills by faculty and learners were conducted and compared. Participants demonstrated gains in knowledge and competence from pretest to posttest, but hands-on exercises demonstrated that understanding did not translate well from theory into practice. On average, faculty observations estimated learners incorrectly placed injections 58% of the time, using unguided techniques. Using a 4-point scale (1=poor, 2=fair, 3=good, 4=excellent), faculty observed learner’s skills and gave their first hands-on attempts average ratings in properly reading ultrasound (US) displays (1.7) and localizing target muscles (1.6). Following practice and feedback, faculty rated learners 3.1 on both. Of learners responding to a commitment to change question on post-activity evaluations, 100% intended to change their practice. Two months later, 100% of respondents to a followup survey indicated they had implemented practice changes based on what they learned.

SUMMARY/CONCLUSION: The effective, engaging CME workshop improved learner knowledge, competence, and performance. Assessments by learners and faculty identified that further education, specifically more hands-on practice, is needed to continue to improve clinicians’ knowledge and skills.
MILL'S SYNDROME AS A PROGRESSIVE ASYMMETRIC LIMB WEAKNESS
Shailesh Reddy (Austin, TX), Yessar Hussain (Austin, TX)

INTRODUCTION/BACKGROUND: There is no universally accepted definition of Mill's syndrome. We present 3 cases suggesting that Mill's syndrome is a slowly progressive asymmetrical spastic paresis.

CASE REPORT: A 75-year-old female presented with 2 years' progressive right-hand weakness/spasticity. Examination showed 4/5 strength of right first dorsal interosseous and finger flexors. She had increased spasticity in the right-upper extremity. Laboratory work/EDX studies were normal. MRI showed degeneration in the left precentral gyrus. A 72-year-old female experienced sudden right upper extremity pain/weakness. She developed spasticity of the left-upper extremity and 4 years later asymmetrical bilateral lower extremity pain/weakness. Examination showed 1/5 strength and hyperreflexia in left-upper extremity. Spasticity was noted in bilateral upper extremities. Laboratory work/EDX studies were normal. MRI-brain was negative. Fluorodeoxyglucose-positron emission tomography (FDG-PET) of the brain demonstrated diminished activity in the right precentral gyrus. A 73-year-old male presented for evaluation of possible ALS. He had 5 months' right grip weakness. MRI-brain showed chronic white matter changes. Examination showed decreased strength throughout the right upper/lower extremity compared to left side. Modified Ashworth was 1+ in the right upper/lower extremities with no spasticity contralaterally. Deep tendon reflexes 3+ on the right compared to the left with positive cross-adductor reflex. EDX studies showed symmetric sensory axonal polyneuropathy. FDG-PET was negative.

SUMMARY/CONCLUSION: Mill's syndrome may be thought of as slowly progressive asymmetrical spastic hemiparesis without sensory abnormalities. The slow progression and natural course suggests unique pathophysiological basis different from primary lateral sclerosis.

INCORPORATION OF ELECTRODIAGNOSTIC CASE REVIEWS TO THE MORNING REPORT IN A NEUROLOGY RESIDENCY PROGRAM
Stephanie Wyrostek (Danville, PA), Jose David Avila (Danville, PA)

INTRODUCTION: EDX training is variable among residency programs in the United States. At our institution, the goal for residents is to accurately interpret EDX studies independently. We have observed that while most acquire the necessary knowledge to achieve this goal, they have difficulty applying and retaining such knowledge. Adult learning theory indicates that repeated exposure over time enhances knowledge accumulation and retention.

OBJECTIVE: To create a longitudinal learning experience focused on the interpretation of EDX studies.

METHODS: Monthly EDX case review was incorporated into the morning report in August 2018. Resident's knowledge and feedback was assessed after 7 months.

RESULTS: We developed a step-wise approach to EDX studies aligned with the Accreditation Council for Graduate Medical Education milestones for neuromuscular disorders and NCSs/needle EMG. This includes how to order EDX studies appropriately, the formulation of NCS and needle EMG plans, use of appropriate terminology, description and interpretation of data, identification of pitfalls, and interpretation of EDX study results in the clinical context. Ten out of 11 residents took a knowledge test. Six (55%) scored 70% or higher, 3 scored between 50-60%, and 1 scored below 50%. All residents completed a feedback survey and 10 (91%) wanted to continue this model for the next academic year.

SUMMARY/CONCLUSION: Incorporating EDX case reviews to the morning report is feasible. Residents were satisfied with this model and want it to continue. We plan to implement a pre-test to evaluate baseline knowledge of new residents before the intervention and repeat a test after 6 months to assess knowledge retention.

Stephanie Wyrostek, DO
Resident and Fellow Member Award Recipient
THE PATH TO DIAGNOSING CHARCOT–MARIE–TOOTH DISEASE: THE PATIENT EXPERIENCE
Robert N Moore (New York, New York), Allison T Moore (New York, NY), Florian P Thomas (Hackensack, NJ), Joy M Aldrich (Seattle, WA), Courtney L Hollett (Chesterfield, VA)

INTRODUCTION: Patients with Charcot–Marie–Tooth (CMT) disease cite a long path to obtaining an accurate diagnosis of their disease, even with a family history of CMT.

OBJECTIVE: To assess the path to diagnosis experienced by CMT patients, considering family history of disease, initial presentation of symptoms, and length of time to obtain a diagnosis.

METHODS: The Hereditary Neuropathy Foundation created the Global Registry for Inherited Neuropathies (GRIN) to capture detailed inherited neuropathy (IN) patient history via an online, IRB-approved patient survey over 2013-2019. IN patients (n=2,195) were queried regarding family history of CMT and diagnosis.

RESULTS: Seventy-six percent of CMT patients have a family history of the disease. For length of time to get a CMT diagnosis, 59% of patients take over 1 year, with 23% taking 5 years. Symptoms present at age 15 years or younger for 42%, with 26% being 30 years or older. Thirty percent of patients were the first to notice their CMT symptoms, while 27% were first identified by a healthcare practitioner (HCP). Neurologists were overwhelmingly identified as the HCP who first diagnosed CMT (33%). Genetic testing was the leading method for obtaining a diagnosis (24%), with EDX studies next (15%).

CONCLUSIONS: CMT patients can present symptoms early in life. While HCP's early identification of patient symptoms is sizably represented, given the large cohort of youthful manifestation of the disease coupled with the length of time to obtain a definitive diagnosis, increased symptom awareness across the spectrum of HCPs is indicated.

Disclosures:
Florian P Thomas - Consultant for Pharnext and Acceleron Pharma.

TRAINING PHANTOMS FOR PERINEURAL INJECTIONS
Elena Shanina (Houston, TX), Robert Glenn Smith (Houston, TX)

INTRODUCTION: In recent years, traditional anatomical landmark-based approaches to needle placement in many procedures have been rendered more accurate by ultrasound (US) guidance. Delicate structure, small size, and frequent location near vasculature make nerves vulnerable to complications. Despite well-known advantages of simulation training, models for perineural injections are not readily available. Commercial phantoms are large, expensive, and not suitable for small areas like wrists.

OBJECTIVE: To analyze different materials used to simulate different organs and tissues, and to create a simple phantom of the wrist for practice carpal tunnel injections.

METHODS: We used plastisol, IV tubing, latex glove material, and rubber strings to produce a model for simulated median nerve perineural injections. This model was compared to other phantom materials to assess optimal US visualization of the target structure, needle advancement, and solution injection.

RESULTS: Compared to other materials for human tissue simulation, including poultry, pork, tofu, and gelatin, all having short shelf lives and requiring refrigeration after each training session, this model can be kept at room temperature, does not lose qualities after prolonged storage, resembles real tissue echogenic properties, and can be used repeatedly. This model also allowed realistic visual imaging of the target and needle during insertions. The presence of simulated vascular structures promoted needle track planning and safe repositioning.

SUMMARY/CONCLUSION: An US-compatible nerve model is inexpensive and easy to make, allowing trainees to develop more confidence and skill before attempting such procedures on patients. This should significantly improve patient safety and effectiveness of the procedure.
FACILITATED LEARNING OF MEDICAL STUDENTS IN THE ELECTROMYOGRAPHY LABORATORY BY PRIOR PREPARATORY ORIENTATION AND INDIVIDUALIZED EDUCATION TO MEET PERSONAL EXPECTATIONS: A PILOT STUDY FROM A LARGE ACADEMY
Sankar Bandyopadhyay (Hershey, PA)

INTRODUCTION: Third and fourth year medical students rotate through EMG laboratories with both faculty and students unprepared regarding expectations.

OBJECTIVE: To study the outcome of these rotations where both students and faculty are aware of expectations.

METHOD: The author (EMG attending) emailed 10 medical students 1-3 days prior to a scheduled rotation a slideshow explaining the basics of needle EMG, its clinical usefulness, application, contraindications, and safety concerns felt necessary by the attending. The students in turn, let the attending know what specific topics they specifically would like to be discussed, in addition to the standard discussion at the laboratory. An optional survey was conducted at the end.

RESULT: Participation in the optional survey was 100%. Responders stated that this was (1) a novel experience across the university in other fields: 100%, (2) more useful and involving than the standard random rotations: 100%, (3) not time consuming, delaying, or problematic: 100%, (4) definitely facilitated training: 100%, (5) provided scope for personalized learning: 100%, and (6) recommendable in all other types of rotations: 100%. Comments included: fostered constructive discussion, reflected on individual gaps in knowledge, provided an incentive to look up subject matter beforehand, facilitated educational discussion, enhanced the learning process, cleared the usual confusion short rotations usually produce, feel valued by the faculty, and was simply a great idea.

SUMMARY/CONCLUSION: This pilot study showed that without adding resources, cost, or delays, it is possible to get higher levels of satisfaction and involvement, with probable facilitated learning. The key is a learning method of individualization that does not compromise the standard core curriculum.

IMPROVING THE EDUCATIONAL EXPERIENCE OF NCS/EMG TRAINING FOR NEUROLOGY RESIDENTS: A PILOT PROJECT
Preston Douglas (Providence, RI), Kara Stavros (Providence, RI), George Sachs (Providence, RI)

INTRODUCTION: Neurology residents today face a rapidly expanding field and ever-increasing time demands, potentially limiting exposure to techniques such as NCSs/needle EMG. In turn, neuromuscular educators face increasing pressure to improve the educational yield of resident rotations. Few published NCS/needle EMG curricula address these evolving challenges; none are customizable or web-based.

OBJECTIVE: To improve educational outcomes in the NCS/needle EMG rotation for neurology residents at the Rhode Island Hospital (RIH).

METHODS: A series of quizzes and cases consisting of multiple choice, matching, and fill-in-the-blank questions were developed, based on AANEM specifications, each designed to highlight specific high-yield teaching points. These were grouped into 6 weekly experiences, with questions becoming increasingly sophisticated over time, culminating in real world interpretive challenges based on patient cases taken from the RIH EMG laboratory. The weekly experiences were digitized with Google Forms, which automates feedback and aggregates performance data to allow question optimization. Google Sites was used to centralize access to both weekly quizzes and relevant textbook chapters via the library website. Anonymous pre- and post-test surveys were administered to gauge resident perception of the curriculum's value.

RESULTS: Four neurology residents have used the curriculum in tandem with laboratory experience. Anecdotal and survey data suggest a benefit from the curriculum in both knowledge base and confidence in NCS/needle EMG techniques.

SUMMARY/CONCLUSION: Interactive quizzes emphasizing high-yield topics may enhance the educational experience of neurology residents when learning NCSs/needle EMG. In the future, additional material will be added to make a more comprehensive review for a broader audience.

Preston Douglas, MD
Resident and Fellow Member Award Recipient
FACIAL ONSET SENSORIMOTOR NEURONOPATHY SYNDROME ASSOCIATED WITH NON-HODGKIN LYMPHOMA
Stephan Botez (Outremont, Canada), Rami Massie (Montreal, Canada), Daniel Alejandro Vargas Mendez (Montreal, Canada)

INTRODUCTION: Facial onset sensorimotor neuronopathy syndrome (FOSMN) is a recently described neurological syndrome, characterized by slow onset of facial sensory abnormalities and motor deficits, often followed by more diffuse lower motor neuron abnormalities. Other motor neuron disorders secondary to hematological malignancies have been previously reported with variable response to treatment.

CASE REPORT: We describe a clinical case of FOSMN associated with non-Hodgkin lymphoma (NHL). We report clinical data, laboratory and neurophysiological findings, genetic testing results, and followup after treatment of the lymphoma. A 49-year-old female presented with progressive left perioral/chin paresthesias, slowly spreading to the cheek and the contralateral side and subsequently developed bilateral asymmetric facial palsies within 1 year. Over the following 4 years, she noticed sensory symptoms in her right hand, followed by diffuse weakness in the right, and then left, upper limb, progressive bulbar dysfunction, and Adie's pupil. Examination confirmed sensory loss and diffuse lower and upper motor neuron dysfunction, with atrophy, fasciculations, and hyperreflexia. Electrophysiology showed delayed left blink reflex and sensorimotor neuronopathy. Extensive workup, including bone marrow biopsy, revealed a clonal cell expansion consistent with an indolent free kappa light chain lymphoma. Aggressive treatment with immunomodulation and chemotherapy failed to slow down the progression.

SUMMARY/CONCLUSION: To our knowledge, this is the first case of FOSMN associated with NHL. Despite previous reports of improved paraneoplastic motor neuron disorders with lymphoma treatment, we suspect the association to be incidental given failure of response to treatment. We expand the phenotype to describe atypical features, including upper motor neuron and pupillary involvement.

ASSOCIATION OF NEUROPATHY WITH NOCTURNAL OXYGEN DESATURATION IN PATIENTS WITH SLEEP APNEA
Hebatallah Rashed (Cairo, Egypt), Salem Taha (Cairo, Egypt), Nagia Fahmy (Cairo, Egypt)

INTRODUCTION: Recurrent nocturnal intermittent hypoxemia, as in obstructive sleep apnea syndrome (OSAS), may be an independent risk factor for peripheral sensory nerve dysfunction.

OBJECTIVE: To look at different factors that determine the risk of neuropathy in patients with sleep apnea.

METHODS: Thirteen patients diagnosed clinically and electrophysiologically with sleep apnea were included. Apnea hypopnea index (AHI) and O2 desaturation were determined. Patients with symptoms of neuropathy, illness predisposed to neuropathy, heavy smoking, age over 50, and a family history of neuropathy were excluded. Body mass index (BMI) was calculated. All patients with no signs of neuropathy underwent neurophysiological examination. Patients included in the study underwent NCs. Patients were categorized into 2 groups: group I (apnea+neuropathy) and group II (apnea only).

RESULTS: Six out of 13 patients (46.15%) had electrophysiological abnormalities consistent with neuropathy. Patients in group I showed statistically significant O2 desaturation (mean SaO2=64%) compared to patients in group II (mean SaO2=74%). Five out of 6 patients in group I had OSAS with SaO2 <70%, and 1 patient had central sleep apnea and his SaO2 is 84%. Age, AHI, and BMI are not statistically different between both groups.

SUMMARY/CONCLUSION: Nerve function critically depends on a sufficient oxygen supply as axonal transport is an energy requiring process and its impairment by hypoxemia can cause axonal degeneration. Experimental chronic hypoxemia causes a resistance to ischemic conduction block (RICB), also seen in diabetic neuropathy. The RICB is likely to be an adaptation to endoneurial hypoxemia caused by reduced O2 requirements.
FACIAL PALSY: A RETROSPECTIVE STUDY OF 416 CASES BASED ON ELECTRONEUROMYOGRAPHY

Vanessa Fernanda Moreira Ferreira (Sao Jose do Rio Preto, Brazil), Carla Renata Graca (Sao Jose do Rio Preto, Brazil), Joao Aris Kouyoumdjian (Sao Jose do Rio Preto, Brazil)

INTRODUCTION: Facial palsy (FP) is a common cause for EDX evaluation. OBJECTIVE: To conduct a prognostic and reinnervation evaluation of FP.

METHODS: In this retrospective study of FP evaluations extracted from an electroneuromyography database, 520 examinations from 416 patients over a 28-year period were reviewed. Sex, age, etiology, comorbidities, and electrophysiological parameters were analyzed.

RESULTS: Cases (53.4% female; mean age: 41 years, range: 3-82) were grouped as Bell's palsy (BP) (70.7%), injury (16.4%), surgery (10.3%), and Ramsay–Hunt syndrome (RHS) (2.6%). BP was found more in Autumn. Diabetes was the most frequent comorbidity. Severe axon loss (>90%) was found in 50% of the cases, but these were more frequent in the surgery group. The amplitude drop of the compound muscle action potentials (CMAPs) was proportional in the orbicularis oculi, orbicularis oris, and nasalis muscles. The absence of CMAPs was more frequent in the surgical group and less frequent in the BP one. BP associated with diabetes was more severe. R1 latency (blink reflex) was significantly longer in the BP group (p>0.001). Late crossed reinnervation was much more frequent in the BP and RHS groups.

SUMMARY/CONCLUSION: Regarding FP: (1) BP was the most common cause. (2) Estimated axon loss was equal in all facial regions. (3) Facial nerve inexcitability was more frequent in the surgical/injury groups. (4) R1 latency was prolonged in the BP group and the only good prognosis indicator in some cases. (6) Crossed reinnervation was more frequent in BP and RHS groups. (7) There were more BP cases in Autumn, and there was no sex or side predominance.

CLINICAL AND ELECTROPHYSIOLOGICAL INVESTIGATION OF 5 PATIENTS WITH SUSPECTED “ELECTROMYOGRAPHY DISEASE”

Fumie Konoeda (Tokyo, Japan), Mari Shibukawa (Tokyo, Japan), Takashi Chiba (Tokyo, Japan), Yuki Hatanaka (Tokyo, Japan), Mana Higashihara (NSW, Australia), Masahiro Sonoo (Itabashi Ku, Japan)

INTRODUCTION: Positive sharp waves (PSWs) are abnormal activities which are observed at rest during needle EMG. Wiechers and Johnson (1979) first reported 10 patients with no organic disorder who presented with widespread PSWs following needle insertion. Later, this condition was named "EMG disease." There are few subsequent reports regarding this concept.

OBJECTIVE: To investigate clinical and electrophysiological features of EMG disease.

METHODS: We searched our EMG database for 2006-2018 using a search for “EMG disease,” and retrospectively reviewed clinical and EMG records.

RESULTS: Enrolled patients were 5 men (mean age: 34.8±15.5 years, range: 21-60). Diagnoses by the referring physicians were ALS, fasciitis, ulnar neuropathy, post-traumatic injury, and radial nerve palsy, respectively. Neurological findings were normal, and clinical myotonia was absent for all patients. Needle EMG showed abundant PSWs lasting several milliseconds following almost every insertion for all muscles examined. Voluntary activities were normal. One patient was examined 3 times over 6 years; needle EMG findings were essentially the same for all examinations. We eventually diagnosed 2 patients with nonorganic palsy. For the other patients, we also judged that the observed PSWs had no relation with their symptoms.

SUMMARY/CONCLUSION: It is important that EDX consultants know this condition to avoid misdiagnosis with true neuromuscular disorders.
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TARSAL TUNNEL SYNDROME CASE DUE TO UNCOMMON IATROGENIC ETIOLOGY
Cheran Elangovan (Hershey, PA), Colleen Newhard (Hershey, PA), Aiesha Ahmed (Hershey, PA)

INTRODUCTION/BACKGROUND: Tarsal tunnel syndrome (TTS) is caused by compression of the tibial nerve and its branches at the tarsal tunnel, causing pain and paresthesia in the medial plantar aspect of the foot. External compression due to footwear or casts, mass lesions, and fracture are common causes. Chronic postoperative TTS can be due to scar tissue. Acute postoperative TTS is very rare; association with deltoid ligament reconstruction surgery has never been reported before.

CASE REPORT: A 58-year-old woman underwent open reduction with internal fixation (ORIF) after a left ankle fracture. She underwent deltoid ligament reconstruction surgery about 1 year later for talus tilting and pain. Immediately after surgery, she had numbness and pain in the medial plantar aspect of her foot. She had a positive Tinel sign, absent sensation, and reduced intrinsic muscle strength. She was referred for needle EMG/NCSs about 8 months later. NCSs showed reduced amplitude at the abductor hallucis with normal latency and conduction velocity. Medial and lateral plantar mixed responses were absent on the left. Needle EMG revealed large motor units with decreased recruitment in left sided intrinsic foot muscles. No active denervation was seen.

SUMMARY/CONCLUSION: Literature review showed 3 cases of acute TTS from lateralizing calcaneal osteotomy surgery in patients with Charcot–Marie–Tooth disease and 1 case of acute TTS in ORIF of ankle fracture. Deltoid ligament reconstruction surgery causing TTS has not been reported until now. This patient’s diagnosis was prolonged due to delayed identification/referral for needle EMG. This case highlights prompt identification of compression postoperatively. Early release could lead to better recovery.

Cheran Elangovan, MD
Resident and Fellow Member Award Recipient

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THE INFLUENCE OF THE RIGHT–LEFT ERROR OF THE PLACEMENT OF THE CONTRALATERAL CENTRAL AREA ELECTRODE IN TibIAL NERVE SOMATOSENSORY EVOKED POTENTIALS
Kazusa Takahashi (Setagaya-ku, Japan), Chizuko Oishi (Mitaka Shi, Japan), Marjorie Anne Bagnas (Manila, Philippines), Masahiro Sonoo (Itabashi Ku, Japan)

INTRODUCTION: At our laboratory, we routinely record tibial nerve somatosensory evoked potentials (SEPs) using 5 channels, including the second cervical vertebrae (C2S)–contralateral central area (Cc) and Cz’ (2 cm posterior to Cz)–Cc derivations. In this method, there is a possibility that the Cc electrode is placed on the wrong side.

OBJECTIVE: To investigate the influence of the right–left error for the placement of the Cc electrode.

METHODS: Tibial nerve SEPs were recorded in 13 healthy volunteers (8 men, 5 women; age: 28-61 years) with no neurological abnormalities in the Cz’–Cd, Cz’–ipsilateral central area (Ci), C2S–Cc, C2S–Ci, Cz’–Fz, Ci–Cc, Cz’–contralateral ear (Ac), and Ci–Ac leads for 8 channels.

RESULTS: P38 potentials were observed in both Cz’–Ac and Ci–Ac leads in all subjects. The amplitude of P38 was 18-86% smaller in the Cz’–Ci lead than those in the Cz’–Cc lead, completely disappeared in 2 subjects, and became negative in 2 subjects. For the C2S–Ci lead, a large negative potential corresponding to the phase reversal of P38 was observed in many subjects.

SUMMARY/CONCLUSION: When the Cc electrode is placed on the opposite side, the P38 potential may decrease its amplitude, disappear, or become negative because the Ci electrode is roughly equipotential to Cz’. When P38 disappears, later potentials may be erroneously identified as P38, and also the phase reversal of P38 in the C2S–Ci lead may be misidentified as N30. When the latency of P38 or N30 potential is unusually prolonged, the right–left error of the Cc electrode position should be checked.
THE EFFECT OF BOTULINUM TOXIN INJECTIONS ON NEEDLE ELECTROMYOGRAPHY
Robin Warner (New York, NY), Dawn Deike (Albany, NY)

INTRODUCTION: Many neurological conditions lead to lower extremity spasticity, including cerebral palsy, traumatic brain injury, multiple sclerosis, stroke, and spinal cord injury. Many patients are treated with intramuscular botulinum toxin injections for relief of spasticity. These patients may also benefit from operant conditioning of the H reflex. Currently, there are no studies comparing operant condition to botulinum toxin injections.

OBJECTIVE: To survey the H reflex and M wave of patients with spasticity receiving botulinum toxin injections to standardize the changes that occur and to control for them in future experimentation.

METHODS: Inclusion criteria were clinically stable injury, ability to ambulate >10 m, spasticity in plantar flexion, and receiving botulinum toxin injections for spasticity. Patients with lower motor neuron disease or cognitive deficits were excluded. Pre-treatment and several post-treatment H reflex and M wave measurements were collected by NCSs. H/M ratios were calculated and recruitment curves created. Physical therapy evaluations and kinematic gait analysis were performed pre-treatment and at 4 and 12 weeks post-treatment.

RESULTS: The H-max and M-max decreased with botulinum toxin injections, then increased as the toxin wore off. The H reflex and M wave were lowest 2-4 weeks after treatment, then slowly trended up until they returned to baseline at 10 weeks. Likewise, the amount of current required to elicit an H reflex increased initially, then returned to baseline after 10 weeks.

SUMMARY/CONCLUSION: According to these data, botulinum toxin injections wear off at the 10 week mark. This supports administration every 10 weeks instead of the conventional every 12 week interval.

Robin Warner, DO
Resident and Fellow Member Award Recipient

REINNERVATION IN FACE TRANSPLANTATION: THE ROLE OF NEEDLE ELECTROMYOGRAPHY

INTRODUCTION/BACKGROUND: Over 40 facial transplantations (FTs) have been reported with little standardized use of needle EMG. While studies report using interval post-transplant needle EMG to monitor success, only a few include pre-transplant baseline facial nerve needle EMGs.

CASE REPORT: Pre/post needle EMG of 2 patient’s FTs: (1) Pre-transplant needle EMG showed normal facial nerve function in a 41-year-old male with extensive facial burns. Neurological examination 1 month post-transplant demonstrated difficulty in lip puckering and mildly dysarthric speech with bilateral loss of sensation in the V3 distribution of the trigeminal nerve, otherwise non-focal. Post-transplant needle EMG consistent with denervation and reinnervation with nil voluntary units in the left orbicularis oculi. (2) Pre-transplant needle EMG showed axonal damage to the facial nerve bilaterally in a 25-year-old male with extensive facial disfigurement secondary to ballistic injury. Neurological examination 1 month post-transplant showed wrinkling of the forehead and closure of the eyes (left stronger than right); facial motor activity otherwise absent. Post-transplant needle EMG showed difficulty in obtaining compound muscle action potentials of the right nasalis/orbicularis oris; right orbicularis oris showed membrane instability.

SUMMARY/CONCLUSION: Pre-transplant needle EMGs for 2 FTs correlated with neurological outcomes 1 month post-transplant. Combining neurological examinations with facial nerve needle EMGs increases sensitivity to motor activity detection and signs of reinnervation. Standardized baseline facial nerve needle EMG assessment prior to FT can help determine surgical candidacy and better understand nerve regeneration. Predicting post-transplant facial reinnervation is critical for prognosticating neurological outcomes and guiding patient expectations.
APPROACH TO REFERENCE VALUES FOR SYMPATHETIC SKIN RESPONSES IN A CLINIC IN TOLIMA, COLOMBIA
Thomas Torres Cuenca (Bogotá, Colombia), Jonatan Gomez-Núñez (Ibague, Colombia), Sandra Torres-Cuenca (Ibague, Colombia)

INTRODUCTION: Sympathetic skin response (SSR) is a simple neurophysiological test that evaluates changes in skin conductance after the activation of sudoriferous glands under neural control of sympathetic cholinergic type C fibers. It can be useful as a marker of axonal neuropathy. The absence of response has been correlated with disorders that affect unmyelinated axons preferentially.

OBJECTIVE: To establish an approximation of the autonomic function in healthy people and the reference values of the SSR.

METHODS: The technique and records of SSR are based on the procedures described in the literature. One of the researchers carried out all the studies. The SSR was recorded on the hands or feet of asymptomatic volunteers using a Cadwell Sierra Wave EMG machine.

RESULTS: For the 21 volunteers (15 women; 37±12 years of age), we found latencies in their hands or feet of 1.82s (range: 1s- 2.4s) and amplitudes of 0.344 mV. These obtained values of latency are similar and consistent to those previously reported in the literature for healthy people.

SUMMARY/CONCLUSION: The great variability of the amplitude of the SSR hardly makes reproducibility an index of normality. In the literature, an SSR has been described abnormal only when it is absent. In this study, an approximation was made to the reference values similar to those reported in the literature. The usefulness of this test, not so frequently performed in our setting, is highlighted as a complement in patients with suspected autonomic dysfunction.

Thomas Torres Cuenca, MD
Resident and Fellow Member Award Recipient

ELECTRODIAGNOSTIC STUDIES IN TRAUMATIC INJURY TO PERIPHERAL NERVES
Vo Don (Ho Chi Minh City, Vietnam)

INTRODUCTION: Traumatic peripheral nerve injuries (TPNIs)—commonly due to the result of motor vehicle accident, occupational injury, accident at home, or penetrating injury—can potentially lead to significant disability. Needle EMG is the best method for localizing and assessing the severity of a TPNI.

OBJECTIVE: To describe the epidemiology of TPNIs, including the frequency of each injury by anatomic location, the etiologies, and the clinical characteristics.

METHODS: A cross-sectional descriptive study was conducted at Hospital for Traumatology and Orthopaedics, Ho Chi Minh City, from January 2017 to April 2017 in patients with TPNIs. Collected variables included individual characteristics, medical examination, and needle EMG index according to data sheet.

RESULTS: We studied 226 patients (83.6% male, 16.4% female; mean age: 33±11 years) with TPNIs. Motor vehicle accident was the most common cause of TPNIs. The ulnar, median, and radial nerves and the brachial plexus were most the commonly injured. NCSs and needle electrode examinations showed variation in compound muscle action potentials (CMAPs) and sensory nerve action potentials (SNAPs) as well as spontaneous activity in the ulnar (33%), median (29.6%), and radial (25.2) nerves and brachial plexus (23.9%). Axonal injuries and the level of a complete injury were most commonly seen.

SUMMARY/CONCLUSION: TPNIs are more common in males than females. Motor vehicle accident is the most common cause of TPNIs. CMAPs, SNAPs, and spontaneous activity were the most affected. Axonal damages and level of complete damage are dominant in the ulnar, median, and radial nerves and the brachial plexus.
ELECTROPHYSIOLOGICAL EVALUATION OF DIABETIC PERIPHERAL NEUROPATHY AFTER HYPERBARIC OXYGEN THERAPY
Hazem Elkarabaty (Alexandria, Egypt)

INTRODUCTION: Diabetic peripheral neuropathy is the most common complication of diabetes mellitus (DM) with involvement of the peripheral and autonomic nervous systems. The duration and severity of hyperglycemia is an important risk factor for development of diabetic peripheral neuropathy in patients with type I and type II diabetes.

OBJECTIVE: To study the role of hyperbaric oxygen therapy in the management of patients with diabetic peripheral neuropathy.

METHODS: Sixty patients with DM for more than 5 years were included in the study. They were divided into 2 groups, with 30 patients in each group. Group I received hyperbaric oxygen sessions in addition to their regular medications for 6 weeks. Group II received medications only. NCSs—including sensory conduction of the sural nerve and motor conduction of the posterior tibial and common peroneal nerves—were performed for both groups at the start of the study and after 6 weeks.

RESULTS: Group I showed significant improvement (p<0.001) in all the NCS parameters, including decreased motor distal latency, increased nerve conduction velocity, and reappearance or decreased H reflex latency, while group II did not show significant improvement.

SUMMARY/CONCLUSION: Hyperbaric oxygen therapy is considered an important adjuvant therapeutic modality for management of diabetic patients with peripheral neuropathy.

IMAGE AND NEUROPHYSIOLOGICAL FINDINGS IN AMYOTROPHIC LATERAL SCLEROSIS
Bárbara Hernandez (Havana, Cuba), Ariel González (Havana, Cuba), Evelio González (Havana, Cuba), Belkis Reyes (Havana, Cuba), Joe Michel López (Havana, Cuba), Ruben Periche (Havana, Cuba)

INTRODUCTION: ALS is an uncommon illness caused by motor neuron degeneration in which upper, lower, and bulbar muscles are affected. The diagnosis is based on El Escorial criteria. Some research also reports degeneration in non motor structures of the brain.

OBJECTIVE: To evaluate electrophysiological and imaging findings in ALS diagnoses and to correlate these results.

METHODS: During January 2016 to January 2018, 26 patients with an ALS diagnosis and 20 healthy subjects were evaluated. Sensory and motor NCSs, needle EMG, and somatosensory evoked potentials (SSEPs) were conducted on the patients. 3T MRIs were obtained from the patients and the healthy subjects. Post-processing MRI techniques were applied.

RESULTS: NCSs were positive in 90% of the patients, SSEPs were positive in 60%, and needle EMGs were positive in 100%. Anatomic MRIs were positive in 50% of the patients; they showed cortical atrophy, ventricle enlargement, and hyperintensity of the corticospinal tract. Fractional anisotropy (FA) was reduced in the ALS group in comparison with the healthy group. Fiber numbers of the corticospinal tract and corpus callosum were diminished in the ALS group. Also, grey and white matter were reduced in the ALS group in relation to the healthy group. FA abnormality in the corticospinal tract at the cortex, internal capsule, brainstem, and corpus callosum was in correlation with the revised ALS Functional Rating Scale and neurophysiologic abnormalities.

SUMMARY/CONCLUSION: Electrophysiological studies confirmed ALS diagnosis in 100% of cases. MRIs showed abnormalities in motor and non motor structures of the brain in ALS patients.
STIFF PERSON SYNDROME, ABOUT A CASE
Rezoug Chahrazed (Ain Beida, Algeria)

INTRODUCTION/BACKGROUND: The stiff person syndrome is a rare and underestimated pathology, often mistaken for a psychiatric disease. It is a neurological autoimmune disease affecting the central nervous system related to an anomaly of the synthesis of gamma-aminobutyric acid (GABA).

CASE REPORT: The patient is a 28-year-old man with no antecedents apart from being pursued in psychiatry for abnormal trunk movements which were labeled as psychogenic and treated with psychiatric drugs since 2012. His abnormal movements extended to the 4 limbs, and his spasms presented a considerable hinderance in daily life obliging the patient to abandon his job after being able to pursue and finish his studies in the university with minor symptoms. Treatment was stopped 8 months ago without engendering any negative repercussion on his clinical state. His cerebral MRI had no particularities. Laboratory results showed that the anti-glutamic acid antibodies (anti GAD Ab) are negative, and needle EMG uncovered the presence of a continued activity in the spinal and abdominal muscles. When put on baclofen, his symptoms improved after a month of treatment.

SUMMARY/CONCLUSION: The stiff person syndrome can be taken for a psychiatric disease. The ineffectiveness of the psychiatric treatment demands the extension of explorations, especially needle EMG which leads to the diagnosis.

NEUROPHYSIOLOGICAL STUDY OF THE PUDENDAL NERVE IN A PATIENT WITH CHRONIC GENITAL PAIN
Nelsy Rocio Huertas-Romero (Bogotá, Colombia), Thomas Torres Cuenca (Bogotá, Colombia), Jorge Diaz-Ruiz (Bogotá, Colombia)

INTRODUCTION/BACKGROUND: Pudendal neuralgia is a painful neuropathy that produces symptomatology in the pudendal nerve innervation area. The diagnosis is based on clinical and neurophysiological findings.

CASE REPORT: A 50-year-old male patient with no significant history of disease presented with several months of chronic pain at the genital level with left side predominance. Strength and sensitivity in the lower limbs are preserved. Electrophysiological studies were performed; somatosensory evoked potentials (SEPs) of the pudendal nerve, stimulating separately each side of the penis, demonstrated prolonged and low latency amplitude on the left side (P1 44.22 ms, P1–N1 0.68 μV) and normal values on the right side (P1 39.84 ms, P1–N1 1.57 μV). A bulbocavernosus reflex was also performed, stimulating separately each side of the penis, evidencing latency significantly prolonged on the left side (67.38 ms) with normal values on the right side (32.84 ms). Pudendal NCSs presented normal latencies, with a decrease in the amplitude of the left compared to the right side (33%).

SUMMARY/CONCLUSION: In the neurophysiological evaluation of the pudendal nerve, different methods can be used. Studies such as SEPs, the bulbocavernosus reflex, and NCSs among others could be useful. It is recommended to evaluate separately each side of the penis or clitoris; in this way unilateral lesions of the pudendal nerve can be differentiated.
SEGMENTAL BIOIMPEDANCE MEASUREMENTS IN VARIOUS NEUROMUSCULAR DISEASES
Tulio Bertorini (Cordova, TN), Yu Zhao (Memphis, TN), Jeffrey Metter (Memphis, TN), William Mays (Memphis, TN), Laura Talbot (Memphis, TN)

INTRODUCTION: Segmental bioimpedance is a useful tool to measure limb and total body mass. We are reporting our experience in healthy individuals and those with various neuromuscular diseases who were examined on 1 or more occasions clinically and with segmental bioimpedance.

METHODS: Forty-one control subjects had 67 segmental bioimpedance studies using the RJL System (Clinton Township, Michigan). Twenty-nine neuromuscular disease subjects had 61 studies, which included segmental bioimpedance and a clinical evaluation. Studied patients included 3 with spinal muscular atrophy (SMA), 9 with ALS, 7 with inclusion body myositis (IBM), 3 with limb girdle muscular dystrophy (LGMD), 1 with dermatomyositis, 2 with Pompe disease, 1 with myotonic dystrophy, 2 with undefined myopathy, and 1 with benign motor neuron disease.

RESULTS: Little variability was found between repeated measurements in healthy control subjects. The control subjects had much higher muscle mass than the neuromuscular disease subjects. Decreased muscle mass correlated with the distribution of weakness in ALS, LGMD, and SMA but not IBM. Changes over time were only detected in ALS, LGMD, and dermatomyositis.

SUMMARY/CONCLUSION: Segmental bioimpedance is a reproducible test and correlates with clinical findings when whole limbs are affected. Changes in segmental bioimpedance over time were noted in most diseases. This method can be used clinically in trials depending on observation times.

ASSESSING THE EFFECT OF SHORT EXPERIMENTAL ISCHEMIA ON MEDIAN AND ULNAR NERVE CONDUCTION IN IMPROVING THE DIAGNOSTIC ACCURACY OF CARPAL TUNNEL SYNDROME IN DIABETIC PATIENTS
Hanan Soliman (Giza, Egypt), Marwa Eljaly (Beni Suef, Egypt), Saly Elkholy (Giza, Egypt), Al Metwally Youssof (Giza, Egypt)

INTRODUCTION: CTS is the most common entrapment neuropathy encountered in diabetic patients.

OBJECTIVE: For future treatment planning, it is important to determine whether CTS is an entrapment of the median nerve under the transverse carpal ligament or it results from diabetic mononeuropathy.

METHODS: In this study, 75 patients were divided into 3 groups: 25 nondiabetic patients with idiopathic CTS, 25 diabetic patients with CTS (without clinical or electrophysiological evidence of peripheral neuropathy), and 25 age- and sex-matched healthy control subjects. Ischemia was induced by placing a tourniquet around the arm to elevate the pressure higher than the patient systolic pressure by 30 mm Hg for 1 minute. Median and ulnar motor and sensory NCSs were performed before, during, and 1 minute after compression relief.

RESULTS: The diabetic group showed statistically significant affects in all neurophysiological conduction parameters of the median nerve and the evoked response amplitude of the ulnar sensory nerve during compression (p<0.05) when compared to the pre-compression values. The recovery of median nerve conduction was significantly delayed in diabetic patients (p<0.01) in comparison to the nondiabetic group and control subjects.

SUMMARY/CONCLUSION: Diagnosis of CTS in patients with diabetic polyneuropathy is important as with early focal ischemia nerves are physiologically impaired and conduction block is a rapidly reversible, so early interventions may prevent further nerve damage.
REAL-WORLD ANALYSIS OF NEUROLOGIC SYMPTOMS, DIAGNOSTIC PATTERNS, AND PROVIDER PERSPECTIVE OF ACUTE HEPATIC PORPHYRIA
Stephen Meninger (Cambridge, MA), John Ko (Cambridge, MA), Sarah Murray (Cambridge, MA), Nicole Lyn (Cambridge, MA), Chitra Karki (New York, NY), Katherine Krautwurst (Parsippany, NJ), Renata Mustafina (Parsippany, NJ), Jigar Amin (Cambridge, MA)

INTRODUCTION: Acute hepatic porphyria (AHP) is a family of rare genetic diseases, the most common being acute intermittent porphyria (AIP). AHP results from enzyme deficiencies involved in heme synthesis, leading to accumulation of neurotoxic heme intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG), causing potentially life-threatening attacks and chronic symptoms.

OBJECTIVE: To describe neurologists’ experience diagnosing AHP and characterize patients from the United States, European Union-5, Canada, and Japan.

METHODS: Physicians (n=175) who actively managed AHP patients in the preceding year completed an online survey probing demographics, familiarity with diagnostic tests, and symptoms. Physicians reviewed a subset of patients’ charts (n=546) and shared anonymized data (demographics, medical history, attacks, and symptoms).

RESULTS: Physicians practiced a mean of 18 years and 21% were neurologists (n=36). Neurologic symptoms informing AHP diagnosis included abdominal pain (88%), muscle weakness (63%), vomiting (62%), tachycardia (61%), seizures (56%), muscle pain (61%), and palpitation (57%). Patients were aged 40 years (mean), female (53%), and had AIP (82%). Neurologists considered urinary PBG (78%), ALA (67%), and several nonspecific tests indicative of AHP. For most patients (69%), diagnoses were assessed as uncertain (43%) or incorrect (26%). Misdiagnoses reported included polyneuropathy (56%), psychosis (44%), and fibromyalgia (47%). Patients had a mean of 1.8 attacks and 1.1 hospitalizations in the past year. Neurologists reported chronic symptoms including pain (60%), weakness (59%), and fatigue (57%).

SUMMARY/CONCLUSION: This study highlights the challenges diagnosing AHP due to nonspecificity of symptoms and limited understanding of diagnostic procedures. AHP patients reported acute attacks and chronic symptoms, implicating both in the disease.

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Stephen Meninger - Consultant of Alnylam Pharmaceuticals receiving payment through a postdoctoral fellowship grant.
John Ko, Jigar Amin, & Sarah Murray - Employee and ownership interest including stock options of Alnylam Pharmaceuticals.
Nicole Lyn - Employee of Alnylam Pharmaceuticals.
Katherine Krautwurst, Chitra Karki, & Renata Mustafina - Employee of Ipsos-Insight LLC.

A HIDDEN COMMON REASON BEYOND DELAYED PHRENIC NERVE DISTAL MOTOR LATENCY
Rowaida Ali (New Cairo, Egypt), Mai Farouk (Cairo, Egypt), Salwa Moussa (Cairo, Egypt)

INTRODUCTION: The phrenic nerve arises in the neck from C4 with contribution of C3,5 levels. This anatomical location makes it vulnerable to traumatic injury. Limited data are published regarding how it is affected in patients with cervical spondylosis. However, cervical spondylotic radiculopathy or myelopathy can lead to phrenic nerve root compression and weakness.

OBJECTIVE: To investigate possible subtle phrenic nerve affection in patients with cervical spondylosis.

METHODS: A comparative cross-sectional cutoff study was conducted on 30 patients suffering from cervical spondylosis above C6 (previously diagnosed and graded by plain X-ray on cervical spines, excluding associated neuropathy) as well as 30 healthy volunteers. All were subjected to thorough clinical assessment and electrophysiological studies in the form of: determination of both phrenic nerves’ distal motor latencies and amplitudes, and both median and ulnar nerves’ latencies, amplitudes, and conduction velocities.

RESULTS: Normative data of phrenic nerve distal motor latency was less than 8.5 ms, while amplitude was greater than 378 μV in our control group. Our patients showed a statistically significant prolongation of phrenic nerve distal motor latency on both sides than control subjects (p<0.01), but showed nonsignificant difference regarding amplitude (p>0.05). Phrenic nerve distal motor latency was delayed (in comparison to other side) in 23 patients (76.7%), while it was not prolonged in 7 patients (23.3%).

SUMMARY/CONCLUSION: There is possible associated phrenic nerve affection in patients with cervical spondylosis. Consequently, we should be aware of cervical spondylosis as a reason for delayed phrenic nerve distal motor latency.
PROXIMAL ULNAR MONONEUROPATHY IN YOUNG WOMEN
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INTRODUCTION: We often experience patients with acute-onset ulnar mononeuropathy of unknown cause. However, clinical features including prognosis of these patients remain unclear.

OBJECTIVE: To investigate the clinical features of patients with acute-onset ulnar mononeuropathy of unknown cause.

METHODS: We retrospectively reviewed our EMG laboratory database from January 2014 to December 2018. The inclusion criteria were acute-onset ulnar mononeuropathy, sensorimotor axonal neuropathy without conduction block, and absence of abnormalities in other nerves. Cases of entrapment neuropathies such as Guyon's canal syndrome or cubital tunnel syndrome were excluded. Patients with trauma, postoperative onset, and disorders known to be associated with peripheral neuropathy were also excluded. The affected region along the ulnar nerve, clinical features, and prognosis were evaluated.

RESULTS: Seven patients were identified (age: 26.6±4.2 years; body mass index: 19.9±2.8). All patients were right-handed women. Five patients had impairment on the left side. Six patients had pain at onset. NCSs documented a lesion between the upper arm and Erb’s point in 2 patients. Tinel sign suggested a lesion at the upper arm or more proximal in 3 patients. No patients experienced recurrence or progression to other nerves during the follow-up period (9.0±10.4 months, range: 2-30). The prognosis was relatively good, although mild sensory disturbance or weakness remained in all patients.

SUMMARY/CONCLUSION: We identified a group of young women presenting with painful proximal ulnar mononeuropathy, with a relatively good prognosis.

THE SYMMETRY OF BILATERAL CARPAL TUNNEL SYNDROME
Elliot Bodofsky (Camden, NJ), Stephen Cohen (Voorhees, NJ), Rohini Kumar (Camden, NJ), Adam Schindelheim (Camden, NJ), Sabana Malik (Camden, NJ)

INTRODUCTION: CTS is by far the most common focal peripheral nerve disorder, with over 1,000,000 cases per year in the United States alone. Bilateral presentation is quite common, ranging from 40-70% in different studies. Previous studies have indicated that bilateral cases are often symmetric on NCSs.

OBJECTIVE: To determine whether bilateral CTS symmetry on NCSs will allow more limited testing while maintaining accuracy.

METHODS: A review was conducted of the academic Physical Medicine and Rehabilitation department database of upper extremity NCSs for 2013-2017 for patients with symptoms and NCS diagnosis of bilateral CTS. Patients with other symptoms (i.e., neck pain) were excluded. All studies were performed by a single researcher on 2 EDX machines; prior testing indicated no significant differences between the machines.

RESULTS: There were 111 cases of bilateral CTS. NCS symmetry was quite high. Correlation of median motor distal latency (MMDL) was 0.58, motor amplitude 0.53, median sensory latency (MSL) 0.54, and sensory amplitude 0.82 (all p<0.001). In only 2 cases (1.8%), was CTS mild on 1 side and severe contralaterally. In all but 1 case (99%) with moderate CTS by NCS on 1 side and 4.2 ms<MMDL<6.0 ms on the other side, 3.5 ms<MSL<7.0 ms, and the diagnosis was also moderate CTS (bilaterally moderate CTS).

SUMMARY/CONCLUSION: In patients presenting with symptoms of bilateral CTS exclusively, NCS results are quite symmetric. In some cases with only moderate CTS on NCS on 1 extremity, more limited NCS testing may be possible. More research is needed.
SAFETY OF NEEDLE ELECTROMYOGRAPHY IN CRITICALLY ILL INTENSIVE CARE UNIT PATIENTS
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INTRODUCTION/BACKGROUND: Needle EMG is a relatively safe procedure, and in most cases, the yield of the study outweighs the risks associated with it. However, the safety of needle EMG in critically ill ICU patients, including those with multiple medical comorbidities, remains unknown.

OBJECTIVE: To evaluate the safety of needle EMG in patients who are critically ill and in the ICU. METHODS: Retrospective chart review was conducted of patients in the ICU who underwent needle EMG.

RESULTS: Twenty-nine patients (17 [58.6%] males; mean age: 60.8±16.7 years) were included. The mean prothrombin time, partial thromboplastin time, and international normalized ratio were 15.2 and 36.5 seconds and 1.13 IU, respectively. At the time of the study, 14 (48.2%) patients were on subcutaneous (SC) low molecular weight heparin and 8 (7.5%) were on SC heparin for deep vein thrombosis prophylaxis. Therapeutic heparin was being used in 3 (10.3%) patients and sequential compression devices in 4 (13.7%). Twenty (69%) patients had at least 1 comorbid condition such as cardiovascular risk factors, malignancy, renal failure, and diabetes mellitus. A total of 228 muscles were tested of which 38 (16.6%) were deep muscles. There were no major bleeding complications at the time of each procedure and for the following 7 days in any of the patients including those with multiple medical comorbidities.

SUMMARY/CONCLUSION: Needle EMG of both superficial and deep muscles is safe in critically ill patients, and even those with multiple medical comorbidities.

CONCURRENT SCIATIC AND FEMORAL NEUROPATHIES AS A RARE COMPLICATION OF KNEE SURGERY: WAS IT THE TOURNIQUET?
Melissa Cook (JBSA Fort Sam Houston, TX), Sarah Pierrie (JBSA Fort Sam Houston, TX), Daniel Simmons (JBSA Fort Sam Houston, TX)

INTRODUCTION/BACKGROUND: Sciatic and peroneal mononeuropathies are well-known complications of knee surgery, while femoral neuropathies are rare. The definitive mechanism of injury is often difficult to establish. We argue that prolonged compression from a limb-positioning device led to concurrent sciatic and femoral neuropathies during a complex anterior cruciate ligament (ACL) reconstruction.

CASE REPORT: A 22-year-old male sustained ACL and lateral meniscus tears. Reconstructive surgery was completed without anesthetic nerve blocks. A tourniquet over the proximal thigh was used for 167 minutes at 300-350 mmHg with 10 minutes rest. Total operative time was 9 hours. At completion there was circumferential erythema and blistering at the mid-thigh in the location of the limb-positioning device. In recovery, the patient reported weakness and numbness below the knee. At 6 months, there was atrophy and weakness of tibial- and peroneal-innervated muscles, hamstrings, and distal vastus muscles; absent and diminished ankle and knee reflexes; and sensory loss below the knee. EDX studies revealed sciatic and distal femoral neuropathies.

SUMMARY/CONCLUSION: The association of tourniquet use with perioperative nerve injury is controversial. Our patient was exposed to nearly 3 hours of tourniquet time. However, on the basis of EDX localization we favor prolonged use of a limb-positioning device as the most reasonable etiology. Allowing intermittent rest from tourniquet compression is standard practice, but there are no such guidelines for limb-positioning devices. We suggest that the targeted use of neurophysiologic intraoperative monitoring may help prevent such complications.
HETEROGENEOUS NEUROPHYSIOLOGICAL FEATURES OF THREE CASES WITH MYOFIBRILLAR MYOPATHY
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BACKGROUND: The clinical and neurophysiological features of myofibrillar myopathy (MFM) are heterogeneous, making it a diagnosis difficult.

CASE REPORT: We diagnosed 3 patients with MFM by genetic testing and pathology over the preceding 3 years. (1) A 58-year-old man presented with weakness and atrophy of the right lower extremity for 8 years, and he was diagnosed with myotilinopathy. NCSs were normal. On needle EMG, diffuse abnormal spontaneous activity (SA) and small amplitude and short duration motor unit action potentials (MUAPs) were demonstrated. (2) A 15-year-old girl complained of difficulties in squat movements for 7 years and dyspnea for 1 year, whose diagnosis was BAG3-opathy. NCSs showed sensorimotor, axonal-demyelinating neuropathies, and needle EMG revealed lots of SA in tibialis anterior and polyphasic MUAPs with large amplitude and long duration. (3) A 15-year-old boy developed gait abnormalities and dyspnea for 4 years, and he was diagnosed with α-β- crystallinopathy. His NCSs were normal. On needle EMG, a bit of abnormal SA in the deltoid and myotonic discharges in the quadriceps were detected; both polyphasic small and short MUAPs and large and long MUAPs were noted.

SUMMARY: MFM patients demonstrate various neurophysiological features. NCSs might indicate peripheral neuropathy, and needle EMG could manifest as neurogenic, myogenic, or combined damages. The interpretations of EDX data should be cautious and made together with clinical characteristics.

T1 INVOLVEMENT IN POSTMEDIAN STERNOTOMY PLEXOPATHY
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INTRODUCTION: The post-median sternotomy plexopathy is known as a plexopathy that predominantly affects the C8 anterior ramus. However, we sometimes experience patients in whom the T1 component was affected.

OBJECTIVE: To document the lesion site of a post-median sternotomy plexopathy.

METHODS: We searched our EMG database from 2005-2018 using appropriate keywords. For extracted cases, we retrospectively reviewed clinical and needle EMG records and enrolled patients who developed sensorimotor disturbances documented as plexopathy after surgery with post-median sternotomy.

RESULTS: Enrolled were 7 patients (all male; age: 52-83 years). Five patients had predominantly C8 lesions. All patients showed weakness of C8 muscles, whereas the abductor pollicis brevis (APB) muscle innervated by the T1 root showed no weakness except in 1 case with CTS. On NCSs, the sensory nerve action potential (SNAP) of the ulnar nerve was depressed in all patients, and the median nerve SNAP from the ring finger was depressed in 3 patients. In 2 patients with normal median-ring finger SNAP, the involvement of C8 muscles such as extensor pollicis brevis was documented by needle EMG. One patient showed predominantly T1 involvement, documented by a weak APB and loss of SNAP of the median antebrachial cutaneous nerve with normal ulnar SNAP. The last patient showed both C8 and T1 involvement.

SUMMARY/CONCLUSION: Post-median sternotomy plexopathy most frequently involves the C8 anterior ramus, although associated or isolated T1 involvement may occur.
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IMPACT OF QUANTITATIVE ASSESSMENT OF FASCICULATIONS FOR CLINICAL SEVERITY IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS
Akihiro Nishida (Fukuoka, Japan), Jun Tsugawa (Fukuoka, Japan), Hiromu Ogura (Fukuoka, Japan), Maiko Doi (Fukuoka, Japan), Shinsuke Fujiioka (Fukuoka, Japan), Yoshio Tsuboi (Fukuoka, Japan)

INTRODUCTION: The detection of fasciculations is an important neurophysiological feature for the diagnosis of ALS. Recently, muscle ultrasound (MUS) has been widely used as a supportive diagnostic tool for detecting fasciculations in ALS. However, few studies have focused on the quantitative assessment of fasciculations by MUS in ALS.

OBJECTIVE: To investigate the impact of quantitative assessment of fasciculations in patients with ALS.

METHODS: Twenty-one ALS patients (11 male, 10 female; age at MUS test: 68.4±9.6 years; ALS Functional Rating Scale- Revised: 36±10.0; disease duration: 30±47.6 months) were enrolled. Patients underwent MUS to determine muscle fasciculations in 25 regions, including the tongue, trunk, and all 4 limbs. The sum was calculated as the MUS fasciculation score. We analyzed the correlation between this score and clinical parameters in ALS.

RESULTS: Overall, the fasciculation positive rate on MUS was 62.4±23.4%. The flexor carpi ulnaris muscle had the highest MUS positive rate (80.9%), while the abdominal muscle had the lowest (28.5%). Disease duration negatively correlated with overall (r=−0.591, p=0.007) and upper limb (r=−0.609, p=0.00561) MUS fasciculation score. Respiratory function (SaO2) positively correlated with the MUS fasciculation score (r=0.513, p=0.00175), and the compound muscle action potential on NCSs negatively correlated with the MUS score (r=−0.577, p=0.0193). There is no association between the MUS fasciculation score and swallowing function.

SUMMARY/CONCLUSION: We confirmed that the MUS fasciculation score was higher in the early stage in ALS patients. Quantitative assessment of fasciculations by MUS may be correlated with the stage of ALS and may predict respiratory outcome.

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SAFETY OF NERVE CONDUCTION STUDIES IN A PATIENT WITH A VENTRICULAR ASSIST DEVICE
Eunji Yim (Ann Arbor, MI), Benjamin Claytor (Ann Arbor, MI), James Wolfe (Ann Arbor, MI), Zachary London (Ann Arbor, MI), Reema Hasan (Ann Arbor, MI)

INTRODUCTION/BACKGROUND: Experimental studies suggest that as little as 200 μA of current, when applied directly to myocardial tissue, may induce a life-threatening arrhythmia. The skin and pericardial soft tissues provide substantial electrical resistance, but ventricular assist devices have a transdermal conduit with mechanical connections to the heart. It is unknown if stray electrical discharges from NCSs can be transmitted through this device and induce cardiac conduction abnormality.

CASE REPORT: A 66-year-old man with ischemic cardiomyopathy and a left ventricular assist (HeartWare™) device presented for evaluation of suspected demyelinating neuropathy. Under continuous 12-lead electrocardiogram monitoring, the patient underwent NCSs of the right sural, peroneal, tibial, median, ulnar, and radial nerves. There were a total of 52 stimulations at various sites, with 100 mA of current and durations ranging between 0.02-0.7 ms. A minimum of 10 seconds of electrocardiographic data were reviewed after each stimulation. No malignant arrhythmias or conduction abnormalities were found during the study. The patient had no dyspnea, palpitations, or other symptoms suggestive of arrhythmia or reduced cardiac output.

SUMMARY/CONCLUSION: Standard NCSs may be safe in patients with ventricular assist devices.
NEEDLE ELECTROMYOGRAPHY FINDINGS IN DERMATOMYOSITIS/POLYMYOSITIS: THE UTILITY OF ILIOPSOAS
Keiichi Hokkoku (Tokyo, Japan), Yuki Hatanaka (Tokyo, Japan), Masahiro Sonoo (Itabashi Ku, Japan)

INTRODUCTION: Presence of fibrillation potentials and positive sharp waves (Fib/PSWs) in needle EMG is essential for diagnosing dermatomyositis and polymyositis (DM/PM). Selection of the muscle to be examined is important as the yield for Fib/PSWs varies between muscles in DM/PM. In our laboratory, we routinely examine the iliopsoas, and have experienced sufficiently high sensitivity of Fib/PSWs in this muscle.

OBJECTIVE: To assess the utility of needle EMG on iliopsoas for detecting Fib/PSWs in DM/PM patients.

METHODS: We retrospectively reviewed the presence of Fib/PSWs on needle EMG of DM/PM patients admitted to our department from 2009-2018.

RESULTS: Fifty patients (17 DM, 33 PM) were enrolled. DM patients consisted of 11 classical DM and 6 clinically amyopathic DM (CADM) patients. The 2 muscles examined the most were the biceps brachii (BB) and iliopsoas (Ip), and the numbers of examined muscles were 43 and 38, respectively. The presence of Fib/PSWs in the Ip and BB were 92% and 72%, respectively. Ip showed significantly higher sensitivity for Fib/PSWs compared to BB (p<0.05). In the CADM patients, the BB showed no Fib/PSWs (0/6), whereas the Ip showed Fib/PSWs in 50% of examined muscles (3/6).

SUMMARY/CONCLUSION: Needle EMG of the Ip has high sensitivity for Fib/PSWs in DM/PM patients. Improved identification of the Ip by our laboratory might have resulted in superior sensitivity compared to past reports. In CADM patients, needle EMG on the BB is insufficient to detect Fib/PSWs, and further examination on the Ip should be considered.

PREVALENCE OF MALE SEXUAL DYSFUNCTION IN TYPE 1 DIABETES
Ana Calzada-Reyes (Havana, Cuba)

INTRODUCTION: Sexual dysfunction is a common complication of diabetes that adversely affects patients’ quality of life. Somatic and autonomic neuropathy are common complications of diabetes mellitus.

OBJECTIVE: To investigate the prevalence of sexual dysfunction in a sample of males with type 1 diabetes.

METHODS: The bulbocavernosus reflex and somatosensory evoked potentials of the pudendal nerve were studied in 62 patients with type 1 diabetes to explore nervous structures of the pelvic floor which participate in sexual function.

RESULTS: Seventy-one percent of patients had abnormalities and 21% had clinical manifestations, while 38% had electrophysiological abnormalities without clinical manifestation. Needle EMG showed patterns of abnormality in 92%, with synchronism and amplitude parameters the most affected. The highest incidence of abnormalities in pelvic floor studies was observed in patients with more than 5 years of evolution and metabolic decontrol of diabetes mellitus.

SUMMARY/CONCLUSION: Sexual dysfunction is a common complication in diabetic patients. The combination of anamnesis and an ad hoc neurophysiological protocol showed its high prevalence and provided a more accurate prognosis.
EARLY ELECTRODIAGNOSTIC FINDINGS IN CHARCOT–MARIE–TOOTH DISEASE SECONDARY TO A PATHOLOGIC VARIANT OF DYNAMIN 2: A CASE STUDY

Cynthia Wozow (Houston, TX), Suzanne Woodbury (Houston, TX), Gabrielle Nguyen (Houston, TX)

INTRODUCTION/BACKGROUND: Charcot–Marie–Tooth (CMT) disease has significant genetic heterogeneity with more than 30 genes identified, including mutation to Dynamin 2 (DNM2).

OBJECTIVE: To describe early EDX findings in CMT type 2M secondary to a mutation in DNM2.

CASE REPORT: An 11-year-old female was referred for EDX testing to evaluate for hereditary neuropathy following genetic workup positive for a DNM2 mutation. This mutation is known to cause CMT2M or centronuclear myopathy (CNM). Clinically, the patient had distal weakness and areflexia with pes cavus and an inverted champagne bottle appearance to her calves. She also had a steppage gait. EDX testing showed normal sensory NCSs of the median and sural nerves and normal motor NCSs of the peroneal and tibial nerves, with mild-to-moderate decreased amplitude of the median nerve. Needle EMG showed denervation potentials with decreased recruitment in all muscles tested. Brief runs of myotonia were present in the left gastrocnemius and left extensor hallucis longus.

SUMMARY/CONCLUSION: Given the patient’s clinical appearance and genetic testing results, the needle EMG findings are most consistent with axonal CMT rather than CNM, although the nearly normal NCSs findings were unexpected and likely represent an early presentation. This case illustrates the utility of EDX studies in the diagnosis of CMT2M in conjunction with genetic testing.

Cynthia Wozow, DO
Resident and Fellow Member Award Recipient

MOTOR UNIT NUMBER INDEX IN THE QUANTITATIVE ASSESSMENT OF SEVERITY AND SURGICAL OUTCOME IN CERVICAL SPONDYLOTIC AMYOTROPHY

Chaojun Zheng (Shanghai, China), Yu Zhu (Syracuse, NY), Jianyuan Jiang (Shanghai, China)

INTRODUCTION: Cervical spondylotic amyotrophy (CSA), an uncommon type of cervical spondylosis, is always treated by surgery. Both disease progression and surgical outcome in CSA are typically assessed by scoring systems. However, these assessment methods are suboptimal to detect subtle changes in progression.

OBJECTIVE: To investigate motor unit number index (MUNIX) as a method to quantitatively evaluate CSA.

METHODS: MUNIX was performed on the abductor pollicis brevis, abductor digiti minimi, biceps brachii, and middle deltoid in 41 normal control subjects and 47 patients with CSA (distal-type versus proximal-type: 25 versus 22). Additionally, patients were assessed on handgrip strength; the disabilities of arm, shoulder, and hand (DASH); and MRC scales. These examinations were re-evaluated approximately 18 months after operation in 37 of these CSA patients.

RESULTS: MUNIX values were noticeably lower in the mainly affected muscles of CSA patients than those in control subjects (p<0.05), and 49.0% (51/104) of the tested muscles with abnormal MUNIX measurements showed normal muscle strength. Significant correlations between MUNIX measurements and both DASH and MRC scores were observed in both CSA patient groups (p<0.05). Postoperative longitudinal followup analysis identified significant increase in motor unit number in both CSA patient groups within approximately 18 months (p<0.05), with or without improved measures of motor function.

SUMMARY/CONCLUSION: A significant reduction in MUNIX values related to motor impairment was found in patients with CSA, even in the pre-symptomatic stage. Compared with measures of motor function, the MUNIX measurements in the patients with CSA improved more noticeably after surgical intervention.
SPINAL ACCESSORY NEUROPATHY DUE TO SEQUELA OF EPSTEIN–BARR VIRUS MONONUCLEOSIS: A CASE REPORT
Filip Cheng (Okemos, MI), Michael Andary (East Lansing, MI), Ryan Keating (Detroit, MI)

INTRODUCTION/BACKGROUND: The spinal accessory nerve (SAN) provides primary motor innervation to the sternocleidomastoid (SCM) and trapezius muscles. SAN injury is most often associated with surgical procedures, local trauma, or tumors.

OBJECTIVE: To describe the first reported case, to our knowledge, of SAN neuropathy due to Epstein–Barr virus (EBV) mononucleosis-mediated lymphadenopathy.

CASE REPORT: An 18-year-old right-hand dominant woman recently diagnosed with EBV mononucleosis presented with persistent right-sided neck pain, right arm weakness, and right hand paresthesias. Her symptoms began 6 weeks earlier in the setting of extensive cervical lymphadenopathy, most prominent at level II bilaterally as demonstrated on CT soft tissue. The symptoms persisted despite dramatic improvement in her lymphadenopathy. Initial physical examination revealed minimal weakness in right shoulder abduction to 90 degrees. Focused examination revealed right periscapular atrophy, subtle winging of the right scapula, and the inability to actively abduct at the right shoulder above 150 degrees. Needle EMG revealed fibrillations in the right SCM and trapezius, while NCSs revealed a 66% decrease in amplitude of the right SAN compared to the left. The remainder of EDX testing was normal, including NCSs of the right arm and left SAN, and needle EMG of the right arm, serratus anterior, supraspinatus, infraspinatus, and cervical paraspinals. EDX findings were classic for right SAN neuropathy, proximal to the innervation of the SCM.

SUMMARY/CONCLUSION: SAN neuropathy can occur from apparent pressure from lymphadenopathy from EBV mononucleosis.

CONCENTRIC NEEDLE VOLUNTARY JITTER ABNORMALITIES IN PATIENTS WITH CONGENITAL MYOPATHY
Vitor Caldas (São Paulo, Brazil), Carlos Otto Heise (São Paulo, Brazil), Edmar Zanoteli (São Paulo, Brazil)

INTRODUCTION: There are few reports of classic single-fiber EMG (SFEMG) abnormalities in patients with congenital myopathies (CMs) but no studies involving the disposable concentric needle electrode (CNE) technique.

OBJECTIVE: To compare CNE jitter abnormalities in the orbicularis oculi muscle (OOM) using voluntary activation in CM patients and healthy control subjects.

METHODS: We selected 9 subjects (mean age: 21.4 years) with a CM. Five patients had ryanodine receptor 1 gene-related CM (RYR1-CM), 2 had nebulin gene-related CM, 1 had tropomyosin gene-related CM, and 1 had titin gene-related CM. We also studied 14 healthy patients as a control group (mean age: 38.4 years). In all patients, we collected 20 apparent single-fiber action potential (ASFAP) pairs during voluntary activation of OOM using disposable CNEs. CNE jitter assessments with 3 or more abnormal ASFAP pairs and/or mean jitter above 31 μs were considered abnormal.

RESULTS: Two RYR1-CM patients presented an abnormal jitter analysis. The first presented 6 abnormal ASFAP pairs, with 3 pairs with objective impulse blocking and an average jitter of 53.6 μs. The other patient had only 2 abnormal ASFAP pairs, but had a mean jitter of 32 μs. Clinically, none of those patients had a fatigable weakness. The 7 remaining CM patients had normal tests. The average jitter of all CM patients was 24.3 μs. In the control group, no patient presented a single abnormal ASFAP pair and/or mean jitter above 31 μs were considered abnormal.

SUMMARY/CONCLUSION: CNE voluntary jitter assessment, like classic SFEMG, can present abnormalities, including impulse blocking, in patients with RYR1-CM.
UTILITY OF A TWO-STEP APPROACH TO SMALL FIBER NEUROPATHY EVALUATION USING THE SYMPATHETIC SKIN RESPONSE AND SKIN PUNCH BIOPSY
Lawrence Zeidman (Maywood, IL), Ali Zandieh (Chicago, IL), Dilip Pandey (Chicago, IL)

INTRODUCTION: Isolated small fiber neuropathy (SFN) is typically undetectable on routine needle EMG studies. However, the sympathetic skin response (SSR), available on standard EMG equipment, is a quick and noninvasive method of detecting autonomic dysfunction, which can be seen with SFN. The skin punch biopsy (sensitivity 88%) has become a gold standard in SFN diagnosis, yet is invasive and costly.

OBJECTIVE: To evaluate the utility of a 2-step approach to diagnose SFN using the SSR first and skin punch only in negative or equivocal cases. We hypothesized that the SSR could, in some cases, prevent the need for skin biopsy. To our knowledge, this comparison has never been performed previously.

METHODS: In this retrospective study of 25 patients with clinical SFN seen in a university EMG laboratory (2015-2017), patients included had normal needle EMG and had SSR and skin punch biopsies. Clinical, SSR, and nerve fiber density (NFD) data were collected.

RESULTS: Using a cutoff of 2 SSRs being abnormal, 72% had normal results and 28% abnormal. Comparatively, punch biopsies were positive in 84%. Thus, compared to punch biopsy, the SSR sensitivity was 29% and specificity 75%. In patients with more severe SFN (low NFD in both sites), having 4 absent SSRs resulted in a sensitivity of 14% and specificity of 94%.

SUMMARY/CONCLUSION: The SSR is insensitive but has a high specificity compared to punch biopsy in diagnosing SFN with this 2-step approach. Thus, in patients with SFN clinically, having an abnormal SSR study may be sufficient and obviate the need for skin punch, especially if all SSRs are absent.

Disclosures: Lawrence Zeidman - Research support from Shire (Takeda) Inc for clinical trials.

QUANTITATIVE ANALYSIS OF THE SOUND WAVES PRODUCED BY ABNORMAL SPONTANEOUS POTENTIALS: DIFFERENCES BETWEEN MYOKYMIC AND LOW FREQUENCY COMPLEX REPETITIVE DISCHARGES
Alexandre Recchia (Sao Paulo, Brazil)

INTRODUCTION: Myokymic discharges (MDs) and complex repetitive discharges (CRDs) are usually different and frequently do not cause confusion in their identification. Nevertheless, CRDs, when spontaneously firing at low frequencies, can produce a sound similar to MDs, generating doubts and misinterpretations.

OBJECTIVE: To quantify the differences between sound waves produced by MDs and low frequency CRDs through analysis of their frequencies and correlate them with the pitch of the sound.

METHODS: Fifteen MDs and 6 low frequency CRDs were collected from distinct patients using concentric needle electrodes. Afterwards, a small portion of each discharge of 10 seconds duration (15 MDs/6 CRDs), named long samples (LSs), were selected. Then, 2 samples of bursts discharges (30 MDs/12 CRDs), named short samples (SSs), were isolated from the LSs. Once isolated, the sounds produced by both, LSs and SSs, were recorded and submitted to a Fast Fourier Transform spectrum analyzer to make frequency domain measurements.

RESULTS: Mean frequencies and standard deviations were 723.40±72.35 Hz/681.53±53.40 Hz in the LSs and 1128.39±89.23 Hz/823.39±47.28 Hz in the SSs for MDs and CRDs, respectively. There were no significant differences between the frequencies in the LSs when the 2 types of discharges were compared. Nonetheless, the differences became quite evident when the frequencies in the SSs were compared.

SUMMARY/CONCLUSION: Analysis of the frequencies of the bursts of discharges individualized in the SSs allowed a differentiation between MDs and CRDs. When they were continuously analyzed (LSs), similar frequencies were observed, which produced sound waves very alike, making them difficult to be differentiated by hearing.
USE OF COMPOUND MOTOR ACTION POTENTIALS TO ASSESS RESPONSE TO INTRATHECAL NUSINERSEN IN CHILDREN WITH SPINAL MUSCULAR ATROPHY

INTRODUCTION: Spinal muscular atrophy (SMA) is a neurodegenerative devastating disease of the motor neuron due to defects in the SMN1 gene. As a consequence, NCSs in children affected with this disease show reduced or absent compound motor action potentials (CMAPs).

OBJECTIVE: With the arrival of new therapies, there is a need to provide objective outcome measures to assess response and optimize the use of treatments.

METHODS: Clinical, genetic, and complementary data including NCSs and motor scales were reviewed in 20 children treated with nusinersen (SMA-I, 7; SMA-II, 12; SMA-III, 1; age range: 3 months-11 years). CMAPs, Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), and Hammersmith Infant Neurological Examination (HINE) Section 2 scores (infants) and Motor Function Measure (MFM) scores (after 2 years) were analyzed to describe their course and correlations.

RESULTS: Significant increase of CMAP amplitudes were observed during the first year of treatment in the younger infants in whom NCSs had been performed before and after treatment (type 1 infants treated before 7 months). They also showed the highest changes in CHOP INTEND scores (all HINE >2). CMAP changes and motor function tests were less important during the first year of treatment in more chronic patients.

SUMMARY/CONCLUSION: Measurement of CMAP amplitudes may be useful in the followup of SMA children treated with nusinersen and can be correlated with motor function tests. While changes were striking in infants at early stages of the disease, older children with chronic disease may require longer followup. Further studies are needed to seek establishing a correlation with response to nusinersen.

Charbel El Kosseifi, Fellow
Resident and Fellow Member Award Recipient

FACTORS ASSOCIATED WITH TIMING OF COMPLETION OF ELECTRODIAGNOSTIC TESTS
Lonni Schultz (Detroit, MI), Vyom Grover (Troy, MI), Shabnam Pakneshan (Detroit, MI), Kavita Grover (Detroit, MI)

INTRODUCTION: Optimal patient management requires appropriate and timely investigations to guide treatment.

OBJECTIVE: To identify the factors associated with time to perform needle EMG tests after order entry in electronic medical records and correlation between pre- and post-test diagnoses.

METHODS: A retrospective chart review of needle EMGs April-June 2018 at Henry Ford Hospital EDX laboratories was conducted. Demographic data, residential zip code, referring department, time interval between order entry and test completion, and pre/post-test diagnoses were collected.

RESULTS: Needle EMGs from 689 patients (65% women; mean age: 55.4 years) were included. Participants were 55% African American, 36% Caucasian, 2% Hispanic, and 7% other. Primary physicians (38%), neurologists (35%), and orthopedists (11%) had the most referrals. Tests were performed within ≤2 weeks (median: 7 days) for 73%; only 5% were >30 days. Delayed tests >2 weeks (66%) were due to patient factors. For delay due to laboratory scheduling, median time between scheduling and completion was 6 days. Women were less likely to have tests within 2 weeks (p=0.016). Patients from Detroit were more likely to have tests within 2 weeks and patients from north of Detroit less likely (p=0.002). No other time differences were significant.

There was a correlation between specific pre-test diagnosis and abnormal results for orthopedics referrals only (p=0.04). For all referrals, this correlation was not significant (p=0.472).

SUMMARY/CONCLUSION: Correlation between the specific pre-test diagnosis and abnormal results was seen only for orthopedics. Women and patients north of Detroit were less likely to have their tests performed within 2 weeks of being ordered.
TRAUMATIC BRACHIAL PLEXOPATHY WITH MIXED SPARING OF C5 AND C6 MOTOR AND SENSORY FIBERS WITH CONCOMITANT SPINAL ACCESSORY NERVE INJURY
Collin Grant (Columbus, OH), William Pease (Columbus, OH)

INTRODUCTION/BACKGROUND: Trauma to the upper extremity and neck can cause a variety of injuries to the brachial plexus. Often more than one injury is sustained, the severity of which is difficult to assess with imaging alone. Vigilant and detailed history taking, physical examination, and EDX studies are key in identifying the injury, its severity, and its prognosis.

CASE REPORT: A 56-year-old woman was referred to our outpatient EDX laboratory for evaluation of her left upper limb weakness and paresthesias. Forty days prior she suffered a traction and prolonged compressive injury to her left neck/shoulder in a car accident. In addition to multiple bone fractures, her left arm was not moving so an MRI was completed showing edematous changes to the superior aspects of the brachial plexus extending laterally towards the shoulder. Over the coming weeks she slowly began to regain feeling and strength distally, but proximally she remained very weak. NCSs of bilateral upper limbs demonstrated moderate CTS bilaterally and normal lateral antebrachial cutaneous nerves bilaterally. Needle EMG showed signs of left brachial plexopathy with C5 and C6/upper trunk most affected with possible C5 root avulsion (partial sparing sensory) and partial C6 motor sparing, as well as incomplete left spinal accessory nerve injury.

SUMMARY/CONCLUSION: No two brachial plexopathies are exactly alike, and as demonstrated in this case they often have chronic and acute injuries mixed into their clinical picture. Vigilant and detailed EDX studies allow for the diagnosis, treatment, and functional prognostication of complex neurological injuries.

Collin Grant, MD
Resident and Fellow Member Award Recipient

ORTHODROMIC MEDIAL DORSAL CUTANEOUS NERVE CONDUCTION
Amit Sachdev (Okemos, MI), Dale Turpin (East Lansing, MI), George Zakhia (Brighton, MI), Lindsay Bliss (Lansing, MI)

INTRODUCTION: The first and second dorsal digital nerves join to form the medial dorsal cutaneous nerve. Confirming an isolated dorsal digital injury may be clinically relevant, in particular in the assessment of persisting pain. Nerve conduction has been demonstrated antidromically. To our knowledge, orthodromic conduction is not routinely practiced and has not been the subject of recent interest.

OBJECTIVE: To demonstrate a technique for orthodromic stimulation of the first and second dorsal digital cutaneous nerves.

CASE REPORT: A 43-year-old man presented after a right Lisfranc fracture with surgical repair. Fixation was achieved through a combination of plate and screws. Despite good foot stability, persisting dorsal burning and tingling sensations involving the big toe prompted referral and concern for peripheral nerve impingement. Literature search for medial dorsal cutaneous nerve conduction revealed few publications with a focus on antidromic conduction. Ultrasound, antidromic nerve conduction, and gradual symptom improvement argue against persisting focal impingement. This case prompted intellectual curiosity to pursue an additional conduction technique for this nerve. Utilizing a Natus® (Pleasanton, California) EMG machine with Viking® software, a stimulator was placed at the first and second metatarsophalangeal joints. The recording electrode was placed on the anterior shin, adjacent but lateral to the tibialis anterior ligament and 14 cm from the stimulator. The procedure utilized steady pressure, standard filters, and low level stimulation. Low amplitude but reproducible waveforms were obtained reliably.

SUMMARY/CONCLUSION: It is technically feasible to obtain low amplitude orthodromic stimulation of the first and second dorsal digital cutaneous nerves.
BICKERSTAFF BRAINSTEM ENCEPHALITIS

Bickerstaff brainstem encephalitis (BBE) was initially described in 1951 by Bickerstaff and Cloake. It presents with the triad of external ophthalmoplegia, ataxia, and altered level of consciousness. It is preceded by a bacterial infection with Campylobacter jejuni or Haemophilus influenzae. The pathophysiology underlying the disease process is IgG anti-Gq1b antibodies. We report an atypical case of BBE following a group A Streptococcus (GAS) infection.

CASE REPORT: This is a retrospective review of a single case of a 29-year-old Caucasian female with a medical history of migraine who presented with altered mental status, impaired gait, and generalized weakness. She presented with a 1-week history of sore throat, headache, and fatigue. She was treated with a 10-day course of amoxicillin for treatment of GAS, suggested by a positive strep antigen test. She was readmitted a week later with weakness, nausea, vomiting, and fever. Neurologic examination was significant for somnolence, restricted upward gaze, absent corneal and oculocephalic reflexes, impaired eye-opening, dysarthria, hyperreflexia with bilateral Babinski, and ataxia. Blood work and brain MRI were unremarkable. She was started on antibiotics and antivirals for a central nervous system infection. Lumbar puncture revealed pleocytosis and an elevated antistreptolysin O titer of 409 IU/ml. Electroencephalogram showed background slowing. NCSs revealed abnormal blink reflexes without an underlying demyelinating process. A 5-day course of IVIg and methylprednisolone was administered with improvement in speech and motor strength. Blood work was positive for Gq1b antibody.

CONCLUSION: History suggestive of an antecedent infection preceding clinical presentation should raise concern for this spectrum of illness.

UPDATED REFERENCE VALUES FOR JAPANESE PERONEAL NERVE CONDUCTION STUDY

INTRODUCTION: Many Japanese doctors think the peroneal nerve of Japanese patients is often affected by the traditional Japanese lifestyle of sitting seiza-style (cross-legged). However, lifestyle changes through the eras. Japanese reference values for peroneal NCSs need to be updated for the correct diagnosis.

OBJECTIVE: To determine current reference values for NCSs of the peroneal nerve (deep peroneal nerve) in the Japanese population.

METHODS: In 30 patients (male-female ratio: 11:19; mean age: 55±16 years) with no lower leg symptoms, the peroneal nerve was stimulated at 2 sites (ankle, proximal to the fibular head) by surface electrical stimulation. The recording site is extensor digitorum brevis muscle with surface electrodes. These NCSs were performed December 1, 2018-February 28, 2019.

RESULTS: The compound muscle action potential amplitude (baseline-to-negative peak)/area (negative area) was 4.1±1.8 mV/13.0±6.2 mVms. The duration of negative area was 5.7±0.8 ms. The distal motor latency was 4.6±0.8 ms. The conduction velocity was 53±4 m/s. The amplitude reduction rate between the ankle and knee was 99.5±25.1%.

SUMMARY/CONCLUSION: These values are better than are expected by many Japanese doctors. Using these reference values, more peroneal nerve damage will be correctly diagnosed in Japan.
Carolina Vivar (Danville, PA), Jose David Avila (Danville, PA)

INTRODUCTION/BACKGROUND: Ganglioside-induced differentiation-associated protein 1 (GDAP1) mutations represent up to 1% of all forms of Charcot–Marie–Tooth (CMT) disease and 2-4% of autosomal recessive CMT (AR CMT). These mutations are associated with 4 CMT subtypes: 4A, 2H, recessive intermediate type A (RIA), and 2K. The c.692C>T variant has only been reported in 3 siblings from a single Amish family with AR CMT.

CASE REPORT: A 33-year-old Puerto Rican man presented with weakness. He had a normal motor development but started falling at age 6. Symptoms progressed slowly over time. He developed hand weakness and bilateral foot drop a few years before his presentation. There was no family history of similar symptoms. Examination demonstrated distal arm and leg weakness, sensory loss, and areflexia. There was no extraocular, facial, bulbar, or respiratory muscle weakness, and no upper motor neuron signs. An EDX study demonstrated a non–length-dependent, sensorimotor, primarily axonal neuropathy. Workup for acquired causes of neuropathy led to a new diagnosis of type 2 diabetes (hemoglobin A1C 10.6%, normal <5.7%). Genetic testing identified a homozygous mutation of c.692C>T (p.Pro231Leu) in GDAP1.

SUMMARY/CONCLUSION: The c.692C>T mutation in GDAP1 is associated with AR CMT. Our case suggests that the mutation is not restricted to the Amish population. The phenotype seems to be milder compared to other forms of GDAP1-related AR CMT. In our case, diabetes likely contributed to the neuropathy but did not fully explain the phenotype.

Carolina Vivar, MD
Resident and Fellow Member Award Recipient

MILLER–FISHER SYNDROME AFTER VACCINATION IN THE UNITED STATES: A CENTERS FOR DISEASE CONTROL AND PREVENTION/FOOD AND DRUG ADMINISTRATION VACCINE ADVERSE EVENT REPORTING SYSTEM STUDY, 1999-2017
Kazi Md Asif Hilmi (Newark, NJ), Kevin Nolasco (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Miller–Fisher syndrome (MFS) can occur after vaccination in the United States and is included in the Centers for Disease Control and Prevention (CDC)/FDA Vaccine Adverse Event Reporting System (VAERS).

OBJECTIVE: To investigate the correlation between MFS and vaccination in adults.

METHODS: Using data from the VAERS database for over 1999-2017, we identified cases of MFS and characterized their temporal relationship with different vaccinations. The initial 6 weeks after vaccination were defined as the risk period for possible cause–effect between vaccination and MFS, while the subsequent 6 weeks were defined as the control period. Only case-centered analysis was utilized.

RESULTS: There were 87 MFS cases (male 61%; mean age: 45 years) reported following influenza, hepatitis AB, and human papillomavirus (HPV) 4 vaccination between 1999 and 2017. Reporting rate of post-vaccination MFS was 0.36-0.47/1,000,000, which is within the range expected for the general population. Of these, 76% were reported within 6 weeks after vaccination, with 24% of these reported in the first 2 weeks. Case-centered analyses demonstrated that 76.1% cases of MFS cases were reported within the risk period.

SUMMARY/CONCLUSION: Although we did not observe an increase in the incidence of MFS after vaccination as compared to the general population, the unbalanced distribution of cases within the first 6 weeks is unlikely to be coincidental. Furthermore, case-centered analyses demonstrated that majority of MFS cases were reported within the 6-week risk period. These results warrant the implementation of active surveillance and careful evaluation of patients with signs and symptoms of MFS after vaccination.
AMYOTROPHIC LATERAL SCLEROSIS PRESENTING AS SYNDROME OF INAPPROPRIATE ANTI DIURETIC HORMONE SECRETION
Sadia Waheed (Lexington, KY), Fawad Yousuf (Lexington, KY), Adam Gray (Lexington, KY)

INTRODUCTION: ALS presents with insidious onset progressive muscle atrophy, fasciculations, and respiratory muscle dysfunction. Presentation varies depending on motor neurons involved. Bulbar findings (difficulty chewing, speaking, or swallowing) are common.

CASE REPORT: A 72-year-old man presented with 2 weeks of confusion and recently diagnosed hyponatremia. Family reported several months of progressive fatigue and diffuse generalized weakness limiting ability to care for himself. He had dysphagia, anorexia, weakened voice, and depression. Vital signs were normal. He appeared fatigued, had a flat affect, hypophonia, and was not very interactive to questions. He had muscle atrophy in the left leg and bilateral arms with 3/5 strength throughout; fasciculations in tongue and all extremities. Reflexes were brisk, and Babinski sign on the right. Cranial nerves/sensation were intact. Sodium was 122 mmol/L, serum osmolality 260 mmol/L, urine osmolality 389 mmol/L, and urine sodium 72 mEq. Arterial blood gas demonstrated chronic hypercapnic respiratory failure. Needle EMG/NCSs showed diffuse proximal lower motor neuron injury. Head MRI showed a non-enhancing intramedullary lesion from C3-7 with posttraumatic myelomalacic changes. Symptoms improved with medical management but with residual bilateral upper extremity weakness. Daily rehabilitation (physical and occupational therapy) conducted for 3 weeks resulted in the patient's functional independence and return to school.

CONCLUSION: There is a known association of ALS with SIADH, which is potentially related to the hypercapnic respiratory failure or emotional/physical stressors. Our patient presented with confusion, hyponatremia, and chronic hypercapnia that led to ALS diagnosis. Treatment of the respiratory failure with NIPPV has been shown to improve the SIADH.

CENTRAL CORD SYNDROME SECONDARY TO TRAUMATIC SYRINGOMYELIA WITH CONCOMITANT BILATERAL BRACHIAL PLEXUS INJURY: A CASE REPORT
Maria Corazon Riego-Pedro (Manila, Philippines), Anna Cecilia Tiangco (Manila, Philippines), Monalisa Lim-Dungca (Manila, Philippines)

INTRODUCTION/BACKGROUND: Spinal cord injury with concomitant brachial plexus injury is rare, with a frequency of 0.6-1.8%. Early detection is important to determine prognosis and to achieve favorable functional outcomes. MRI, EDX studies, and musculoskeletal ultrasound (US) as diagnostic tools in rehabilitation medicine can help in the diagnosis of combined traumatic injuries.

OBJECTIVE: To describe a case of central cord syndrome secondary to traumatic syringomyelia with concomitant brachial plexus injury, its diagnostic management, as well as its rehabilitation management.

CASE REPORT: A 17-year-old, left-handed, male student gradually developed tetraplegia with sensory deficits at the level of the C5 dermatome and below as well as bladder incontinence after lifting a gas tank. Cervical MRI contrast showed a non-enhancing intramedullary lesion from C3-7 with posttraumatic myelomalacic changes. Symptoms improved with medical management but with residual bilateral upper extremity weakness. Needle EMG and NCSs revealed bilateral brachial plexus injury at C5-6 root levels. Diagnostic musculoskeletal US showed hypoechoic and enlarged left C5, C6, and C7 nerve roots. Daily rehabilitation (physical and occupational therapy) conducted for 3 weeks resulted in the patient's functional independence and return to school.

SUMMARY/CONCLUSION: Early diagnosis of combined spinal cord and brachial plexus injuries can be accomplished with the use of MRI, EDX studies, and musculoskeletal US. Together with timely and appropriate rehabilitation intervention the patient achieved a favorable functional outcome.
FIRST USE OF NEEDLE ELECTRICAL IMPEDANCE MYOGRAPHY IN THE ELECTRODIAGNOSTIC LABORATORY
Benjamin Sanchez (Boston, MA), Seward Rutkove (Boston, MA)

INTRODUCTION: Improved technologies are needed to enhance diagnosis and therapeutic monitoring of neuromuscular disorders (NMDs). A novel modality with promise in the evaluation of NMDs is needle electrical impedance myography (nEIM).

OBJECTIVE: To investigate the feasibility of nEIM as a tool to diagnose neuromuscular disorders.

METHODS: We created a novel disposable concentric EIM needle for intramuscular readings. Concentric EIM needles are similar to standard concentric EMG needles, with an additional thin layer of insulation material re-covering the barrel of the needles to prevent any shortcut of the electrical current applied to the exposed metal. Under IRB approval and signed informed consent, we inserted 2 concentric EIM needles and measured the first dorsal interosseous muscle bilaterally in a 66-year-old man with moderate, chronic right cervical polyradiculopathy with normal strength on the unaffected side and weakness on the right side.

RESULTS: The patient tolerated well the insertion of 2 concentric EIM needles in the muscle separated a distance of 1 cm. The data collection lasted 1 second with the muscle at rest. Different multifrequency EIM data were obtained between the unaffected and affected sides.

SUMMARY/CONCLUSION: This is the first use of nEIM in the clinic. It has the potential to provide powerful insights into the electrical properties of muscle that are closely tied to pathological and physiological changes in the muscle, including myofiber atrophy, fat deposition, and muscle edema. Ultimately, nEIM can augment the EDX toolbox for NMD diagnosis and as serve as an enhanced biomarker of disease alteration and therapeutic intervention.

Disclosures: Benjamin Sanchez - Consultant to Myolex, Inc, and Impedimed, Inc; Co-Founder of Haystack Diagnostics, Inc; Dr. Sanchez is a named inventor. This study did not employ any relevant company technology.
Seward Rutkove - Scientific advisor and consultant to Myolex, Inc; Co-Founder of Haystack Diagnostics, Inc; Dr. Rutkove is a named inventor. This study did not employ any relevant company technology.

NERVE-SPECIFIC LOCAL AND SYSTEMIC ANALGESIC EFFECTS OF ACUPUNCTURE IN HEALTHY ADULTS, MEASURED BY QUANTITATIVE SENSORY TESTING
Alexandra Dimitrova (Portland, OR), Dana Colgan (Portland, OR), Barry Oken (Portland, OR)

OBJECTIVE: To assess whether acupuncture analgesia is mediated via a dose response and whether its effects are local or systemic.

METHODS: Twenty-eight healthy volunteers aged 18-45 were randomized to 2 doses of acupuncture, using points closely associated with peripheral nerves in the legs. The lower dose group involved acupoints overlying the deep peroneal nerve (DP) and the higher dose acupoints overlying the deep peroneal and posterior tibial nerves (DPTN). Baseline and post-acupuncture quantitative sensory testing (QST) were obtained locally in the calf and big toe and systemically at the hand. Results were analyzed using factorial repeated measures ANOVA for each of the QST variables—cold detection threshold (CDT), vibration detection threshold (VDT), heat pain threshold (HP0.5), and heat pain 5/10 (HP5.0). Location (leg/arm) and time (pre/post-acupuncture) were within-subject factors. Intervention (DP/DPTN) was between-subject factor.

RESULTS: CDT was increased locally in the calf (p<0.001) and systemically in the hand (p<0.001). VDT was increased locally in the toe (p<0.001), but not in the hand. HP0.5 was increased locally in the calf (p<0.001) and systemically in the hand (p<0.001). HP5.0 was increased in the calf (p=0.002) and in the hand (p<0.001), with the local effect significantly greater than the systemic (p=0.004). In all modalities there was no difference between low- (DP) and high-dose (DPTN) acupuncture groups.

CONCLUSION: Acupuncture caused comparable local and systemic analgesic effects in cold detection and heat pain perception and only local effects in vibration perception. There was no clear acupuncture dose response to these effects.
DO WE NEED ANALGESIA COVER DURING ELECTRODIAGNOSTIC TESTING?—PATIENTS’ PERCEPTION OF PAIN DURING ELECTRODIAGNOSTIC TESTING AT THE AGA KHAN UNIVERSITY HOSPITAL

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INTRODUCTION: EDX testing is instrumental in investigating peripheral nervous system disorders. Unfortunately, this involves considerable discomfort to the patient. To make this procedure less painful multiple strategies have been proposed. We assessed pain perception during EDX testing in our patients to determine requirements of pre-procedure analgesic cover.

OBJECTIVE: To determine the level of pain perception and factors affecting it during EDX testing in our patients to determine requirements of pre-procedure analgesic cover.

METHODS: This prospective analytical cross-sectional study was conducted at Aga Khan University Hospital, Karachi. Non-probability purposive sampling was used. Patient and procedure-specific data along with post-procedure pain scores were recorded. Patients were asked their opinion regarding need of pre-procedure analgesic cover. All p-values were considered as statistically significant if <0.05.

RESULTS: Included in the study were 95 participants who had an anticipated post NCS pain score of 5 (interquartile range [IQR] 4-7) with an actual post NCS pain score of 6 (IQR 5-7; p=0.074). The median anticipated post needle EMG pain score was 6 (IQR 5-8) with an actual post EMG pain score of 8 (IQR 5-9; p=0.000442). There were statistically significant differences in post-EMG scores between body mass index groups, type of needle, and whether endplate noise was detected (all p-values <0.05). Higher post needle EMG pain scores were predictive of the need for painkillers during the procedure as assessed by a logistic regression model (p=0.025).

SUMMARY/CONCLUSION: EDX examination is a painful test and warrants administration of an effective pre-procedure analgesic cover.

PAIN DRAWINGS FOR PATIENTS WITH LENGTH-DEPENDENT SMALL FIBER NEUROPATHY AND NON-LENGTH-DEPENDENT SMALL FIBER NEUROPATHY

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INTRODUCTION: Small fiber neuropathy (SFN) has rarely been observed in a pain clinic. Her, we explore pain drawings from patients with both length-dependent and non-length-dependent SFN to look for any defining patterns of pain in this population.

OBJECTIVE: To determine the pain patterns with length-dependent and non-length-dependent SFN.

METHODS: A total of 111 patients with length-dependent and non-length-dependent SFN completed a pain drawing. If the patient only exhibited pain in the spine it was classified as axial pain. If the pain was in a typical glove and stocking pattern it was called peripheral. If the drawing was completed in both axial and peripheral, it was called labeled as both. We then analyzed this data.

RESULTS: Of 111 patients, 45 (40.54%) have non-length-dependent SFN. Of those 45 patients, 11 (24.44%) have axial pain, 7 (15.56%) present peripheral pain, and 27 (60%) have both. Sixty-five patients (58.56%) of the total sample (111) have length-dependent SFN. Of those, 16 (24.62%) have axial pain, 5 (7.69%) peripheral pain, and 44 (67.69%) both.

SUMMARY/CONCLUSION: Rarely will patients only complain of distal burning, tingling, and pain in the extremities. We show that most patients will complain of diffused pain throughout their body, even if it is length-dependent. For patients to have complete resolution of their pain, the correct diagnoses and appropriate treatments need to be rendered for all of their conditions.
POSTHERPETIC NEURALGIA TREATED WITH BOTULINUM TOXIN
Richard Weiss (Roanoke, VA)

INTRODUCTION/BACKGROUND: Reactivation of dormant varicella virus can cause postherpetic neuralgia (PHN) involving chronic pain or dysesthesias. Multiple treatment options exist including antiviral medications, topical lidocaine, and capsaicin, as well as oral neuroleptics and antidepressants. For recalcitrant cases interventional procedures including epidural steroids can be effective. More recently botulinum toxin type A (BTX-A) has been shown to be effective for this type of pain.

CASE REPORT: A 77-year-old Caucasian male was referred to the author’s clinic with 12 years of neuropathic pain (9-10 on the visual analog scale, VAS) primarily in a T1-4 distribution due to a previous herpetic lesion. He was initially not treated with oral antiviral agents due to a delay in diagnosis. He had tried traditional and some nontraditional treatment options including bee venom therapy without success. The patient opted to proceed with a trial of intradermal BTX-A. After mapping out the area of maximal pain, BTX-A diluted in 4 ml of unpreserved normal saline was injected intradermally into the skin 1.5-3.0 cm apart (0.2 ml/5 units injected per site for 40 sites: 200 units total). The patient had good relief of his symptoms for 2 months duration with reduction of pain to 2-4/10 on the VAS. He reported he was able to wear a shirt for a longer duration and that the BTX-A was the only thing that has really helped with his PHN pain and that he would like to repeat the injections.

SUMMARY/CONCLUSION: BTX-A can be an effective treatment for incalcitrant cases of PHN.

QUALITATIVE AND QUANTITATIVE VOICE ACTIVATION TECHNOLOGY CAPTURES PATIENT REPORTED OUTCOMES TO INFORM THE FOOD AND DRUG ADMINISTRATION ON CHARCOT–MARIE–TOOTH DISEASE
Robert N Moore (New York, NY), Allison T Moore (New York, NY), Joy M Aldrich (Seattle, WA), Florian P Thomas (Hackensack, NJ), Courtney L Hollett (Chesterfield, VA)

OBJECTIVE: Patient reported outcomes (PROs) are essential to understanding disease state and what is important to patients when considering treatments and therapeutics. The Hereditary Neuropathy Foundation (HNF) deployed novel voice activation technology (VAT) to capture important PROs regarding pain, mobility, and impact on quality of life (QOL) for patients with Charcot–Marie–Tooth (CMT) disease.

METHODS: HNF created the Global Registry for Inherited Neuropathies (GRIN) to capture detailed inherited neuropathy patient history. Via an automated telephone IRB-approved patient survey over 2017-2018, CMT patients (n=380) were queried on the impact of pain and impaired mobility on QOL.

RESULTS: Forty-five percent of CMT patients identified pain as having a significant impact on QOL. Patients use a wide lexicon to describe their pain; 25 individual descriptives were identified, with 50% describing their pain as shooting, stabbing, burning, or severe. Pain impacts a wide range of activities of daily living (ADL), including work, household chores, and sleep. Patients are using varying modalities to cope with pain, ranging from over-the-counter remedies to cannabis to opiates. Patient mobility is cited as the number 1 impairment by CMT patients, impacting multiple aspects of ADL. Weakness, atrophy, and balance issues have a significant negative impact on QOL. Falls are common, and simple tasks such as standing can be a challenge.

CONCLUSIONS: Deploying VAT to capture CMT patient PROs in their own voice allowed investigators to conduct a quantitative and qualitative analysis of CMT patients experience with pain and mobility, providing deeper insight into the CMT patient experience.

Disclosures:
Florian P Thomas - Consultant for Pharnext and Acceleron Pharma.
PAIN TREATMENT CONSIDERATIONS FOR NERVE INJURY DUE TO UNUSUAL WORK-RELATED SITUATIONS
Barathi Sreenivasan (Toronto, Canada)

INTRODUCTION: Patients who have neuropathic symptoms from unusual work-related injuries, with normal EDX studies, can be treated using a number of methods to improve pain.

OBJECTIVE: To present a case of a patient who developed ulnar neuritis and CTS from work-related tar injury and discuss challenges and approaches to treatment of pain in this population.

CASE REPORT: A 30-year-old male who sustained a work-related tar injury to the posterior neck, scalp, and both arms and hands was treated with skin grafting. His symptoms included bilateral upper extremity paresthesias, especially in the left little and ring fingers and the right hand dorsum, nocturnal paresthesias, and some subjective weakness. Physical examination was in keeping with abnormalities in the ulnar and median distributions. EDX studies showed essentially normal NCSs and needle EMG. The patient was diagnosed with clinical bilateral CTS and left ulnar neuritis in the setting of essentially normal NCSs. The patient was treated with therapy including active nerve gliding stretches, systematic desensitization, and hand function retraining, as well as splinting for nerve tension reduction and scar management strategies. Post treatment, the Numeric Rating Scale for pain improved from 7/10 to 3/10, the Wong–Baker Faces pain rating scale improved from 6 to 2, and the Patient Rated Ulnar Nerve Evaluations Scores improved especially with lifting heavy objects, nocturnal and work-related symptoms, and frequency of pain.

SUMMARY/CONCLUSIONS: Unusual work-related nerve injuries with normal EDX studies can be addressed using a number of methods to significantly decrease pain levels.

SPATIAL VARIABILITY IN HAND SURFACE TEMPERATURE PRIOR TO WARMING FOR ELECTRODIAGNOSTIC STUDIES
Michael Lin (Madison, WI), David Schwanebeck (Waukesha, WI), Bonnie Weigert (Madison, WI)

INTRODUCTION: EDX measurements are susceptible to temperature dependent effects, which can be addressed with standard protocols for skin temperature measurement and warming.

OBJECTIVE: To determine, through a quality improvement study, the variability in skin temperature between 2 sites on the hand commonly used for electrode placement in upper extremity (UE) EDX studies, and to consider the impact this may have on the decision to warm patients.

METHODS: Temperatures were recorded with an infrared probe over the ipsilateral first dorsal interosseous muscle (FDI) and dorsal fifth proximal interphalangeal joint (PIP) in 77 patients prior to UE EDX examinations. Standard protocol at our study site recommends warming for 5 minutes if skin temperature over the FDI is less than 31.5°C.

RESULTS: Temperature over the fifth PIP was on average 2.3°C lower than over the FDI. Eighteen percent of patients with a FDI temperature greater than 31.5°C, had a fifth PIP temperature less than 31.5°C. These results prompted modification to our standardized protocol, instead measuring surface temperature over the fifth PIP in UE studies prior to decision to warm patients. Our data suggest more patients would need to be warmed prior to their studies for a fixed temperature cutoff if measured at the fifth PIP.

SUMMARY/CONCLUSION: There is considerable variability between surface temperatures at the FDI and fifth PIP in our study population, impacting the number of patients who were warmed prior to their EDX examination. Future studies are needed to determine if the spatial temperature variability on the hand significantly alters study results.

Michael Lin, MD
Resident and Fellow Member Award Recipient
IS THE PAIN FIBER NERVE CONDUCTION STUDY USEFUL IN DIAGNOSING RADICULOPATHY
Nicholas Tranchitella (York, PA), Vincent Tranchitella (York, PA)

INTRODUCTION: The pain fiber NCS (pf-NCS) purports to identify pain pathology by selectively stimulating, and subsequently recording, the A delta sensory pain fiber response to a cutaneous electrical stimulus at a frequency of 250 Hz. It allegedly predicts nerve root pathology with a sensitivity of 94.6%, and specificity of 70.2%.

OBJECTIVE/METHODS: We performed a retrospective review of cervical pf-NCSs performed on patients who were involved in a motor vehicle accident (MVA). The frequency with which pf-NCSs diagnosed cervical radiculopathy, and at which root levels, was compared to published scientific literature.

RESULTS: A total of 278 cervical pf-NCSs were analyzed. Radiculopathy was diagnosed in 233/278 (84%) of the studies. The root levels involved, in order of descending frequency, included T2, C6, T1, C8, C5, C7, C4, C3, and C2. Three or more nerve roots were involved in 156/233 (67%) of the pf-NCSs that were positive for radiculopathy. Published scientific literature indicates that cervical radiculopathy occurs with a frequency of 8% following MVA. These studies show it occurs most frequently at C7, followed by C6, then C8 and C5, and may involve multiple levels up to 30% of the time.

SUMMARY/CONCLUSION: The pf-NCS overdiagnosed cervical radiculopathy with a frequency and at root levels inconsistent with the current scientific literature. The pf-NCS does not appear to be useful in diagnosing cervical radiculopathy. The role of pf-NCSs in the radiculopathy diagnostic algorithm needs to be re-evaluated using current standard criteria.

PATHOPHYSIOLOGY, DIAGNOSIS, AND MANAGEMENT OF PRIMARY PERIODIC PARALYSIS: IDENTIFICATION OF GAPS IN KNOWLEDGE AND COMPETENCE AMONG NEUROLOGISTS
Thomas Finnegan (New York, NY), Pakinam Aboulsaoud (New York, NY), Deborah Susulka (New York, NY), Stephen Cannon (Los Angeles, CA)

INTRODUCTION: The 2 primary forms of primary periodic paralysis (PPP) are hyperkalemic periodic paralysis (hyperkPP) and hypokalemic periodic paralysis (hypokPP). Because PPP is a rare condition, the knowledge and competency base among neurologists has not been established.

OBJECTIVE: To identify gaps in knowledge and competence among neurologists regarding PPP.

METHODS: A continuing medical education-certified 24 multiple-choice survey on knowledge, clinical preferences, and competence was made available to neurologists in the United States. The questions were based on clinical trials, guidelines, and expert faculty recommendations regarding the pathophysiology, diagnosis, and management of PPP. The survey posted on the Medscape Education website and responses were collected from September 17, 2018 through October 30, 2018.

RESULTS: Ninety-seven neurologists completed the survey during the study period. On average, 60% of neurologists were not familiar with the mechanisms responsible for the presentation of either hyper or hypokPP. Additionally, 43% of neurologists were unaware of PPP symptoms; 65% incorrectly identified the appropriate clinical testing for PPP; and less than 45% correctly identified the FDA indication for dichlorphenamide, the appropriate treatment of acute weakness in hypokPP, or any of the case vignettes requiring treatment-related decision making. A subanalysis of the data indicated no differences in outcomes based on whether or not the neurologist managed patients with PPP.

SUMMARY/CONCLUSION: This research yielded important insights into current clinical knowledge and competence gaps of neurologists regarding the pathophysiology, diagnosis, and management of PPP. The results indicated a need for comprehensive education across all areas of PPP.

Disclosures:
Stephen Cannon - Advisor/consultant for Strongbridge Biopharma.
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VARIABLE PRESENTATION AND PATHOLOGIC OVERLAP OF HEREDITARY AMYLOIDOSIS
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INTRODUCTION/BACKGROUND: Hereditary amyloidosis (HaTTR) is thought to have either cardiac or neurologic phenotype. We present several cases showing HaTTR can have diverse presentations and even be mistaken histologically for other diseases.

CASE REPORT: The following cases confirmed HaTTR by genetic testing and biopsy. A 58-year-old male with history of heart failure presented with grip weakness, quadriceps atrophy, bilateral foot drop, and paresthesias. EDX studies showed mixed peripheral large fiber neuropathy and myopathic changes in the quadriceps. Initial muscle biopsy revealed inflammatory cell infiltration and basophilic-rimmed vacuoles suggesting inclusion body myopathy. A 75-year-old male presented with ascending paresthesias and burning pain. He was treated for 2 years with IVIg and plasma exchange with a diagnosis of chronic inflammatory demyelinating polyneuropathy. A 65-year-old male presented with orthostasis and peripheral neuropathy (PN). A 74-year-old male presented with constipation, bloating which progressed to orthostasis, and PN. A 65-year-old male with history of heart failure presented with peripheral sensory neuropathy. A 65-year old male with history of heart failure presented with progressive lower extremity weakness and paresthesias. A 79-year-old man with history of heart failure presented with 2 years of progressive PN.

SUMMARY/CONCLUSION: HaTTR has many different presentations and histologically overlapping features. Commonly, HaTTR is not diagnosed correctly until cardiac symptoms arise. We contend that, although the statistical yield is low, sending HaTTR as standard testing for patients with neuropathy has the potential to save them time, money, and stress by not allowing misdiagnosis or mislabelling as “idiopathic” when an etiology may exist.

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IS VITAMIN D DEFICIENCY AN INDEPENDENT RISK FACTOR FOR PERIPHERAL NEUROPATHY?
Jin Jun Luo (Philadelphia, PA), Favio Bumanlag (Oreland, PA), Nae Dun (Philadelphia, PA)

INTRODUCTION: We previously reported vitamin D deficiency (VDD) may potentially serve as a biomarker contributing to the etiology causing paresthesia (Muscle Nerve 2018;58 [suppl 2]:S7.). However, whether VDD is an independent risk factor for neuropathy remains to be elucidated.

OBJECTIVE: To study whether isolated decreased plasma level of vitamin D occurs in patients with paresthesia.

METHODS: Charts of patients with paresthesia seen from January 1, 2015 to December 31, 2017 were retrospectively reviewed. Their medical history, demographic, clinical, laboratory, and electrophysiologic data were recorded. Patients with identifiable established etiologies for neuropathy in history, body mass index >30 kg/m2, any abnormal laboratory derangement, other than vitamin D25-hydroxyl (VD25OH), were excluded. Symptoms and VD25OH before and after vitamin D were compared.

RESULTS: Of 217 patients with paresthesia, 78 who had a VD25OH laboratory test were initially recorded. Of those, 14 met the inclusion criteria. They were 46.1±11.0 years old, with VD25OH=19.9±5.1 ng/mL, comprised of 9 males (age: 43.1±9.1, VD25OH=20.3±4.6) and 5 females (age: 51.4±13.1, VD25OH=19.2±6.4). Supplementation of vitamin D (2714.3±2812.8 IU/day) slightly increased the VD25OH level and partially ameliorated 6/12 (50%) patients’ symptoms in 8.7±6.9 months.

SUMMARY/CONCLUSION: In conjunction with our previous study showing a significantly increased frequency of decreased vitamin D levels (p<0.0001) in patients with paresthesia, the present study provides additional evidence that isolated VDD may potentially be an independent risk factor, and serve as a biomarker paralleling others such as hemoglobin A1C, for peripheral neuropathy. Validation in a large scale study is warranted.
TREATMENT OF CHARCOT–MARIE–TOOTH DISEASE IN THE UNITED KINGDOM AND UNITED STATES: INSIGHTS FROM A DIGITAL REAL-WORLD OBSERVATIONAL STUDY

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INTRODUCTION: Charcot–Marie–Tooth (CMT) disease is a hereditary neuropathy that affects the peripheral nervous system.

OBJECTIVE: To explore patient-reported treatment patterns and care standards for CMT in the United Kingdom and United States.

METHODS: Adults with CMT were recruited to a 2-year international observational study exploring the real-world burden of the disease. Data were collected via CMT&Me, a bespoke “bring your own device” app, through which participants were asked questions about their CMT and its management. This interim analysis examined treatment patterns and care standards reported by U.K. and U.S. participants.

RESULTS: Treatment standards were generally consistent with guidelines. Most participants had at least annual access to several different healthcare professionals, including family doctors, neurologists, orthotists, physical/physiotherapists, and occupational therapists. However, the type and number of professionals visited varied considerably between participants. The majority of participants had received some form of physical therapy for their CMT, the most common being physio/physical therapy and occupational therapy. Analgesics/painkillers and antidepressants were the most frequently used medicines. Most participants reported using some form of orthosis or walking aid, with insoles and ankle/leg braces being the most common. Additionally, around half had undergone a surgical procedure for their CMT.

SUMMARY/CONCLUSION: CMT management in the U.K. and U.S. is multifaceted, involving physical and surgical therapies, medications, orthoses, and aids. Standards of care are broadly consistent with guidelines; however, there remains scope to improve access to suitable healthcare professionals. This ongoing study will provide further real-world insights into areas for the development of CMT care.

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Emma Bagshaw, Hara Kousoulakou & Mark Larkin - Employees of Vitaccess, paid by Pharnext to conduct this study.

UTILITY OF REPEAT ELECTRODIAGNOSTIC STUDIES IN AN OUTPATIENT SETTING

Aimee Boegle (Boston, MA), Jillian Alderson (Boston, MA), Neil Datta (Boston, MA), Pushpa Narayanaswami (Boston, MA)

INTRODUCTION: EDX studies are frequently used for the diagnosis of neuromuscular disorders. Repeat EDX studies may be requested for individual patients for evaluation of the same or different conditions. The outcome/usefulness of repeat studies in patient management has not been studied.

OBJECTIVE: To evaluate the frequency, indications for, and outcome of repeat EDX studies in a tertiary level academic medical center over 3 years.

METHODS: A retrospective review of outpatient EDX studies performed between January 1, 2015 and December 31, 2017 was conducted to identify patients who had undergone repeat studies. The reason for repeat testing was obtained from the referral diagnosis for the initial and repeat studies. Data were then categorized based on referral indications. Referral patterns for repeat EDX studies were evaluated. Medical records of patients undergoing repeat studies for the same indication were reviewed to determine the impact of EDX diagnoses on clinical outcome. Descriptive statistics were used.

RESULTS: Out of 4,882 outpatients who had EDX studies, 276 (5.6%) returned for 1 or more additional studies. The most common reasons for repeat studies were evaluation of CTS, cervical radiculopathy, and lumbosacral radiculopathy. Approximately 20% of patients were referred for the same indication as their initial study. Neurologists most frequently requested repeat studies, followed by orthopedic and primary care physicians.

SUMMARY/CONCLUSION: Only 5% of patients underwent repeat EDX testing. Details of reasons for the repeat studies, resulting changes in management, referral patterns, and potential correlations between referral patterns and repeat EDX studies will be presented.
FACTORS ASSOCIATED WITH TIMELINESS OF TEST RESULT COMMUNICATION
Rebecca Bond (Detroit, MI), Ahmad Siddiqi (Detroit, MI), Vyom Grover (Troy, MI), Lonni Schultz (Detroit, MI), Kavita Grover (Detroit, MI)

INTRODUCTION: Effective and timely communication is imperative for quality patient care.

OBJECTIVE: To evaluate communication of NCS/needle EMG results between physicians’ offices and patients.

METHODS: A retrospective chart review of needle EMGs during March-June 2018 at Henry Ford Hospital EDX laboratories was conducted. Demographic data, residential zip code, referring department, time interval between test and result communication, and specifics of communication were collected.

RESULTS: Needle EMGs of 832 patients (68% women; mean age: 55.4 years) were included. This review included African Americans (66%), Caucasians (25%), Hispanics (3%), and others. Results were communicated to 682 (82%) patients. Highest numbers of referrals were from Neurology (35%) and Internal Medicine (29%). Results were communicated to 31% telephonically, 29% at clinic visit, and 17% by letter and electronically. Most of the communication was conducted by physicians (85%). Median time to communicate was 5 days (range: 0-290). Communication rate was not associated with patient demographics. The overall difference in the rate of communication among different geographic locations was not significant (p=0.163). The overall difference in rate of communication was not significant across departments (p=0.053). However, the rate for Pain Clinic was the lowest (53%) with Family Medicine the highest (88%), with others ranging 76-84%. Time to communicate using clinic visits was significantly longer (median 17 days versus 4-5 for others, p<0.001).

SUMMARY/CONCLUSION: Majority of test results were communicated. Patient demographics did not influence the rate of communication. Pain Clinic had the lowest and Family Medicine had the highest rate of communication. Results provided at clinic visits were the least timely.

A CASE SERIES OF HEREDITARY NEUROMUSCULAR DISORDERS IN PATIENTS WITH NEUROMUSCULAR IMMUNE-RELATED ADVERSE EVENTS SECONDARY TO IMMUNE CHECKPOINT INHIBITORS
Nadim Jiwa (Boston, MA), Donald Lawrence (Boston, MA), Amanda Guidon (Boston, MA)

INTRODUCTION: Treatment with immune checkpoint inhibitors (ICIs) for cancer may result in neuromuscular immune-related adverse events (irAEs). To our knowledge, coincident hereditary neuromuscular disorders have not been described, but may affect evaluation and management.

OBJECTIVE: To present 3 cases of neuromuscular irAEs with new diagnoses of hereditary neuromuscular disorders in patients treated with ICIs for melanoma.

CASE REPORT: Patient A is a 70-year-old man who developed immune-related myositis and lumbosacral radiculitis after pembrolizumab. Prior history of transient creatine kinase elevation and cardiomyopathy prompted genetic studies that revealed a pathogenic variant in TTN. A muscle biopsy showed myopathic features, confirming a coexisting titinopathy. Patient B is a 72-year-old man who developed truncal and appendicular paresthesias secondary to immune-related sensory ganglionopathy following ipilimumab and nivolumab. In addition to sensory neuronopathy, EDX studies revealed diffuse myotonic discharges. He had a long history of muscle stiffness. Genetic testing showed a pathogenic variant in CLCN1, diagnostic of myotonia congenita. Patient C is a 71-year-old man with rapidly progressive dysphagia following pembrolizumab. EDX studies revealed waning myotonic discharges, and genetic testing revealed a mutation in CNBP consistent with type 2 myotonic dystrophy (DM2). His dysphagia was more than expected in DM2 and improved with IVIg, suggesting an immune-mediated component.

CONCLUSION: This case series illustrates the importance of considering comorbid hereditary neuromuscular conditions when evaluating patients for irAEs to ICIs. Neuromuscular evaluation should include a detailed review of symptoms predating ICIs and family history. Further study into genetic risk factors for the development of neuromuscular irAEs may be warranted.
COGNITIVE DEFICITS IN PATIENTS WITH MYASTHENIA GRAVIS: ASSOCIATION WITH GLUCOCORTICOIDS AND DEPRESSION
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INTRODUCTION: Cognitive deficits in patients with myasthenia gravis (MG) have been described in the literature since the 1980s, but at the moment the results are conflicting.

OBJECTIVE: To verify the cognitive profile of patients with MG.

METHODS: This is a cross-sectional descriptive study. The patients were recruited in the Neuromuscular outpatient clinics of a reference Hospital in Porto Alegre/Brazil. A standardized battery of instruments was utilized for assessing the cognitive profile. Clinical and sociodemographic data were extracted from medical records.

RESULTS: Forty patients (70% female; mean age: 50.10±18.0 years; mean education period: 9.18±4.39 years) were assessed. With regard to drug use, 50% (20) used immunomodulators, 90% anticholinesterase inhibitors, and 57.5% glucocorticoids. The percentage of patients with altered scores in each cognitive test, according to normative values, was 45% in Mini-Mental State Examination (MMSE), 67.5% Montreal Cognitive Assessment (MoCA), 20% in phonological verbal fluency (PVF), and in Rey Auditory Verbal Learning Test (RAVLT) 57.5% in learning memory, 42.5% in immediate memory, and 55.0% in recent evocation. After the regression analysis of Poisson, a higher prevalence of depression was observed in patients who had the PVF (7.85 [IC: 2.42, 25.47], p=0.056), MoCA (1.65 [IC: 1.25, 2.17], p=0.048), and MMSE (1.94 [IC: 1.14, 3.31], p=0.024) altered. In addition, there was a higher prevalence of glucocorticoid use in patients with altered RAVLT (9.36 [IC: 1.19, 73.42, p=0.001).

SUMMARY/CONCLUSION: We observed a high percentage of individuals with cognitive impairment in executive functions and memory in this sample. These deficits have strong associations with the use of glucocorticoids and depression.

STANDARD REFERENCE DATA OF MEDIAN NERVE CONDUCTION STUDY WITH CONSIDERATION OF EXTENDED UNCERTAINTY
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INTRODUCTION: The NCS is an essential tool for assessing peripheral nerve function and pathological condition. However, there is no standardized reference data in South Korea, or the world. This allows for various reference values in each laboratory, confusing the diagnosis and causing unnecessary re-examination. Therefore, there is a need for producing standard reference data.

OBJECTIVE: To derive standard reference values of median NCSs, including the calculation of measurement uncertainties, in the South Korean population.

METHODS: We enrolled 97 healthy subjects (50 subjects in their 20s, and 47 subjects in their 50s). We performed standardized median motor NCSs on 5 NCS machines calibrated with the standard signal generator. We included uncertainty factors in the subjects group, correction of NCS machines, distance measure with a tape, skin surface temperature measurement, instrument resolution, and moving the cursor by the examiner. The indoor temperature and humidity of unknown effect on the examination were controlled in specific ranges. We produced standard data for onset latency, baseline-to-peak amplitude, peak-to-peak amplitude, area, duration, and velocity.

RESULTS: Standardized reference values from the 97 subjects, considering uncertainty, were produced. The mean values for 194 median nerves with wrist stimulation were 3.03 ms, 11.07 mV, 17.55 mV, 33.77 mVms, 5.64 ms, and 59.43 m/s for the data points listed in Methods, respectively. Expanded uncertainties were 0.81, 4.84, 8.53, 17.89, 1.29, and 10.35, respectively.

SUMMARY/CONCLUSION: We produced national median NCS reference data for South Korea. Distribution of this data will precipitate reliable NCS results being shared between laboratories and reduction of unnecessary tests.
FUNCTIONAL OUTCOME OF PATIENT WHO WAS DIAGNOSED WITH GUILLAIN–BARRÉ SYNDROME DUE TO IMMUNE CHECK POINT INHIBITORS
Ying Guo (Houston, TX), Amy Ng (Houston, TX), Diana Molinares (Houston, TX)

INTRODUCTION: Check point inhibitors (CPIs) have shown the most promising results by increasing the survival of patients with advanced cancer. However, neurological complications such as Guillain–Barré syndrome (GBS) have been reported.

OBJECTIVE: To report the strength and function of a patient after 2 treatments for CPI-induced GBS.

CASE REPORT: A 21-year-old female diagnosed with acute lymphoblastic leukemia (ALL) for 5 months was enrolled on a protocol with hyper-CVAC and inotuzumab. Two to 3 weeks after the inotuzumab, she developed ascending weakness in her bilateral lower extremities and required a cane to walk. After being admitted to hospital, a needle EMG showed no definitive evidence for GBS. Cerebrospinal fluid (CSF) protein was normal. She received 5 doses of IVIg with partial improvement. At day 17 of hospitalization, she was transferred to inpatient rehabilitation. Her functional level was minimal assistance for transfer and walking 40 feet with bilateral ankle brace and rolling walker (RW). A few days later, she required maximum assistant for walking. Repeat needle EMG showed no definitive evidence for GBS, but CSF protein was elevated. She was given daily plasma exchange (PE) for 5 days. On day 33, her CSF protein was normalized. On day 37, she was discharged home and continued outpatient therapy. Four weeks after discharge, she was walking without brace or RW.

SUMMARY/CONCLUSION: GBS caused by CPI may not respond to IVIg and require PE. If the patient's strength and function deteriorate, it is crucial to re-consult neurology service and seek additional treatment options.

A CASE OF ATAXIC SENSORY AXONAL POLYNEUROPATHY WITH ANTI-FIBROBLAST GROWTH FACTOR RECEPTOR 3 ANTIBODY, RAPIDLY RESPONSIVE TO IMMUNE THERAPY
Leila Darki (Los Angeles, CA), Said Beydoun (Los Angeles, CA)

INTRODUCTION/BACKGROUND: This case presents the identification of anti FGFR3 antibody as a potential cause of neuropathy in a patient previously characterized with idiopathic neuropathy.

CASE REPORT: A 75-year-old male with subacute onset of progressive balance impairment, frequent falls, paresthesia, difficulty with fine skills, and neuropathic pain was referred with a diagnosis of idiopathic polyneuropathy. He was noted to have significant sensory ataxia, pseudoathetosis, loss of vibration and proprioception in the extremities, slight distal lower extremity weakness, and areflexia. An EDX study showed non–length-dependent severe sensory axonal loss with moderate length-dependent motor axonal loss. There was no evidence of gammopathy. Paraneoplastic antibody panel and imaging studies to rule out malignancy were negative. Cerebrospinal fluid examination showed a protein of 112 mg/dl without cells. Sensory neuropathy antibody panel showed elevated IgG FGFR3 antibody by ELISA assay at titer of 4800 (normal <3000). Treatment with IVIg was initiated. Improvement began to be noted 3 weeks post treatment with significant improvement in his sensory ataxia, absence of falls, and diminution of pain. Current plan is to continue monthly maintenance therapy and assess objective response to IVIg therapy.

SUMMARY/CONCLUSION: Anti FGR3 polyneuropathy has been previously reported in sensory neuropathies associated with ataxia and pain. The subacute onset of symptoms, rapid progression, and predominant sensory ataxia are not typical for idiopathic polyneuropathy. Hence, further investigation for possible immune-mediated etiologies and looking for nonconventional antibodies is crucial, even in cases with underlying axonal process due to potential response to immunomodulatory treatment, which was quite rapid in our case.
EFFICACY AND SAFETY OF PXT3003 IN PATIENTS WITH CHARCOT–MARIE–TOOTH DISEASE TYPE 1A: RESULTS OF PLEO-CHARCOT–MARIE–TOOTH: AN INTERNATIONAL PIVOTAL PHASE III TRIAL
Florian Thomas (Hackensack, NJ), Youcef Boutalbi (Issy-les-Moulineaux, France), Serge Fitoussi (Issy-les-Moulineaux, France), Philippe Rinaudo (Issy-les-Moulineaux, France), Viviane Bertrand (Issy-les-Moulineaux, France), Rodolphe Hajj (Issy-les-Moulineaux, France), Serguei Nabirotchkin (Issy-les-Moulineaux, France), Daniel Cohen (Issy-les-Moulineaux, France)

INTRODUCTION: Charcot–Marie–Tooth (CMT) disease type 1A is a rare, inherited peripheral neuropathy affecting 1/5000. Patients suffer from distal muscle atrophy compromising gait, stocking-glove sensory loss, and reduced quality of life. No current treatment stabilizes or reverses the disease. PXT3003 is a novel oral fixed-dose 3 drug combination.

OBJECTIVE: To assess the effect of PXT3003 on disability measured by the mean change from baseline of Overall Neurology Limitations Scale (ONLS) score at months 12 and 15. The 10-meter Walk Test (10-mWT) constituted 1 of the secondary efficacy endpoints.

METHODS: PLEO-CMT is an international, multicenter, randomized, double-blind, placebo (Pb) controlled phase III trial, assessing the efficacy and safety of 2 doses of PXT3003 given twice daily for up to 15 months to mild-to-moderate severity, genetically-confirmed CMT1A patients ages 16-65, with Dose 1 (D1) (3 mg baclofen, 0.35 mg naltrexone, and 105 mg sorbitol) and Dose 2 (D2) at twice D1.

RESULTS: Three randomized groups (n=323; D1=109, D2=113, Pb=101) were comparable at baseline. D2 met the primary endpoint: a clinically-meaningful reduction of 0.37-point ONLS (95% CI [0.1, 0.64], p=0.008) was observed versus Pb. In D2, a trend for improvement in ONLS was observed versus baseline −0.20 (95% CI [−0.447, −0.039], p=0.098). A reduction of 0.47 seconds (95% CI [0.09, 0.85], p=0.016) was observed on the 10-mWT with D2 versus Pb. The rate of treatment-emergent adverse events leading to treatment withdrawal was low and similar between groups (D2=5.3%, D1=5.5%, Pb=5.6%).

SUMMARY/CONCLUSION: PXT3003 is the first treatment for CMT1A demonstrated to be effective, safe, and well tolerated.

Disclosures:
Florian Thomas - Researcher with Pharnext & Acceleron and compensation as principal investigator; Member of the speakers bureau for Novartis, Acceleron, Genentech.
Youcef Boutalbi, Serge Fitoussi, Philippe Rinaudo, Viviane Bertrand, Rodolphe Hajj,Serguei Nabirotchkin, & Daniel Cohen - Employees of Pharnext.

BOTULINUM TOXIN TYPE B INJECTION FOR SIALORRHEA IN AMYOTROPHIC LATERAL SCLEROSIS: A SINGLE CENTER EXPERIENCE
Neelam Goyal (Palo Alto, CA), Srikanth Muppidi (Palo Alto, CA)

INTRODUCTION: Sialorrhea is a common disabling symptom in ALS at times resistant to routine therapies. Treatment with botulinum toxin type B (BoNT-B) injection has shown benefit.

OBJECTIVE: To review benefits, side effects, and barriers to using BoNT-B in the treatment of sialorrhea in patients with ALS.

METHODS: A retrospective chart review was performed. Detailed clinical information was recorded, including response to treatment using patient reported analog scale ranging from 1 (no sialorrhea) to 9 (max sialorrhea) as well as mean daily tissue use, duration of benefit, side effects, drop out, and time to insurance approval. A 2-tail paired t-test was used for analysis.

RESULTS: Twelve patients were treated from October 2015 to February 2019. Eleven had previously tried 1-2 other agents. Eight received 2 or more injections (range: 1-7). Pre- and post-treatment outcome data were available for 7 patients. All reported improvement with mean decline of 4 points (p=0.001). Mean daily tissue decline was 57% (range: 0-100%). The benefit lasted on average of 8.3 weeks (range: 6-10). Three reported side effects of dry mouth and increased saliva thickness, with no progression of bulbar weakness related to treatment. Seven patients stopped treatment, 4 due to death, 3 due to declining health, and none due to side effects. Five patients had private insurance, and rest Medicare. Median time to approval was 1 day (range: 1-14) with no insurance denials.

SUMMARY/CONCLUSION: BoNT-B treatment of sialorrhea in patients with ALS is safe and effective with minimal barriers to treatment.
INCREASED FREQUENCY OF THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY TREATED WITH INTRAVENOUS IMMUNOGLOBULIN THROUGH CENTRAL VENOUS CATHETERS

Ami Patel (King of Prussia, PA), Billie Durn (Fuquay Varina, NC), Sanders Clark (Wayne, PA), Tara Grabowsky (Wayne, PA), Rob Curry (Wayne, PA), Ann Leon (King of Prussia, PA)

INTRODUCTION: IVIg therapy is approved for chronic inflammatory demyelinating polyneuropathy (CIDP). Central venous access devices (CVADs) provide reliable venous access for patients treated with IVIg but may be associated with increased risk of thromboembolic events (TEEs).

OBJECTIVE: To characterize the relationship between CVAD-based IVIg administration and TEE occurrence.

METHODS: This study utilized claims data collected in the United States between 2006-2018. The study cohort was identified via a CIDP diagnosis claim and a procedure/drug code for IVIg after diagnosis. CVAD exposure was defined as having a placement procedure code up to 2 months prior to initial CIDP diagnosis and without removal before the end of IVIg treatment. The TEE outcome comprised arterial, venous, and vascular prostheses-related TEE codes. Event frequency in patients with a CVAD was compared with demographically matched non-CVAD control subjects.

RESULTS: The study cohort comprised 882 (11.8%) CVAD and 6565 (88.2%) non-CVAD patients with ≥1 IVIg claim. Among CVAD patients, 46% were male and median age was 53 years at IVIg initiation. Frequency of TEEs was 25.0% in patients with a CVAD versus 11.2% in control subjects (p<0.0001). The most frequently observed arterial TEE was occlusion/stenosis of the carotid artery (5.3% in CVAD versus 2.8% in non-CVAD). Acute venous embolism and thrombosis of lower extremity deep vessels (7.0% in CVAD versus 1.8% in non-CVAD) was the most prevalent venous TEE.

SUMMARY/CONCLUSION: CIDP patients treated with IVIg using a CVAD may experience TEEs with greater frequency compared to those treated with IVIg without using a CVAD.

Disclosures:
Ami Patel, Billie Durn, & Ann Leon - Employees of CSL Behring.

EFFICACY AND SAFETY OF IMMUNOGLOBULIN CAPRYLATE/CHROMATOGRAPHY PURIFIED (IGIV-C) IN PATIENTS WITH MYASTHENIA GRAVIS EXACERBATIONS: A MULTICENTER, PROSPECTIVE, OPEN-LABEL, NONCONTROLLED CLINICAL TRIAL

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INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disorder affecting neuromuscular transmission. MG exacerbations can present with sudden respiratory failure and bulbar weakness and produce major functional disability. MG exacerbation treatments include plasma exchange (PE) and IVIg. Studies comparing PE and IVIg in MG have demonstrated equal efficacy, but fewer side effects with IVIg.

OBJECTIVE: Grifols conducted a clinical trial of immunoglobulin caprylate/chromatography purified (IgIV-C) in subjects with MG exacerbations since additional clinical trial data is needed.

METHODS: MG Foundation of America (MGFA) class IVb or V status were required for inclusion. Forty-nine subjects enrolled in this 28-day study and received a total IgIV-C dose of 2 g/kg over 2 consecutive days (1 g/kg/day). Quantitative myasthenia gravis (QMG) score was measured at Day 0 and weekly thereafter, with the QMG on day 14 representing the primary endpoint. Categorical response was defined as 3-point decrease in QMG and MG Composite, and 2-point decrease in MG-Activities of Daily Living (MG-ADL). Weekly safety evaluations were performed.

RESULTS: Analysis of primary efficacy endpoint results showed a statistically significant decrease of 6.4 points (evaluable population n=43) and 6.7 points (safety population n=46) in mean QMG score from Baseline to Day 14; 77%, 86%, and 88% of evaluable subjects were responders for QMG, MG Composite, and MG-ADL at day 14, respectively. IgIV-C showed good tolerability.

SUMMARY/CONCLUSION: Both primary and secondary efficacy objectives were achieved, demonstrating the efficacy of IgIV-C in an MG exacerbation. IgIV-C was also well tolerated in MG exacerbations.

Disclosures:
Elsa Mondou, Rhonda Griffin, Junliang Chen, Beatriz Garcia, Sandra Camprubi, & Jaume Ayguasanosa - Employees of Grifols. This study was funded by Grifols, a manufacturer of IgIV-C.
INTRAVENOUS IMMUNOGLOBULIN TREATMENT-RELATED FLUCTUATIONS IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY PATIENTS USING DAILY GRIP STRENGTH MEASUREMENTS: STUDY UPDATE

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INTRODUCTION: Although IVIg efficacy for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) has been demonstrated in randomized controlled trials, the optimal treatment approach for patients on chronic therapy is unknown.

OBJECTIVE: To update progress on the investigator-initiated, multicenter “GRIPPER” study that prospectively evaluates “wear-off” or other IVIg treatment-related fluctuations in patients with CIDP.

METHODS: The primary outcome measure is Jamar grip strength (GS), performed daily for 6 months. Home nursing visits also capture Rasch-built Overall Disability Score (R-ODS), Timed Up and Go Test (TUGs), Overall Neuropathy Limitations Scale (ONLS), Modified Fatigue Severity Scale (mFSS), and Visual Analog Pain Severity Scale (VAS) weekly for 6 months. The Quality of Life Short Form Physical Component Summary (SF-36v2®) is collected at baseline, week 12, and week 24. Serum IgG levels are collected at 3 time-points surrounding IVIg infusions (peak, trough, and mid-cycle). Study “wear-off” frequency data is currently being analyzed by assessing the proportion of subjects with any given degree of GS and R-ODS intracycle fluctuation and the proportion of cycles in which GS and R-ODS fluctuation occurs. To determine the extent of “wear-off” the degree of difference between maximum and minimum GS, R-ODS, TUGs, ONLS, and VAS scores are being analyzed.

RESULTS: Study enrollment (n=29) and data collection are now complete. Preliminary study results are forthcoming.

SUMMARY/CONCLUSION: By better understanding the frequency and extent of IVIg treatment-related fluctuations we expect that these results will help facilitate development of CIDP treatment optimization strategies.

NEO1 AND NEO-EXT STUDIES: PHARMACODYNAMIC/EXPLORATORY BIOMARKER AND SAFETY ASSESSMENTS FOLLOWING REPEAT AVALGLUCOSIDASE ALFA DOSING FOR UP TO 4.5 YEARS IN PATIENTS WITH LATE-ONSET POMPE DISEASE

Mazen Dimachkie (Kansas City, KS), Richard Barohn (Kansas City, KS), Priya Kishnani - Served on advisory boards for Sanofi Genzyme, Amicus, BioMarin, Octapharma, and Terumo. Grants from Amicus, Alnylam, Audentes, BioMarin, CSL-Behring, Genzyme, Mallinckrodt, Novartis, NuFactor, Octapharma, and Terumo. Grants from Amicus, Alnylam, Audentes, BioMarin, CSL-Behring, Genzyme, Mallinckrodt, Novartis, NuFactor, Octapharma, UCB Biopharma, Viromed, and TMA.

INTRODUCTION: In NEO1 (NCT01898364;EudraCT:2012-004167-42), safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of repeat avalglucosidase alfa dosing (5, 10, or 20 mg/kg every 2 weeks) for 6 months were evaluated in late-onset Pompe disease patients, either treatment-naïve (Naïve) or having received alglucosidase alfa for ≥9 months (Switch). In the ongoing NEO-EXT study (NCT02032524;EudraCT:2013-003321-28), long-term safety and pharmacokinetics of repeat avalglucosidase alfa dosing will be monitored for ≥6 years following NEO1.

OBJECTIVE: To report pharmacodynamic/exploratory biomarker and safety data after ≤4.5 years’ avalglucosidase alfa exposure.

METHODS: NEO1 began in July 2013. After NEO1, patients could enter NEO-EXT on the same avalglucosidase alfa dose. During 2016, all NEO-EXT patients switched to 20 mg/kg every 2 weeks. Creatine kinase (CK), hexose tetrasaccharide (Hex4), aspartate transaminase (AST), and alanine aminotransferase (ALT) were assessed as secondary endpoints at baseline and every 6 months.

RESULTS: 24 patients entered NEO1; 19 entered NEO-EXT, with 17 currently participating. At NEO1 enrolment, patients’ mean±SD age was Naïve: 44.8±20.3 years; Switch: 46.7±14.1 years. Mean±SD (range) avalglucosidase alfa exposure durations were Naïve: 1025±611 (109-1572) days; Switch: 1179±570 (102-1658) days. All treatment groups demonstrated mean % reductions from Baseline to Week 208 in Hex4 (range, 38.4-44.1%), CK (25.1-38.7%), and ALT (20.6-39.0%). No deaths/life-threatening serious adverse events (SAEs) were reported during NEO1/NEO-EXT; 1 Switch patient discontinued NEO1 for a treatment-related SAE (respiratory distress/chest discomfort).

SUMMARY/CONCLUSION: Avalglucosidase alfa treatment in NEO1/NEO-EXT for up to 4.5 years resulted in persistent biomarker improvements from baseline in muscle (CK), disease substrate (Hex4), liver/muscle (AST), and heart/liver/muscle (ALT) with a consistent safety profile. Funding: Sanofi Genzyme.

Disclosures:
Mazen Dimachkie - Consultant, advisor or is on speakers’ bureaus for Apliedym, Audentes, BioMarin, Catalys, CSL-Behring, Genzyme, Mallinckrodt, Novartis, NuFactor, Octapharma, and Terumo. Grants from Amicus, Alnylam, Alexion, BioMarin, Bristol-Myers Squibb, Catalys, CSL-Behring, FDA/OPD, GSK, Grifols, MDA, NIH, Novartis, Genzyme, Octapharma, UCB Biopharma, Viromed, and TMA.
Richard Barohn - Research support from Ra Pharma, Sanofi Genzyme, PTC, and Alexion.
Priya Kishnani - Served on advisory boards for Sanofi Genzyme, Amicus, Baebies, Vertex,
AUTONOMIC MANIFESTATIONS OF HEREDITARY TRANSTHYRETIN-MEDIATED AMYLOIDOSIS: LONGTERM SAFETY AND EFFICACY FROM THE PATISIRAN GLOBAL OPEN-LABEL EXTENSION STUDY

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INTRODUCTION: Hereditary transthyretin-mediated (hATTR) amyloidosis is a progressive, multisystem disease; the majority of patients develop a mixed phenotype of polyneuropathy, including dysautonomia, and cardiomyopathy. The safety and efficacy of patisiran in hATTR amyloidosis patients with polyneuropathy have been evaluated in phase 2 and phase 3 (APOLLO) studies.

OBJECTIVE: To present interim data on dysautonomia in the ongoing patisiran Global Open-Label extension (OLE) study.

METHODS: Multicenter, OLE safety and efficacy study (NCT02510261) in eligible patients, including APOLLO patients randomized to placebo (APOLLO/placebo, n=49) or patisiran (APOLLO/patisiran, n=137) and phase 2 OLE patients (n=25).

RESULTS: Two hundred eleven patients enrolled into Global OLE; 189 had 12-month assessments as of September 24, 2018. Safety profile remained consistent with previous studies. After 12 months of additional patisiran treatment in Global OLE, durable improvement was seen in COMPASS-31 (mean change [standard error of the mean]) in APOLLO/patisiran (−4.0 [1.5]) and stabilization in the phase 2 OLE (0.1 [2.1]) compared to parent study baselines. APOLLO/placebo patients experienced improvement after 12 months of patisiran (COMPASS-31: −4.0 [1.5]) and stabilization in the phase 2 OLE (0.1 [2.1]) compared to Global OLE baseline. mBMI increased across all groups at 12 months compared to Global OLE baseline.

SUMMARY/CONCLUSION: Dysautonomia is a debilitating, early symptom of hATTR amyloidosis. Patients showed sustained durable improvement in dysautonomia during longterm patisiran treatment. APOLLO/placebo patients experienced improvement after 12 months of patisiran on Global OLE; however, the treatment delay resulted in worse dysautonomia at baseline for them.

Disclosures:
Elizabeth A Mauricio - Honorarium from Alnylam.
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Dianna Quan - Compensation from Alnylam – regional medical advisory board, Research
ZILUCOPLAN, A MACROCYCLIC PEPTIDE INHIBITOR OF COMPLEMENT COMPONENT 5 (C5), DEMONSTRATES MECHANISTIC AND PHARMACOLOGICAL DIFFERENTIATION FROM ANTI-C5 MONOCLONAL ANTIBODIES

Alonso Ricardo (Cambridge, MA), Michelle Hoarty (Cambridge, MA), Steven DeMarco (Cambridge, MA), Petra Duda (Cambridge, MA), Ramin Farzaneh-Far (Cambridge, MA), Zhong Ma (Cambridge, MA), Simon Read (Cambridge, MA), Camil Sayegh (Cambridge, MA), Guo-Qing Tang (Cambridge, MA), Evan Thackaberry (Cambridge, MA), Douangsone Vadyviraisack (Cambridge, MA), Nanqun Zhu (Cambridge, MA)

INTRODUCTION: Zilucoplan is a convenient, subcutaneously self-administered inhibitor of component 5 (C5) currently in advanced clinical development for multiple complement-mediated disorders, including myasthenia gravis. Zilucoplan is a fully synthetic peptide product that is approximately 40 times smaller than a therapeutic monoclonal antibody (mAb).

OBJECTIVE: To characterize potential pharmacological differences between zilucoplan and anti-C5 mAbs.

METHODS: Pharmacological differentiation for zilucoplan and anti-C5 mAbs was determined using: binding site and mechanism of inhibition studies, in vitro permeability across basement membrane models, in vivo clearance in the presence of concomitant IVIg or anti-FcRn therapies, and activity against clinically-relevant C5 mutations.

RESULTS: Zilucoplan binds to C5 and inhibits its cleavage of C5 by canonical complement pathway convertases. Zilucoplan additionally binds C5b, preventing the formation of the membrane attack complex induced by non-canonical cleavage of C5. Zilucoplan’s binding and inhibitory activities are not affected by the presence of clinically-relevant human C5 polymorphisms (including p.R885>H/C). Unlike eculizumab, a C5 mAb inhibitor, zilucoplan does not bind to surface-bound C5b-9 or soluble membrane attack complex (sC5b-9). Zilucoplan displays superior permeability (about 4 times higher) across a basement membrane model as compared with eculizumab, suggesting preferential tissue penetration. Zilucoplan pharmacokinetics and pharmacodynamics did not change with concomitant dosing of an anti-FcRn mAb in cynomolgus monkeys. In addition, no changes in zilucoplan levels were observed in a patient receiving concomitant therapeutic doses of IVIg.

SUMMARY/CONCLUSION: These data highlight mechanistic and pharmacological differences of zilucoplan as compared with eculizumab and other monoclonal antibody inhibitors of C5.

Disclosures:
Alonso Ricardo, Michelle Hoarty, Steven DeMarc, Petra Duda, Ramin Farzaneh-Far, Zhong Ma, Simon Read, Camil Sayegh, Guo-Qing Tang, Evan Thackaberry, Douangsone Vadyviraisack, & Nanqun Zhu - Employees and stockholdera of Ra Pharmaceuticals.
INTRODUCTION/BACKGROUND: Repetitive transcranial magnetic stimulation (rTMS) is FDA approved for major depressive disorder (MDD) but not for cognition.

CASE REPORT: In 2015, a 57-year-old man presented with weakness and cognitive issues. Examination showed asymmetric twitching and weakness in arms, normally active reflexes, and cognitive deficits. Needle EMG was consistent with ALS, and brain MRI revealed midbrain atrophy while positron emission tomography was consistent with front temporal dementia (FTD). ALS genetic panel was negative. Neuropsychological testing in 2017 revealed significant impairment of executive function/cognition-related AEs in a pooled HYP/HOP analysis.

OBJECTIVE: To evaluate long-term (9 weeks blinded plus 52 weeks open-label) efficacy and characterize paresthesia and cognition-related AEs in a pooled HYP/HOP analysis.

RESULTS: Of 63 patients (DCP/DCP, n=36; PBO/DCP, n=27), 47 (74.6%) completed 61 weeks. Median weekly attack rates improved from baseline to week 61: DCP/DCP (1.75 versus 0.00; p<0.0001 [93.8% reduction]); PBO/DCP (2.25 versus 0.25; p=0.01 [75.0% reduction]); severity-weighted rates were similarly reduced. For paresthesia, 25 (39.7%) patients had ≥1 event; 2 (3.2%) severe; 4 (6.3%) discontinued; and 6/16 (37.5%) had dose reductions. AE onset was typically during the first month on DCP.

SUMMARY/CONCLUSION: Long-term DCP treatment durably reduced attack frequency and severity in PPP patients. Paresthesia and cognition-related AEs (mild/moderate) occurred within 1 month of therapy initiation and resolved spontaneously with few discontinuations.

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Nicholas Johnson – Research support from Biogen Idec, Ionis Pharmaceuticals, Muscular Dystrophy Association, Myotonic Dystrophy Foundation, and Valerian Therapeutics, and being a consultant for AMO Pharma, FulcrumTherapeutics, and Strongbridge Biopharma.
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Fredic Cohen - Employee of Strongbridge Biopharma.
DEVELOPMENT OF MICRO-DYSTROPHIN VECTORS FOR GENE THERAPY OF DUCHENNE MUSCULAR DYSTROPHY
Jeffrey Chamberlain (Seattle, WA), Guy Odom (Seattle, WA), Julie Crudele (Seattle, WA), Stephen Hauchka (Seattle, WA)

INTRODUCTION: Our group has been developing vectors for gene therapy of Duchenne muscular dystrophy (DMD) for more than 25 years, culminating in 2 of our microdystrophin vectors having entered into clinical trials in the past year.

OBJECTIVE: Despite the early promise of this approach, a number of features of adeno-associated viral (AAV) microdystrophin vectors can be further optimized. Key features of this system include the AAV serotype, gene regulatory cassettes (RC) for high level, muscle-restricted expression, and the structure of the encoded microdystrophin protein. Our group has focused on vectors derived from AAV6, which displays high tropism for striated muscles. We have also developed a series of muscle-restricted gene RCs derived from the muscle creatine kinase enhancer plus promoter.

METHODS: Components of the vectors are cloned into AAV plasmids and prepared at high titer, then tested by systemic delivery to mdx mice, a model for DMD.

RESULTS: Our previous studies described MHCK7 and CK8, which are both being used in the clinic. However, a number of newer RCs are available that provide higher-level expression in the context of AAV. Finally, while 2 of our microdystrophin cDNAs have been used successfully in the clinic, these microdystrophins are only about 30% of the size of the full-length dystrophin mRNA and can likely be further optimized.

SUMMARY/CONCLUSION: We will discuss strategies used to develop the current clinical vectors and newer developments that may improve functional outcome for DMD gene therapy trials.

Disclosures:
Jeffrey Chamberlain - Inventor on patents covering ΔR4-R23/ΔCT and μDys5 microdystrophin proteins being used in clinical trials by Sarepta and Solid Biosciences. Member of Solid Biosciences' scientific advisory board.
Stephen Hauchka - Inventor on patents covering muscle-specific expression of genes for gene therapy

ARE THE CHOICES OF THERAPEUTIC OPTIONS FOR THE MANAGEMENT OF MYASTHENIA GRAVIS CRISIS WITH ACUTE RESPIRATORY FAILURE INFLUENCED BY THE PATIENT’S AGE: A NEW YORK STATE PLANNING AND RESEARCH COOPERATION
Shuja Sheikh (Newark, NJ), Kevin Nolasco (Newark, NJ), Abu Nasar (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Previous studies reported that myasthenia gravis (MG) crisis complicated by acute respiratory failure (ARF) is more likely to be treated with plasma exchange (PE).

OBJECTIVE: To investigate the age group difference for use of IVIg, PE, and steroids in the treatment of MG crisis with ARF.

METHODS: We used New York Statewide Planning and Research Cooperation System (SPARCS) database for the 1998-2014 period. Data was analyzed using IBM SPSS software.

RESULTS: A total of 496 patient encounters with MG crisis with ARF receiving treatment were identified (47.6% male; mean age: 63.3±18.1 years) of which 20.2% were treated with IVIg, 30.66% with PE, and 4.2% with steroids. Of these, 66 (13.3%) patients were 20-49 years of age, 125 (25.2%) were 50-79, and 54 (10.9%) were over 80. Patients 80 years and older were more likely to develop ARF (23.7%) than patients 50-79 (13.5%) and patients 20-49 (9.8%) (p<0.05). Of those patients 80 years and older, 46.3% were treated with IVIg, compared to 30.3% of patients 20-49 and 32.8% of patients 50-79 (p=0.41). Of those patients 80 years and older, 50% were treated with PE, compared to 59.1% of patients 20-49 and 60.8% of patients 50-79 (p=0.77).

SUMMARY/CONCLUSION: Elderly patients are more likely, compared to younger patients, to develop ARF with MG crisis. We found no significant difference in the use of IVIg versus PE for the treatment of MG crisis between different age groups, suggesting that age does not influence the choice of therapeutic options.

Shuja Sheikh, MD
Resident and Fellow Member Award Recipient
ARE THERE GENDER DIFFERENCES IN THE OUTCOMES OF MYASTHENIA GRAVIS CRISIS TREATMENT? A NEW YORK STATE PLANNING AND RESEARCH COOPERATION SYSTEM DATABASE ANALYSIS (1998-2014)
Shuja Sheikh (Newark, NJ), Kevin Nolasco (Newark, NJ), Abu Nasar (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Previous studies demonstrated that there is no long-term benefit difference between IVIg and plasma exchange (PE) treatment of myasthenia gravis (MG) crisis. However, gender difference response to IVIg versus PE was not studied.

OBJECTIVE: To investigate the long-term gender difference of use of IVIg, PE, and steroids in the treatment of MG crisis.

METHODS: We used New York Statewide Planning and Research Cooperation System database for the 1998-2014 period. Data was analyzed using IBM SPSS software.

RESULTS: A total of 1007 individual patients with MG crisis who received treatment were identified (44.6% male; mean age: 59.5±19.2 years); 22.4%, 20.0%, and 2.2% of males and 27.2%, 24.9%, and 3.3% of females were treated with IVIg, PE, and steroids, respectively. There was no significant difference in acute respiratory failure rates among males and females (52.6% versus 46.6%, p=0.27). There was also no significant difference in the recurrence of MG crisis in males versus females between the 3 treatment groups: IVIg, PE, and steroids (36 versus 28%, 39 versus 31%, and 30 versus 55%, respectively; p=0.16, 0.2, and 0.24, respectively).

SUMMARY/CONCLUSION: Our study demonstrated no significant difference of recurrence of MG crisis in patients treated with IVIg, PE, or steroids between males and females. Work is in progress to determine the effect of mechanical ventilation and other comorbid conditions on the outcome of these therapies.

Shuja Sheikh, MD
Resident and Fellow Member Award Recipient

CHARCOT–MARIE–TOOTH DISEASE TYPE 1A AND IMPAIRED PATIENT MOBILITY: EXPRESSIONS, REMEDIES, AND IMPACT ON QUALITY OF LIFE
Allison T Moore (New York, NY), Robert N Moore (New York, NY), Joy M Aldrich (Seattle, WA), Florian P Thomas (Hackensack, NJ), Courtney Hollett (Chesterfield, VA)

INTRODUCTION: Impaired mobility is cited by Charcot–Marie–Tooth (CMT) disease type 1A patients as the number one phenotypical expression of their disease, significantly impacting daily activities.

OBJECTIVE: To assess the most prevalent symptoms that cause mobility impairments of CMT1A patients.

METHODS: The Hereditary Neuropathy Foundation created the Global Registry for Inherited Neuropathies (GRIN) to capture detailed inherited neuropathy (IN) patient history via an online, IRB-approved patient survey over 2013-2019. IN patients (n=2,142) were surveyed, yielding a 34% CMT1A (n=770) cohort. This cohort was queried against a subset of questions to test for causal relationships between disease state, level of impairment, and quality of life.

RESULTS: The 770 CMT1A patients identified mobility (63%) as the activity of daily life impacted most by their disease. Multiple expressions of their disease that have an impact on their mobility, the most common being weak ankles (79%). Additionally, 58% of patients can neither walk on their heels or toes, 48% reported using some type of orthotic or mobility device to assist them with mobility, and 51% have had orthopedic surgery. Maintaining balance and walking stamina were cited as most challenging by 28% of patients. A significant by-product of mobility challenges is fatigue, reported by 85% of CMT1A patients. Pain is cited by 77%.

CONCLUSIONS: Mobility impairments are represented in a large cohort of CMT1A patients, affecting their physical and psychological well-being. While use of orthotics, mobility devices, and surgery can have a positive impact on mobility, CMT1A patients need a more comprehensive approach to addressing mobility impairment.

Disclosures:
Florian P Thomas – Consultant for Pharnext and Acceleron Pharma.
**NUSINERSEN IN ADULT SPINAL MUSCULAR ATROPHY PATIENTS**

*Mithila Fadia (Houston, TX), Sheetal Shroff (Houston, TX), Ericka Simpson (Houston, TX)*

**INTRODUCTION:** Spinal muscular atrophy (SMA) is an autosomal recessive disease caused by mutation in survival motor neuron 1 (SMN1) gene leading to decreased SMN1 protein synthesis. Nusinersen is an antisense oligonucleotide that modifies pre-mRNA resulting in increased synthesis of SMN2 protein. It was FDA approved for adult and pediatric patients. There are limited data regarding its benefit in adults.

**OBJECTIVE:** To collect data regarding changes to post-nusinersen revised upper limb module (RULM) scores in adult SMA patients.

**METHODS:** We did a retrospective chart review of all clinic patients with SMA by collecting data regarding age, gender, genetic test, RULM score pre- and post-nusinersen, and muscle (subcutaneous tissue ratio on ultrasound [US]).

**RESULTS:** Of 21 SMA patients identified, 12 refused treatment or were receiving treatment at another institution. Of the 9 patients (8 female, 1 male; age: 26-49 years) included, their SMN2 copy numbers were n=6: 3 copies, n=1: 4 copies, n=1: pending result, and n=1: unavailable. Four patients had US for muscle (subcutaneous ratio prior to infusion) and are pending US post-infusion; 8 had already received nusinersen; 5 had pre- and post-nusinersen RULM scores documented, and 4 had pre- RULM scores documented so far. Of the 5 patients with pre- and post-nusinersen RULM scores, 4 showed improvement by 2 points each and 1 had an unchanged score. A paired t-test analysis on these 5 patients showed a significant (p=0.0213) difference in the pre- and post-nusinersen RULM scores.

**CONCLUSION:** We continue to collect data and will present updated data in the future.

**Disclosures:**
Ericka Simpson - Paid speaker for Alexion, Inc Pharmaceuticals and CSL Behringher, Inc.

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**THE MMPOWER-2 OPEN-LABEL EXTENSION TRIAL: OBSERVATIONS AT 18 MONTHS OF ELAMIPRETIDE THERAPY**

*Bruce Cohen (Twinsburg, OH), Amy Goldstein (Philadelphia, PA), Richard Haas (San Diego, CA), Gerard Vockley (Pittsburgh, PA), Amel Karaa (Boston, MA)*

**INTRODUCTION:** Primary mitochondrial myopathies (PMMs) are caused by genetic defects that result in impaired mitochondrial function, manifesting clinically as fatigue, exercise intolerance, and muscle weakness, which negatively impact physical function, exercise capacity, and quality of life (QOL). Elamipretide penetrates cell membranes, localizing to the inner mitochondrial membrane where it associates with cardiolipin to improve mitochondrial cristae architecture and enhance mitochondrial respiratory chain efficiency and adenosine triphosphate production. These effects are now being evaluated in clinical trials.

**OBJECTIVE:** To assess the longterm safety, tolerability, and efficacy of single daily subcutaneous (SC) doses of elamipretide for up to 260 weeks in patients with PMMs.

**METHODS:** Subjects who completed the end-of-study visit in the MMPOWER-2 trial (elamipretide 40 mg SC daily for 4 weeks; n=30) were eligible to enroll in the MMPOWER-2 Open Label Extension (OLE) trial of elamipretide 40 mg SC daily (n=28).

**RESULTS:** There were 23 patients with 18 months of data (3 male, 20 female; average age: 48.7 years). Consistent with previous elamipretide trials, including the blinded MMPOWER-2 study, injection site reactions were the most commonly reported adverse events. At the end of the 18-month observation period, patients continued to demonstrate improvements (reductions) in their fatigue assessment scores (PMM-Symptom Assessment: 12.18 to 10.30 and Neuro-QOL Fatigue Short Form: T-score 57.1 to 53.2, baseline to 18-months, respectively) and EuroQOL 5-Dimension analyses (Individual Domain and Problem-to-No Problem Transition).

**SUMMARY/CONCLUSION:** On average, patients receiving elamipretide therapy demonstrated a continued treatment effect over the 18-month observation period.

**Disclosures:**
Bruce Cohen, Amy Goldstein, Richard Haas, Gerard Vockley, & Amel Karaa - Research grant, reimbursement for travel, and consulting payments from Stealth BT.
MMPOWER-3 STUDY DESIGN: A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF ELAMIPRETIDE IN PRIMARY MITOCHONDRIAL MYOPATHY

Michael DiMatteo (Newton, MA), Anthony Aiudi (Newton, MA), Jim Carr (Newton, MA)

INTRODUCTION: Primary mitochondrial myopathies (PMM) are genetic disorders that negatively impact mitochondrial function, adversely affecting physical function, exercise capacity, and quality of life (QOL). Elamipretide localizes to the inner mitochondrial membrane to associate with cardiolipin, thereby improving adenosine triphosphate production/exercise capacity. Currently, no approved treatments are available. Elamipretide is being developed for the treatment of patients with PMMs.

OBJECTIVE: MMPOWER-3 is a pivotal, phase-3 randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of elamipretide in PMM patients (n=202 target enrollment). Daily subcutaneous injections of elamipretide 40 mg or placebo are being administered to PMM patients for 24 weeks. Participants completing this study will be eligible to enter the open-label treatment extension of up to 144 weeks.

METHODS: MMPOWER-3 was designed to assess the effect of elamipretide on the primary family endpoints, 6-minute walk test and Total Fatigue on the Primary Mitochondrial Myopathy Symptom Assessment (PMMSA), in patients with genetically confirmed PMMs. Secondary endpoints include changes in Fatigue During Activities on the PMMSA, the Neuro-QOL Fatigue Short Form, and the Most Bothersome Symptom on the PMMSA scores. Elamipretide safety/tolerability will also be evaluated. Exploratory endpoints will measure changes in individual PMMSA symptoms, individual items of the Neuro-QOL Fatigue Short Form, EQ-5D-5L, Patient Global Impression Scales, and Clinician Global Impression Scales.

RESULTS: MMPOWER-3 includes 16 enrollment sites in North America and 12 within the United Kingdom and the European Union.

SUMMARY/CONCLUSION: Results from MMPOWER-3 will provide evidence for the safe and effective use of elamipretide in patients with PMMs.

Disclosures:

PHASE 3 STUDY OF HYQVIA® FOR CHRONIC INFLAMMATORY Demyelinating Polyradiculoneuropathy: ADVANCE CIDP-1 INFUSION PROTOCOL

Shabbir Hasan (Cambridge, MA), Kim Duff (Lexington, MA), Andras Nagy (Vienna, Austria), Leman Yel (Cambridge, MA)

INTRODUCTION: IVIg, the mainstay of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) treatment, is limited by venous access and increased risk of systemic adverse events, and volume of subcutaneous Ig (SCIg) administration is limited by hyaluronan. HYQVIA® (Immune Globulin Infusion [Human] 10% with recombinant human hyaluronidase [rHuPH20]; facilitated SCIg [SCIg]) allows for dispersion and absorption of large-dose SCIg by self-infusion and can be infused at rates and frequencies similar to IVIg, with better systemic tolerability. fSCIg is being investigated in CIDP.

OBJECTIVE: To describe fSCIg infusion protocol in ADVANCE CIDP-1 (NCT02549170).

METHODS: Planned enrollment in this prospective, global, multicenter study is 174 adults. Patients with CIDP receiving stable IVIg for ≥12 weeks will be randomized equally to fSCIg or placebo (with rHuPH20). The primary outcome is relapse rate. Recommended sites for infusion are upper to middle abdomen and thighs with a 24 gauge needle(s). The number of infusion sites can be 1, 2, or 3, and a needle set can be single, bifurcated, or trifurcated. Maximum infusion volume per infusion site is 600 mL for patients ≥40 kg and 300 mL for patients <40 kg. Per infusion day, maximum infusion volume should not exceed 1200 mL for patients ≥40 kg or 600 mL for patients <40 kg. After the initial 2 infusions, the infusion rate may be increased up to 300 mL/h/site. Patients will receive fSCIg with the same frequency as pre-randomization IVIg treatment.

RESULTS: This study is ongoing and blinded.

SUMMARY/CONCLUSION: fSCIg, enabling infusion rates and volumes similar to IVIg, is being evaluated for CIDP.

Disclosures:
Shabbir Hasan, Kim Duff, Andras Nagy & Leman Yel - Employees of the Takeda group of companies.
**EFFECT OF ATALUREN ON AGE AT LOSS OF AMBULATION IN NONSENSE MUTATION DUCHENNE MUSCULAR DYSTROPHY: OBSERVATIONAL DATA FROM THE STRIDE REGISTRY**

Abdallah Delage (Zug, Switzerland), Filippo Buccella (Rome, Italy), Isabelle Desguerre (Paris, France), Francesco Muntoni (London, United Kingdom), Andrés Nascimento (Barcelona, Spain), Már Tulinius (Gothenburg, Sweden), Salvatore Colucci (South Plainfield, NJ), Allan Kristensen (South Plainfield, NJ), Rich Able (Lynnfield, MA), Claudio Santos (South Plainfield, NJ), Panayiota Trifillis (South Plainfield, NJ), Olivia Zhang (South Plainfield, NJ), E Mercuri (Rome, Italy)

**INTRODUCTION:** Duchenne muscular dystrophy (DMD) is a fatal, X-linked disease, characterized by progressive muscle weakness. Loss of ambulation (LoA) is a major milestone in disease progression. About 10-15% of cases of DMD are caused by a nonsense mutation (nmDMD) in the dystrophin gene, which leads to translation of truncated, non-functional dystrophin. Ataluren is the first approved therapy to target the underlying cause of nmDMD, enabling formation of full-length, functional dystrophin.

**OBJECTIVE:** To evaluate LoA in patients with nmDMD taking ataluren ≥12 months while enrolled in the international, multicenter STRIDE (Strategic Targeting of Registries and International Datasets of Excellence) Registry.

**METHODS:** Data were extracted from the STRIDE Registry on July 9, 2018 regarding age at LoA in patients with nmDMD taking ataluren ≥12 months (n=207). Kaplan–Meier analyses were used to investigate age at LoA.

**RESULTS:** Mean (SD) age of registry participants starting ataluren treatment was 9.1 (3.1), and 89.2% were being treated with corticosteroids in addition to ataluren. At the date of data extraction, registry participants had a mean (SD) age of 11.6 (3.6) years. Mean (SD) exposure to ataluren within the registry was 372.6 (211.6) patient-years, and 44.6% of patients had been on ataluren for more than 720 days. Mean (SD) age at LoA in registry participants was 15.5 (0.3) years, and 50% of patients were still ambulatory at the age of 16.5 years. Safety outcomes were consistent with the known safety profile of ataluren.

**SUMMARY/CONCLUSION:** Ataluren may delay LoA in patients with nmDMD.
INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare, progressive disease caused by an abnormal autoimmune response to peripheral nerve myelin. Its characteristic muscle weakness and sensory and other neurological impairments result in limited mobility, numbness, and impaired balance.

OBJECTIVE: To summarize the literature on burden and treatment options for CIDP.


RESULTS: Of 462 unique publications identified, 26 focusing on epidemiology (n=10), clinical/humanistic burden (n=7), and treatment patterns (n=9) were analyzed. Prevalence is 1.61-12.00/100,000 people, and incidence is 0.15-1.40/100,000, depending on country and diagnostic criteria. Misdiagnosis is common (≤47% of cases) because of its similarities with other polyneuropathies. Quality of life is impaired due to mobility limitations, with use of gait aids reported in 16-27% of patients and wheelchair use in 10-17%. IVIg and corticosteroids are the most commonly recommended/prescribed first-line treatments, with plasma exchange mostly reserved for severe cases. In real-world studies, more patients receiving IVIg responded to therapy than patients receiving corticosteroids (≤80% versus ≤70%, respectively), and those receiving IVIg had fewer adverse events (4-16% versus 13-51%, respectively). Subcutaneous Ig, approved as maintenance therapy only, is administered weekly for 1-2 days, through several injection sites.

SUMMARY/CONCLUSION: CIDP is a rare disease, with relatively unknown pathogenesis, that can impose considerable burden on patients. Increased awareness, timely and correct diagnosis, and prompt treatment remain paramount.

Disclosures:
Maria Fernandez, Margaret Mordin, Mackenzie Neighbors, & Sprios Tzivelekis - Employees of RTI Health Solutions, that received consulting fees from the Takeda group of companies.
PRESERVATION OF FUNCTION OVER TIME AS MEASURED BY NORTH STAR AMBULATORY ASSESSMENT IN AMBULATORY BOYS WITH NONSENSE MUTATION MUSCULAR DYSTROPHY TREATED WITH ATALUREN

Craig McDonald (Sacramento, CA), Lee-Jen Wei (Boston, MA), Gary Elfring (South Plainfield, NJ), Panayiota Trifillis (S Plainfield, NJ), Rich Able (Lynnfield, MA), Marcio Souza (South Plainfield, NJ), Joseph McIntosh (South Plainfield, NJ), Stuart Peltz (South Plainfield, NJ), Francesco Muntoni (London, United Kingdom)

INTRODUCTION: Ataluren is the first drug approved to treat the underlying cause of disease in patients with nonsense mutation Duchenne muscular dystrophy (nmDMD) by promoting read-through of a nonsense mutation to produce full-length functional dystrophin. ACT DMD was a 48-week, multicenter, randomized, double-blind, placebo-controlled study that compared the efficacy and safety of ataluren versus placebo in ambulatory boys with nmDMD.

OBJECTIVE: To assess whether ataluren can preserve physical function in boys with nmDMD.

METHODS: ACT DMD enrolled boys aged 7-16 years with nmDMD, a baseline 6-minute walk distance ≥150 m, and ≤80% of the predicted normal value at baseline (n=228). The North Star Ambulatory Assessment (NSAA) is a validated tool that assesses disease progression in ambulatory boys with DMD. NSAA is comprised of 17 tasks that patients are evaluated on at each clinic visit, with the possible values for each item being 0=unable to perform task, 1=performs with difficulty, or 2=able to perform. Loss of function (failures) from 17 tasks was evaluated for each patient (i.e., 2-0, or 1-0) at various time points over the entire study duration. The average cumulative number of failures over time was then obtained over all patients in each treatment group, and was plotted to show the temporal profile of treatment.

RESULTS: This analysis resulted in a ratio of 0.73 (95% CI 0.55-0.97; p=0.027), indicating that ataluren treatment significantly reduces the cumulative number of failures by 27% over 48 weeks compared to placebo.

SUMMARY/CONCLUSION: Ataluren may preserve physical function in ambulatory boys with nmDMD.
LONGTERM EFFICACY OF ATALUREN FOR THE TREATMENT OF NONSENSE MUTATION DUCHENNE MUSCULAR DYSTROPHY: OBSERVATIONAL DATA FROM THE STRIDE REGISTRY

Abdallah Delage (Zug, Switzerland), Filippo Buccella (Rome, Italy), Isabelle Desguerre (Paris, France), Francesco Muntoni (London, United Kingdom), Andrés Nascimiento (Barcelona, Spain), Már Tulinius (Gothenburg, Sweden), Salvatore Colucci (South Plainfield, NJ), Allan Kristensen (South Plainfield, NJ), Claudio Santos (South Plainfield, NJ), Rich Able (Lynnfield, MA), Panayiota Trifillis (South Plainfield, NJ), Olivia Zhang (South Plainfield, NJ), E Mercuri (Rome, Italy)

INTRODUCTION: Duchenne muscular dystrophy (DMD) is a fatal, X-linked disease, with progressive muscle weakness; 10-15% of patients have a nonsense mutation (nmDMD), resulting in truncated, non-functional dystrophin. Ataluren is the first approved therapy targeting the cause of nmDMD, enabling formation of full-length, functional dystrophin.

OBJECTIVE: To evaluate the longterm effectiveness of ataluren (40 mg/kg/day) in routine clinical practice in nmDMD patients in the international STRIDE (Strategic Targeting of Registries and International Datasets of Excellence) Registry (n=213).

METHODS: Data from registry participants (≥48 weeks between first and last assessment) and Study 020 participants receiving ataluren or placebo for 48 weeks were compared. Registry data were extracted on July 9, 2018.

RESULTS: Mean (SD) age at first assessment of registry participants and Study 020 participants receiving ataluren or placebo was 9.1 (3.1), 8.9 (1.8), and 9.0 (1.7) years, respectively. Mean exposure to ataluren ranged 71.8-121.6 patient years. Registry participants experienced smaller 48-week mean (SD) functional declines than Study 020 participants receiving ataluren or placebo, respectively: 6-minute walk distance (−35.0 [69.7] versus −42.2 [84.9], and −57.6 [98.8] m), time to walk/run 10 m (1.6 [3.2] versus 2.3 [5.2], and 3.5 [6.4] seconds), stand from supine (2.9 [5.0] versus 3.8 [6.1], and 3.9 [6.9] seconds), climb 4 stairs (1.2 [2.2] versus 2.7 [5.3], and 4.5 [7.3] seconds) and descend 4 stairs (0.5 [1.5] versus 2.2 [5.3], and 4.0 [7.9] seconds). Safety outcomes were consistent with ataluren's known safety profile.

SUMMARY/CONCLUSION: Registry participants were older and showed smaller functional declines, suggesting ataluren may slow disease progression in nmDMD patients in routine clinical practice.

Disclosures:
Filippo Buccella - Consultant fees from PTC Therapeutics, Santhera Pharmaceuticals and Sarepta Therapeutics.
Isabelle Desguerre - Consultant fees from AveXis, Biogen, BioMarin and PTC Therapeutics.
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Andrés Nascimiento - Speaker and consultant fees from PTC Therapeutic; investigator on clinical trials sponsored by Biogen, F. Hoffman-La Roche, Italfarmaco, Sarepta Therapeutics and TAMDMD.
Már Tulinius - Lecture fees from Biogen and PTC Therapeutics; a consultant on DMD clinical trials for BioMarin, PTC Therapeutics, ReversaGen and Sarepta Therapeutics, advisory board member for AveXis, Biogen and PTC Therapeutics.
Abdallah Delage, Salvatore Colucci, Allan Kristensen Claudio Santos, Rich Able, Panayiota Trifillis, and Olivia Zhang - Employees of PTC Therapeutics.
E Mercuri - Advisory board member for AveXis, Biogen, BioMarin, Bristol-Myers Squibb, Ionis Pharmaceuticals, Italfarmaco, Prosensa, PTC Therapeutics, Roche, Santhera Pharmaceuticals, Sarepta Therapeutics and Summit Therapeutics.
NOVEL INTRANEURAL FACILITATION AS A TREATMENT FOR CARPAL TUNNEL SYNDROME: A PILOT STUDY
Nancy Baker (Loma Linda, CA), Diep Vuong (Loma Linda, CA), Sarah Humbert (Loma Linda, CA), Mark Bussell (Loma Linda, CA), Bryan Tsao (Loma Linda, CA)

INTRODUCTION: Intraneural facilitation (INF) is a novel noninvasive technique designed to stimulate vascular growth at the vasa nervorum level in peripheral nerve using stretches and holds. INF performed twice weekly for 6 weeks has been shown to improve clinical function in patients with diabetic polyneuropathy, a model of ischemic neuropathy. CTS is a common focal mononeuropathy with ischemia at the area of compression.

OBJECTIVE: To perform a pilot study to assess the efficacy of INF in CTS using clinical and ultrasound (US) measures.

METHODS: This prospective, blinded, and sham-controlled study enrolled patients with clinical and EDX evidence of CTS. The Boston CTS Questionnaire (BCTQ) severity and functional status scale was performed at enrollment and 1 week and 3 months after treatment. Subjects were randomized into INF or sham treatment twice weekly for 3-6 weeks. US of the median nerve at the wrist and forearm was performed before and after treatment.

RESULTS: A total of 10 subjects completed the trial, 5 each in the treatment and sham groups. Nine were female with an average age of 51.3 years and duration of symptoms of 28.5 months. The average score for the BCTQ functional outcomes showed a statistically significant benefit with INF treatment compared to the sham group (p=0.03) whereas the BCTQ sum score for symptoms and US measures did not.

CONCLUSION: This pilot study shows that INF can improve functional symptoms in CTS. Further study is warranted to confirm if INF can improve sustained symptomatic and US outcomes.

CHARACTERIZING TREATMENT EXPERIENCE AMONG PATIENTS WITH TRANSTHYRETIN AMYLOIDOSIS
Asia Sikora Kessler (Johnston, RI), Sean O'Connor (Johnston, RI), Michael Pollock (Boston, MA), Spencer Guthrie (Boston, MA), Kristen L. McCausland (Johnston, RI)

INTRODUCTION: Transthyretin amyloidosis (ATTR) is a rare, systemic, progressive and fatal condition resulting from amyloid deposits of misfolded transthyretin proteins in peripheral nerves and organs. Little is known about patients’ experience and satisfaction across available therapies.

OBJECTIVE: To examine treatment-related tolerability, hospitalizations, and satisfaction experienced by patients with ATTR amyloidosis.

METHODS: Adults with ATTR amyloidosis enrolled in an online longitudinal observational study (n=92). Items assessed patients’ current treatment regimens, ability to tolerate treatment, hospitalizations due to side effects, and treatment satisfaction. Treatment tolerability was characterized with a single 4-point scale item; treatment-related hospitalizations with a single “Yes/No” item. The Treatment Satisfaction Questionnaire for Medication (TSQMvII) assessed treatment satisfaction along 4 domains; higher scores indicate greater satisfaction. All outcomes were summarized descriptively by treatment.

RESULTS: Fifty-eight (63%) of patients were currently receiving treatment. The 4 most prevalent were diflunisal (n=28), doxycycline+tauroursodeoxycholic acid (TUDCA; n=11), patisiran (n=13), and inotersen (n=10). Median duration for common treatments ranged 0.3-2.0 years. Among treated patients, tolerability was high (≥70% reported tolerating treatment “very well”). Treatment-related hospitalizations were uncommon; 3 reported diflunisal-related hospitalizations and 1 patisiran-related. Patients receiving diflunisal reported highest satisfaction regarding side effects (mean score=94.8); whereas patients receiving inotersen reported highest satisfaction regarding effectiveness (68.3). Convenience was similar for diflunisal, inotersen, and doxycycline+TUDCA (71.1-79.4). Across all treatments, patients receiving inotersen reported the highest global satisfaction (82.5).

SUMMARY/CONCLUSION: Patient treatment experience for available ATTR therapies showed high levels of tolerability and low incidence of hospitalizations. Overall, treatment satisfaction was highest with inotersen.

Disclosures:
Asia Sikora Kessler, Kristen L. McCausland & Sean O’Connor - Employee of Optum, which received payment from Akcea Therapeutics to conduct this research.
Michael Pollock & Spencer Guthrie - Employee of and owns stock in Akcea Therapeutics.
BASELINE DEMOGRAPHICS OF MMPOWER-3: A CLINICAL TRIAL OF ELAMIPRETIDE IN PRIMARY MITOCHONDRIAL MYOPATHY
Michael DiMatteo (Newton, MA), Mary Kay Koenig (Houston, TX)

INTRODUCTION: Primary mitochondrial myopathies (PMMs) are genetic disorders of the mitochondrial respiratory chain affecting predominantly, but not exclusively, skeletal muscle. Clinical manifestations include fatigue, exercise intolerance, and muscle weakness which adversely affect physical function, exercise capacity, and quality of life. The investigational product elamipretide localizes to the inner mitochondrial membrane and associates with cardiolipin to improve mitochondrial respiratory chain efficiency and adenosine triphosphate production.

OBJECTIVE: MMPOWER-3 is an ongoing, phase-3 randomized, double-blind, placebo-controlled trial evaluating the efficacy/safety/tolerability of elamipretide.

METHODS: Genetically-confirmed PMM patients were administered daily subcutaneous injections of elamipretide 40 mg or placebo for 24 weeks. A 144-week open label treatment extension will follow for eligible patients.

RESULTS: As of March 7, 2019, 147 subjects (50 male, 83 female, 14 gender not provided; mean age: 44.2 years; 84% white) were enrolled. Genetic tests showed that the majority of defects (75.5%) were mitochondrial DNA mutations, while the remainder were nuclear DNA mutations. At baseline, the mean distance walked for evaluable patients (n=145) on the 6-minute walk test was 329.8±77.6 m, the mean score for total fatigue on the Primary Mitochondrial Myopathy Symptom Assessment questionnaire (n=141) was 10.5±2.4, and the mean T-score for the Neuro-QOL Fatigue Short Form (n=145) was 54.3±7.9. Complete descriptions for assessments will be provided.

SUMMARY/CONCLUSION: Compared to literature control subject and previous trial data, patients in the MMPOWER-3 trial were impaired in their baseline functional and patient-reported assessments. MMPOWER-3 will provide safety and efficacy data for elamipretide in patients with PMMs.

DISCLOSURES:
Michael DiMatteo - Employee of Stealth BioTherapeutics. Submitted this abstract on behalf of the MMPOWER-3 Investigators.
Mary Kay Koenig - Research grant, reimbursement for travel, and consulting payments from Stealth BioTherapeutics.
SUSTAINED FUNCTIONAL BENEFITS AFTER A SINGLE INJECTION WITH ABOBOTULINUMTOXINA USING A 2 ML INJECTION VOLUME IN ADULTS WITH CERVICAL DYSTONIA

Atul Patel (Overland Park, KS), Mark Lew (Los Angeles, CA), Allison Brashear (Winston Salem, NC), Khashayar Dashtipour (Loma Linda, CA), Stuart Isaacson (Boca Raton, FL), Robert Hauser (Tampa, FL), William Ondo (Houston, TX), Pascal Maisonobe (Boulogne-Billancourt, France), James Otto (Basking Ridge, NJ)

INTRODUCTION: This open-label extension (OLE) of a 12-week, randomized, placebo-controlled trial included adults with primary idiopathic cervical dystonia (CD) who completed the lead-in week (Wk) 12 visit or whose Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score decreased ≤15% from baseline to Wk4.

OBJECTIVE: To evaluate long-term safety and efficacy of repeat treatment cycles (Cs) of abobotulinumtoxinA using 2 mL dilution (NCT01753336).

METHODS: For C1, patients toxin-naïve at baseline received 500 U, and non-naïve received 250-500 U based on prior dose. For C2/C3, adjustments were limited to ≤250 U/cycle and maximal total dose limited to 1000 U/cycle. Re-treatment occurred every 12-16 weeks, for ≤3 cycles, based on clinical judgment. Endpoints included TWSTRS and treatment-emergent adverse events (TEAEs).

RESULTS: Of 112 treated patients, 92 completed the Wk36 visit (C3-Wk12). Mean TWSTRS total score decreased from 42.2 (baseline) to 30.1 (C3-Wk12), with change from baseline of −11.7 at C3-Wk12. For each cycle, TWSTRS scores decreased from D1 to Wk4 and increased between Wk4 and Wk12, though Wk12 scores remained lower than D1 scores. Mean TWSTRS scores at Wk4 and Wk12 were primarily lower for each successive cycle (no worsening to baseline). Seventy patients (62.5%) reported TEAEs; most frequent: dysphagia, muscular weakness, and neck pain (10.7% each). Most TEAEs (70.9%) were not considered treatment-related and none led to discontinuation/death.

SUMMARY/CONCLUSION: Results were consistent with the lead-in double-blind study; abobotulinumtoxinA at approved doses using 2 mL dilution remained effective and well tolerated over 4 cycles, demonstrating sustained improvements within/across cycles.

Disclosures:
Mark Lew - Advisor/consultant fees from Teva, US World Meds, UCB, Lundbeck, Abbvie, Adamas, Cynapsus, Revance, Acadia, Neurocrine, Acorda and Speaker fees from Teva, UCB, Lundbeck, Adamas, Acadia, Neurocrine and Researcher support from Parkinson’s Study Group, Michael J. Fox Foundation, Biotive, Neuroderm, Enterin Inc., Pharm2B
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William Ondo - Compensation from UCBPharma, TEVA, USWorldMeds, Neurocrine, ADAMAS, and research support from Lundbeck, Sunovian, Neuroderm.
Pascal Maisonobe - Compensation from Ipsen.
Abstracts

ABOBOTULINUMTOXINA USING 2 ML DILUTION MAINTAINS DURABLE FUNCTIONAL IMPROVEMENTS ACROSS MULTIPLE TREATMENT CYCLES
Khhashayar Dash-tipoor (Loma Linda, CA), James Otto (Basking Ridge, NJ), Pascal Maisonobe (Boulogne-Billancourt, France), Laxman Bahroo (Washington, DC), Daniel Truong (Fountain Valley, CA), Richard Trosch (Fountain Valley, CA)

INTRODUCTION: This open-label extension (OLE) of a 12-week, randomized, placebo-controlled trial included adults with primary idiopathic cervical dystonia (CD) who completed the lead-in week (Wk) 12 visit or whose Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score decreased ≤15% from baseline to Wk4.

OBJECTIVE: To evaluate longterm safety and efficacy of repeat treatment cycles (Cs) of abobotulinumtoxinA using 2 mL dilution (NCT01753336).

METHODS: For C1, patients toxin-naïve at baseline received 500 U, and non-naïve received 250-500 U based on prior dose. For C2/C3, adjustments were limited to ≤250 U/cycle and maximal total dose limited to 1000 U/cycle. Re-treatment occurred every 12-16 weeks, for ≤3 cycles, based on clinical judgment. Endpoints included TWSTRS and treatment-emergent adverse events (TEAEs).

RESULTS: Of 112 treated patients, 92 completed the Wk36 visit (C3-Wk12). Mean TWSTRS total score decreased from 42.2 (baseline) to 30.1 (C3-Wk12), with change from baseline of −11.7 at C3-Wk12. For each cycle, TWSTRS scores decreased from D1 to Wk4 and increased between Wk4 and Wk12, though Wk12 scores remained lower than D1 scores. Mean TWSTRS scores at Wk4 and Wk12 were primarily lower for each successive cycle (no worsening to baseline). Seventy patients (62.5%) reported TEAEs; most frequent: dysphagia, muscular weakness, and neck pain (10.7% each). Most TEAEs (70.9%) were not considered treatment-related and none led to discontinuation/death.

SUMMARY/CONCLUSION: Results were consistent with the lead-in double-blind study; abobotulinumtoxinA at approved doses using 2 mL dilution remained effective and well tolerated over 4 cycles, demonstrating sustained improvements within/ across cycles.

Disclosures:
James Otto - Employee of Ipsen during time of study.
Pascal Maisonobe - Compensation from Ipsen.
Richard Trosch - Consultation fees from Ipsen and speakers bureau fees from Acadia Pharmaceuticals and Impax Pharmaceuticals.

EVALUATION OF THE BENEFIT AND RISK PROFILE OF MEDICAL CANNABIS IN CHARCOT–MARIE–TOOTH DISEASE AND HEREDITARY NEUROPATHY WITH PRESSURE PALSIES
Brian Péper (Scranton, PA), Allison Moore (New York, NY), Meg D’Elia (Burlington, VT), Leah Perkinson (Brattleboro, PA), Joy M Aldrich (Seattle, WA), Marion McNabbb (Arlington, MA), Andrew Westerkamp (Arlington, MA), Robert N Moore (New York, NY), Gregory Carter (Spokane, WA)

INTRODUCTION: Charcot–Marie–Tooth (CMT) disease is a group of hereditary sensory and motor neuropathies. A review of various treatment guidelines determined that the evidence base was substantial for medical cannabis (MC) for chronic pain (CP) and moderate-to-substantial in peripheral neuropathy.

OBJECTIVE: To determine the risks and benefits of MC in CMT and to contrast this profile with that obtained previously with CP.

METHODS: CMT participants (n=82) were recruited from the Global Registry for Inherited Neuropathies. Two-fifths (44.1%) were type 1A and one-fifth (20.6%) were hereditary neuropathy with liability to pressure palsy. CP patients (n=705; age: 47.7 years) were recruited from New England.

RESULTS: Among the subset of CMT respondents to this online survey that used MC for CMT (n=34), one-third (32.4%) had completed the certification process and one-third (34.5%) communicated with their healthcare providers about their MC use. The primary route of administration was smoking for half (51.6%) and edibles for one-third (29.0%). MC use was reported as 78.3% medical on a continuum from 0% medical/100% recreational to 100% medical/0% recreational. CP cohort respondents reported pain from multiple sources, including back/neck (71.6%), neuropathic (34.3%), trauma (22.3%), post-surgery (19.7%), abdominal (12.5%), menstrual (5.1%), and cancer (1.4%). Qualitative analyses identified strengths (efficacy and limitations (cost) of MC. Further analyses examining the MC response by CMT type are ongoing.

SUMMARY/CONCLUSION: These studies provide a detailed patient-centric understanding of the utility of MC. This research may form the foundation for additional controlled trials in CMT and other neuropathies.

Disclosures:
Meg D’Elia - Employed by an organization that sells medical cannabis.
Marion McNabb - CEO and co-founder of the C3 Research Network.
POOLED DOSE-RESPONSE ANALYSIS OF PATISIRAN FROM FOUR STUDIES
Xiaoping Zhang (Stoneham, Massachusetts (MA)), Gabriel Robbie (Cambridge, Massachusetts (MA))

INTRODUCTION: Hereditary transthyretin mediated (hATTR) amyloidosis is an inherited life-threatening disease caused by accumulation of amyloid fibrils, consisting of both mutant and wild-type transthyretin (TTR). Patisiran is an RNAi therapeutic approved for the treatment of hATTR amyloidosis with polyneuropathy at a dose of 0.30 mg/kg IV administered every 3 weeks (Q3W).

OBJECTIVE: To evaluate the dose-response relationship for serum TTR by pooling data across various doses and studies.

METHODS: Data from 4 patisiran clinical studies were pooled, including 2 phase 1, 1 phase 2, and 1 phase 3 trials. Healthy subjects or patients received single or multiple ascending doses in a phase 1 or phase 2 study, respectively. Patients received 0.30 mg/kg Q3W patisiran for 18 months in a phase 3 study. The effect on serum TTR reduction over a wide dose range of 0.01, 0.05, 0.15, 0.30, and 0.50 mg/kg and 2 regimens (0.30 mg/kg Q3W and every 4 weeks [Q4W]) were evaluated.

RESULTS: A total of 197 subjects were included in the analysis. Maximum median TTR reduction was dose dependent: 30.8%, 40.4%, 75.4%, 87.2%, 89.2%, 87.8%, and 93.4% at 0.01, 0.05, 0.15, 0.30, 0.30* (reduced premedication), 0.30** (phase 3) and 0.50 mg/kg, respectively. The TTR reduction at peak and trough were substantially greater in patients with 0.30 mg/kg Q3W than for those with 0.30 mg/kg Q4W.

SUMMARY/CONCLUSION: Patisiran dose of 0.30 mg/kg Q3W was in the plateau portion of the dose-response curve and yielded a high level of TTR reduction that was maintained over the entire dosing interval.

Disclosures:
Xiaoping Zhang, Gabriel Robbie - Employees of Alnylam Pharmaceuticals Inc and has stock options.

PHASE 1 INVESTIGATION OF A LIGAND-CONJUGATED ANTISENSE OLIGONUCLEOTIDE FOR THE TREATMENT OF TRANSTHYRETIN AMYLOIDOSIS
Nicholas Viney (Carlsbad, CA), Li-Jung Tai (Carlsbad, CA), Shiangtung Jung (Carlsbad, CA), Spencer Guthrie (Boston, MA), Brenda Baker (Carlsbad, CA), Richard Geary (Carlsbad, CA), Eugene Schneider (Carlsbad, CA), Shuling Guo (Carlsbad, CA), Brett Monia (Carlsbad, CA)

INTRODUCTION: Hereditary transthyretin amyloidosis (hATTR) is a rare, progressive, fatal disease caused by pathogenic variants in the transthyretin (TTR) gene that induce formation of insoluble, extracellular amyloid deposits in multiple organ systems. Wild-type TTR amyloid deposits can also occur, leading to progressive congestive heart failure. Inotersen is an antisense oligonucleotide (ASO) approved for treatment of hATTR patients with polyneuropathy that inhibits production of both mutant and wild-type TTR protein by degradation of TTR mRNA. AKCEA-TTR-LRx (ION-682884) is an ASO of similar design and sequence that is conjugated to a ligand for selective, receptor-mediated delivery to hepatocytes, the principal source of systemically circulating TTR. In preclinical studies, AKCEA-TTR-LRx produced significant dose-dependent reductions of TTR mRNA and protein levels, with a significant increase in potency compared to inotersen. AKCEA-TTR-LRx is in early phase development for the treatment of both hereditary and wild-type ATTR.

OBJECTIVE: To evaluate AKCEA-TTR-LRx in a phase 1/2 study of healthy volunteers and patients with transthyretin-mediated amyloidosis (NCT03728634).

METHODS: In phase 1, eligible subjects were assigned to 1 of 2 multiple-dose cohorts (45 and 90 mg, 12 per cohort) and randomized 10:2 (active:placebo) to receive 4 monthly subcutaneous doses of study drug. A higher, single-dose cohort of healthy volunteers is planned.

RESULTS: This study is ongoing. Safety, tolerability, pharmacokinetics, and pharmacodynamics of AKCEA-TTR-LRx in healthy volunteers will be presented.

SUMMARY/CONCLUSION: These results will guide selection of the dose/treatment schedule for the cohort of ATTR patients and upcoming phase 3 studies.

Disclosures:
Nicholas Viney, Li-Jung Tai, Shiangtung Jung, Spencer Guthrie, Brenda Baker, Richard Geary, Eugene Schneider, Shuling Guo, Brett Monia - Employees and shareholders of Ionis Pharmaceuticals, Inc.
INTRODUCTION: Hereditary transthyretin amyloidosis (hATTR) is a rare protein misfolding disorder causing progressive and debilitating polyneuropathy. A randomized, placebo-controlled phase 3 trial (NEURO-TTR; NCT01737398) demonstrated inotersen efficacy/safety in hATTR polyneuropathy patients.

OBJECTIVE: To update inotersen longterm efficacy/safety after 24 months in open label extension (OLE) (NCT02175004).

METHODS: Patients who completed NEURO-TTR were eligible for OLE. Assessments included modified Neuropathy Impairment Score +7 (mNIS+7) neurophysiologic tests, Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN), Short Form 36 Health Survey version 2 (SF-36v2) Physical Component Summary (PCS), and safety monitoring.

RESULTS: OLE enrollment was chosen by 135/139 (97.1%) patients who completed NEURO-TTR. As of May 31, 2018, some ongoing patients hadn’t yet completed 24 months, and longest inotersen exposure was 5.2 years. Patients switched from placebo to inotersen in OLE demonstrated slowing of neurologic disease progression by mNIS+7 and QOL-DN as early as 6 months after starting inotersen (mean change OLE baseline to month 6/ year 2: 6.22/5.08-mNIS+7, 0.54/2.26-QOL-DN). Patients who received inotersen for 39 months (15 months NEURO-TTR + 24 months OLE) continued to show benefit (mean change OLE baseline to year 2: 11.18-mNIS+7, 5.22-QOL-DN), and showed health-related QOL stabilization per SF-36v2 PCS. No evidence of increased risk of grade 4 thrombocytopenia or severe renal events has been observed with increased exposure duration and no new safety concerns identified.

SUMMARY/CONCLUSION: In OLE, inotersen improved, halted, or slowed progression of hATTR polyneuropathy, with greater stabilization observed in patients who initiated inotersen earlier.

Disclosures:
Shiangtung Jung – Employee of Ionis.
Michael Pollock, Spencer Guthrie - Employees of Akcea.

INTRODUCTION: Hereditary transthyretin amyloidosis (hATTR) is a rare, progressive, and fatal disease that manifests as buildup of TTR protein in major organ systems, resulting in organ failure. Inotersen, a TTR-directed antisense oligonucleotide indicated for the treatment of hATTR polyneuropathy, demonstrated therapeutic benefit on sensorimotor peripheral neuropathy and quality of life in a global, randomized, double-blind, placebo-controlled phase 3 study (NEURO-TTR, NCT01737398).

OBJECTIVE: To evaluate the impact of inotersen on Neuropathy Symptoms and Change (NSC) scores. The NSC score is a standardized measure of motor, sensory, and autonomic symptoms in generalized polyneuropathy that quantitates and assesses the distribution and severity of muscle weakness, sensory symptoms, and autonomic symptoms.

METHODS: Adults with stages 1 and 2 hATTR amyloidosis were randomized (2:1) to receive 300 mg weekly subcutaneous inotersen or placebo for 15 months. The NSC score (total, individual domains) was assessed in tandem with the primary endpoints at 9 and 15 months.

RESULTS: Of the 172 patients evaluated, inotersen-treated patients experienced significant therapeutic benefit versus those receiving placebo in NSC total score from baseline to 9 months (least-square mean [LSM] difference −3.32; 95% CI −5.70 to −0.86; p=0.008) and 15 months (LSM difference −6.33; 95% CI −9.12 to −3.55; p<0.001). Patients receiving inotersen also experienced therapeutic benefit versus placebo in NSC subdomains of muscle weakness, sensory, pain, and autonomic symptoms at 15 months. Notably, autonomic symptoms also showed therapeutic benefit at 9 months.

SUMMARY/CONCLUSION: Inotersen conferred therapeutic benefit on neuropathic symptoms in patients with hATTR amyloidosis consistent with previously reported benefits.

Disclosures:
Elizabeth Ackermann - Employee of Ionis.
Spencer Guthrie, Michael Pollock - Employees of Akcea.
MODIFIED NEUROPATHY IMPAIRMENT SCORE +7 COMPONENTS AND LOWER LIMB FUNCTION RESPONSIVENESS IN INOTERSEN TREATMENT OF HEREDITARY TRANSTHYRETIN AMYLOIDOSIS POLYNEUROPATHY

James Dyck (Rochester, MN), John Kincaid (Indianapolis, IN), Janice Wissman (New York, NY), Michael Polydoros (Baltimore, MD), William Litchy (Rochester, MN), Michelle Mauermann (Rochester, MN), Elizabeth Ackermann (Carlsbad, CA), Spencer Guthrie (Boston, MA), Michael Pollock (Boston, MA), Shiangtung Jung (Carlsbad, CA), Brenda Baker (Carlsbad, CA), Peter Dyck (Rochester, MN)

INTRODUCTION: The modified Neuropathy Impairment Score +7 (mNIS+7) was developed from NIS+7 to better represent neuropathic impairments in transthyretin amyloidosis (ATTR) polyneuropathy. In the 15-month phase 3 trial (NEURO-TTR; NCT01737398), inotersen, an antisense oligonucleotide inhibitor of TTR production, demonstrated significant beneficial effect compared with placebo in primary outcomes (mNIS+7 and Norfolk Quality of Life-Diabetic Neuropathy questionnaire scores) in patients with hereditary ATTR (hATTR).

OBJECTIVE: To evaluate performance of mNIS+7 in assessing the efficacy of inotersen.

METHODS: Efficacy of inotersen was tested utilizing the 7 major components of mNIS+7 (NIS-weakness, NIS-reflexes, NIS- sensation loss, 5 nerve conduction amplitudes, touch and heat-pain somatotopic quantitative sensation testing, and heart rate response to deep breathing [HRDB]) and lower limb function (LLF) (3 functions: ability to walk on toes or heels, and to arise from kneeling).

RESULTS: In NEURO-TTR, 5/7 main components of mNIS+7 showed significant benefit by 15 months in inotersen versus placebo patients. HRDB and touch did not reach significance; however, HRDB cannot be assessed in active pacing or atrial fibrillation, both common in hATTR. All mNIS+7 components assessed by upper and lower limbs showed statistically significant benefit in patients receiving inotersen versus placebo except NIS-reflexes (upper) and touch pressure (upper, lower). Overall and individual LLF scores showed statistically significant benefit by 15 months in patients receiving inotersen compared with placebo.

SUMMARY/CONCLUSION: These data support beneficial effects of inotersen on many different neurological functions including muscle weakness, muscle stretch reflexes, sensation, attributes of nerve conduction of limb nerves, and LLF.

Disclosures:
Elizabeth Ackermann, Brenda Baker, Shiangtung Jung – Employees of Ionis.
Spencer Guthrie, Michael Pollock – Employees of Akcea.

ACUTE FLACCID MYELITIS WITH DRAMATIC IMPROVEMENT AFTER INTRAVENOUS IMMUNOGLOBULIN TREATMENT

Malik Ghannam (Eagan, MN), Brent Berry (Minneapolis, MN), Stephanie Reeder (Minneapolis, MN), Tanner Verderer (Minneapolis, MN), Gaurav Guliani (Saint Paul, MN), Georgios Manousakis (Minneapolis, MN), Jetter Robertton (Minneapolis, MN), Jeffrey Allen (Minneapolis, MN), Michael Howell (Minneapolis, MN)

INTRODUCTION: Acute flaccid myelitis (AFM) is a rare polio-like illness with growing prevalence in the United States since 2014. Confirmed AFM is defined as acute flaccid paralysis (AFP) present in ≥1 limbs plus MRI gray matter spine lesion, and probable AFM if AFP is present with cerebrospinal fluid (CSF) pleocytosis. AFM has unclear etiology; viruses are thought to play a pathogenic role. Various coxsackie and enteroviruses were detected in 4/542 confirmed AFM cases. We present a case of probable AFM that showed dramatic improvement after treatment with IVIg.

CASE REPORT: A 20-year-old African male patient with no known antecedent illnesses developed rapidly progressive bilateral lower greater than upper limb flaccid paralysis. Time from symptom onset to inability to walk and first hospital admission was 7 days. CSF showed lymphocytic pleocytosis and elevated protein. He had a transient improvement of strength after high dose methylprednisolone treatment, but subsequently deteriorated. Viral serologies were normal except for West Nile IgG antibodies that were detected on the second, but not the first, CSF examination. MRI showed no spinal cord or brain lesions. Serial EDX studies showed denervation changes principally in lumbosacral segments, and a central pattern of reduced motor unit action potential activation. After treatment with 2 g/kg of IVIg he showed major improvement. Two months later he required no gait support and his upper limb strength was normal.

CONCLUSION: To our knowledge, this is the first reported case of AFM that improved after IVIg exposure.
TWO BROTHERS WITH LOWER EXTREMITY WEAKNESS
Yessar Hussain (Austin, TX), Chaitanya Konda (Austin, TX), Shailesh Reddy (Austin, TX)

INTRODUCTION/BACKGROUND: We present a case of juvenile-onset of an ALS variant with a rare gene variant.

CASE REPORT: A 25-year-old male of French descent who is a competitive swimmer with no significant past medical history presented with 8 years of progressive distal lower extremity weakness and gait imbalance. He developed right foot weakness, then slowly progressed with a left foot weakness. He has had frequent falls due to progressive stiffness in his legs; currently, he is mostly using a wheelchair. He has no sensory complaints, and denies bulbar and ocular symptoms. His motor examination showed moderate distal lower extremity weakness and minimal distal upper extremity weakness. His reflexes are 3+ throughout, but diminished at the ankles, with an intact sensory examination. He has proximal lower extremity spasticity, and notable bilateral pes cavus. On his initial encounter, there was no prior family history. However, on subsequent visits, it was discovered that his younger brother had also been experiencing similar signs and symptoms around the age of 16. Examination of his mother showed she was asymptomatic except for bilateral pes cavus. Brain and spinal cord MRI were normal, and needle EMG/NCSs showed denervation in the distal lower extremities with sensory sparing. Genetic testing was diagnostic for 2 variants of the senataxin (SETX) gene.

SUMMARY/CONCLUSION: ALS variant with juvenile onset can mimic other disease processes. Looking at the implications of genetic variants to diagnose different anterior horn cell disease processes will be an area of future evaluation. The SETX gene variant should be further explored for motor neuron diseases.

CLINICAL FINDINGS AND SEGMENTAL BIOIMPEDANCE STUDIES IN ADULTS WITH SPINAL MUSCULAR ATROPHY RECEIVING INTRATECAL NUSINERSEN
Tulio Bertorini (Cordova, TN), Janna Knickerbocker (Memphis, TN), Jeffrey Metter (Memphis, TN), Yu Zhao (Memphis, TN) William Mays (Memphis, TN), Kim Carter (Memphis, TN), Laura Talbot (Memphis, TN)

INTRODUCTION: The antisense oligonucleotide therapy with nusinersen is beneficial in children with spinal muscular atrophy (SMA), but no clinical trials have been reported in adult-onset SMA. We are reporting our experience in 6 adults with SMA (3 nonambulatory SMA2, 3 ambulatory SMA3) who received nusinersen treatment and were clinically followed for more than a year after treatment. The 3 ambulatory patients were evaluated with bioimpedance.

METHODS: We performed clinical and functional evaluations, forced vital capacity, serum creatinine measurements, and segmental bioimpedance using the RJL System (Clinton Township, Michigan) periodically for more than a year following treatment.

RESULTS: On clinical evaluation, all patients had minor clinical benefits. All were weaker in their legs than their arms. During followup after treatment, strength remained the same or showed modest improvement. By segmental bioimpedance, both leg and arm muscle mass were below normal correlating with the weakness. The greatest weakness being in the lower extremities. At most, small improvements were observed in the bioimpedance readings in the arms and legs during followup.

SUMMARY/CONCLUSION: Treatment showed overall minimal improvement in these 6 individuals. This could be secondary to lack of sensitivity of the evaluation. We cannot determine if the treatment slowed progression. Larger control studies will be necessary.
EDARAVONE USE IN NORTHEASTERN PENNSYLVANIA: A SINGLE CLINIC EXPERIENCE
Mathieu Cuchanski (Danville, PA), Eric Veloso (Bloomsburg, PA), Rachel Dragano (Danville, PA), Laura Fierke (Danville, PA), Jose David Avila (Danville, PA)

INTRODUCTION: A recent Japanese study demonstrated that edaravone slows the progression of ALS in a well-defined subgroup of patients. The FDA approved the drug for use in the United States in May 2017. There is limited evidence on the use of edaravone in the United States.

OBJECTIVE: To report the use of edaravone in the Geisinger Wyoming Valley (GWV) ALS Clinic.

METHODS: Retrospective review of all patients seen in the GWV ALS Clinic from August 2017 to December 2018.

RESULTS: Twenty-five patients (12 men, 13 women; median age: 60 years, range: 42-85) were reviewed. Disease phenotypes included: limb-onset ALS, 13 patients (52%); bulbar-onset ALS, 11 patients (44%); and primary lateral sclerosis, 1 patient (4%). The diagnosis of ALS according to the revised El Escorial criteria was definite in 5 (20%), probable in 16 (64%), not documented in 3 (12%), and not applicable in 1 (4%). Edaravone was offered to 16 patients (64%), of which only 3 (12%) met the criteria of the study that showed efficacy. The drug was started in 4 patients (16%). Mean time to the first infusion was 20 weeks. Duration of therapy ranged 13-47 weeks. Two patients remain on the drug. No serious adverse effects have been reported.

SUMMARY/CONCLUSION: Edaravone was not consistently offered in our clinic. Only a minority of patients resembled the population in which the drug showed efficacy. There was insufficient data to analyze the Revised ALS Functional Rating Scale before and after the initiation of therapy.

Mathieu Cuchanski, DO
Resident and Fellow Member Award Recipient

PHENOTYPIC PATTERNS OF AMYOTROPHIC LATERAL SCLEROSIS: A SINGLE CENTER STUDY FROM SOUTH INDIA
Sruthi S Nair (Thiruvananthapuram, India), Jaffer Vali Sayyed (Thiruvananthapuram, India), Muralidharan Nair (Thiruvananthapuram, India)

INTRODUCTION: The phenotypic variability of ALS is well recognized but poorly explored from India.

OBJECTIVE: To study the ALS phenotypes and ALS plus syndromes from a single tertiary care center in South India.

METHODS: We retrospectively collected the data of patients from over 2 years (2017-2018) with diagnoses of definite, probable, or possible ALS by the revised El Escorial criteria and classified them into the 8 established phenotypes by review of the clinical and needle EMG data.

RESULTS: The study included 132 patients (77 males, M:F 1.4; mean age: 55.1 years, range: 28-83) with mean disease duration of 14.5±12.1 months. Bulbar onset was noted in 44 (33.3%), limb onset in 86 (65.2%), and neck drop in 2 (1.5%). The common ALS phenotypes were classic ALS in 64 (48.5%), bulbar in 23 (17.4%), pyramidal in 17 (12.9%), and pure lower motor neuron in 13 (9.8%). Young-onset ALS commonly had classic (8/15, 53.3%) phenotype. Female predominance was noted in the bulbar group alone (M:F 0.43). Ten (7.6%) had ALS plus syndromes: 4 frontotemporal dementia, 4 parkinsonism, and 2 cerebellar ataxia. Other observations were gaze abnormalities in 13 (9.8%) and bladder symptoms in 12 (9.1%). Among 6 with positive family history, 2 were confirmed to have heterozygous mutations in the FUS gene.

SUMMARY/CONCLUSION: The classic, bulbar, and pyramidal phenotypes were the most common. Male dominance was seen in all except bulbar phenotype. ALS plus syndromes were noted in less than 10%.
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IMPAIRED HORIZONTAL SACCHADES IN JUVENILLE ONSET AMYOTROPIC LATERAL SCLEROSIS WITH FUSED IN SARCOMA (FUS) MUTATION

Mark Ross (Scottsdale, AZ), Alan Zhang (Sacramento, CA), Benn Smith (Scottsdale, AZ)

INTRODUCTION/BACKGROUND: Juvenile onset ALS with the FUS mutation is a rapidly progressive form of ALS. Slow horizontal saccade movements have not been reported in ALS patients.

OBJECTIVE: To report slow horizontal saccadic eye movements in a patient with juvenile onset ALS with the FUS mutation.

CASE REPORT: A 20-year-old man developed asymmetrical arm weakness first involving the right arm and next the left. He reported difficulty focusing his vision. He had no diplopia or ptosis. He next developed difficulty holding his head up. Two months after onset he developed leg weakness and difficulty swallowing. Four months after onset he could no longer use his arms and he was unable to walk. Examination revealed diffuse muscle weakness and atrophy without fasciculations. Horizontal saccades were extremely slow, while vertical saccades were preserved. Reflexes were initially hypoactive without pathologic reflexes but 1 month after onset hyperreflexia and extensor plantar responses were observed. MRI of the brain and cervical spine were unremarkable. Needle EMG revealed diffuse fibrillation potentials and large motor unit potentials with reduced recruitment. DNA testing confirmed a mutation in the FUS gene.

SUMMARY/CONCLUSION: Slow horizontal saccades have not been reported in ALS. This may be a specific finding in patients with juvenile ALS with the FUS mutation. We speculate the impaired horizontal saccades are due to the disease involving the pons where control of horizontal saccades resides. Physicians should be aware that slow horizontal saccades may be seen in juvenile ALS patients with the FUS mutation.

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PATTERNS OF DYSTROPHIN GENE DELETION/ DUPLICATION IN A SAMPLE OF DUCHENNE MUSCULAR DYSTROPHY PATIENTS LIVING IN SAUDI ARABIA

Ayman Abdelhady (Cairo, Egypt), Mostafa Madkor (Jeddah, Saudi Arabia), Ahmed Safwat (Jeddah, Saudi Arabia), Ashraf Soliman (Jeddah, Saudi Arabia), Salem Abdelhady (Cairo, Egypt), Hebatallah Rashid (Cairo, Egypt), Mona Wahideldin (Cairo, Egypt)

INTRODUCTION: Duchenne muscular dystrophy (DMD) is caused by the lack of functional dystrophin molecules, either due to nonsense mutations (premature stop codons) or by large rearrangements (deletions or duplications) that disturb the reading frame and in consequence abolish the production of dystrophin in muscles.

OBJECTIVE: To detect patterns of dystrophin gene deletion/duplication among DMD patients living in Saudi Arabia.

METHODS: Twenty patients with DMD diagnosed by clinical history, family pedigree, and creatine kinase total were subjected to screening for all 79 exons of the dystrophin gene for deletions and duplications.

RESULTS: Dystrophin gene deletion was detected in 80% of patients; 25% of them had only 1 exon deletion. The most frequently deleted exon was exon 45, followed by exon 51, and deletion mutation in exon 33. The other 75% had multiple exon deletions (from 19 exons), most of which were in the major hotspot region between exons 44 and 52, and only 1 patient with deletion in exons 8-18. Fifteen percent of the patients showed dystrophin gene duplication, seen mainly in exons 8-9, then exons 44-50, and lastly exons 31-43. Only 1 patient had neither deletion nor duplication but nucleotide substitution (c.10033C>T) in exon 69.

SUMMARY/CONCLUSION: Our study detected higher incidence of gene deletion compared to other studies; the most common deletion is multi-exon deletion in the major hot spot of the gene (exons 44-52). Also, we detected lower incidence of duplication with higher percentage of duplication in the distal region of dystrophin gene.
DELAYED DIAGNOSED ATYPICAL ANDERSEN–TAWIL SYNDROME WITH FULL RECOVERY WITH ACETAZOLAMIDE
Ahmet Burakgazi (Roanoke, VA)

INTRODUCTION: Andersen–Tawil syndrome (ATS) is characterized by a triad of periodic paralysis (PP), cardiac arrhythmias, and distinctive dysmorphic features. Due to its rarity and high degree of clinical and phenotypic variability, a diagnosis of ATS can be very perplexing and challenging.

CASE REPORT: A 28-year-old male was referred for PP. He first noticed significant weakness in the 10th grade. He went hunting and was maintaining a squatting position for a prolonged period of time. The weakness was apparently isolated to his legs. Over the following month, he slowly returned back to 75% of his prior strength. The initial neurological workup including blood tests, multiple needle EMGs, and muscle biopsy was inconclusive. He had more paralytic episodes over time with no full recovery between episodes. He had significant weakness for a few days that gradually improved, but he did not return to full strength. No remarkable facial or body dysmorphic features were detected. He developed recurrent syncope episodes at age 27. Cardiac workup showed prolonged QT and polymorphic ventricular tachycardia with deterioration to ventricular fibrillation.

Molecular genetic tests showed mutations in the KCNJ2 gene. He was put on acetazolamide 250 mg 3 times a day. At 3 months followup, he demonstrated maximum improvement and no new spells.

CONCLUSION: ATS is very rare PP with highly variable clinical presentations. The diagnosis can be very challenging. A neuromuscular specialist should be familiar with an atypical presentation of ATS due its high degree of clinical and phenotypic variability.

NON-DYSTROPHIC MYOTONIA SYNDROME INCIDENTALLY FOUND IN PATIENT WITH RIGHT CARPAL TUNNEL SYMPTOMS
Tyler Klein (Madison, WI)

INTRODUCTION: Myotonic muscle disorders can be a cause of pain, stiffness, and weakness. Myotonic discharges found during needle EMG are easy to recognize and associated with or without dystrophic changes. In our asymptomatic patient (other than CTS symptoms), myotonic discharges were an incidental finding.

CASE REPORT: A 44-year-old male with right upper extremity (RUE) pain was referred for needle EMG/NCSs with suspected CTS. He had a 1-year onset of pain (with numbness/tingling) to right shoulder, elbow, and thumb and index and middle fingers. He denied neck pain/inciting event or weakness/stiffness. Examination revealed: sensation intact, 5/5 strength to bilateral upper and lower extremities, positive Phalen's on the right, cranial nerves II-XII intact, and no fasciculations or muscle atrophy/hypertrophy. NCSs with prolonged bilateral transcarpal median latencies consistent with CTS. Needle EMG with short bursts of prominent myotonia in all 5 RUE muscle studies. Motor unit action potentials were normal, consistent with a non- dystrophic myotonia syndrome.

CONCLUSION: Myotonic discharge is a common spontaneous pattern seen during needle EMG. Possible causes in this patient are myotonia congenita, sodium channel myotonia congenita, and myofibrillar myotonia. Acid maltase deficiency can cause non- clinical myotonia, but myotonic discharges are typically only proximal. Paramyotonia congenita and hyperkalemic periodic paralysis are also possible, but usually present at a younger age and with more profound weakness. For this patient no interventions were recommended. It is important to recognize non-dystrophic myotonia syndromes. Some patients will only require education and monitoring.

Tyler Klein, DO
Resident and Fellow Member Award Recipient
CAN HISTORICALLY AUTOSOMAL RECESSIVE MUSCULAR DYSTROPHIES PRESENT IN A CARRIER OF TWO SEPARATE DYSTROPHY GENES?
George Small (Pittsburgh, PA)

INTRODUCTION: Clinically manifesting muscular dystrophy genes in single copy carriers have been occasionally described in subjects with characteristically autosomal recessive disorders.

CASE REPORT: Our patient developed proximal lower extremity weakness in middle age, with stiffness and electrical myotonia along with serum creatine phosphokinase elevation. Previously diagnosed with Mobitz type-1 heart block on medical therapy, no family history of neurological disease noted. Normal development and sports participation as a youth. Severe psoas and paraspinal muscle atrophy on MRI. Dried blood spot testing revealed a single nucleotide deletion in the HSPG2 gene, resulting in a frameshift mutation. Another missense variant aspartic acid substitution was noted in the TTN (titin) gene. The HSPG2 genetic variant is seen in Schwartz–Jampel syndrome, and the second genetic mutation noted, although not previously described, is in the gene for titin, a major sarcomeric protein where other genetic mutations result in autosomal recessive forms of limb girdle muscular dystrophy.

RESULTS/CONCLUSION: Our patient’s stiffness and myotonia are characteristic of Schwartz–Jampel syndrome, along with limb girdle weakness seen in both limb girdle muscular dystrophy (LGMD) type 2) and Schwartz–Jampel syndrome. The pathophysiology appears to encompass both the deficiency in effective acetylcholinesterase activity thought to result in the stiffness of Schwartz–Jampel patients, and the weakness from abnormal titin in stabilizing muscle cell sarcomeres in LGMD2J. How this phenotype can occur may be the result of a clinically significant "second hit" in a patient rare enough to have 1 abnormal gene, inheriting yet another uncommon, pathogenic gene.

EFFECTIVE IMMUNOTHERAPY OF ANTI-TIF1-GAMMA-POSITIVE PARANEOPLASTIC DERMATOMYOSITIS WITH CONCURRENT DIAGNOSIS OF OVARIAN CANCER
Noushin Jazebi (Galveston, TX), Elena Shanina (Houston, TX)

INTRODUCTION/BACKGROUND: The association between malignancy and inflammatory myopathies, particularly dermatomyositis (DM), is well established. Anti-TIF1-gamma antibody positive DM patients have significantly higher risk of cancer. Treatment of underlying malignancy is considered a cornerstone of cancer-associated myositis management. However, there is little evidence to guide additional treatment options. Here, we report a case with concurrent clinical manifestations of anti-TIF1-gamma-positive DM and advanced ovarian cancer with remarkable response to immunotherapy, despite delay of cancer treatment.

CASE REPORT: A 63-year-old female with newly diagnosed metastatic ovarian cancer presented with a 4-week history of progressive proximal muscle weakness, restricting her to bed. Needle EMG demonstrated a myopathic pattern with increased membrane irritability. Muscle biopsy showed inflammatory infiltrates with CD4 predominance but no classical perifascicular atrophy. Skin biopsy of the limb macular rash was typical for DM. She had positive anti-TIF1-gamma antibody. The patient was successfully treated with IVIg, significantly improving in strength and walking with a walker at discharge. For non-medical reasons, her cancer treatment was initiated 2 months later. At 4 months followup, DM remained stable.

SUMMARY/CONCLUSION: This case demonstrates that early initiation of immunotherapy is beneficial in patients with DM and advanced cancer, and improves quality of life even when cancer treatment is delayed. The parallel diagnosis of cancer and DM requires a multidisciplinary approach, including close collaboration of oncologists and neuromuscular specialists for treatment and monitoring. Considering challenges of early diagnosis of ovarian cancer, anti-TIF1-gamma antibody can be used in addition to other cancer screening in DM patients.

Noushin Jazebi, MD
Resident and Fellow Member Award Recipient
MITOCHONDRIAL CYTOPATHY IN NECROTIZING MYOPATHY
Kenkichi Nozaki (Birmingham, AL)

INTRODUCTION: Necrotizing myopathy consists of multiple etiologies. Its precise cytopathic mechanism is not fully elucidated, and its presentation is frequently difficult. Mitochondrial cytopathy is well known in myositis associated with poor response to treatment, but is not well known in necrotizing myopathy.

OBJECTIVE: To examine mitochondrial cytopathy in necrotizing myopathy.

METHODS: A retrospective review was conducted of muscle pathology of necrotizing myopathy and clinical information of patients whose muscle biopsy shows necrotizing myopathy with mitochondrial cytopathy. Mitochondrial cytopathy is defined as presence of significant number of cytochrome oxidase negative/succinic dehydrogenase positive myofibers (COX−/SDH+) and/or ragged red fibers.

RESULTS: Mitochondrial cytopathy was seen in 6/31 (19%) patients with necrotizing myopathy. Muscle pathology of the 6 patients shows inflammation (rare-to-mild) in 3/6 (50%), rimmed vacuoles (rare) in 1/6 (17%), and amyloid or inclusions in 0/6. Among 4 of these patients in whom clinical information is available, weakness is seen in a proximal dominant manner in 2/4 (50%) and in a diffuse distribution in 2/4 (50%). Myalgia is seen in 2/4 (50%). Associated medical conditions include polyneuropathy and heavy alcohol use (1/4, 25%), Wernicke's encephalopathy (1/4, 25%), and interstitial lung disease and connective tissue disease (1/4, 25%). Immunosuppressive/modulating therapy was given in 3/4 (75%) and improvement of strength was seen in 1 (1/3, 33%).

SUMMARY/CONCLUSION: Mitochondrial cytopathy is seen in necrotizing myopathy. It consists of various medical backgrounds. While the number is limited, the condition may be associated with poor response to immunosuppressive/modulating therapy.

INCREASED DIAGNOSTIC SENSITIVITY FOR ANTI-SRP MYOPATHY USING TISSUE-BASED IMMUNOFLUORESCENCE COMPARED TO TRADITIONAL SRP54 RECOMBINANT-BASED METHODS
Shahar Shelly (Rochester, MN), Matthew Roforth (Rochester, MN), Sean Pittcock (Rochester, MN), Divyanshu Dubey (Rochester, MN), Christopher Klein (Rochester, MN), John Mills (Rochester, MN)

INTRODUCTION/BACKGROUND: Anti-SRP myopathy is a disabling yet treatable necrotizing myopathy. Several different testing methodologies can detect SRP antibodies. In clinical practice there are limited reports of how well these methods correlate.

OBJECTIVE: To demonstrate that tissue indirect immunofluorescence (IIF) assays can detect SRP antibodies in biopsy-confirmed immune-mediated necrotizing myopathy (IMNM) that have tested negative by the “gold-standard” radioimmunoprecipitation assay (RIA).

CASE REPORT: Three patients were reported negative for SRP antibodies at a Clinical Laboratory Improvement Amendments (CLIA)-certified national reference laboratory that utilizes RIA, yet had IIF staining patterns consistent with SRP antibodies upon testing at Mayo Clinic. Patient 1 was a 52-year-old female with proximal lower limb weakness which rapidly progressed and extended to the upper limbs. Biopsy of the quadriceps was consistent with IMNM. Her creatine kinase (CK) was 15,000 U/L, and her needle EMG showed myopathic changes with fibrillation potentials but no myotonic discharges. Patient 2 was a 64-year-old female with progressive muscle weakness. Her CK was 17,000 U/L, and her needle EMG showed myopathic changes and fibrillation potentials in majority of muscles. A left deltoid biopsy was consistent with IMNM. Her CK was 17,000 U/L, and her needle EMG showed myopathic changes and fibrillation potentials in majority of muscles. A left deltoid biopsy was consistent with IMNM. Patient 3 was a 54-year-old female with 3 months of bulbar weakness and profound proximal muscle weakness. Her biopsy was consistent with IMNM, and her CK was 30,000 U/L.

SUMMARY/CONCLUSION: In pathologically-confirmed IMNM patients SRP antibodies may be missed when utilizing a single testing methodology such as RIA. Our experience suggests SRP IIF is important to incorporate into comprehensive autoantibody evaluation of IMNM.
TWO CASES OF VALOSIN-CONTAINING PROTEIN ASSOCIATED NEUROMUSCULAR DISEASE
Lise Phan (Los Angeles, CA), Leila Darki (Los Angeles, CA), Said Beydoun (Los Angeles, CA)

INTRODUCTION/BACKGROUND: Valosin-containing protein (VCP) is involved in cell cycle control and protein degradation. VCP disease is an autosomal dominant syndrome associated with progressive inclusion body myopathy with Paget disease of bone and frontotemporal dementia (IBMPFD) and ALS. There is inter- and interfamilial phenotypic heterogeneity.

CASE REPORT: We describe 2 patients, 1 with extensive family history which aided in the diagnosis. The other was misdiagnosed and found to have VCP mutation after not improving with immunotherapy. Case 1 is a 50-year-old female who presented with 4 years of proximal leg weakness. Her deceased father and paternal aunts also had progressive weakness. The children of the affected aunt developed early dementia and ALS. Her half-sister was diagnosed with IBMPFD with VCP mutation. Our patient got tested and had mutation as well, with predominant proximal lower extremity myopathy phenotype. Case 2 is a 59-year-old female with 20 years of asymmetric weakness in distal arms, initially diagnosed as multifocal motor neuropathy without objective improvement with IVIg. Family history is unknown as patient was adopted. EDX studies showed motor axonopathy, without conduction block, and acute and chronic denervation. Muscle biopsy showed chronic denervation and large type 1 fibers. She had heterozygous mutation of VCP gene R159H, c.476 G>A with motor neuron disease phenotype.

SUMMARY/CONCLUSION: The VCP gene mutations demonstrate phenotypic pleiotropy with significant intra- and interfamilial variation in phenotype. VCP-associated neuromuscular disease should not only be considered in cases with family history of progressive weakness, myopathy, bone disease, and dementia but also in atypical cases with overlapping phenotype.
EFFICACY AND SAFETY OF ABOBOTULINUMTOXINA IN ADULTS WITH CERVICAL DYSTONIA: SIMILAR RESULTS BETWEEN 1 AND 2 ML DILUTION METHODS

Khayyaz Dashtipour (Loma Linda, CA), Robert Hauser (Tampa, FL), Stuart Isaacsen (Boca Raton, FL), Daniel Truong (Fountain Valley, CA), Loochan Babroo (Washington, DC), Atul Patel (Overland Park, KS), Pascal Maisonneuve (Boulogne-Billancourt, France), James Otto (Basking Ridge, NJ)

INTRODUCTION: AbobotulinumtoxinA is approved (United States only) for the treatment of cervical dystonia (CD) using 1 or 2 mL dilution. Dilution flexibility allows clinicians to individualize care, which may improve outcomes.

OBJECTIVE: To evaluate efficacy and safety of a single injection of abobotulinumtoxinA using 1 or 2 mL dilution in adults with CD.

METHODS: AbobotulinumtoxinA was evaluated in 3 double-blind, placebo-controlled trials (1 mL: Trials 1 and 2; 2 mL: Trial 3). In Trials 1 and 2, patients were randomized to abobotulinumtoxinA 500 U or placebo. In Trial 3, patients were randomized to abobotulinumtoxinA 500 U if toxin-naïve at baseline; 250-500 U based on previous onabotulinumtoxinA dose, if non-naïve) or placebo. Eligible adults had primary idiopathic CD, baseline Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score ≥20 (2 mL) or ≥30 (1 mL), and TWSTRS severity subscale score >10 (2 mL) or ≥15 (1 mL). The primary endpoint was change in TWSTRS total score (week 4-baseline). Treatment-emergent adverse events (TEAEs) were assessed.

RESULTS: In Trial 1 (n=80), 37 patients received abobotulinumtoxinA, 43 placebo. In Trial 2 (n=116), 55 patients received abobotulinumtoxinA, 61 placebo. In Trial 3 (n=133) 88 patients received abobotulinumtoxinA, 45 placebo. All trials met the primary endpoint (Trial 1: Δ-6.0, p=0.013; Trial 2: Δ-8.8, p<0.001; Trial 3: Δ-8.3, p<0.001). AbobotulinumtoxinA’s safety profile was similar across trials. Dysphagia was the most common TEAE (about 9-16%).

SUMMARY/CONCLUSION: Although trial designs differed, abobotulinumtoxinA was efficacious using 1 or 2 mL dilutions, offering treatment flexibility and individualized care.

Disclosures:
Robert Hauser - unable to insert Dr. Hauser’s conflicts 6/25/19 emailed
CLINICAL AND ELECTRODIAGNOSTIC FEATURES OF SPORADIC INCLUSION BODY MYOSITIS
Payam Soltanzadeh (Los Angeles, CA) Nimish Thakore (Cleveland, OH) Richard Prayson (Cleveland, OH), Kerry Levin (Cleveland, OH)

INTRODUCTION: Early diagnosis of sporadic inclusion body myositis (sIBM) can be challenging. In this study, we present data from a large series of patients with sIBM.

OBJECTIVE: To provide clinical and EDX characterization of patients with sIBM and explore EDX features that can help with early diagnosis of sIBM.

METHODS: We identified sIBM patients referred to the Cleveland Clinic Neuromuscular Center. Griggs, European Neuromuscular Centre (ENMC), and MRC criteria were used to stratify patients into different diagnostic categories based on clinical, EDX, and pathologic findings. Creatine kinase levels, age of onset, presenting features, and needle EMG findings were collected from the clinical charts.

RESULTS: Among 107 identified patients with IBM, 51 had detailed biopsy findings consistent with the diagnosis of sIBM, among whom 1 had HIV infection and 1 had chronic hepatitis C disease. In patients with ENMC definite sIBM, 23 (60%) presented with proximal leg weakness and 2 with asymptomatic hyperCKemia. Irritable myopathy with mixed neurogenic and myopathic motor units was the most common EDX pattern in patients with sIBM. Electrical muscle irritability in the form of fibrillations/positive sharp waves was noted with a high frequency in some of the forearm muscles: 82% in the brachioradialis and 69% in the flexor pollicis longus.

SUMMARY/CONCLUSION: More sIBM patients are now diagnosed based on clinical and EMG criteria rather than biopsy criteria. Needle EMG examination of forearm muscles can help with the diagnosis of sIBM. Infectious and genetic muscle diseases can mimic sIBM and asymptomatic hyperCKemia may be a presenting feature.
LUMBOSACRAL PLEXOPATHY SECONDARY TO RETROPERITONEAL HEMATOMA: CORRELATING RADIOGRAPHIC IMAGING WITH ELECTRODIAGNOSTIC FINDINGS
Kacper Pierwola (Hershey, PA), Colleen Newhard (Hershey, PA), Aiesha Ahmed (Hershey, PA)

INTRODUCTION/BACKGROUND: Although it is not the most common underlying etiology of lumbosacral plexopathy (LSP), a retroperitoneal hematoma should be considered when evaluating a patient complaining of flank or back pain with lower extremity weakness, pain, and altered sensation. Imaging is a useful modality to confirm the variable causes of LSP, but EDX studies are a valuable adjunct in evaluation and prognostication.

CASE REPORT: A 65-year-old male with a history of atrial fibrillation on apixaban presented to the ER 4 days after falling onto his side complaining of back pain, leg pain/numbness, and difficulty with ambulation. Radiographic imaging revealed a 9.7 x 8.8 cm retroperitoneal hematoma which was managed conservatively and the patient was discharged home. EDX testing 15 weeks later revealed a femoral neuropathy with ongoing denervation of the iliopsoas, vastus medialis, and vastus lateralis. Physical examination at that time was notable for atrophy of the thigh.

SUMMARY/CONCLUSION: LSP secondary to retroperitoneal hematoma primarily results in sensory and motor deficits involving the femoral nerve (35%), but the obturator (9%) and lateral femoral cutaneous (4%) nerves can also be affected. Interestingly, the size and extent of the hematoma has not been shown to correlate with sensory and motor deficits, emphasizing the importance of the physical examination and EDX testing on evaluating the extent of nerve involvement.

Kacper Pierwola, MD
Resident and Fellow Member Award Recipient

PROXIMAL WEAKNESS WITH GAIT DISTURBANCE SECONDARY TO HYPOKALEMIC CHANNELOPATHY
Stephen Anderson (Columbus, OH), Jonathan Pedrick (Columbus, OH)

INTRODUCTION/BACKGROUND: Hypokalemic channelopathy is characterized by painless generalized muscle weakness usually affecting proximal muscles greater than distal muscles, and lower more than upper limbs. Episodes of weakness can last from minutes to several days, can be triggered by stress, and are often associated with low plasma potassium levels. Needle EMG can be used to discriminate other causes of intermittent muscle weakness and assist in the correct diagnosis of hypokalemic channelopathy.

CASE REPORT: A 32-year-old female, 19 weeks pregnant with twins, presented to the ER with worsening weakness for the past 2 weeks. She was admitted 2 days prior with progressive weakness, culminating with her legs buckling at work after which she could not walk. The patient endorsed weakness that was worse in the bilateral lower extremities, proximal greater than distal. She denied numbness or tingling, bowel or bladder incontinence, or visual disturbances. Laboratory studies were significant for elevated creatine phosphokinase, c-reactive protein, erythrocyte sedimentation rate, and hypophosphatemia, and decreased serum potassium level at 1.8 mEq/L. Needle EMG demonstrated positive fibrillation potentials and positive sharp waves in left upper and lower extremities with decreased amplitude and increased early recruitment. Weakness gradually improved with correction of potassium.

SUMMARY/CONCLUSION: Hypokalemic channelopathy can present like a myopathy and cause acute attacks of weakness in the setting of low serum potassium levels. Needle EMG can aid in narrowing the differential and assist in correctly diagnosing this neuromuscular disorder.
RHABODYMYOLYSIS ASSOCIATED WITH LEGIONELLA INFECTION
Lincoln Darla (Malden, MA), Ritu Bagla (Burlington, MA) Michal Vytopil (Peabody, MA)

INTRODUCTION/BACKGROUND: Rhabdomyolysis is characterized by muscle pain and elevation in creatine kinase (CK). Muscle necrosis leading to release of intracellular muscle constituents underlies this clinical syndrome. Potential causes include infections, toxins, hyperthermia, and trauma. Here we report a case of rhabdomyolysis in the setting of Legionella pneumonia.

CASE REPORT: A 50-year-old man was admitted with diffuse myalgias and proximal leg weakness resulting in 2 falls. Fever and cough had begun 4 days before the onset of myalgias. Medical history was notable for gout on daily colchicine. Chest X-ray performed upon admission revealed right lower lobe infiltrate, and he was started on levofloxacin. Examination was significant for fever (103.1°F) and mild symmetric proximal leg weakness (hip flexion 3+/5 and hip adduction 4/5, bilaterally). The remainder of neurological examination was normal. Laboratory testing demonstrated positive Legionella urinary antigen, and CK of 9227 IU/L. MRI of the thighs showed symmetric adductor musculature signal changes consistent with rhabdomyolysis or myositis. Needle EMG revealed myopathic units in proximal limb muscles, without features of muscle membrane irritability. CK gradually declined and was 446 IU/L on discharge 9 days later, along with improved muscle strength (normal hip adduction and 4/5 hip flexion). Muscle biopsy was contemplated but deferred due to spontaneous improvement.

SUMMARY/CONCLUSION: Systemic Legionella infection is a rarely reported cause of rhabdomyolysis, and should be thought of in patients presenting with pneumonia, myalgias, and elevated CK. Mechanism of the muscle involvement is unknown. Myotoxic medications such as colchicine may be a predisposing factor in the development of Legionella rhabdomyolysis.

Lincoln Darla, MD
Resident and Fellow Member Award Recipient

IS THERE AN ASSOCIATION BETWEEN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND OTHER AUTOIMMUNE DISORDERS? A NEW YORK STATE PLANNING AND RESEARCH COOPERATION SYSTEM DATABASE ANALYSIS
Sanjila Islam (Newark, NJ), Yueqing Zhang (Newark, NJ), Kevin Nolasco (Newark, NJ), Jaideep Vaidya (Newark, NJ), Vijay Atluri (Newark, NJ), Basit Shafiq (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: Chronic inflammatory demyelinating polyneuropathy (CIDP) has been associated with other autoimmune disorders in few case reports.

OBJECTIVE: To investigate the association of CIDP with other autoimmune disorders.

METHODS: Patient data were retrieved from the Statewide Planning and Research Cooperative System (SPARCS) database for 1998-2014 using the Principal Diagnosis Code for CIDP. We compared the incidence of 4 autoimmune disorders—Guillain–Barré syndrome (GBS), myasthenia gravis (MG), acute disseminated encephalomyelitis (ADEM), and systemic lupus erythematosus (SLE)—in CIDP to their incidence in multiple sclerosis (MS), an autoimmune disorder, and in migraine, a disorder without an autoimmune component.

RESULTS: We identified 2850 patients with CIDP, 29,808 with MS, and 27,5631 with migraines. The incidence of the above autoimmune disorders was significantly higher in the CIDP group compared to the MS and migraine groups, respectively (13.1% versus 0.7% versus 0.45%; p<0.0001). GBS was reported in 11.2% of CIDP, 0.11% of MS, and 0.03% of migraine patients (p<0.0001); MG was reported in 11.2% of CIDP, 0.11% of MS, and 0.03% of migraine patients (p<0.0001); GBS was reported in 11.2% of CIDP, 0.11% of MS, and 0.03% of migraine patients (p<0.0001); MG was reported in 11.2% of CIDP, 0.11% of MS, and 0.03% of migraine patients (p<0.0001); ADEM was reported in 0.07% of CIDP, 0.02% of MS, and 0.0007% of migraine (p=0.10); SLE was reported in 0.74% of CIDP, 0.35% of MS, and 0.37% of migraine (p<0.0015).

SUMMARY/CONCLUSION: CIDP patients are more likely to also develop other autoimmune disorders compared to patients with MS and migraine. Work is in progress to determine the temporal association between autoimmune disorders and CIDP and the role of age, gender, and comorbid conditions in the occurrence of autoimmune dysfunction in CIDP.
QUANTITATIVE ASSESSMENT OF MUSCLE SIZE AND STRUCTURE USING IMAGE PROCESSING TECHNOLOGY
Robert Smith (Houston, TX), Ekaterina Shanina (Houston, TX)

INTRODUCTION: MRI is a useful tool for detection of structural abnormalities in muscle due to denervation, disease, and aging. Increased signal intensity is the most common finding, but the degree and pattern of this change varies and is often difficult to evaluate. Automated methods may provide objective quantitation of muscle thickness and composition in the areas of interest.

OBJECTIVE: To evaluate the utility of automated post-processing of MRI images to compare normal and abnormal lumbar paraspinal muscle in young and elderly populations.

METHODS: MRI images were obtained from 4 groups of people: young normal, young abnormal (lumbar radiculopathy), elderly normal, and elderly abnormal. Images were de-identified and blindly assessed by 2 raters on 2 separate occasions. ImageJ software was used to analyze grayscale distributions within selected regions of interest. Cross-sectional areas (CSAs) of the paraspinal muscles were calculated. Analysis was performed at multiple segments within the axial plane at the level of intervertebral disks.

RESULTS: CSAs and signal intensity plot profiles for normal and radiculopathy patients were analyzed and compared. Chronic or active denervation changes were confirmed by needle EMG. Inter- and intra-rater reliability was excellent. Grayscale range was highest between normal and abnormal muscles in young individuals, and lowest in the elderly groups.

SUMMARY/CONCLUSION: This automated technique is reliable, user-friendly, and potentially applicable not only to patients with radiculopathies, but also to patients with other neuromuscular disorders. Reduced grayscale range in elderly groups results from sarcopenia.

IS GUILLAIN–BARRÉ SYNDROME DIFFERENT IN PAKISTAN?
Waseem Iqbal (Peshawar Cantt, Pakistan), Tahir Sayed (Islamabad, Pakistan), Wasim Wali (Quetta, Pakistan), Nadeem Ahmed (Rawalpindi, Pakistan), Aamir Butt (Rawalpindi, Pakistan), Zaheer Gill (Rawalpindi, Pakistan)

INTRODUCTION: Guillain–Barré syndrome (GBS) is an autoimmune inflammatory polyneuropathy presenting classically as a rapid, progressive ascending paralysis with global areflexia. The diagnosis of GBS is based upon history, relevant clinical examination, albuminocytological dissociation in cerebrospinal fluid, and characteristic electrophysiological studies. Acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and Fisher syndrome are 3 different variants of GBS described in the literature in addition to the classic acute inflammatory demyelinating polyneuropathy (AIDP). The geographical distribution of various electrophysiological subtypes of GBS has been described in the literature.

OBJECTIVE: To assess clinical presentations and subtypes of GBS in Pakistan.

METHODS: The study was conducted at CMH Lahore, Abbottabad, Quetta & Armed Forces Institute of Rehabilitation Medicine from January 2007 to February 2015. The relevant history, demographic features, clinical presentations, and subtypes of GBS in 211 patients (62.7% male, 37.3% female; average age: 37.36 years) fulfilling the clinical and EDX criteria were investigated.

RESULTS: Clinically, 66.8%, 17.8%, and 15.4% of the patients presented with ascending paralysis, simultaneous quadriparesis, and paraparesis, respectively. About 38.1% of the patients presented with cranial nerve involvement, 87.4% presented with areflexia, while 59.5% reported pain. GBS subtypes identified were AIDP (21.9%), AMAN (38.9%), AMSAN (35.6%), and Fisher syndrome (3.6%).

SUMMARY/CONCLUSION: GBS presents in the young, as an ascending paralysis, and the main subtypes of GBS in Pakistan are axonal, and this highlights the importance of local management guidelines and preventive medicine.
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AN ATYPICAL CASE OF ULNAR NEUROPATHY AT THE MID-FOREARM
Jordan Powell (Bethesda, MD), Matthew Miller (Potomac, MD), Edward Dolomisiewicz (Bethesda, MD)

INTRODUCTION/BACKGROUND: Ulnar neuropathy at the mid-forearm is exceptionally rare, and has only been reported twice within the literature (when in the absence of tumor, significant trauma, or diabetes mellitus), both of which reported entrapment from a fibrovascular band supplying blood to a hypertrophied flexor carpi ulnaris muscle.

CASE REPORT: A 45-year-old woman presented with a 4-year history of left-hand intrinsic weakness and atrophy. She had no neurologic symptoms or history of trauma. Physical examination revealed ulnar-distribution left hand weakness, no sensory deficits, and positive Tinel’s sign at the ulnar aspect of the forearm. NCSs showed decreased sensory nerve action potential and compound motor action potential amplitudes, with slowed conduction velocity in the forearm. Needle EMG showed reduced insertional activity and chronic neuropathic changes in the left adductor digiti minimi and first dorsal interosseous, with normal findings in the ulnar flexor digitorum profundus. A short segment incremental study demonstrated focal slowing throughout a large segment of the mid-forearm, 6.5-12.5 cm proximal to the wrist crease. Subsequent ultrasound revealed loss of fascicular architecture and marked enlargement of the ulnar nerve throughout this same segment of the forearm. An MRI with contrast showed corresponding ulnar nerve enlargement and no evidence of neural sheath tumor. She was recommended for surgical decompression of the ulnar nerve and neurotization of the pronator quadratus branch of the anterior interosseous nerve to the distal ulnar nerve.

SUMMARY/CONCLUSION: Although ulnar neuropathy at the elbow is a common EDX finding, clinicians must be mindful of other causes of ulnar neuropathy outside of conventional entrapment sites.

Jordan Powell, MD
Resident and Fellow Member Award Recipient

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A NOVEL CASE OF AXONAL FORM OF ADULT GUILLAIN-BARRÉ SYNDROME PRECEDED BY ACUTE RENAL FAILURE
Chichun Emily Sun (Hershey, PA), Sankar Bandyopadhyay (Hershey, PA)

INTRODUCTION/BACKGROUND: Guillain–Barré syndrome (GBS) is an acute/subacute form of polyradiculoneuropathy that can commonly cause ascending paraplegia and sensory deficits, and can result in quadriplegia and respiratory failure requiring intubation. There are different subtypes of GBS. Th axonal form is the predominant form in the pediatric population in the United States and many Asian countries. There is paucity of literature about such cases preceded by acute renal failure in adults.

CASE REPORT: A 72-year-old man presented with acute onset of paraplegia and areflexia shortly after acute renal failure, confirmed by laboratory testing, and was intubated for respiratory failure. Besides respiratory compromise, there was no cranial nerve or autonomic involvement. Sensory impairment was restricted to the lower extremities only. Infectious workup was unrevealing. Cerebrospinal fluid studies showed albuminocytologic dissociation. MRI of the brain and entire spine did not show any significant abnormalities. Needle EMG showed severe, generalized, axonal, motor and sensory polyneuropathy. GBS was diagnosed. The patient received a course of IVIg without improvement. Plasma exchange was subsequently performed. He was successfully extubated without any improvement of his motor and sensory profile.

SUMMARY/CONCLUSION: An acute axonal form of GBS causing diffuse motor and sensory neuropathy usually has an early age of onset, slower recovery, and incomplete resolution of symptoms. This is a novel case of an axonal variant of GBS preceded by renal failure, as per our review of literature for North America. A broad differential diagnosis should be kept in mind in patients with acute/subacute paraplegia preceded by acute renal failure.

Chichun Emily Sun, DO
Resident and Fellow Member Award Recipient
CHRONIC MOTOR NEURONOPATHY AS A UNIQUE PRESENTATION OF NIEMANN–PICK DISEASE TYPE C
Ahmad Yusuf Solaiman (Galveston, TX), Ahmad Shawafjeh (Galveston, TX)

BACKGROUND: Niemann–Pick disease type C is an autosomal recessive neurometabolic disorder associated with cognitive decline, movement disorders, vertical supranuclear gaze palsy, and seizures. The clinical spectrum ranges from a neonatal rapidly fatal disorder to an adult-onset chronic neurodegenerative disease. Chronic neuronopathy can be seen as paraneoplastic syndrome, but never reported in Niemann–Pick C.

CASE REPORT: A 39-year-old Caucasian female presented with recurrent falls, slowly progressive imbalance, dysarthria, oropharyngeal dysphagia, psychomotor slowing, apathy, and cognitive decline over the last 12 years. Examination showed generalized clasp knife spasticity, bilateral Babinski/Hoffmann, hyperreflexia in lower extremities, general dysmetria, and wide-based gait. Needle EMG/NCSs showed mild diffuse chronic neurogenic changes seen in proximal and distal upper and lower extremities, which relates to chronic lower motor neuron disease. Metabolic workup and brain MRI were unremarkable. Biochemical studies showed elevation of oxysterols and 7-ketocholesterol suggestive of a biochemical diagnosis of Niemann–Pick C. Whole Exome Sequencing showed a heterozygous mutation in the Niemann–Pick C gene which explains her neurological symptoms/findings, except those from the needle EMG.

CONCLUSION: Niemann–Pick C is characterized by visceral, neurological, and psychiatric symptoms. It's known that neurological/psychiatric symptoms are predominant in older children, adolescents, and adults. Vertical supranuclear gaze palsy, ataxia, and dysphagia have a high prevalence in patients older than 10 years. Our patient has these symptoms in addition to motor neuronopathy which was not explained by any vitamin deficiency or other etiology. This is the first case to report chronic motor neuronopathy in Niemann–Pick C.

A THIRD ENTRAPMENT SITE OF THE ULNAR NERVE
Drew Parkhurst (Lansing, MI), Rani Gehara (Okemos, MI), Michael Andary (East Lansing, MI), Ryan Fajardo (East Lansing, MI)

INTRODUCTION: There are few reports of isolated dorsal ulnar cutaneous nerve (DUC) neuropathy and most have failed to describe a consistent entrapment site.

OBJECTIVE: To describe entrapment of the DUC nerve secondary to extensor carpi ulnaris (ECU) tendinosis with ultrasound (US), EDX, and MRI results.

CASE REPORT: A 49-year-old female presented to the EMG clinic with right hand paresthesias on the dorsal ulnar side of the hand. She had a history of cervical spine fusion 8 years prior. The onset of symptoms was insidious as pain and paresthesias progressively worsened to the dorsal aspect of the ring and little fingers. The patient had been employed as a clerk requiring repetitive typing. Physical examination revealed 5/5 strength in ulnar-, median-, and radial-innervated muscles bilaterally. Needle EMG/NCSs demonstrated significantly decreased amplitude of the right DUC compared to the left. Amplitude was 4 μV on the right and 40 μV on the left. Needle EMG did not reveal fibrillation potentials in the right upper extremity, including ulnar-innervated muscles. Follow-up US and MRI demonstrated tendinosis of the ECU tendon with mild tenosynovitis with no injury to the triangular fibrocartilage complex or localized cyst.

SUMMARY/CONCLUSION: Tendinosis of the ECU should be considered as a possible etiology explaining DUC neuropathy. We present the first case with concomitant NCS, MRI, and US data.

Drew Parkhurst, DO
Resident and Fellow Member Award Recipient
GULLIAN–BARRÉ SYNDROME AS A COMPLICATION OF ATEZOLIZUMAB, A MONOCLONAL ANTIBODY AGAINST PROGRAMMED CELL DEATH LIGAND-1
Sri Raghav Sista (Peoria, IL), Editha Johnson (Peoria, IL), Gregory Blume (Peoria, IL)

INTRODUCTION/BACKGROUND: Guillain–Barré syndrome (GBS) is among the neuromuscular complications that have previously been reported with programmed cell death inhibitor agents like nivolumab, pembrolizumab, and ipilimumab. We report a case of GBS associated with atezolizumab, a monoclonal antibody against programmed cell death-ligand 1.

CASE REPORT: A 62-year-old gentleman presented with 2 days of right hand numbness and weakness. One month prior, he was started on atezolizumab for adenocarcinoma of lung. He received his second cycle 2 days before the first noted symptom. By the second day following symptom onset, his neurological examination was significant for movement with gravity eliminated in all extremities, decreased sensation to light touch in all limbs, and absent deep tendon reflexes. MRI of the brain and whole spine with and without contrast were unremarkable. Spinal fluid showed 17 nucleated cells with lymphocytic predominance but normal protein, glucose, and cytology. Further, spinal fluid also showed strong positivity for antibodies against Asialo-GM1, GD1a, and GD1B with weak positivity against GM1 and GM2. EDX study was consistent with acute inflammatory demyelinating polyneuropathy. After treatment with IVIg therapy and 1 month of rehabilitation, the patient was able to walk but with maximal support.

SUMMARY/CONCLUSION: To our knowledge this is the first report of atezolizumab associated with GBS, although we should emphasize that this was mentioned in manufacturer’s drug labelling. With the growing list of immune check point inhibitors associated with neuromuscular complications, it is of utility to the neurologist to familiarize oneself with various agents and their indications as they aid in early recognition.

Sri Raghav Sista, MD
Resident and Fellow Member Award Recipient

ULTRASOUND IN THE DIAGNOSIS OF MEDIAN NEUROPATHY PROXIMAL TO THE ELBOW
Paige Harrison (Baltimore, MD), Eric Buchner (Ellicott City, MD), Edward Soriano (Baltimore, MD)

INTRODUCTION/BACKGROUND: EDX testing is the gold standard for diagnosis of median neuropathy at the wrist and forearm, however these studies are of limited use when median neuropathy is proximal to the elbow. The case presented here highlights high-resolution ultrasound (US) as an complement to EDX testing in localizing proximal median neuropathy.

CASE REPORT: A left-handed 28-year-old male presented with complaints of paresthesia in a median distribution and pain in the right hand and forearm. He was involved in a motor vehicle collision 4 weeks prior requiring medical attention and IV placement at the right antecubital fossa. He noted onset of symptoms immediately after the IV was removed. Examination findings included altered sensation in median distribution of right hand, absence of weakness, and negative Tinel sign at the wrist. EDX testing was notable for reduced amplitude of right median sensory nerve to the middle finger, and evidence of muscle membrane instability in right abductor pollicis brevis, flexor digitorum superficialis, and pronator teres. All other EDX findings were normal. High-resolution US revealed enlarged median nerve (0.33 cm2) 7 cm proximal to medial epicondyle. Additionally, the nerve appeared to be surrounded by homogenous and hyperechoic soft tissue structure. The contralateral side was normal in size (0.11 cm2) and appearance. The patient has followup with physical medicine and rehabilitation and orthopedic surgery specialists to monitor symptoms and for possible intervention.

SUMMARY/CONCLUSION: High-resolution US was valuable in providing anatomical information for median neuropathy proximal to the elbow.

Paige Harrison, DO
Resident and Fellow Member Award Recipient
ULTRA-HIGH FREQUENCY ULTRASOUND AS A BIOMARKER IN AMYOTROPIC LATERAL SCLEROSIS

Paige Laverick (Winston-Salem, NC), Michael Cartwright (Winston Salem, NC)

INTRODUCTION: Ultrasound (US) of nerve and muscle has demonstrated promise as a biomarker in ALS. As US technology advances, resolution continues to improve. The goal of this study is to determine if an ultra-high frequency US (70 MHz transducer) can identify changes in nerve fascicles in individuals with ALS.

OBJECTIVE: To compare fascicle counts in the median nerves of individuals with ALS to those in healthy control subjects.

METHODS: Ten individuals with ALS will be evaluated with ultra-high frequency US, examining their bilateral median nerves at the wrists. Nerve area, fascicle count, and fascicle area will be determined and compared to previously collected values from 20 healthy individuals.

RESULTS: To date, 5 individuals with ALS have been studied (4 male, 1 female; mean age: 56.20 years). The mean area for the median nerve is 14.23 mm² compared to 10.83 mm² in healthy control subjects, fascicle count is 19.70 compared to 22.67 in healthy control subjects, and fascicle density is 1.39 fascicles/mm² compared to 2.09 fascicles/mm² in healthy control subjects.

SUMMARY/CONCLUSION: This study will provide insight into changes at a fascicle level, which can be obtained with ultra-high frequency US, in individuals with ALS. This may illuminate findings that can be used to improve diagnosis, prognosis, and monitoring of disease in the future.

THE ROLE FOR SURGICAL MANAGEMENT IN NEURALGIC AMYOTROPHY: A CASE SERIES


INTRODUCTION: Large observational studies of neuralgic amyotrophy (NA) suggest that greater than 50% of patients experience long-term sequelae. Emerging evidence suggests focal, hourglass-like constrictions develop in affected nerves, and that nerve surgery may improve patient outcomes.

OBJECTIVE: To present 2 cases of NA with persistent neuropathies managed surgically to improve function. Clinical features, EDX, neuroimaging, and neuropathology are presented.

CASE REPORT: Patient A presented with musculocutaneous, axillary, median, and anterior interosseous nerve (AIN) involvement. By 6 months post onset, there was clinical and EDX evidence of improvement in the musculocutaneous and median nerves, but not the axillary or AIN. Ultrasound demonstrated persistent inflammation of the involved nerves. Surgical exploration revealed focal constriction of the axillary nerve proximal to the quadrangular space and no function intraoperatively across this segment. A branch of radial nerve to the triceps was transferred end-to-side to the axillary nerve. The AIN was surgically decompressed along its course. Postoperatively, the patient regained deltoid and AIN function.

Patient B developed idiopathic axillary and suprascapular nerve (SSN) involvement (MRC 0/5, no motor units on needle EMG). By 9 months post onset, the axillary nerve improved (MRC 3/5, reinnervated motor units). SSN had no clinical or EDX improvement. MRI demonstrated focal constriction of the SSN proximal to the suprascapular notch. Surgical exploration revealed focal corkscrew compression and no function across this segment. The segment was excised; neuropathology demonstrated atrophy with regenerative clusters. Postoperatively, the patient regained active shoulder function.

CONCLUSION: Refractory neuropathy from NA should be investigated for focal nerve constrictions as surgical intervention can improve outcomes in these patients.

E. Ali Bateman, MD
Resident and Fellow Member Award Recipient
WEIGHTLIFTER’S CHEST ATROPHY
Sakinah Sabadia (New York, NY), Howard Sander (New York, NY)

INTRODUCTION/BACKGROUND: A 56-year-old male weightlifter presented with progressive bilateral medial pectoral muscle atrophy. He developed isolated thinning of his medial chest bilaterally over 2 years.

CASE REPORT: Chest examination revealed severe wasting of the bilateral inferomedial portions of the pectoralis major, in contrast to hypertrophy of the remainder of the pectoralis and other muscles. Strength, sensation, and reflexes were normal, apart from relative ankle hyporeflexia. NCSs were normal in the arms and left leg. Needle EMG showed fibrillation potentials and positive sharp waves in the pectoralis major sternal heads bilaterally. The right sternal head had a single motor unit firing pattern with a prolonged duration polyphasic motor unit. Motor recruitment was absent in the left sternal head. Needle EMG was normal in bilateral clavicular heads. These findings demonstrate severe bilateral medial pectoral nerve dysfunction.

SUMMARY/CONCLUSION: The pectoralis major muscle is innervated by the medial (MPN) and lateral (LPN) pectoral nerves. The MPN innervates the pectoralis major sternocostal portion, while the LPN supplies the remainder, including the clavicular head. The LPN passes medially to the pectoralis minor muscle before reaching the pectoralis major. The MPN has a variable course, usually piercing through the pectoralis minor before innervating the pectoralis major, less often coursing laterally around the pectoralis minor first. During the trajectory of the MPN within the pectoralis minor, pectoralis minor hypertrophy could result in MPN compression causing denervation and atrophy of the sternocostal portion of the pectoralis major muscle. Early recognition of medial pectoral neuropathy could prompt a recommendation to adjust any weightlifting regimen.

Disclosures:
Howard Sander - Consultant for CSL Behring.

TARGETED GENETIC TESTING IN THE EVALUATION OF NEUROPATHY
Sasha Zivkovic (Pittsburgh, PA), Michael Isfort (Pittsburgh, PA), Araya Puwanant (Pittsburgh, PA), Paula Clemens (Pittsburgh, PA), David Lacomis (Pittsburgh, PA)

INTRODUCTION: Inherited neuropathies are a heterogeneous group of disorders caused by mutations in more than 80 genes affecting 1/2500. Recent advances in next-generation sequencing facilitated clinical use of genetic testing in neuropathy evaluation.

OBJECTIVE: To describe the use of targeted next-generation sequencing in evaluation of patients with neuropathy.

METHODS: Eighty five patients with peripheral neuropathy underwent next-generation sequencing with targeted panel of 70 genes between May 2017 and February 2019.

RESULTS: The cause of neuropathy was found in 15 patients (18%); 4 had single putative pathogenic mutations of autosomal recessive disorders (5%). There were 39 patients with genetic variants of unknown significance (VUS, 46%), and testing was negative in 27 (32%). Identified causes included Charcot–Marie–Tooth (CMT) disease type 1A (n=8); hereditary neuropathy with liability to pressure palsies and CMT1X (n=2); and CMT1B, 2E, and hereditary sensory and autonomic neuropathy (HSAN) type 2B (n=1). Heterozygous mutations were found in genes associated with CMT2S, 4C, 4F, and 2B1/HSAN6 (n=1). Positive genetic testing was found in 5/6 patients with familial and 3/11 with sporadic demyelinating neuropathy, and in 1/11 patients with familial and 1/25 with sporadic axonal neuropathy. Overall, genetic testing was positive in 9/27 patients with familial and 5/57 with sporadic neuropathy.

SUMMARY/CONCLUSION: Positive family history was associated with higher yield of genetic testing in patients with suspected inherited neuropathy, especially with demyelinating neuropathy. The yield was lowest in patients with sporadic axonal neuropathy. High occurrence of VUS may suggest that some variations may represent unrecognized pathogenic mutations.
CONCOMITANT CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY AND MYASTHENIA GRAVIS: TWO CASES
Nan Jiang (Birmingham, AL), Mohamed Kazamel (Birmingham, AL)

INTRODUCTION/BACKGROUND: Few cases of coexisting chronic inflammatory demyelinating polyneuropathy (CIDP) and seropositive myasthenia gravis (MG) are reported. However, there are no reports on coexistence of CIDP with seronegative MG or on response to treatment.

CASE REPORT: (1) A 38-year-old African American female presented with progressive sensory deficit and weakness over 5 months. She developed left ptosis, diplopia, mild dysphagia, chewing fatigue, and dyspnea a few weeks prior. EDX study was consistent with acquired demyelinating polyneuroradiculopathy. Repetitive nerve stimulation (RNS) testing was equivocal. Acetylcholine receptor (AChR-Ab) and muscle specific kinase antibodies were negative. Single-fiber EMG (SFEMG) of the frontalis muscle showed that 83% of tested pairs (n=6) were abnormal with mean consecutive difference of 72.3 μs. Bulbar symptoms improved significantly with average doses of prednisone and pyridostigmine, but not limb muscle strength, even with plasma exchange. (2) A 65-year-old British male developed dysphagia, slurred speech, ptosis, diplopia, and fatigue 3-4 weeks after a flu shot. MG was diagnosed based on positive AChR-Ab and RNS study. Bulbar symptoms improved significantly with IVIg; however, he developed paraparesis and difficult walking a few months later. EDX study was consistent with acquired demyelinating polyneuroradiculopathy. Cerebrospinal fluid analysis showed albuminocytologic dissociation. His limb weakness has been refractory to treatment, currently requiring 2 g/kg IVIg every 3 weeks, mycophenolate, and prednisone medium dose.

SUMMARY/CONCLUSION: The first case underscores the importance of performing SFEMG on cranial muscles in cases of CIDP with cranial nerve involvement. In both cases, bulbar symptoms were more responsive to immunomodulatory treatment than limb symptoms.

NEOPLASTIC BRACHIAL PLEXOPATHY VERSUS BRACHIAL PLEXITIS/CERVICOBRACHIALGIA/RADICULOPATHY
Oksana Haiko (Kyiv, Ukraine), Roman Tretiakov (Kyiv, Ukraine), Yulianna Halii (Kyiv, Ukraine)

INTRODUCTION/BACKGROUND: Neoplastic brachial plexus compression (NBPC) usually involves the inferior trunk or medial cord of the brachial plexus (BP).

CASE REPORT: A 49-year-old man presented with a 5-month history of progressive neck, shoulder, and chest pain on the right side not relieved with analgesic drugs for few last weeks as well as numbness of the arm. Previous chest X-rays were normal; cervical spine MRI detected moderate degenerative changes. Physical examination revealed painful but not restricted movements of the right shoulder and neck, tactile hypoesthesia on the medial brachial area of the arm, weakness and wasting of the latissimus dorsi (LDM) and pectoralis major muscles (PMM), and positive Spurling test and Tinel sign over the infraclavicular fossa. His NCs were normal and his needle EMG showed denervation and neurogenic changes only in the LDM and PMM. Brachial plexus MRI scan revealed osteolytic destruction of 2-3 ribs with a pronounced soft tissue component adjacent to the bones that compresses the subclavian part of the BP. A further CT with contrast enhancement in 3 days revealed a pancreas carcinoma.

SUMMARY/CONCLUSION: In this case report, clinical and electrophysiological investigations suggested BP pathology with involvement of its short branches (pectoral nerve, thoracodorsal nerve, and medial cutaneous nerve of the arm). MRI revealed the NBPC. Neoplastic brachial plexopathy can show different and sometimes unusual clinical patterns and mimic symptoms of plexitis, shoulder orthopedic problems, or cervical spine pathology.
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NEUROPATHIC ARTHROPATHY OF THE SHOULDERR
AND SCAPULA FRACTURE AS INITIAL SYMPTOMS OF
IDIOPATHIC SYRINGOMYELIA
Oksana Haiko (Kyiv, Ukraine), Sergiy Strafun (Kyiv, Ukraine), Roman
Tretiakov (Kyiv, Ukraine), Yulianna Halii (Kyiv, Ukraine)

INTRODUCTION/BACKGROUND: The clinical symptoms,
severity, and time of their occurrence can widely vary in patients
with syringomyelia (SM).

CASE REPORT: A 40-year-old man was admitted to our institute
with deformation and restricted movements (RMs) of the
left shoulder (LS). About 3 months ago he noticed a painless
 crunch, shoulder swelling, and RMs after overhead lifting of the
arm. Shoulder ultrasound showed bursitis. After 1.5 months of
unsuccessful conservative treatment, the patient was further
investigated with shoulder X-ray, CT, and MRI. He was presented
with a preliminary diagnosis of possible scapula fracture, synovial
chondromatosis, synovioma, or pyrophosphate arthropathy of
the LS. Physical examination indicated: non-painful RMs and
deformity of the LS; dissociated sensory disturbances in the form
of the "half jacket," reduced tendon reflexes in the left upper
limb, and increased knee reflexes; and weakness and wasting of
the left first dorsal interosseous muscle. The patient underwent
NCSs/needle EMG and shoulder, whole spine, and brain MRI.
MRI scans revealed SM from C2 to T8 level without brain and
craniovertebral abnormalities, shoulder joint pathology (shoulder
dysplasia and osteoarthritis, bursitis, and soft tissue calcification),
and scapula fracture. NCSs demonstrated severe elbow ulnar
neuropathy and reduction in the median and radial sensory
potential amplitudes; needle EMG-neurogenic changes were
found only in ulnar-innervated muscles on the affected side.

SUMMARY/CONCLUSION: Neuropathic changes of the bones
and joints can be seen in 20-25% of all SM cases. Shoulder
involvement and fractures are quite rare. Rapid onset of SM can
occur with bone and joint pathology only.

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RISK OF DYSPNEA WITH WATER IMMERSION IN
PATIENTS WITH PHRENIC NEUROPATHIES
Rocio Vazquez Do Campo (Rochester, MN), Shahe Sheheli (Rochester, MN),
Pritikanta Paul (Rochester, MN), Hongyan Bi (Rochester, MN), Robert
Vassallo (Rochester, MN), Christopher Klein (Rochester, MN)

INTRODUCTION: Phrenic neuropathies result in diaphragmatic
weakness or paralysis often presenting with dyspnea on exertion
and orthopnea. During water-related activities (bathing, swimming)
diaphragmatic descent is further compromised by the effect of hydrostatic pressure over abdominal contents worsening
respiratory distress.

OBJECTIVE: To bring awareness of the risk of dyspnea with water
immersion in patients with phrenic neuropathies and to assess
potential risk factors for its occurrence.

METHODS: We compared demographics, body mass index,
smoking history, comorbid cardiopulmonary conditions,
respiratory symptoms, chest X-ray/CT, "sniff" test, phrenic NCSs,
diaphragm needle EMG and ultrasound (US), and pulmonary
function parameters, including vital capacity, maximal inspiratory
and expiratory pressures (MIP, MEP), and MEP/MIP ratio
between phrenic neuropathy patients with documented dyspnea
in water and control subjects.

RESULTS: We identified 21 patients and 23 control subjects
among 535 phrenic neuropathy cases diagnosed January 1, 2000
to December 31, 2018. Patients were predominantly middle-
age (85.7% male; mean age: 55 years, range: 31-79) with right-
sided (47.6%) or bilateral (52.4%) phrenic neuropathies most
commonly due to Parsonage–Turner syndrome (76.2%). Dyspnea
with water immersion was the only symptom in 1 patient, the
presenting respiratory symptom in 8/21 (38.1%), resulting in
near- drowning in 3/21 (14.3%). Left phrenic involvement was
more common in control subjects (p<0.002); other variables were
not significantly different between groups.

SUMMARY/CONCLUSION: Dyspnea in water occurs most
commonly with right-sided and bilateral phrenic neuropathies.
Clinico- demographic features, pulmonary function, EDX tests,
and diaphragm US do not strongly predict risk. All phrenic
neuropathy patients should be counseled about risks of water
exposure.

Rocio Vazquez Do Campo, MD
Resident and Fellow Member Award Recipient
RECONFIRMATION OF NEWLY DISCOVERED RISK FACTORS OF DIABETIC PERIPHERAL NEUROPATHY
Ming-Hong Chang (Taichung, Taiwan)

OBJECTIVE: To investigate the major determinants of diabetic peripheral neuropathy (DPN) in patients with type 2 diabetes, especially considering both the newly discovered and traditional risk factors.

METHODS: A total of 2,837 patients with type 2 diabetes were recruited in Taiwan and screened for DPN using the Michigan Neuropathy Screening Instrument. We analyzed biochemistry data, including hypoglycemia, albuminuria, and variability of fasting sugar. A stepwise selection of variables was used based on the Akaike Information Criterion (AIC) and the Schwarz Criterion (SC). Multivariate analysis was performed using the identified variables obtained from stepwise selection.

RESULTS: Among the recruited patients, 604 (21.3%) were found to have DPN in which 275 patients were randomly selected and paired with 351 consecutive patients with type 2 diabetes without DPN. The results of the stepwise selection showed that the presence of albuminuria had the lowest values of AIC and SC, which indicates the best predictive performance. Multivariate analyses demonstrated that the presence of previous hypoglycemia, albuminuria, and greater glycemic variability significantly increased the risk of DPN, with a corresponding odds ratio of 2.59 (95% CI 1.08-6.23), 2.22 (95% CI 1.36-3.62), and 1.76 (95% CI 1.16-2.67), respectively.

SUMMARY/CONCLUSION: Albuminuria is an important predictor of DPN in adults with type 2 diabetes, and if present, previous hypoglycemic events might be the most potent risk factor for type 2 DPN.

CLINICAL SPECTRUM OF POSTSURGICAL PARSONAGE–TURNER SYNDROME
Vasudeva Iyer (Louisville, KY)

INTRODUCTION: Parsonage–Turner syndrome (PTS) is a rare disorder characterized by acute onset of severe pain in the shoulder/ scapular area, followed by muscle weakness in the distribution of nerves arising from the brachial plexus (BP). Surgical procedures are known to be one of several preceding events in patients developing PTS. Reports of single cases or small series of postsurgical PTS (PSPTS) abound, but the pattern of neural involvement in a large series is unavailable.

OBJECTIVE: To describe the clinical spectrum of PSPTS in a large series.

METHODS: A retrospective chart study (covering 10 years) showed 154 patients diagnosed with PTS; the clinical criteria included new onset of severe pain 2 days to 4 weeks after surgery followed by weakness of muscles innervated by 1 or more nerves derived from the BP. EDX criteria included documentation of denervation localizing to the BP or its branches.

RESULTS: Patients who underwent surgery at remote body part (19 cases) were considered definite PSPTS, and those who had a surgical procedure in the ipsilateral limb (27) or cervical spine (5) probable PSPTS. The most common single nerve affected was anterior interosseous nerve (AIN) (33%), followed by the posterior interosseous (12%) and suprascapular (9%) nerves; the lower trunk was more frequently involved than the upper trunk.

SUMMARY/CONCLUSION: The clinical pattern of PSPTS seen in our facility appears different from that reported in the literature, especially the significant AIN involvement. It is unclear whether this is due to high proportion of patients coming through hand clinics.
DIAGNOSIS AND TREATMENT OF PROXIMAL LEVEL TUNNEL NEUROPATHIES OF UPPER EXTREMITY
Albina Tretiakova (Kyiv, Ukraine), Lidia Chebotariova (Kyiv, Ukraine), Igor Tretyak (Kyiv, Ukraine), Alexander Gatskiy (Kyiv, Ukraine), Ludmila Suliy (Kyiv, Ukraine), Oleksandr Solonovych (Kiev, Ukraine), Roman Tretiakov (Kyiv, Ukraine)

INTRODUCTION: Tunnel neuropathies of the upper extremity at the proximal level are difficult to recognize; atypically manifested cases are frequently found.

METHODS: We analyzed data obtained from 22 patients (77.3% male; mean age: 41 years) with compression mononeuropathies: tunnel neuropathy of the suprascapular (5), axillary (6), radial (8), and long thoracic (3) nerves. We used clinical evaluation, NCSs, needle EMG, ultrasound of nerve trunks. In 11 (50%) patients with tunnel neuropathies, after the decompression/neurolysis a Neuro-Si 3M neurostimulation system (Vel, Ukraine) was installed. In 3 severe cases of axonal nerve damage, neurolysis was used.

RESULTS: In all cases, to determine the indications for the choice of surgical treatment of compression mononeuropathies, an individualized approach based on an evaluation of the degree of loss of functional capacity of nerve structures was used. Positive dynamics was observed in 20/22 patients. The application of the method of prolonged electrostimulation (after 3-6 months) in 11 patients allowed for a more complete restoration of motor function. Indicators of treatment effectiveness were (1) restoration of the function of muscles innervated by the corresponding nerves in the form of an increase in M responses and (2) signs of effective reinnervation according to the needle EMG data (decrease/absence of spontaneous activity, appearance of motor unit action potentials of sufficient amplitude and duration).

SUMMARY/CONCLUSION: Needle EMG helps to identify anatomical abnormalities, exclude other diagnoses, and minimize risks of surgical decompression. The application of the long-term electrostimulation technique allows us to achieve a more complete restoration of motor function.

CASE OF VASCULITIC NEUROPATHY FOLLOWING PNEUMOCOCCAL VACCINATION
Khatuna Gurgenashvili (Chambersburg, PA), Aiesha Ahmed (Hershey, PA)

INTRODUCTION/BACKGROUND: Several autoimmune disorders have been linked to vaccination. One that stands out is Guillain–Barré syndrome (GBS) following influenza vaccine. Molecular mimicry is a proposed mechanism. As opposed to GBS, the vasculitic neuropathy is a rare subtype of immune-mediated neuropathy. It may or may not be associated with systemic vasculitis. The most common phenotype is multifocal neuropathy known as mononeuritis multiplex. To the best of our knowledge distal symmetric axonopathy due to vasculitic neuropathy has not been described following pneumococcal vaccination.

CASE REPORT: A 60-year-old previously healthy non-diabetic woman developed purpuric rash 3 days after she received a pneumococcal vaccine. The rash was biopsied showing vasculopathy. For persistent eosinophilia that was noted after vaccination she underwent bone marrow biopsy without any evidence of malignancy. She developed acute onset lower extremity weakness worse in distal muscles. She became nonambulatory prompting her admission to neurology service. Cerebrospinal fluid was normal, spine MRIs were negative. NCSs/needle EMG revealed acute axonal neuropathy. She was treated with IVIg for possible axonal GBS without any improvement. A radial sensory nerve biopsy was undertaken showing perivascular lymphocytes in the epineurial connective tissue. Rheumatology was consulted and confirmed the diagnosis of eosinophilic granulomatosis with polyangiitis. The patient was treated with high dose steroids, cyclophosphamide followed by azathioprine.

SUMMARY/CONCLUSION: Vasculitic neuropathy is a rare entity. When it occurs, the typical presentation is multifocal neuropathy. Here, we describe the unique case of vasculitic neuropathy that developed in the setting of pneumococcal vaccination and presented as a distal symmetric axonal neuropathy causing weakness.
CONCURRENT ONSET OF AUTOIMMUNE DIABETES MELLITUS AND DEMYELINATING NEUROPATHY: CASE REPORT AND REVIEW OF THE LITERATURE
Jacob Manske (Chicago, IL), Ryan Jacobson (Chicago, IL)

INTRODUCTION/BACKGROUND: The relationship between diabetes mellitus and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) has been a topic of debate. Here, we present an individual who simultaneously presented with CIDP and antibody-positive type 1 diabetes.

CASE REPORT: A 32-year-old male, previously healthy, presented with 3 months of progressive distal lower extremity paresthesia and weakness. Initial neurologic examination showed weakness in bilateral ankle dorsiflexion, eversion, and inversion, as well as diffuse areflexia and distal lower extremity sensory loss. On presentation hemoglobin A1C was elevated at 11.8%. Anti–glutamic acid decarboxylase (GAD) antibodies were also elevated, consistent with a new diagnosis of autoimmune or type 1 diabetes. NCSs demonstrated slowing of conduction velocity with evidence of conduction block and temporal dispersion in the peroneal and tibial nerves. F responses were absent. Based on these results and the time course of symptoms, a diagnosis of CIDP was made. Treatment with methylprednisolone and IVIg was given, followed by maintenance IVIg infusions. At followup 6 months later, he had slowly improved and neurologic examination showed normal strength.

SUMMARY/CONCLUSION: A simultaneous onset of CIDP and type 1 diabetes would seemingly support an association between the 2 conditions. At least 1 other similar case report of a simultaneous presentation was found in the literature. However, population-based studies have not found an association between CIDP and type 1 or type 2 diabetes. Larger population-based studies are still needed to address this question. In the meantime, clinicians should consider dysimmune neuropathies in patients with diabetes of recent or remote onset in the appropriate clinical context.

A CASE OF ACUTE-ONSET CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY WITH POSITIVE ANTI–NEUROFASCIN-155
Leila Darki (Los Angeles, CA), Said Beydoun (Los Angeles, CA)

INTRODUCTION/BACKGROUND: Anti–Neurofascin-155 (NF-155) antibodies occur in a subset of acute-onset chronic inflammatory demyelinating polyneuropathy (CIDP) patients with distal dominant involvement and tremor.

CASE REPORT: A 47-year-old female was referred to us with 3 years of progressive weakness and tremor. Retrospectively, symptoms started acutely with painful ascending weakness 4 days after a diarrheal illness. Cerebrospinal fluid protein was mildly elevated (59 mg/dl). She was diagnosed with Guillain–Barré syndrome (GBS) and treated with 2 g/kg IVIg with no improvement. Symptoms continued to progress with no response to subsequent IVIg. Examination 3 years later demonstrated postural hand tremor. MRC muscle strength was 3/5 in distal and 4/5 in proximal upper extremities. Strength in lower extremities was 4/5 proximally and 0/5 distally. Reflexes were preserved except for absent Achilles. Sensory examination was normal. EDX study showed significant motor axonal neuropathy with marked reduction in compound muscle action potential amplitudes and normal sensory responses. Workup for metabolic etiologies and serum immunofixation were unremarkable. IgG antibody to NF-155 by Western blot was positive.

SUMMARY/CONCLUSION: IgG NF-155 testing should be considered in patients presenting with an acute-onset CIDP resembling GBS because of potential therapeutic implications and refractoriness to IVIg treatment. Rapidly progressive distal motor neuropathy has been described in positive anti–NF-155 CIDP cases. This case is unique as (1) the patient presented as GBS but continued to progress, manifesting as acute-onset CIDP, and (2) EDX studies showed predominant axonal loss. Treatment with rituximab has been considered in this case.
REFERENCE VALUES FOR CONDUCTING NERVE ULTRASOUND IN ADULT HEALTHY SUBJECTS
Jun Tsugawa (Fukuoka, Japan), Hiromu Ogura (Fukuoka, Japan), Maiko Doi (Fukuoka, Japan), Shinji Oma (Fukuoka, Japan), Toshio Higashi (Fukuoka, Japan), Yoshio Tsuboi (Fukuoka, Japan)

INTRODUCTION: Nerve ultrasound (NUS) is useful for evaluating the condition of nerves and can inform the diagnoses of several types of neuromuscular disease, especially demyelinating neuropathy. However, as NUS procedures differ slightly among facilities and examiners, there are consequences for the differential performance of NUS.

OBJECTIVE: To standardize NUS procedures and reference values to help the diagnosis of neuromuscular disease.

METHODS: NUS was administered to 21 adult healthy subjects (4 females; age: 28±9.0 years; height, 166.5±7.7 cm) according to a standardized procedure, and the results obtained were compared to those of previous studies. Following 8 nerves (median, ulnar, radial, peroneal, tibial, sural, vagus, and C6 cervical), a total of 32 cross-sectional areas were examined using an ultrasound machine with a 9-22 MHz linear-array transducer.

RESULTS: Most of the evaluated nerves indicated sizes similar to those observed in previous studies, while some of the recorded sizes tended to be slightly smaller than those found by previous studies. Our relatively small sample size composed of younger subjects than those enrolled by other investigations may account for these findings.

SUMMARY/CONCLUSION: Most of the NUS data acquired in the present study can be applied as NUS reference values. However, data from older subjects are needed for more accurate NUS reference values.

A RARE GENETIC ETIOLOGY OF HEAD DROP
Vinod Ravikumar (Saratoga, CA), Kunal Desai (Harrison, NY)

INTRODUCTION/BACKGROUND: Head drop is defined as a chin-on-chest abnormality with neck extensor weakness or increased tone in neck flexor muscles. It impairs activities of daily living including any movement with a forward vision component.

CASE REPORT: A 56-year-old woman presented with difficulty holding up her head upright while driving, and while at the hairdresser. She noted worsening fatigue, dysphagia, muscle soreness, balance, and difficulty projecting her voice. Examination is significant for tongue fasciculations, dysarthria, and weakened neck flexion compared with extension. Proximal arm weakness, hyperreflexia, dysmetria, and an unsteady ataxic gait were prominent. Family history includes a brother with “tongue dystonia.” Contrast-enhanced brain MRI demonstrated cerebellar and brainstem atrophy. Needle EMG was significant for evidence of diffuse lower motor neuron dysfunction of cranial and cervical segments. Vitamin B12, thyroid function, creatine kinase, acetylcholine receptor antibody, and autoimmune panel were within normal limits. Cerebellar and motor neuron dysfunction, in the setting of an MRI showing brainstem and cerebellar atrophy, raised suspicion for a genetic disorder. Sequencing analysis was performed, revealing heterozygous pathogenic variant in the SPG7 gene (A510V).

SUMMARY/CONCLUSION: Hereditary spastic paraplegia is a group of inherited diseases featuring progressive corticospinal tract degeneration, with the subtype spastic paraplegia type 7 (SPG7) caused by a mutation in the paraplegin gene. SPG7 is characterized by adult-onset progressive weakness, spasticity, hyperreflexia, dysphagia, dysarthria, cerebellar ataxia, amyotrophy, and motor and sensory neuropathy, most of which our patient experienced. This patient’s family history may offer insights into the hereditary pathway, as autosomal dominant variants have been described.

Disclosures:
Vinod Ravikumar - Stock ownership in Solid Biosciences.
TRAUMATIC NEUROPATHY OF THE MEDIAL ANTEBRACHIAL CUTANEOUS NERVE: A LESS APPRECIATED CONDITION

James Noto (Hershey, PA), Sankar Bandyopadhyay (Hershey, PA)

INTRODUCTION/BACKGROUND: Neuropathy of the medial antebrachial cutaneous (MAC) nerve is a diagnosis that is infrequently documented outside of the postsurgical setting or association with proximal brachial plexus lesions. Only 6 cases have been reported in the literature.

CASE REPORT: A 22-year-old gentleman presented with left elbow pain and numbness of the medial forearm and hand following a fall from a skateboard. X-rays showed moderate soft tissue edema over the posterior aspect of the left forearm and elbow but no joint effusion or fracture. Examination was significant for left elbow swelling and tenderness, normal muscle bulk, full strength, intact reflexes, and decreased sensation to pinprick of the medial left forearm with intact sensation in the hand. Four months after the injury, EDX testing was ordered without a mention of any possible MAC involvement by the ordering provider. NCSs revealed absence of the left MAC sensory response with a normal comparative study in the right arm. Ulnar sensory and motor NCSs were normal. Needle EMG of selected muscles of the left arm and cervical paraspinal muscles were normal. A non-contrasted MRI of the left elbow revealed a fluid collection over the olecranon with a fluid–fluid level as well as edema in the dorsal forearm subcutaneous tissues around the course of the MAC. These findings were consistent with an olecranon hematoma causing bursitis and generalized edema that resulted in a focal neuropathy of the left MAC.

SUMMARY/CONCLUSION: MAC injury should be suspected with sensory disturbance of the forearm following elbow trauma and can be evaluated by comparative EDX testing.

James Noto, DO
Resident and Fellow Member Award Recipient

SPINAL ACCESSORY NEUROPATHY: A RETROSPECTIVE CHART REVIEW OF MORE THAN 200 CASES

Michael Christiansen (Scottsdale, AZ), Akta Patel (Scottsdale, AZ), Leslie Zuniga (Phoenix, AZ), Nan Zhang (Scottsdale, AZ), Julie Khoury (Scottsdale, AZ), Ruple Laughlin (Rochester, MN), Benn Smith (Scottsdale, AZ)

INTRODUCTION: The major causes of spinal accessory (SA) nerve injuries are thought to be well known; however, there are limited large retrospective reviews identifying the most common etiologies.

OBJECTIVE: To identify the major causes and characteristics of SA nerve injuries.

METHODS: All patient records with EDX confirmation of SA neuropathy between January 1, 1994 and December 31, 2017 were reviewed. Clinical and demographic data for each patient were collected.

RESULTS: We identified 203 patients in our cohort with EDX confirmation of SA neuropathy in 118 males (58%) and 85 females (42%) (median age: 47 years, range: 15-84). The most common etiology was postoperative trauma (55.2%), with lymph node biopsy as the most common surgical type (42.9%). Idiopathic or presumed inflammatory causes represented the next most common cause (18.7%) followed by other external trauma (15.3%), which typically occurred more often in men (83.9%), and most often was trauma secondary to motor vehicle accidents (61.3%).

SUMMARY/CONCLUSION: This retrospective review provides evidence regarding the major causes of SA neuropathy. Future studies could be undertaken to evaluate whether etiology or demographic factors play a role in predicting prognosis or recovery.
NEUROPHYSIOLOGICAL DISSONANCE IN THE DIAGNOSIS OF MUCOPOLYSACCHARIDOSIS

Oleksandr Solonovych (Kiev, Ukraine), Albina Tretiakova (Kyiv, Ukraine), Lidia Chebatariova (Kyiv, Ukraine), Ludmila Suliy (Kyiv, Ukraine)

INTRODUCTION: Most types of mucopolysaccharidosis are accompanied by gross changes in the central and peripheral nervous systems.

METHODS: Data of 16 children aged 4-15 with various types of mucopolysaccharidosis were analyzed; 7 underwent motor and sensory NCSs, short-latency somatosensory evoked potentials (SSEPs), and transcranial magnetic stimulation (TMS).

RESULTS: In all cases, the conduction disturbance on the median nerves was determined. In 14 children, the changes were from moderate to pronounced; in 2, motor fibers were preserved, but there was a marked decrease in sensitive fibers (less than 30 m/s). Elbow nerves suffered much less frequently, which was confirmed in 5/16 cases. Four showed a significant increase in central motor conduction time on 1 or both sides, which correlated with MRI data (spinal cord compression at the cervical level). SSEPs indicated pronounced changes in the peripheral and spinal components (at the border of registration) in 6 patients. The remaining 10 children showed a moderate increase in the latency of N11, N13, and/or inter-peak intervals. Parameters of the latent periods and amplitudes of the cortical components were within the normal range.

SUMMARY/CONCLUSION: The use of needle EMG, SSEPs, and TMS allows assessment of the level and extent of damage, which is essential for solving the problem during surgical treatment. However, the absence of deviations in the parameters of the cortical components (according to SSEPs) contradicts clear conduction disturbances along the afferent fibers at different levels. This dissonance can be partially explained by the relative integrity of conduction along type Aβ fibers.

A CASE OF EXEMESTANE-INDUCED CARPAL TUNNEL SYNDROME

Melissa Lau (Columbus, OH), William Pease (Columbus, OH)

INTRODUCTION/BACKGROUND: Peripheral neuropathies are the most common neurotoxic side effect of chemotherapy use, particularly polyneuropathies. Rarely, mononeuropathies are observed. In the case of exemestane, an aromatase inhibitor used to treat breast cancer, CTS is a rare side effect.

CASE REPORT: A 51-year-old female with breast cancer currently on exemestane with symptomatic cervical stenosis and fibromyalgia presented with 2 months’ duration of bilateral whole hand numbness and paresthesias; her symptoms were worse with typing for her part-time job, and alleviated by stretching. Examination revealed intact strength and sensation to light touch in bilateral upper limbs, and negative Spurling sign. On EDX study, bilateral median nerve sensory studies had reduced amplitude across the carpal tunnel; additionally the right side also had had prolonged peak latency on sensory NCSs and high normal onset latency on motor NCSs. Bilateral ulnar and radial NCSs and upper limb needle EMG testing were unremarkable. Her EDX study was consistent with bilateral CTS (mild on the left and mild-to-moderate on the right).

SUMMARY/CONCLUSION: Immunohistochemical stains have identified estrogen receptors in the transverse carpal tunnel ligament and flexor tendons. As such, sex steroid treatments such as exemestane can cause fluid accumulation around the flexor tendons and predispose patients to CTS symptoms. However, exemestane rarely causes severe CTS; patients generally tolerate its musculoskeletal side effects well, with less than 1% of patients discontinuing its use because of CTS.
RUCKSACK AND BODY ARMOR USE RESULTING IN SPINAL ACCESSORY NERVE PALSY IN ACTIVE DUTY SOLDIER

Jordan Powell (Bethesda, MD)

INTRODUCTION/BACKGROUND: Rucksack palsy is a well-described entity in which a prolonged load over the shoulders results in a brachial plexus palsy due to either traction or a compressive injury. However, spinal accessory nerve (SAN) palsy following a similar load has only once been described in the literature. Most literature on SAN injury focuses on either iatrogenic or acute traumatic injuries.

CASE REPORT: A 29-year-old active duty male soldier presented with left shoulder pain and weakness with shrugging exercises. His symptoms began gradually 5 years prior during which he was frequently wearing body armor and carried rucksacks for his military occupation. During this time, he noticed progressive weakness and pain when carrying the loads. He underwent a left shoulder arthroscopy without substantial relief. Physical examination showed left-sided lateral scapular winging on provocative testing, and no other neurologic findings. When stimulating at Erb’s point and recording over the left upper trapezius, a NCS demonstrated markedly reduced left SAN combined motor action potential, as well as a 50% prolongation in onset latency relative to the right SAN. Needle EMG of the left trapezius and left serratus anterior were both normal. A diagnosis of chronic, incomplete, left spinal accessory neuropathy was made. The patient subsequently underwent ultrasound-guided hydrodissection of the left SAN.

SUMMARY/CONCLUSION: Although loads such as rucksacks are commonly associated with brachial plexus palsies, other nerve injuries can occur, such as spinal accessory neuropathy. Suprascapular neuropathy and long thoracic neuropathy have also been described in the literature as resulting from similar loads.

Cristina Valencia Sanchez (Scottsdale, AZ), Chia-Chun Chiang (Scottsdale, AZ), Leslie Zuniga (Phoenix, AZ), Mark Ross (Scottsdale, AZ)

INTRODUCTION/BACKGROUND: Bifacial weakness with paresthesias (BFP) is a rare variant of Guillain–Barré syndrome. Patients present with rapidly progressive bilateral facial weakness, distal limb paresthesias, and hyporeflexia, without ataxia, limb weakness, or other cranial neuropathies. It is typically a demyelinating neuropathy. Here, we report a case of BFP with electrophysiologic evidence of axonal degeneration in facial nerves and 

SUMMARY/CONCLUSION: The patient’s clinical presentation is typical of BFP. This is the first report of BFP associated with C. jejuni infection and electrophysiologic documentation of axonal loss affecting the facial nerves.
IS IT A ROOT OR NERVE OR TENDON?
Kevin Moser (Hershey, PA), Aiesha Ahmed (Hershey, PA)

INTRODUCTION/BACKGROUND: Rotator cuff tears and cervical radiculopathy can present with similar symptoms and may coexist. Both etiologies must be considered for proper treatment.

CASE REPORT: A healthy 56-year-old male developed pain over the left shoulder, weakness with shoulder abduction, as well as pectoralis major and deltoid atrophy following a motor vehicle accident. Needle EMG/NCSs performed 2 months later showed normal sensory nerve action potentials in the lateral antebrachial cutaneous, medial antebrachial cutaneous, radial, median, and ulnar nerves as well as normal compound muscle action potentials in the median and ulnar nerves. Active denervation was present in the biceps, deltoid, supraspinatus, and rhomboid muscles with normal left cervical paraspinals. Subsequent shoulder MRI arthrogram revealed full-width, full-thickness supraspinatus tendon tear.

DISCUSSION: In a retrospective analysis of patients with rotator cuff pathology, Vad and colleagues (2003) noted shoulder atrophy to be correlated with peripheral nerve injury in rotator cuff tears. During analysis of the current literature on the coexistence of rotator cuff tear and cervical radiculopathy, Hattrup and Cofield (2010) noted that both conditions are relatively common, but literature on coexistence of these conditions is sparse. In our case, the patient’s pain in a C5 distribution and the presence of muscle atrophy pointed toward cervical radiculopathy, while his weakness with shoulder abduction suggested rotator cuff pathology.

SUMMARY/CONCLUSION: This case highlights the importance of considering non-mechanical or shoulder-related etiology such as cervical radiculopathy in the presence of rotator cuff tears as these conditions can present similarly and coexist. Diagnosis of the presence of both is important for adequate treatment.

Kevin Moser, MD
Resident and Fellow Member Award Recipient

NONALCOHOLIC/ANOREXIC THIAMINE DEFICIENCY LEADING TO SEVERE ACUTE MOTOR AXONAL NEUROPATHY
Anita Bell (Lansing, MI), Alexander Carrese (Lansing, MI), John Tegtmeier (Lansing, MI), Michael Andary (East Lansing, MI)

INTRODUCTION/BACKGROUND: EDX findings of neuropathy associated with vitamin B1 deficiency usually reveal a sensorimotor (or pure sensory) axonal neuropathy, which can mimic Guillain–Barré syndrome variants.

OBJECTIVE: To describe an atypical case of motor-dominant axonal neuropathy caused by B1 deficiency that mimicked acute motor axonal neuropathy (AMAN).

CASE REPORT: A 46-year-old male presented with vomiting, 50-lb weight loss, “magical thinking,” and the inability to ambulate. Extensive neurological workup revealed B-vitamin deficiencies and suspected Wernicke's encephalopathy. His mentation improved with IV thiamine supplementation, but profound weakness (lower greater than upper extremities) persisted. EDX findings were most consistent with AMAN, and he received IVIg therapy without much functional improvement. He was transferred to an inpatient rehabilitation (IPR) facility, where it was revealed that his diet primarily consisted of milk due to limited funds and desire to feed his pets instead.

OUTCOME: The patient was initially bed-bound and dependent on his family for most activities of daily living (ADLs). After 8 weeks of IPR, he was ambulating 10-15 feet with bilateral ankle-foot orthoses and a rolling walker (RW) with minimal assistance and performed ADLs with standby assistance. Four to 5 months later, he was using a RW for household distances, a wheelchair in the community, and was attempting to climb stairs. Repeat needle EMG at that time revealed evidence of sprouting/reinnervation.

SUMMARY/CONCLUSION: This case highlights that nonalcoholic B1 deficiency can cause a motor-dominant axonal neuropathy, which is similar to AMAN but different from alcoholic or post-gastrectomy B1 deficiency.

Anita Bell, DO
Resident and Fellow Member Award Recipient
THE CLINICAL NEUROPHYSIOLOGY TREATMENT AND PROGNOSIS OF HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSY
Dongqing Zhu (Shanghai, China), Lingfen Chen (Shanghai, China), Yu Zhu (Syracuse, NY), Xiangjun Chen (Shanghai, China)

INTRODUCTION: Hereditary neuropathy with liability to pressure palsy (HNPP) is a dominant inherited demyelinating peripheral neuropathy. The diagnosis of HNPP is challenging and treatment is conservative and preventive. To date, no pharmacological treatment has been known to be beneficial.

OBJECTIVE: To explore the correlation among neurophysiology data, treatment, and prognosis of HNPP.

METHODS: We retrospectively collected data of gender, age at onset, family history, initial affected nerve, precipitating factors, neurophysiological studies, gene tests, treatment, and prognosis of HNPP patients.

RESULTS: Ten patients (5 men, 5 women; mean age at onset: 32.30±4.02 years) were studied. The PMP22 gene was deleted in all 6 patients who underwent genetic testing. The nerves affected initially were the common fibular nerve (40%), ulnar nerve (20%), radial nerve (20%), and the brachial plexus (10%). A total of 80 nerves from 10 EDX studies were analyzed. Conduction block was found in 6 patients, 12.5% in total nerves, including the fibular nerve across the head of fibula, ulnar nerve across the elbow, radial nerve across the elbow, and the brachial plexus at Erb’s point. Spontaneous recovery occurred in 4 patients, lasting weeks to months, with incomplete recovery, and secondary axonal degeneration occurred later. Six patients with conduction block received oral corticosteroid therapy, resulting in rapid and almost complete recovery. Two cases underwent repeat EDX study, showing absence of conduction block in the radial nerve and brachial plexus.

SUMMARY/CONCLUSION: Our cases provide evidence of correlation among EDX data, steroid effect, and prognosis, suggesting a potential inflammation mechanism in HNPP.

CORRELATION OF NECK FLEXOR MUSCLE STRENGTH WITH RESPIRATORY WEAKNESS IN GUILLAIN–BARRÉ SYNDROME
Lisa Arnold (Burlington, VT), Michael Hehir (South Burlington, VT), Rup Tandan (Burlington, VT), Noah Kolb (Charlotte, VT), Waqar Waseed (Burlington, VT)

INTRODUCTION: Respiratory failure in Guillain–Barré syndrome (GBS) is common. Forced vital capacity (FVC) is the gold standard for monitoring respiratory muscle strength in GBS. In some clinical situations, FVC testing could be delayed or unavailable, thus there is a need for accurate, fast, and device-free bedside respiratory evaluation.

OBJECTIVE: (1) To determine if admission neck flexion strength can be utilized to predict the need for subsequent intubation in GBS patients, and (2) to correlate neck flexion strength with FVC measurements in GBS patients.

METHODS: The first examination of quantitative neck flexion strength was analyzed in 24 patients (aged 20-71 years) included in the International GBS Outcome Study (IGOS) from University of Vermont Medical Center (Burlington, VT). Neck flexion strength was assessed using the 0-5 point MRC scale as predictor of FVC value. A secondary analysis was conducted to evaluate quantitative neck flexion strength assessed in intubated or not-intubated patients as predictor of respiratory clinical status.

RESULTS: Intubation was required by 100% of patients (n=4) with neck flexion strength MRC score less than 3 and in 0% of patients (n=20) with neck flexion strength MRC score greater than 3, regardless of age or sex. Correlation between neck flexion strength and FVC could not be determined due to small sample size.

SUMMARY/CONCLUSION: Weak neck flexion (MRC score less than 3) correlates with poor respiratory status as measured by need for intubation in GBS patients. Analysis of a larger, multicenter sample from the IGOS trial is needed to evaluate correlation between neck strength and FVC values.
SENSORY AND CRANIAL NEUROPATHIES CAUSED BY CUTANEOUS T CELL LYMPHOMA
Ian Bakk (Cincinnati, OH), Hani Kushlaf (Cincinnati, OH)

INTRODUCTION/BACKGROUND: Secondary neurolymphomatosis is a rare disease typically caused by B-cell lymphomas. Cutaneous T-cell lymphoma causing both sensory and cranial neuropathies has not been reported.

CASE REPORT: A 63-year-old woman with a remote history of lung and ovarian cancers presented initially with an itchy-pigmented rash on her back, stomach, and extremities associated with alopecia at age 59. Skin biopsies revealed cutaneous T-cell lymphoma and patch-stage mycosis fungoides. Positron emission tomography CT of the whole body showed mildly hypermetabolic bilateral axillary and inguinal lymph nodes. Her neurologic symptoms began with facial numbness, facial weakness, and numbness in hands and toes at age 60. Symptoms progressed to diffuse numbness and anhidrosis. Examination showed decreased pinprick sensation in the right V2/V3 distributions and in hands and toes, and severe bilateral facial weakness. EDX studies revealed sensory polyneuropathy, bilateral chronic and severe facial neuropathies, and right V1 trigeminal neuropathy based on blink reflexes. Relevant ancillary workup included no cranial nerve involvement on brain MRI with and without contrast, negative Lyme serology, negative Sjögren’s syndrome A and B antibodies/antineutrophil cytoplasmic antibodies, normal angiotensin-converting enzyme and serum immunofixation, negative cerebrospinal fluid (CSF) and serum paraneoplastic panels, and negative CSF flow cytometry. A left sural nerve biopsy showed a chronic mild axonal neuropathy and epineurial perivascular inflammation consisting predominantly of T cells. T-cell receptor gamma gene rearrangement testing on the nerve biopsy was positive indicating T-cell clonality.

SUMMARY/CONCLUSION: The occurrence of cutaneous T-cell lymphoma with sensory and cranial neuropathies should prompt consideration of secondary neurolymphomatosis.

NEUROLEUKEMIOSIS PRESENTING AS MONONEURITIS MULTIPLEX
Michael Youssef (Houston, TX), Sudhakar Tummala (Houston, TX)

INTRODUCTION/BACKGROUND: Extramedullary tumors can often present at relapse for a patient with acute myeloid leukemia (AML). Uncommonly, this may be accompanied with leukemic nerve infiltration causing painful peripheral neuropathy, including mononeuritis multiplex. When cancer involvement is proven in the peripheral nervous system it is referred to as neuroleukemiosis. Here, we report a case of neuroleukemiosis in a patient who developed an extramedullary scalp lesion concurrently with wrist drop and peripheral neuropathy.

CASE REPORT: After an initial response with induction chemotherapy, the patient developed an extramedullary scalp lesion concurrently with a right wrist drop and a painful peripheral neuropathy. She further developed bilateral wrist drop, then bilateral foot drop as well as a painful peripheral neuropathy in all 4 extremities. Biopsy of the scalp lesion was consistent with a myeloid sarcoma. Needle EMG was consistent with a multifocal sensory motor axonal neuropathy. Biopsy of the sural nerve with lower amplitude was consistent with AML involving the nerve as well. Steroids and plasma exchange were initially attempted to prevent progression for acquired neuropathy. Chemotherapy was initiated as biopsy results were available with stabilization of symptoms without further progression. There was limited improvement of motor strength.

SUMMARY/CONCLUSION: It is important to consider relapsed leukemia in a patient with new neurologic symptoms in the peripheral nervous system since prompt recognition of the symptoms and prompt diagnosis leads to earlier treatment with effective chemotherapy and prevents unnecessary harm to the patient. Scalp lesion biopsy might provide the clue of leukemic infiltration as well.
EARLY DIAGNOSIS OF BRACHIAL PLEXUS TRAUMATIC LESIONS
Roman Tretiakov (Kyiv, Ukraine), Igor Tretyak (Kyiv, Ukraine), Alexander Gatskiy (Kyiv, Ukraine)

INTRODUCTION: Traumatic damage to the brachial plexus (TDBP) is one of the most severe and prognostically adverse diseases of the peripheral nerves.

OBJECTIVE: To provide a comprehensive early diagnosis and evaluation of the results of surgical treatment of patients with TDBP.

METHODS: The results of clinical and instrumental research and surgical treatment of 62 patients (87.1% male) with TDBP were analyzed. Among the methods used are needle EMG and MR neurography.

RESULTS: Total damage to the brachial plexus trunks was detected in 21 (33.9%) patients, partial in 41 (66.1%). Of those with partial damage: the superior trunk separately in 28 (45.2%), in combination with the middle in 8 (12.9%), and inferior in 5 (8.1%). MR data reflecting the degree of denervation changes were an important complement to the clinical picture. MR signs of separation of the roots were indications for surgical intervention at an earlier date (1-2 months) after the injury. Evaluation of the results was carried out within 10-24 months after the operation. In cases of total preganglionic TDBS, partial restoration of the function of individual muscle groups was achieved in 11/21 patients (52.4%). The case followup of patients after reconstructive surgery evaluated the restoration of the functions of the muscles, recorded the processes of collateral sprouting (polyphasic, low-amplitude motor unit action potentials), as well as determined the degree of severity of pathological reinnervation.

SUMMARY/CONCLUSION: Early localization and assessment of the degree of damage to the brachial plexus allows for establishing indications for surgery at an early stage and provides for the best results of surgical treatment.

AXONAL CHARCOT–MARIE–TOOTH DISEASE CAUSED BY A NOVEL YARS VARIANT
Assia Meziane-Tani (Cincinnati, OH), Hani Kushlaf (Cincinnati, OH)

INTRODUCTION/BACKGROUND: Dominant intermediate Charcot–Marie–Tooth (DI-CMT) disease is a CMT variant characterized by mild slowing of motor nerve conduction velocities and axonal and demyelinating features in nerve biopsies. DI-CMT type C is caused by YARS mutations. Prior reports of YARS mutations identified patients with axonal CMT phenotype and pathology on NCSs and nerve biopsies. We report a patient with a novel YARS variant causing axonal CMT.

CASE REPORT: A 61-year-old man with past medical history of lumbar fusion presented with leg weakness, paresthesia in hands and legs, and balance problems for more than 20 years. He recalls not being able to play sports as child due to “coordination problems” and wore leg braces in the third and fourth grades. Paternal grandfather had similar symptoms and was thought to have muscular dystrophy. Examination revealed high-arched feet, distal leg atrophy, sparse fasciculations in calves, absent ankle reflexes, glove-stocking sensory loss to light touch and pinprick sensations, and absent vibration at big toes. He walked with a wide-based gait and was unable to tandem walk. Needle EMG showed chronic, moderate-to-severe, length-dependent, sensorimotor, axonal polyneuropathy. Brain MRI showed incidental remote left cerebellar infarct. Lumbar spine MRI showed no significant changes. Hemoglobin A1C and B12 levels were normal. A neuropathy genetic testing panel including 72 genes showed a novel variant in YARS gene (p.Ala60Thr).

SUMMARY/CONCLUSION: We present a novel YARS variant causing axonal CMT phenotype. The pathogenicity of this variant is supported by its consistency with the clinical phenotype and the results of in silico analysis.

Assia Meziane-Tani, MD
Resident and Fellow Member Award Recipient

Disclosures:
Hani Kushlaf - Consultant on advisory board for Catalyst. Serves on speakers bureau of Genzyme and Alnylam.
SUPRASCAPULAR NEUROPATHY FOLLOWING ARTHROSCOPIC SHOULDER DEBRIDEMENT AND SUBACROMIAL DECOMPRESSIVE ACROMIONOPLASTY: AN UNCOMMON SURGICAL COMPLICATION
Nicholas Spinuzza (Bethesda, MD), Christopher Reece (Bethesda, MD), Matthew Kelly (Washington, DC), Kevin Spencer (Bethesda, MD)

INTRODUCTION/BACKGROUND: A 45-year-old female presented with external rotation (ER) weakness without paresthesias following left shoulder arthroscopic debridement and subacromial decompressive acromioplasty 4 years prior. She experienced pain relief following procedure, however, persistent weakness despite physical therapy. Needle EMG of supraspinatus and infraspinatus 2 years prior did not demonstrate abnormalities despite marked infraspinatus atrophy on MRI.

CASE REPORT: Examination revealed 4/5 strength of left shoulder ER in the setting of subtle palpable infraspinatus atrophy without paresthesia/numbness. Needle EMG was challenging due to a fibrous band at trapezius' deepest aspect just superficial to a thin tissue overlying the scapula demonstrating decreased insertional activity with distant motor unit action potentials (MUAPs) on ER. As this did not fit the clinical picture, the needle was left in place while nearby musculature was activated differentiating between normal infraspinatus versus pathology more congruent with examination/imaging. Activation of trapezius (scapula adduction) and posterior deltoid (shoulder extension at 90 degree abduction) revealed increased activity, confirming infraspinatus had no voluntary MUAPs. Given that the supraspinatus, deltoid, and biceps were normal, we diagnosed axonal neuropathy of right suprascapular nerve prior to innervating infraspinatus.

SUMMARY/CONCLUSION: Arthroscopic debridement and subacromial decompressive acromioplasty is well tolerated; however, due to the proximity of suprascapular and spinoglenoid notches, nerve injury can result from direct iatrogenic trauma or aberrant tissue healing. Furthermore, this case illustrates the importance of utilizing EDX studies as an extension of history/physical, as misdiagnosis is readily possible without appropriate troubleshooting when findings do not correlate. A thorough anatomic understanding can help prevent both iatrogenic injury and aid postoperative diagnosis.

Nicholas Spinuzza, MD
Resident and Fellow Member Award Recipient

ACUTE POST-BARIATRIC SURGERY AXONAL POLYNEUROPATHY ASSOCIATED PARALYSIS: CLINICAL FEATURES AND OUTCOME
Ahmad R. Abuzinadah (Jeddah, Saudi Arabia), Omnijab Albaradei (Jeddah, Saudi Arabia), Hessa Ateeq AlOtaibi (Jeddah, Saudi Arabia), Mohammed H. Alanazy (Riyadh, Saudi Arabia), Aysa Alshareef (Jeddah, Saudi Arabia)

INTRODUCTION: The syndrome of acute post-bariatric surgery axonal polyneuropathy (APAP) may present with various sensory and motor symptoms including paralysis.

OBJECTIVE: To describe the clinical and EDX features and the outcome of APAP associated paralysis (APAP-AP) as it has not been described in a separate cohort previously.

METHODS: We retrospectively reviewed medical charts for patients who presented to our clinical neurophysiology unit with disabling weakness within 24 months post-bariatric surgery.

RESULTS: Thirteen patients (10 women; mean age: 29.8±12.5 years) were identified. All presented with ascending weakness and loss of ambulation resembling Guillain–Barré syndrome. The median time of onset was 4 months (interquartile range [IQR] 3-6) post-surgery and the median time to weakness nadir was 3 weeks (IQR 3-3.5) with an average weight loss of 38.6 kg (SD 17.09). The ability to walk independently was achieved in 66.7% of patients at 6 months. The use of IVIg was not associated with an increased chance to walk independently (16% with IVIg versus 66.7% without IVIg, p=0.242).

SUMMARY/CONCLUSION: The syndrome of APAP-AP develops in the first year post-surgery. The majority of patients regain ability to ambulate independently.
CORRELATION BETWEEN NERVE ULTRASOUND AND ELECTRODIAGNOSTIC PARAMETERS IN THE DIAGNOSIS OF SPINAL ACCESSORY NEUROPATHY
Christopher Reece (Bethesda, MD), Nicholas Spinuzza (Bethesda, MD), Matthew Miller (Potomac, MD)

INTRODUCTION/BACKGROUND: Spinal accessory neuropathy (SAN) is a known complication of surgeries involving the posterior triangle of the neck, but the trapezius is also innervated by C2-4, which may confound EDX evaluation. Ultrasound may add complementary information to neurophysiological studies in the diagnostic workup of postoperative SAN injury.

CASE REPORT: A 47-year-old woman with past medical history significant for C5-6 total disc replacement in February 2017 presented complaining of right neck and shoulder pain, weakness, and difficulty with overhead activities that started insidiously. She initially noted pain in the right side of her neck and into the right shoulder after resuming regular exercise postoperatively. The pain progressed over 3 months with subsequent development of right shoulder abduction and flexion weakness. Focused physical examination revealed right lateral scapular winging, trapezius muscle atrophy, and weakness of shoulder abduction. MRI of the cervical spine showed stable postoperative findings at C5-6 with neuroforaminal narrowing at C3-4. MRI of the neck showed atrophic changes of the right trapezius and mild atrophy of the right sternocleidomastoid. EDX studies revealed a right SAN as evidenced by a decrease in amplitude and prolonged duration of motor unit action potentials with associated spontaneous activity in the right trapezius muscle compared to the left. Focused ultrasound showed greater than 50% side-to-side difference in cross-sectional area of the right compared to the left with associated atrophic changes in the right trapezius.

SUMMARY/CONCLUSION: Given the presentation, cervical radiculopathy cannot be ruled out with just EDX. Ultrasonography demonstrating significant nerve enlargement may aid in differentiating SAN from radiculopathy.

Christopher Reece, MD
Resident and Fellow Member Award Recipient

STUDY OF SOMATOSENSORY EVOKED POTENTIALS OF THE FEMORAL NERVE: COMPARISON OF THREE STIMULATION SITES AND INTER-OBSERVER RELIABILITY
Carolina González Alvarado (Bogotá, Colombia), Juan Camilo Mendoza Pulido (Bogotá, Colombia), Fernando Ortiz-Corredor (Bogotá, Colombia)

INTRODUCTION: Lumbar plexus injuries are the most frequent complications in minimally invasive intercorporeal lumbar spine surgery where a lateral approach is made through the psoas muscle. In order to optimize the postoperative results, it is necessary to define a safe approach through the psoas using neurophysiological techniques.

OBJECTIVE: To determine the best femoral nerve stimulation site that generates reproducible and stable cortical responses during somatosensory evoked potentials (SEPs).

METHODS: In a convenience sample of 30 children with idiopathic scoliosis who were monitored with conventional intraoperative neurophysiologic techniques, we stimulated the femoral nerve over 3 different sites: i) the inguinal ligament lateral to the femoral pulse; ii) the saphenous nerve on the groove between the sartorius and vastus medialis muscles and iii) the safenous nerve located with ultrasound in the distal thigh. Three derivations according to the 10-20 system were used for recording each stimulation site: CPz-FPZ/Ci-Cc/CPz-Cc. Five traces were averaged before the incision. Amplitudes were averaged for each of the three aforementioned stimulation sites. Friedman test with Bonferroni adjustment was used to establish amplitude differences, therefore, statistic significance was set at p<0.01. Responses reproducibility reliability between two observers was assessed with the Kappa statistic.

RESULTS: Stimulation of the femoral nerve in the inguinal ligament showed higher amplitudes, and the ability to identify these responses by trained observers was greater.

CONCLUSIONS: SEPs of the femoral nerve stimulating the inguinal ligament generates reproducible and identifiable cortical responses. This technique may be useful during minimally invasive intercorporeal lumbar fusion surgeries where the integrity of the femoral nerve is at risk.
NEUROPHYSIOLOGICAL ABNORMALITIES OF THE PUDENDAL NERVE AFTER COLPOPEXY TO THE RIGHT SACROSPINOUS LIGAMENT: A CASE REPORT
Carolina González Alvarado (Bogotá, Colombia), David Felipe Cardozo Reyes (Bogotá, Colombia), Jorge Díaz-Ruiz (Bogotá, Colombia), Daniel Otalora Cortes Díaz (Bogotá, Colombia), Jaime Rosas-Jaimes (Bogotá, Colombia), José Wilder Vidal Patiño (Popayán, Colombia)

INTRODUCTION: Pudendal nerve (PN) lesions can be of traumatic, congenital, or surgical origin. The mechanical compression, or entrapment, can be caused by a spasm of the pelvic floor muscles, by the tension generated on the sacrospinous ligament, and by scars secondary to trauma or surgeries in the surrounding area.

CASE REPORT: We present the case of a woman who underwent a hysterectomy plus colpopexy to the right sacrospinous ligament. She presented with neuropathic pain and urinary retention with electrophysiological evidence of a partial lesion in the PN. She had a normal neurography by nuclear magnetic resonance (NMR). She was then initiated with neuromodulation with symptomatic control. She underwent vaginal hysterectomy and anterior colporrhaphy with vaginal colposuspension to the right sacrospinous ligament under general anesthesia. On the second postoperative day, she presented with neuropathic pain in the S2 dermatome and urinary retention. MNR of the lumbosacral spine and PN showed no abnormalities. Somatosensory evoked potentials of the PN, stimulating separately on each side of the clitoris, were normal on the left side and had no response on the right. A bulbocavernosus reflex with stimulation on each side of the clitoris revealed significantly longer latencies on the right compared to the left side.

SUMMARY/CONCLUSION: PN injury should be suspected in patients with pain referred to the inguinal region, as well as a urinary sphincter alteration in the context of an intervention such as in this case. Electrophysiological studies are essential tools to evaluate and follow the progress of PN lesions.

CRYOGENICALLY-INDUCED MONOMELIC NEUROPATHY: A CASE STUDY
Thereseann Huprikar (Freeport, MI), Matthew Saffarian (East Lansing, MI)

INTRODUCTION/BACKGROUND: Ischemic monomelic neuropathy (IMN) is an axonal sensorimotor peripheral neuropathy that occurs after acutely diminished blood flow to an extremity. It is most commonly associated with arteriovenous fistula vascular access procedures. To our knowledge, there have not been any reported cases of cryogenically-induced IMN.

OBJECTIVE: To report a case of acute onset of multiple axonal sensorimotor mononeuropathies in bilateral upper extremities after prolonged cold exposure.

CASE REPORT: A 64-year-old female presented for EDX evaluation of bilateral hand pain and weakness 2 months after she fell and laid in the cold for an unknown period of time. On examination, she had decreased sensation to light touch on all 5 fingers on the left hand, as well as the ring and little fingers on the right. Her strength was intact throughout bilateral upper and lower extremities, except distal median- and ulnar-innervated muscles. Reflexes were intact with no upper motor neuron signs. EDX studies revealed bilateral median, ulnar, and superficial radial neuropathies with axon loss in distal median- and ulnar-innervated muscles. Reflexes were intact with no upper motor neuron signs. EDX studies revealed bilateral median, ulnar, and superficial radial neuropathies with axon loss in distal median- and ulnar-innervated muscles. Reflexes were intact with no upper motor neuron signs.

SUMMARY/CONCLUSION: Prolonged cold exposure to a distal extremity can cause IMN. In this single case, both sensory and motor symptoms seem to improve with hand therapy and time.
ULTRASONOGRAPHIC FEATURES PREDICTIVE OF THE PATHOLOGICAL TYPE OF PERIPHERAL NERVE SHEATH TUMOR
Chaitanya Bonda (Bentonville, AR), John Morren (Cleveland, OH), Steven Shook (Beachwood, OH)

INTRODUCTION: Peripheral nerve sheath tumors are rare. Therefore, there is a paucity of scientific data on the utility of ultrasonographic features in predicting specific tumor type.

OBJECTIVE: To predict the type of peripheral nerve sheath tumor (schwannoma versus neurofibroma) based on specific ultrasonographic features.

METHODS: A retrospective review was conducted for all the neuromuscular ultrasounds (NMUs) performed for various indications at our institution between 2010-2016. The charts of patients with a NMUS diagnosis of peripheral nerve sheath tumor were reviewed for the final diagnosis.

RESULTS: There were a total of 23 patients with peripheral nerve sheath tumors, of which 11 were schwannomas and 12 were neurofibromas. In 22/23 patients, the tumor type was pathologically proven. All the ultrasonographic images of the tumors were characterized for 6 features—Doppler signal (positive/negative), “target” sign, density (hypodense, isodense, or hyperdense), central or eccentric to nerve, number of tumors (one or multiple), and vertical-to-horizontal (VH) ratio of largest tumor in transverse section. Schwannoma patients had a statistically significant larger average VH ratio than neurofibroma patients (p=0.001). No other statistically significant differences between the 2 groups were observed. Doppler signal positivity was seen more often in schwannomas than neurofibromas (50 versus 12.5%). Neurofibroma tumors tended to be multiple compared to schwannomas (54.5 versus 16.7%).

SUMMARY/CONCLUSION: On NMUS, schwannomas tend to be more spherical and neurofibromas tend to be more fusiform/ovoid, which can be used as key ultrasonographic features in the prediction of the tumor pathological type.

ISCHEMIC LUMBOSACRAL PLEXOPATHY: AN UNCOMMON ETIOLOGY FOR PROGRESSIVE LOWER LIMB WEAKNESS
Laura Pesantez Pacheco (Houston, TX)

INTRODUCTION/BACKGROUND: The arterial supply of the lumbosacral plexus usually derives from branches of the internal iliac artery. Given this rich blood supply and the low metabolic demand of the peripheral nerve tissue, ischemic injury is rare. Acute ischemic lumbosacral plexopathy typically presents in patients with prior aortic surgery or thromboembolic phenomenon. Progressive lower limb weakness from lumbosacral plexopathy related to atherosclerotic occlusion is uncommon.

CASE REPORT: A 60-year-old woman with a history of diabetes, hyperlipidemia, and smoking presented with an 8-month history of left lower extremity numbness, pain, and progressive weakness. Examination showed diffuse weakness with distal predominance (absent dorsiflexion), areflexia, atrophy of the tibialis anterior and gastrocnemius muscles, and decreased pinprick, proprioception, and vibration sensation below the knee. EDX studies revealed left lumbosacral plexopathy evidencing active denervation in the sciatic branch and L5–S1-innervated muscles. Lumbosacral spine and pelvis MRI were normal. CT angiography reported total occlusion of the left common iliac, infrarenal abdominal aortic occlusive disease, and right common iliac artery stenosis. An aortobifemoral bypass was performed using a Dacron graft. Aspirin and atorvastatin were started. At discharge, pain improved significantly, and the patient walked with assistance, however the numbness persisted.

SUMMARY/CONCLUSION: This case highlights the need to consider ischemic lumbosacral plexopathy in patients without previous history of aortic surgery or thromboembolism, as the underlying vascular pathology can be successfully treated in some patients.
**ELECTRODIAGNOSTIC EVIDENCE OF NEUROPATHY PROGRESSION IN LEIGH SYNDROME**

*Akash Patel (Chicago, IL), Qin-Li Jiang (Chicago, IL)*

**INTRODUCTION/BACKGROUND:** Leigh syndrome (LS) is a rare neurodegenerative disorder that usually affects the central nervous system. We report a case of acute deterioration in a patient with LS associated with a rapidly progressive neuropathy that is confirmed on sequential EDX studies.

**CASE REPORT:** A 22-year-old male with history of learning disability presented with acute onset of unsteady gait and fever for 3 days. Initial examination was pertinent for diffuse hyporeflexia, bilateral finger dysmetria, and a very ataxic gait. MRI showed symmetric T2 hyperintensity in the basal ganglia, midbrain, and pons. Workup for various inflammatory, infectious, and metabolic etiologies were negative, including unremarkable cerebral spinal fluid analysis and normal pyruvate and lactate. Needle EMG on day 1 of admission showed diffusely absent sensory responses with intact motor responses, consistent with an axonal sensory polyneuropathy or sensory neuronopathy. His condition rapidly deteriorated over the subsequent days to generalized weakness, severe encephalopathy, and respiratory failure, requiring intubation 5 days after admission. Needle EMG on day 9 showed normal routine motor responses; however, F waves, which were previously normal, were now absent suggesting proximal demyelination. A third needle EMG on day 15 showed reduction in motor amplitudes as well as patchy prolongation of distal motor latencies and slowed conduction velocities, consistent with a mixed demyelinating and axonal polyneuropathy. A mitochondrial genome testing revealed a mutation of MT-ATP6 gene consistent with LS.

**SUMMARY/CONCLUSION:** Neuropathy can occur with LS, and it can rapidly progress with evidence of demyelination and axonal injury shown on EDX studies.

**FUNCTIONAL IMPLICATIONS OF MARTIN–GRUBER ANASTOMOSIS AND DETECTION BY MIXED NERVE CONDUCTION STUDY: A CASE REPORT**

*Dominic Femminineo (Lansing, MI), Michael Andary (East Lansing, MI), Joshua Nicholson (Pleasanton, CA)*

**INTRODUCTION/BACKGROUND:** The Martin–Gruber anastomosis (MDA) is a common anatomic variant. Its functional significance is underappreciated and may offer some protection from sequelae of ulnar nerve injury at the elbow.

**OBJECTIVE:** To present the case of a highly functional outcome after complete ulnar nerve injury due to a large MGA, and concurrently the first case of a large MGA documented on mixed nerve NCSs recording from the upper arm after stimulation at the wrist.

**CASE REPORT:** A 60-year-old male, who had suffered a dominant-arm elbow fracture in adolescence and underwent subsequent operative repair, presented with elbow pain and end-stage arthritis. Recent elbow CT (for surgical planning) incidentally demonstrated thickening of the ulnar nerve in the cubital tunnel. Physical examination revealed only mild weakness of the hand. He was recently retired, having worked a full career as an electrical lineman without accommodation. EDX studies revealed complete ulnar neuropathy at the elbow with a large MGA bypassing the ulnar nerve lesion. The MGA was large enough to be confirmed on mixed nerve NCSs across the elbow, which has not previously been described.

**SUMMARY/CONCLUSION:** The contribution of an MGA (if present) to hand function is variable but underappreciated. This MGA prevented devastating functional impairment from occurring after a complete ulnar nerve injury. This is relevant not only to EDX consultants but also to surgeons; this patient subsequently underwent total elbow joint replacement which required recognition and protection of his anomalous anatomy for a functional outcome.

Dominic Femminineo, DO
Resident and Fellow Member Award Recipient
A RARE CASE OF PERIPHERAL BILATERAL FOOT DROP SUPERIMPOSED ON A CERVICAL SPINAL CORD TUMOR

Akash Bhakta (Chicago, IL), Alan Anschel (Chicago, IL)

INTRODUCTION: Bilateral foot drop is typically caused by a central process. Peripheral causes often present unilaterally, and bilateral cases are rare.

CASE REPORT: A 53-year-old male was admitted to acute inpatient rehabilitation 2 weeks after undergoing resection of a recurrent cervical chordoma with occiput-C5 instrumented fusion. Manual muscle testing (MMT) on admission showed 4/5 strength on ankle dorsiflexion. Ten days into the rehabilitation course, he developed bilateral foot drop of unclear etiology with 2/5 strength on MMT. MRI of the brain and cervical and lumbar spines demonstrated stable findings. EDX studies revealed bilateral motor and sensory mononeuropathies of the common peroneal nerve across the fibular head with features of demyelination and acute axonal denervation. His bilateral dorsiflexion weakness improved to 3/5 strength with functional gait training along with support from solid ankle–foot orthoses. The patient had a notable history of a 34-kg weight loss over the year prior due to poor oral intake from dysphagia and permanent trismus. Caloric intake was increased resulting in a 4-kg weight gain during the remainder of the rehabilitation course. He continued to gain weight and strength over the following year with 5/5 strength on ankle dorsiflexion.

SUMMARY/CONCLUSION: Chordomas are very rare primary spinal cord tumors and bilateral foot drop is commonly associated with a central nervous system etiology. However, this study highlights the need to consider peripheral causes, especially when risk factors such as weight loss are present.

DIVERSITY IN THE CHARCOT–MARIE–TOOTH DISEASE POPULATION IN THE UNITED KINGDOM AND UNITED STATES: INSIGHTS FROM A DIGITAL REAL-WORLD OBSERVATIONAL STUDY

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INTRODUCTION: Charcot–Marie–Tooth (CMT) disease is a hereditary neuropathy that affects the peripheral nervous system.

OBJECTIVE: To examine demographics of United Kingdom and United States participants enrolled in a real-world observational study of CMT.

METHODS: Adults with CMT were recruited to a 2-year international observational study exploring real-world disease burden. Data were collected via CMT&Me, a bespoke “bring your own device” app, through which participants were asked questions about demographic characteristics, management of their CMT, and their quality of life. This interim analysis examined the demographics of U.K. and U.S. participants. Differences between the overall population and those who had taken part in clinical trials were explored.

RESULTS: Demographic diversity of study participants was high. Ages were well distributed. At the time of analysis, more females than males were enrolled. Around half of participants in both countries had CMT type 1A, with type 2 and “unknown” being the next most common subtypes. Participants had been diagnosed with CMT at a wide range of ages. The most frequently reported employment statuses were “working for pay” and “unable to work due to disability.” A small proportion of people in both countries had participated in clinical trials. Characteristics of trial participants were largely similar to those of the general study population.

SUMMARY/CONCLUSION: Diversity was high among U.K. and U.S. participants with CMT in this observational study. Demographics were similar between people who had and had not participated in clinical trials. This ongoing study will provide further insights into the real-world impact of CMT.

Disclosures:
Tjalf Ziemssen, Shahram Attarian, Florian P Thomas, Allison Moore, Daniel Tanesse - Compensation for participation in the study from Scientific Advisory Board.
Xavier Paoli, Viviane Bertrand, Youcef Boutalbi - Employees of Pharnext, the study sponsor.
Emma Bagshaw, Hara Kousoulakou, Mark Larkin - Employees of Vitaccess, which was paid by Pharnext to conduct this study.
HANSEN DISEASE WITH 20-YEAR INCUBATION PERIOD, NEGATIVE FITE STAIN, AND ATYPICAL CLASSIFICATION
Marcus Cimino (Torrance, CA), Moshe-Samuel Hendizadeh (Torrance, CA), Margaret Adler (El Segundo, CA), Luis Chui (Palos Verdes Peninsula, CA)

INTRODUCTION/BACKGROUND: Hansen disease (leprosy) is a common cause of neuropathy throughout the world. Its incubation period usually ranges from several months to a few years.

CASE REPORT: A mid-30-year-old male presented with 2 years of progressive upper and lower extremity painless numbness that started in the hands. He had been diagnosed with a left Bell’s palsy during this time. On examination, he had bilateral eye closure weakness, normal lower face strength, decreased sensation in the right face, and severe decreased pinprick and temperature sensation in arms and legs, but nearly normal extremity strength and normal reflexes. He was born in Mexico but had lived in the United States the past 20 years without ever leaving the country. EDX testing revealed absent upper and lower extremity sensory responses and normal motor responses. Ultrasound of the ulnar and median nerves was normal. Skin biopsy and sural nerve biopsies revealed significant vascular inflammation with acid fast bacilli; Fite stain on a second skin biopsy was negative. The patient was treated for borderline lepromatous/lepromatous leprosy and was improving at 4-month followup.

SUMMARY/CONCLUSION: This case of Hansen disease is notable for the extended incubation period of 20 years, a false-negative Fite stain, and highlighting that skin findings can be subtle. This case demonstrates the importance of considering Hansen disease in patients presenting with sensory neuropathy (either length- or non–length-dependent) and facial weakness, particularly if the patient has ever lived in or near an endemic region.

Marcus Cimino, MD, MBA
Resident and Fellow Member Award Recipient

THE COMBINED USE OF ELECTRODIAGNOSIS AND ULTRASOUND TO ASSESS A COMPLICATED POST-SURGICAL INJURY AT THE ELBOW
Austin Grant (Hilliard, OH), Jeffrey Strakowski (Powell, OH)

INTRODUCTION/BACKGROUND: Electrophysiologic measurement and anatomic visualization with ultrasound (US) are complimentary techniques in the assessment of focal neuropathies. In combination, they can provide both physiologic and anatomic information.

CASE REPORT: A middle-aged female presented to clinic with complaints of persistent weakness and numbness 2 months after undergoing an attempted ulnar nerve transposition for ulnar neuropathy at the elbow. The ulnar nerve was inadvertently transected during the procedure and then an in situ repair was performed. Electrophysiologic testing revealed partial function of the flexor carpi ulnaris and medial flexor digitorum profundus but no distal ulnar sensory or motor function. US revealed a large neuroma but intact repair at the injury site at the cubital tunnel that was proximal to the innervation of the ulnar-innervated forearm muscles. There was also secondary focal enlargement and dynamic subluxation of the nerve more proximally at the level of the medial epicondyle. Utilization of the newer innovation of ultra-high frequency US demonstrated continuity of some of the individual fascicles within the repair site.

SUMMARY/CONCLUSION: The combined use of both electrodiagnosis and US can provide valuable physiologic and anatomic information in complicated focal neuropathies. The use of both modalities revealed an intact repair, the presence of 2 sites of neuropathy, the relative severity of the neuropathy, as well as the dynamic influence of elbow movement. These findings were essential in developing an effective treatment program.

Austin Grant, MD
Resident and Fellow Member Award Recipient
LATERAL ANTEBRACHIAL CUTANEOUS NEUROPATHY: REVIEW OF 17 CASES
Anza Memon (Detroit, MI), Bashiruddin Ahmad (West Bloomfield, MI)

INTRODUCTION: Lateral antebrachial cutaneous neuropathy (LABCN) is rare and often underdiagnosed. Less than 100 cases have been described in the literature. The nerve innervates the radial forearm. Common causes of injury to the nerve reported in the literature include strenuous upper extremity exercise, repetitive forceful pronation in athletes, phlebotomy, compression due to a tourniquet, or improperly placed blood pressure cuff.

OBJECTIVE: To understand the etiology, clinical presentation, and EDX findings in patients with LABCN.

METHODS: A retrospective chart review of patients with LABCN who were seen over 16 years was performed. Demographics and detailed clinical information were recorded. EDX data were reviewed and clinical outcome was recorded.

RESULTS: Seventeen patients were included in this study. Postsurgical etiology was the most common (n=6) cause of LABCN, secondary to arm positioning during orthopedic surgeries. Other cases included antecubital fossa phlebotomy (n=3), trauma (n=2), over use (n=2), dog bite (n=1), and arterial and IV line placement (n=2). No etiology was found in 1 case. Fifteen patients had axonal neuropathy and only 2 showed a demyelinating pattern on EDX studies. Nine patients had poor clinical outcome, 3 had good recovery, and 4 patients were lost to followup.

SUMMARY/CONCLUSION: Our study proposes that patient positioning during orthopedic surgeries leading to stretch or compression of the lateral antebrachial cutaneous nerve as the most likely cause of postoperative LABCN. Antecubital fossa phlebotomy is the second common cause of LABCN.

IMMUNE-MEDIATED LUMBOSACRAL RADICULOPLEXUS NEUROPATHY FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANT
Nadim Jiwa (Boston, MA), Isabel Arrillaga-Romany (Boston, MA), Areej El-Jawahri (Boston, MA), Amanda Guidon (Boston, MA)

INTRODUCTION: Immune-mediated neuropathies (IMNs) are rare treatable complications of autologous hematopoietic stem cell transplantation (SCT). Understanding of the pathophysiology and natural history is limited.

OBJECTIVE: To report an IMN following autologous SCT and to review IMNs after autologous SCT.

CASE REPORT: A 64-year-old non-diabetic man with primary central nervous system lymphoma in remission presented 2 months after high-dose chemotherapy with thiotepa-based regimen and autologous SCT. He had asymmetric leg weakness, paresthesias, and pain in back, buttocks, and hip progressing over several weeks. Evaluation for lymphoma recurrence and neurolymphomatosis was negative. Cerebrospinal fluid cell count was normal, with protein of 53 mg/dL. EDX studies at 6 weeks demonstrated a length-dependent, asymmetric, sensory and motor polyradiculoneuropathy with mixed axonal and demyelinating features affecting the lower extremities. He was treated with IVIg and dexamethasone taper without improvement. He was nonambulatory and required methadone for neuropathic pain. EDX studies at 12 weeks demonstrated additional features of acquired demyelination. Sural nerve biopsy revealed perineurial inflammation involving T cells and macrophages with a single granuloma. Pulse methylprednisolone, followed by a tapering infusion schedule for 7 months, resulted in improvement. Weakness improved and pain resolved. At 11 months, he walked with 2 canes and had discontinued pain medications. Lymphoma remained in remission.

CONCLUSION: This case adds to the limited reports of IMNs following autologous SCT. The natural history of this case suggests a painful, monophasic, radiculoplexus neuropathy with features of peripheral nerve demyelination, responsive to IV corticosteroids. This case supports the hypothesized mechanism of immune reconstitution and a subacute but monophasic course with treatment.

Nadim Jiwa, MBBS
Resident and Fellow Member Award Recipient
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PREOPERATIVE ULTRASOUND ACCURATELY LOCALIZES PERIPHERAL NERVE ABNORMALITIES FOR OPERATIVE GUIDANCE
O. Kenechi Nwawka (New York, NY), Esther Zusstone (Cincinnati, OH), Emily Casaletto (New York, NY), Kenneth Serrano (New York, NY), Steve Lee (New York, NY), Scott Wolfe (New York, NY), Joseph Feinberg (New York, NY)

INTRODUCTION: Localization and characterization of nerve abnormality is critical to guide appropriate intervention. Ultrasound (US) provides superb peripheral nerve imaging resolution and is known to be highly accurate in the diagnosis of peripheral neuropathy. An additional benefit US can provide is preoperative localization of nerve abnormalities with skin marking.

OBJECTIVE: To report on the accuracy of US-guided preoperative skin marking for the localization of nerve abnormality in peripheral neuropathy.

METHODS: From July 2016 to February 2019, a search of the radiology information system was performed to identify US examinations performed for preoperative localization of peripheral nerve abnormality. Data collected included: US diagnosis of nerve abnormality, site of nerve lesion on US, surgical diagnosis of nerve abnormality, site of nerve lesion on US, and EDX diagnosis of nerve abnormality.

RESULTS: Twenty-three nerves in 18 patients were identified by the search parameters. Eighteen nerves had undergone surgical intervention, and 14 nerves had undergone EDX evaluation at the time of this study. Nerves imaged included: median, ulnar, radial (and branches), plantar, common peroneal, superficial peroneal, sural, spinal accessory, and musculocutaneous. US diagnoses included: transection, perineural scarring, neuroma, hardware impingement, and nerve constriction. There was 100% accuracy of US findings as confirmed by operative notes. Skin marking by US guidance correlated to the sites of nerve abnormality documented in operative reports in all 18 cases. EDX findings confirmed US diagnoses in all 14 cases.

SUMMARY/CONCLUSION: US-guided preoperative skin marking of nerve abnormality was accurate in localization of peripheral nerve abnormality, and US diagnoses were corroborated by intraoperative EDX findings.

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CHRONIC IMMUNE SENSORY POLYRADICULOPATHY VARIANT IN A HUMAN IMMUNODEFICIENCY VIRUS-POSITIVE PATIENT
Jennifer Martinez-Thompson (Rochester, MN), Michel Toledano (Rochester, MN), P James Dyck (Rochester, MN)

INTRODUCTION/BACKGROUND: We present a patient with findings suggestive of chronic inflammatory sensory polyradiculopathy (CISP) to highlight the clinical spectrum of this disorder.

CASE REPORT: A 54-year-old gentleman developed progressive bilateral foot numbness, gait imbalance, right hand incoordination, and left sixth nerve palsy over 15 years. He was diagnosed with human immunodeficiency virus 1 (HIV-1) shortly after symptom onset and treated successfully with antiretrovirals. Neurologic examination showed a severe sensory ataxia, areflexia, and mainly large fiber sensory loss in the right upper and bilateral lower limbs with preserved strength. Laboratory evaluation included unremarkable serum monoclonal gammapathy screen, vascular endothelial growth factor, myelin-associated glycoprotein, hepatitis B/C screening, cryoglobulins, SSA/SSB, vitamin B12, copper, paraneoplastic antibody panel, and ganglioside antibodies. Cerebrospinal fluid protein was elevated (67 mg/dL). Lumbar spine/lumbosacral plexus MRI showed multiple nerve root T2 hyperintensity, thickening, and enhancement extending into lumbosacral plexus. Needle EMG revealed a chronic, mainly axonal polyradiculoneuropathy with sural sparing. Somatosensory evoked potentials (SEPs) displayed slowing of left median response between the brachial plexus and cervical cord and absent bilateral tibial responses. Superficial radial nerve biopsy showed mainly large fibers loss, small/thinly myelinated fibers, and scant inflammatory cells. A CISP-variant was considered and IVIg initiated with significant improvement of sensory ataxia/numbness and EDX abnormalities.

SUMMARY/CONCLUSION: This case broadens the spectrum of CISP, which classically involves only sensory roots. When sensory ataxia is prominent, SEPs should be included to assess proximal nerve root segments. Although unclear if HIV is related, inflammatory demyelinating neuropathies have been reported in HIV patients shortly after seroconversion.
ASSOCIATION BETWEEN CLINICAL OUTCOMES AND QUALITY OF LIFE IN PATIENTS WITH HEREDITARY TRANSTHYRETIN AMYLOIDOISIS
Aaron Yarlas (Johnston, RI), Spencer Guthrie (Boston, MA), Michael Pollock (Boston, MA), Andrew Lovley (Johnston, RI), Michelle K. White (Johnston, RI)

INTRODUCTION: Hereditary transthyretin (hATTR) amyloidosis is a rare, systemic, progressive disease that often manifests as polyneuropathy.

OBJECTIVE: To assess associations of clinical outcomes with quality of life (QOL).

METHODS: Data were from the NEURO-TTR trial (NCT01737398), a double-blinded, placebo-controlled randomized trial of inotersen in patients with hATTR accompanied by polyneuropathy. Outcomes were assessed at baseline and week 66. QOL was measured using the Norfolk QOL-diabetic neuropathy (DN) questionnaire and Short Form 36 Health Survey version 2 (SF-36v2). Polyneuropathy symptoms and impairment were assessed by scores from polyneuropathy disability (PND), modified Neuropathy Impairment Score+7 (mNIS+7), and Neuropathy Symptoms and Change (NSC). Analysis of covariance models tested differences in baseline QOL scores across PND stage. Correlations measured associations between clinical outcomes and QOL measures. Regression models tested associations between change-from-baseline QOL scores at week 66 and changes in clinical outcomes.

RESULTS: Significantly worse scores in most Norfolk QOL-DN and SF-36v2 domains were observed at higher PND stages. mNIS+7 and NSC scores showed strong correlations with Norfolk QOL-DN activities of daily living, large fiber neuropathy, and small fiber neuropathy domains, and SF-36v2 physical functioning and role-physical domains. In regression models, decreases in NSC scores were associated with improvement in Norfolk QOL-DN domains; decreases in NSC scores and TTR concentration were associated with improvements in SF-36v2 physical functioning and role-physical domains.

SUMMARY/CONCLUSION: Severity of neuropathy predicted both neuropathic-specific and generic QOL. Decreased TTR concentration predicted improvement in generic QOL. Thus, treatments that reduce TTR and neuropathy should produce better QOL in hATTR patients.

SERIAL MAGNETIC RESONANCE IMAGING AND NEEDLE ELECTROMYOGRAPHY IN BRACHIAL PLEXITIS: A CASE REPORT
Robin Warner (New York, NY), Dale Lange (New York, NY)

INTRODUCTION/BACKGROUND: The diagnosis of brachial plexitis is based on history and clinical findings, supported by needle EMG and MRI. MR neurography can detect focal and multifocal inflammation within nerve.

OBJECTIVE: To determine if MR neurography allows objective data mirroring clinical improvement in brachial plexitis.

CASE REPORT: A 39-year-old man developed sudden onset pain in his left shoulder after a mild infection, which intensified over 3-4 days. Weakness followed, being unable to lift his left arm above the level of his shoulder. There were no sensory symptoms. There was a remote history of Bell's palsy, but no relevant family history. Initial examination showed weakness of the left deltoid and infraspinatus (2/4). Reflexes were present. Needle EMG/NCSs showed left C5 radiculopathy, primarily involving the anterior ramus division with severe denervation of C5-innervated muscles, then progressive reinnervation of the C5 muscles through axonal regeneration. A left brachial plexus MR neurography with gadolinium showed an enlarged hyperintensity in the C5 nerve root at the level of the interscalene triangle with a denervation pattern edema of regional muscles. The patient was treated with IVIg with subsequent improvement. Ten months after onset, strength of all muscles is normal, although there is decreased muscle bulk in his deltoid and pectoral muscles. Serial MRIs show progressively decreasing nerve root hyperintensity and size in the post foraminal nerve root. The last MRI and needle EMG/NCSs were normal, correlating with the clinical syndrome.

SUMMARY/CONCLUSION: MR neurography of the brachial plexus may be important in diagnosis and prognosis in patients with brachial plexitis.

Robin Warner, DO
Resident and Fellow Member Award Recipient
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A CASE SERIES HIGHLIGHTING THE ROLE OF ULTRASOUND IN ULNAR NEUROPATHY AT THE WRIST

INTRODUCTION/BACKGROUND: In 1861, Félix Guyon described the passage of the ulnar nerve through a fibro-osseous tunnel, later named Guyon's canal. The canal's volume is dynamic, changing with wrist movement. The use of a gait aid affects the biomechanics and may lead to ulnar nerve compression at the wrist. Ultrasound (US) evaluation of the hypothenar musculature can assist in assessing for palmaris brevis sparing as well as direct localization of potential sites of compression.

CASE REPORT: We present 4 patients with EDX-confirmed ulnar neuropathy at the wrist, highlighting the role of clinical examination and US. Mean age at presentation was 58.5±4.8 years. All patients presented with weakness of the hand intrinsics (first dorsal interosseous [FDI] MRC grade 0-3, abductor digiti minimi [ADM] MRC grade 0-4). Three of 4 were related to the use of a gait aid (2 canes, 1 axillary crutch). All patients had a palmaris brevis sign. All underwent surgical release of Guyon's canal. Postoperatively, all patients had an improvement of 1 or more MRC grade in both FDI and ADM. On EDX studies, 1 patient had no improvement in compound muscle action potential to the FDI, 1 improved from 2.1 to 6.0 mV, and another improved from 0 to 14 mV. Postoperative EDX studies were not conducted on 1 patient who made a full recovery.

SUMMARY/CONCLUSION: The dynamic changes of Guyon's canal are an important factor in the development of ulnar neuropathy at the wrist. US compliments EDX testing in the diagnosis, and can facilitate surgical management in those with axonal loss, ultimately minimizing disability.

Jordan VanderEnde, MD
Resident and Fellow Member Award Recipient

NERVE ROOT HYPERTROPHY CAUSING SPINAL STENOSIS IN HEREDITARY AND AUTOIMMUNE DEMYELINATING NEUROPATHY
Natalia Gonzalez (Durham, NC), Jeffrey Guptill (Durham, NC), Lisa Hobson-Webb (Durham, NC), Vern Juel (Durham, NC), Karissa Gable (Hillsborough, NC)

OBJECTIVE: To describe cases of severe nerve root hypertrophy and spinal stenosis arising from hereditary and autoimmune demyelinating neuropathies.

CASE REPORT: Case 1: A 60-year-old woman with Charcot-Marie-Tooth (CMT) disease type 1B (MPZ mutation) presented with 6 months of rapidly progressive leg weakness along with back and radicular pain with neurogenic claudication. MRI demonstrated marked cauda equina enlargement that resulted in moderate spinal stenosis. She elected to pursue non-surgical pain management. Case 2: A 37-year-old woman presented with several years of lower greater than upper extremity burning dysesthesias, back and radicular pain, and urinary incontinence. A diagnosis of chronic immune sensory polyradiculopathy (CISP) was ultimately established. MRI demonstrated massively enlarged lumbosacral nerve roots. Decompressive laminectomy was performed. S2 nerve root biopsy obtained intraoperatively demonstrated hypertrophic peripheral nerve tissue with chronic inflammation and onion-bulb formations.

CONCLUSION: Nerve root hypertrophy resulting in spinal canal stenosis is well described in chronic inflammatory demyelinating polyneuropathy (CIDP) and CIDP variants and in CMT1A. In CMT1B, only 2 siblings have been previously described who ultimately underwent successful cauda equina decompression. Although nerve root biopsies are rarely pursued, pathological findings both in CIDP and in CMT demonstrate onion-bulb formation suggesting nerve hypertrophy results from chronic demyelination and remyelination in both hereditary and autoimmune disorders. Spine imaging should therefore be considered in patients with demyelinating CMT or inflammatory polyradiculoneuropathies with neurogenic claudication or examination findings suggesting a spinal mass lesion.

Natalia Gonzalez, MD
Resident and Fellow Member Award Recipient
ANALYSIS OF CLINICAL SYMPTOMATOLOGY IN PATIENTS WITH TS-HDS POLYNEUROPATHY VIA CLINICAL QUESTIONNAIRE
Sri Raghav Sista (Peoria, IL), Ruth Arms (East Peoria, IL), Gregory Blume (Peoria, IL)

INTRODUCTION: Trisulfated disaccharide IdoA2SGlcNS-6S (TS-HDS) IgM antibodies are known to be associated with a predominantly sensory axonal and small-fiber neuropathy.

OBJECTIVE: To characterize the clinical features among our patients with TS-HDS antibodies.

METHODS: Review of data collected from 31 patients with TS-HDS antibodies via a pre-prepared in-person questionnaire.

RESULTS: Age range of symptom onset was 19-69 years with a mean symptom onset of 48 years. A male to female ratio of 18:13 was observed with 84% Caucasian, 6% African American, 3% Asian, and 3% Hispanic. Type II diabetes was found in 19% with the age of symptom onset being 55 years. Sensory symptoms at onset were symmetric in 93%, bilateral foot involvement only in 68%, simultaneous hand and foot involvement in 26%, persistent in 58%, and exacerbated by physical activity in 87%, particularly standing in place. In patients whose symptoms started in their feet with subsequent hand involvement, on average 6.5 years elapsed. Excluding patients with diabetes or other pain syndromes, 40% (10/25) endorsed issues with balance and fine hand movements. Prescription medication for neuropathic pain was used in 71% of patients, 19% of which were on 2. Excluding patients with restless leg syndrome, 74% (14/19) reported symptoms interfered with sleep. A positive family history for neuropathy was found in 35%.

SUMMARY/CONCLUSION: In our patients with TS-HDS antibodies we noted predominantly painful sensory symptoms starting in the feet with subsequent hand involvement and exacerbation by physical activity. Sleep disturbance was also common. These clinical findings are comparable with existing literature. Interestingly, the age of symptom onset in non-diabetics was 7 years earlier than diabetics.

Sri Raghav Sista, MD
Resident and Fellow Member Award Recipient

PARSONAGE–TURNER SYNDROME AFTER MELANOMA RESECTION: A CASE REPORT
Christopher Reece (Bethesda, MD), Jennifer Windsor (Bethesda, MD), Matthew Miller (Potomac, MD)

INTRODUCTION/BACKGROUND: Parsonage–Turner syndrome (PTS) is a rare disorder with an unclear etiology, although it has been reported after infection, trauma, and surgery. The identification of the syndrome in the postoperative patient remains a challenge as symptoms may easily be attributed to sequelae of surgery. However, melanoma resection does not require traction or special positioning.

CASE REPORT: A 57-year-old right-handed man with past medical history of melanoma presented complaining of poorly localized, sharp right shoulder pain 5 days after right posterior neck melanoma excision. The pain progressed and worsened with movement and overhead activities. Shortly after the pain started, he developed shoulder abduction and flexion weakness. Focused physical examination revealed right medial scapular winging, trapezius atrophy, and weakness of abduction. MRI of brachial plexus was normal with exception of increased uptake in the right trapezius. EDX evaluation completed 2 months after initial presentation showed severe axonal right spinal accessory (SA) and long thoracic (LT) neuropathy. Focused ultrasound (US) evaluation at that visit showed the SA and LT nerves were intact with evidence of continuity without swelling. The course of the nerves were found to be separated from the surgical site. There was no voluntary contraction of the trapezius muscle on US. Followup EDX studies 6 months after symptoms started showed evidence of ongoing muscle membrane instability with signs of collateral sprouting in the right trapezius indicative of improvement.

SUMMARY/CONCLUSION: Although PTS is known to occur postoperatively, it is usually found after orthopedic or cardiovascular procedures versus superficial skin procedures without traction or nerve blocks.

Christopher Reece, MD
Resident and Fellow Member Award Recipient
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### MEDIAN PALMAR CUTANEOUS NEUROPATHY FOLLOWING RIGHT RADIAL ARTERY ACCESS FOR CARDIAC CATHETERIZATION: A CASE REPORT

Jessica Calandra (Philadelphia, PA), Shawn Peterson (Somerdale, NJ)

**INTRODUCTION/BACKGROUND:** The palmar cutaneous branch of the median nerve is highly susceptible to injury. Reported etiologies include trauma, compression from cysts or neuromas, complications of carpal tunnel release surgery, and compression after radial fracture. Rarely have vascular etiologies been reported in this mononeuropathy. We present a case of mononeuropathy of the palmar cutaneous branch of the median nerve following cardiac catheterization accessed via the radial artery.

**CASE REPORT:** The patient is a 47-year-old female who presented for EDX evaluation of her right arm pain and dysesthesias which began following a radial artery catheterization 8 months prior. Due to prior excessive bleeding, a compression sleeve was placed for approximately 8 hours post procedure predisposing to vascular stasis. One week later, she developed dysesthesias in the volar wrist and burning pain in the wrist radiating up the forearm. Vascular workup revealed occlusion in the right radial artery without mention of aneurysm. Occlusion was treated conservatively. On EDX evaluation she displayed some altered sensation over median digital branches with allodynia over the palmar cutaneous distribution and trace pain limited weakness in the abductor pollicis brevis. NCSs were notable for axon loss of the right median palmar cutaneous sensory branch without signs of demyelination. The digital sensory and motor branches of the right median nerve were electrophysiologically unaffected.

**SUMMARY/CONCLUSION:** It is proposed that this patient developed mild neuronal ischemia related to her radial artery thrombosis. There were no signs of aneurysm on vascular ultrasound. We recommended a dedicated musculoskeletal ultrasound to confirm the absence of compressive etiologies.

Jessica Calandra, DO
Resident and Fellow Member Award Recipient

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### A NOVEL SPASTIC PARAPLEGIA-11 GENE MUTATION CAUSING CHARCOT–MARIE–TOOTH DISEASE TYPE 2X

Nirav Sanghani (Newark, NJ), Leila Maybodi (West Orange, NJ), Nizar Souayah (Westfield, NJ)

**INTRODUCTION/BACKGROUND:** Mutations in the spastic paraplegia-11 (SPG11) gene are known to cause hereditary spastic paraplegia (HSP), ALS, and Charcot–Marie–Tooth (CMT) disease type 2. To date, more than 100 pathogenic mutations have been described. We present a case of CMT2X caused by a novel SPG11 mutation.

**CASE REPORT:** Ms. J.O. is a 34-year-old woman of Peruvian decent who presented with gait disturbance since the age of 10. This problem progressed and by age 25 she was wheelchair dependent. She is adopted and her family history is unknown. Motor milestones had been mildly delayed, and she attended Special Education schooling. Her examination revealed mild psycho-motor slowing, normal cranial nerves, atrophy of proximal and distal muscles of the limbs, more severe in the legs than arms (where distal atrophy was pronounced), hypotonia of legs, and scoliosis. She had weakness (MRC 3 in deltoids, 2 in distal arms, and 1 in both lower extremities), generalized hypo/areflexia, and distal hypesthesia. Brain MRI showed severe thinning of the corpus callosum and “ear of lynx” sign. EDX studies demonstrated severe sensory-motor axonal neuropathy. Next Generation sequencing identified a homozygous nonsense mutation in the SPG11 gene (chromosome 15): c.3121C>T; p.Arg1041Ter. This mutation has been shown to cause HSP, but to our knowledge there has not been any report of it causing CMT2X.

**SUMMARY/CONCLUSION:** This case represents an SPG11 variant syndrome consistent with CMT2X, yet associated with a novel pathogenic mutation. Pleiotropy of this gene producing different phenotypes is again demonstrated.

Nirav Sanghani, MD
Resident and Fellow Member Award Recipient
INCIDENCE OF AUTONOMIC NEUROPATHY AMONG PATIENTS WITH SMALL FIBER NEUROPATHY
Francis Lagattuta (Santa Maria, CA), Cristina Tipei (Santa Maria, CA),
James Tipei (Arroyo Grande, CA), Lane Lagattuta (Chicago, IL),
Austin Tian (Stockton, CA)

INTRODUCTION: Patients with small fiber neuropathy (SFN) may also have autonomic neuropathy (AN), which can be a life threatening condition. We present patients who had symptoms compatible with SFN and AN. They were then tested for both SFN and AN.

OBJECTIVE: To determine the incidence of AN and SFN in patients with symptoms compatible with AN.

METHODS: Patients who answered questions positively for either SFN or AN had a skin biopsy for an epidermal nerve fiber density (ENFD) test and autonomic nerve testing. The autonomic tests were sympathetic sudomotor, parasympathetic cardiovagal, valsala maneuver, and tilt table testing. Results of all tests were analyzed.

RESULTS: A total of 35 patients answered positively to questions regarding symptoms of AN and underwent both a skin biopsy and all 4 autonomic tests: 4 (11%) had normal tests for both ENFD and autonomic testing. Ten (29%) of the patients were diabetic. Twenty-three (66%) had abnormal autonomic tests. Nineteen (54%) had abnormal ENFD results. Twelve (34%) had a normal ENFD and abnormal autonomic testing. Seven (20%) had length-dependent SFN and abnormal autonomic testing. Four (11%) had non–length-dependent SFN and abnormal autonomic testing.

SUMMARY/CONCLUSION: Patients with symptoms of AN should be tested for AN and SFN, including both diabetics and nondiabetics, so treatment can be started immediately.

PERIPHERAL NEUROPATHIES ASSOCIATED WITH NEUROGLIAL ANTIBODIES: CLINICAL, ELECTRODIAGNOSTIC, AND HISTOPATHOLOGICAL CHARACTERISTICS
Pritikanta Paul (Rochester, MN), Christopher Klein (Rochester, MN), Sean Pittcock (Rochester, MN), Andrew McKeon (Rochester, MN),
Rocio Vazquez do Campo (Rochester, MN), ELIA SECHI (Rochester, MN),
Eoin Flanagan (Rochester, MN), Michel Toledano (Rochester, MN),
John Mills (Rochester, MN), Divyanshu Dubey (Rochester, MN)

INTRODUCTION: Descriptions of aquaporin-4 (AQP4), glial fibrillary acid protein-α (GFAPα), and myelin oligodendrocyte glycoprotein (MOG) antibody associated neuropathies are limited.

OBJECTIVE: To describe clinical, EDX, and histopathological characteristics of neuropathies associated with neuroglial antibodies.

METHODS: Inclusion criteria comprised: (1) signs/symptoms of neuropathy, (2) EDX/radiological evidence of peripheral neuropathy, (3) AQP4/GFAPα/MOG seropositivity, and (4) reasonable exclusion of alternative etiologies. Clinical outcome was measured by change in modified Rankin Score.

RESULTS: Nineteen AQP4-IgG (9), MOG-IgG (5), or GFAPα-IgG (5) seropositive patients with neuropathies were identified; 12 (63%; AQP4, 4; MOG, 4; GFAPα, 4) had neuropathies as the initial presentation. Polyradiculoneuropathy/polyradiculopathy were the most common phenotypes (84%). Others included bilateral sciatic neuropathy (1) and subacute length-dependent neuropathy (2). The majority had coexisting myelopathy (68%). Four (GFAPα-IgG, 2; AQP4-IgG, 1; MOG-IgG, 1) had demyelinating EDX features (slow conduction velocity, 2; prolonged/absent F waves, 1; conduction block, 1). Cerebrospinal fluid had inflammatory changes in 87% (13/15). Four (GFAPα-IgG, 2; MOG-IgG, 1; AQP4-IgG, 1) had nerve biopsies. AQP4-IgG case had evidence of increased axonal degeneration and small-to-moderate epineurial and endoneurial perivascular inflammatory collections. GFAPα-IgG and MOG-IgG cases demonstrated increased rate of demyelination and axonal degeneration, along with individual to small collections of inflammatory cells.

Seventeen patients received immunotherapy. Favorable outcome at last followup varied based on antibody specificities: MOG-IgG (60%), GFAPα-IgG (60%), and AQP4-IgG (44%).

SUMMARY/CONCLUSION: Peripheral neuropathy with/without central nervous system involvement is a rare but severe manifestation of neuroglial antibodies. Recognizing the polyradiculoneuropathy/polyradiculopathy phenotype may help in early diagnosis and treatment.

Pritikanta Paul, MBBS
Resident and Fellow Member Award Recipient
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EPIDERMAL NERVE FIBER QUANTIFICATION IN DYSLIPIDEMIC PATIENTS
Francis Lagattuta (Santa Maria, CA), Austin Tian (Stockton, CA), Nancy Tian (Stockton, CA)

INTRODUCTION: Needle EMG methods have been well established for diagnosing peripheral neuropathy but have limited clinical utility in diagnosing small fiber neuropathy (SFN). Epidermal nerve fiber density (ENFD) is quickly becoming the gold standard when assessing for the presence, and the degree, of SFN. In this study, dyslipidemia and SFN in symptomatic patients with normal needle EMG were evaluated with ENFD.

OBJECTIVE: To determine how many dyslipidemic patients with negative NCS/needle EMG results have reduced ENFD.

METHODS: One hundred sixty-six patients with a history of dyslipidemia who had clinically suspected peripheral neuropathy but normal NCS/needle EMG results underwent ENFD. Their results were classified normal or abnormal based on age- and sex- adjusted normative values. Abnormal ENFD results were categorized as length-dependent or non–length-dependent. Patients’ history of dyslipidemia was used to determine whether dyslipidemia is associated with SFN.

RESULTS: Of 166 dyslipidemic patients with normal NCS/needle EMG, 157 (95%) showed reduced ENFD compared to 9 (5%) with normal ENFD results (p<0.001). Among 157 dyslipidemic patients with abnormal ENFD results, 98 (62%) were length-dependent versus 59 (38%) who were non–length-dependent (p>0.05).

SUMMARY/CONCLUSION: There was a significant difference observed in patients with dyslipidemia when patients with reductions in their ENFD tests were compared to patients with normal results. There was also determined to be no significant difference in SFN patients with dyslipidemia when length-dependent SFN was compared to non–length-dependent SFN. Our findings indicate that ENFD is a useful technique for the assessment of SFN in dyslipidemic patients.

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CLINICAL CHARACTERISTICS OF FIBROBLAST GROWTH FACTOR RECEPTOR 3 ANTIBODY RELATED POLYNEUROPATHY: A RETROSPECTIVE STUDY
Sukanthi Kovvuru (New Haven, CT), Bhaskar Roy (New Haven, CT), Richard Nowak (New Haven, CT)

INTRODUCTION: Autoantibodies, such as fibroblast growth factor receptor 3 (FGFR3), are increasingly being used as diagnostic biomarkers of inflammatory neuropathies; however, their role and associated clinical syndrome are not well defined.

OBJECTIVE: To report clinical presentation and therapeutic responses in FGFR3 associated neuropathy. METHODS: This retrospective chart review evaluated patients with neuropathy associated with FGFR3 antibody.

RESULTS: Sixteen patients (9 men, 7 women; age: 29-87 years, mean: 65.3±13.6) with positive FGFR3 antibody were included. Distal lower extremity paresthesia (60%), unsteady gait (30%), and foot drop (12.5%) were common presenting symptoms. Symptom onset was gradual in 80%. Distal lower extremity weakness (mild in 6, severe in 3 patients) was the most frequent motor finding. Decreased distal sensation to pinprick (60%) and loss of vibration sensation (40%) was common. Titer of FGFR3 ranged between 3100-29,000 (normal <3000) with a mean of 10,500±7200. Three patients had additional trisulfated heparin disaccharide (TS-HDS) antibody. Neurofascin antibody, anti-cyclic citrullinated peptide (anti-CCP) antibody, double stranded DNA, and GM1-antibody were positive in 1 patient each. Other common neuropathy workup including vitamin B12, serum protein electrophoresis/immunofixation, vitamin B1/B6, and hepatitis B/C were normal/negative. Needle EMG reflected sensorimotor neuropathy with mixed axonal and demyelinating features in 50% of cases. Pure sensory neuropathy was noted in 2 patients. Three (out of 4) nerve biopsies revealed evidence of demyelination. Five patients were treated with IVIg therapy, all responded.

SUMMARY/CONCLUSION: FGFR3 is probably not specific for sensory neuropathy, as previously reported; clinical presentation may vary. Some patients may respond to immunotherapy. Larger studies are warranted.

Sukanthi Kovvuru, MD
Resident and Fellow Member Award Recipient

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Bhaskar Roy: Consultant for Alexion Pharmaceuticals. Received support from Infinity NeuroNEXT fellowship.
MULTIFOCAL MOTOR NEUROPATHY WITH PARTIAL BLOCK OF NERVE CONDUCTION: A CASE REPORT
Camilo Salazar (Bogota, Colombia)

INTRODUCTION/BACKGROUND: Multifocal motor neuropathy with partial conduction block is characterized as a chronic, demyelinating, autoimmune severely disabling neuropathy. This neuropathy presents clinically in relatively young persons.

OBJECTIVE: To report a patient seen in consultation with progressive symptoms of motor neuropathy mainly affecting their arms.

CASE REPORT: A 33-year-old male presented with progressive motor symptoms affecting his arms. Physical examination revealed severe asymmetrical weakness, with atrophy which was less marked than the weakness, fasciculations, cramps, and myokymia of the affected muscle. He did not have cranial nerve involvement. Reflexes were diminished, and he did not have sensory involvement. NCSs showed partial conduction block in motor nerves, in segments with no conduction block in sensory nerves. Although the initial compromise was in the left radial nerve, the most affected nerves were the medial, right ulnar, and tibial nerves, both clinically and in the conduction block found in the neurophysiological studies, given the greater dispersion of the compound muscular action potential.

CONCLUSION: Clinical interest is due to the patient’s condition being potentially curable. Many cases are wrongly diagnosed as motor neuron disease. It can be affirmed that for the patient reported in this case, neurophysiological studies were definitive to reach the diagnosis of the disease, as well as to demonstrate the topography of the affected nerves and corroborate the demyelinating nature of this disorder. Multifocal motor neuropathy is a variant of chronic inflammatory demyelinating polyneuropathy with predominantly motor and asymmetric involvement.

INTRASPINAL LIPOMA: AN UNUSUAL CAUSE OF LUMBAR RADICULOPATHY
Kacper Pierwola (Hershey, PA), Colleen Newhard (Hershey, PA), Aiesha Ahmed (Hershey, PA)

INTRODUCTION/BACKGROUND: EDX testing is regularly used in addition to radiography and MRI to assist in evaluating radiculopathies. The most common causes of radiculopathies include structural lesions such as herniated discs and bony impingement, but can also include mass lesions such as an abscess or tumor. The tumors involved are typically metastatic, but a rare subset of primary tumors can also be seen. We present a case of lumbar radiculopathy secondary to an intraspinal lipoma.

CASE REPORT: A 60-year-old male with a history of spina bifida and low back lipoma excision 2 years ago presented to an outpatient neurosurgery clinic with complaints of persistent and progressive low back pain which woke him at night. His pain was associated with weakness and numbness radiating to his bilateral lower extremities. Diminished patellar reflexes were documented on examination. MRI revealed an intraspinal lipoma measuring 6.2 cm in the craniocaudal dimension. EDX testing revealed normal sensory and motor responses with motor unit abnormalities in bilateral gluteus medius and tibialis anterior as well as the left vastus medialis, revealing evidence of a right chronic L5 radiculopathy and left chronic L3-5 radiculopathy.

SUMMARY/CONCLUSION: Classic radicular symptoms include pain and paresthesias which radiate in the distribution of a nerve root alleviated by laying down and lumbar spine extension. Pain which wakes a patient at night with an increase in pain when laying may suggest a neoplasm. Radiculopathy secondary to a neoplasm most commonly occurs due to metastatic disease and rarely because of primary tumors such as neurofibromas, meningiomas, dermoids, or lipomas.

Kacper Pierwola, MD
Resident and Fellow Member Award Recipient
CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY IN A PATIENT WITH EMBRYONAL CARCINOMA
Andre Granger (Brooklyn, NY), Patrick Kwon (Brooklyn, NY)

INTRODUCTION/BACKGROUND: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neuropathic disorder characterized by autoimmune demyelination of peripheral nerves. Hematologic malignancies are the most common malignancy associated with CIDP. There has not been a described case of CIDP and embryonal carcinoma. Seminomas have been rarely associated with CIDP, but never the embryonal carcinoma subtype. Features that may suggest underlying malignancy include ataxia, distal/upper limb predominance, and bulbar/pulmonic/autonomic involvement.

CASE REPORT: A 51-year-old male with a history of vertigo and nephrolithiasis presented with toe and fingertip numbness for 2 months and unsteady gait. He denied weakness. Physical examination was notable for length-dependent decreased sensation in lower extremities, decreased deep tendon reflexes throughout, and ataxia. Cerebrospinal fluid analysis showed elevated protein with mild lymphocytic pleocytosis. Needle EMG showed a predominantly demyelinating, generalized polyneuropathy with evidence of conduction block in the left tibial nerve and temporal dispersion diffusely. He was thus diagnosed with CIDP and was started on IVIg. One month later, renal sonogram revealed a 10 cm left sided extrarenal mass, found to be a germ cell tumor of the embryonal carcinoma type. There was also pathologic evidence of a “burnt out tumor” in the left testicle. He is currently arranging for chemotherapy after surgical resection.

SUMMARY/CONCLUSION: This is the first described case of embryonal carcinoma in a patient with CIDP. It seems appropriate that the presence of CIDP should prompt the neurologist to, at a minimum, review the patient profile for signs/symptoms suggestive of concurrent malignancy. This becomes more important in patients with atypical features such as ataxia.
PILOT STUDY OF THE RELIABILITY AND VARIABILITY OF LOWER EXTREMITY MOTOR UNIT NUMBER INDEX IN CHARCOT–MARIE–TOOTH DISEASE TYPE 1A

Ryan Castoro (Nashville, TN)

INTRODUCTION: One of the largest obstacles to conducting clinical trials in Charcot–Marie–Tooth (CMT) disease is the lack of responsive disease markers. Motor unit number index (MUNIX) has emerged as a potential marker of disability in CMT type 1A patients.

OBJECTIVE: To determine the reliability and variability of tibialis anterior (TA) and abductor hallucis brevis (AH) MUNIX in CMT1A patients.

METHODS: We performed MUNIX of the TA and AH on 13 genetically-confirmed CMT1A patients and 10 age-matched healthy control subjects. All MUNIX studies were performed in triplicate from 3 different optimized locations.

RESULTS: In CMT1A patients, peroneal compound muscle action potentials (CMAPs) were obtainable in 12/13 (92.3%), whereas tibial CMAPs were only obtainable in 5/13 (38%). Tibial MUNIX was excluded from this analysis. Compared to healthy control subjects, CMT1A patients had significantly decreased TA MUNIX (149.0±44.8 au; 48.0±29.6 au; p>0.001), whereas motor unit size index (MUSIX) was not significantly different between the 2 groups (56.9±15.0; 51.7±23.1, p=0.5716). In CMT1A patients, 9/12 (75%) had a TA MUNIX less than the 95% confidence interval of that of control subjects. The intraclass correlation for TA MUNIX within CMT1A patients was 0.91, with a between group average coefficient of variance of 7.3±7.5 au. TA MUNIX was significantly associated with CMT Examination Score (CMTES) (p=0.017).

SUMMARY/CONCLUSION: We demonstrate that decreased TA MUNIX is common in patients with CMT1A. Additionally, we show that TA MUNIX independently correlates with CMTES. These data suggest that TA MUNIX may act as a potentially responsive marker of disease in CMT1A.

Ryan Castoro, DO, MS
Resident and Fellow Member Award Recipient

TRENDS IN THE MANAGEMENT OF CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: A STATEWIDE PLANNING AND RESEARCH COOPERATIVE SYSTEM STUDY 2002-2014

Yueqing Zhang (Newark, NJ), Kevin Nolasco (Newark, NJ), Sanjila Islam (Newark, NJ), Jaideep Vaidya (Newark, NJ), Vijay Atluri (Newark, NJ), Basit Shafiq (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: There are several options for chronic inflammatory demyelinating polyneuropathy (CIDP) management.

OBJECTIVE: To investigate trends in inpatient and outpatient charges relevant to IVIg, plasma exchange (PE), and steroids administration from 2002-2014 for the management of CIDP.

METHODS: Patient data from 2002-2014 were retrieved from Statewide Planning and Research Cooperative System (SPARCS) database using the ICD9 code for CIDP. Charges on outpatient and inpatient services per patient were compared on a year-by-year basis to determine the overall trend during 2002-2014. The frequency of inpatient admission per year was also retrieved.

RESULTS: We identified 2850 CIDP patients. The overall charges in outpatient services demonstrated an increasing trend over 2002-2014. For outpatient charges during that period, IVIg represented 56±13% of charges, PE 39±17%, and corticosteroids 5.0±7.8%. The average outpatient charges per patient increased from $7,595 (2002) to $132,696 (2014). The overall trend during 2005-2014 for outpatients who required inpatient services was decreasing (y=(−0.0257*x)+0.9417). Between 2005 and 2010, the frequency in which patients were admitted as inpatients ranged 0.75-1.05 times per year. Between 2011 and 2014, the frequency in which patients were admitted as inpatients ranged 0.56-0.74 times per year.

SUMMARY/CONCLUSION: Our data demonstrated an increased average charge for CIDP management during 2002-2014 for outpatients that was paralleled by a reduction in the frequency of inpatient admissions. Work is in progress to determine trends in charges relevant to the inpatient setting as well as to specific CIDP treatments.
TRENDS IN THE MANAGEMENT OF CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: A STATEWIDE PLANNING AND RESEARCH COOPERATIVE SYSTEM STUDY 2002-2014

Yueqing Zhang (Newark, NJ), Kevin Nolasco (Newark, NJ), Sanjila Islam (Newark, NJ), Jaideep Vaidya (Newark, NJ), Vizy Atluri (Newark, NJ), Basit Shafiq (Newark, NJ), Nizar Souayah (Westfield, NJ)

INTRODUCTION: IVIg, plasma exchange (PE), and corticosteroids have been used as a first line to treat chronic inflammatory demyelinating polyneuropathy (CIDP). However, the trends in longterm outcomes have not been investigated.

OBJECTIVE: To compare trends in outcomes including mortality rates, discharge to a nursing home, and disability of CIDP patients across 2002-2014 treated with IVIg, corticosteroids, and PE.

METHODS: Patient data were retrieved from the Statewide Planning and Research Cooperative System (SPARCS) database for 2002-2014 using the ICD9 code for CIDP. Death was compared between patients receiving IVIg, PE, and steroids.

RESULTS: Of the 2850 patients identified with CIDP, 96 died. All 96 deaths were patients who solely used corticosteroids as their treatment. However, the overall death rate over 2002-2014 steadily decreased (y=-(0.0006*x)+0.0138). The death rate peaked in 2003 at 1.85% and dropped to 0.22% by 2014.

SUMMARY/CONCLUSION: Our preliminary data reported a trend toward the reduction of mortality rates in CIDP over 2002-2014. Death was exclusively observed in patients treated with corticosteroids. Work is in progress to determine the disability and discharge to nursing home rates, as well as the effect of comorbid conditions and socioeconomic factors on CIDP patients treated with IVIg compared to patients treated with corticosteroids and PE.

AXONAL PERIPHERAL POLYNEUROPATHY ASSOCIATED WITH IPILIMUMAB AND MANAGED WITH DEXAMETHASONE

Amit Sachdev (Okemos, MI), Pavel Volkov (East Lansing, MI)

INTRODUCTION: Ipilimumab is a monoclonal antibody targeting human cytotoxic T-lymphocyte-associated antigen 4. It is approved by the FDA for the treatment of metastatic melanoma. Immune-related peripheral neuropathy can occur as a complication of use. The package insert states that this adverse event should be managed with weight-based dosing of prednisone. No guidance is provided regarding longterm outcomes, ongoing management, or experience with the use of alternatives to prednisone in initial management.

CASE REPORT: A 57-year-old man was diagnosed with stage 3 melanoma and initiated on ipilimumab. Two weeks following the conclusion of his fourth cycle, he developed distal symmetric sensory loss in the lower extremities. Numbness progressed slowly for 6 weeks, culminating in foot drop symmetrically. By week 8, hand numbness began. Oncology service initiated dexamethasone. MRI of the brain was normal. MRI of the lumbar spine was normal. Needle EMG shortly after dexamethasone start identified widespread sensory and motor length-dependent defect. Dexamethasone was discontinued, and the patient slowly improved. At 2 years, the patient remained moderately impaired with foot drop.

CONCLUSIONS: While immune-mediated neuropathy has been associated with ipilimumab, a monophasic rather than chronic presentation was seen in this case. Dexamethasone was a reasonable therapeutic option. Neuropathy was severe in that it progressed to irreparable foot drop within 6 weeks.
CLINICAL FEATURES IN IMMUNE-MEDIATED SMALL FIBER NEUROPATHY WITH TS-HDS OR FGFR-3 ANTIBODIES
Lawrence Zeidman (Maywood, IL)

INTRODUCTION: Although up to 50% of small fiber neuropathy (SFN) cases may be idiopathic, an autoimmune etiology may underlie 20%. Novel antibodies to trisulfated disaccharide IdoA2S-GlcNS-6S (TS-HDS) and fibroblast growth factor receptor 3 (FGFR3) have been described in otherwise cryptogenic SFN cases.

OBJECTIVE: To describe clinical, neurophysiologic, and treatment features in cases of otherwise cryptogenic SFN found to have TS-HDS and FGFR3 antibodies.

METHODS: A retrospective analysis of all neuropathy patients in a university neuropathy clinic revealed 34 cases of cryptogenic SFN with normal needle EMG studies but positive skin punch biopsies. Of these, cases with positive TS-HDS and FGFR3 antibodies were identified and compared to the antibody-negative cases. Demographics, clinical features, autonomic results, and treatment responses were analyzed.

RESULTS: Of the cryptogenic SFN cases, 94% were female, and 62% had either TS-HDS or FGFR3 antibodies. Of these, 14% had FGFR3, 81% had TS-HDS, and 5% had both. In the antibody-positive and negative groups, 38% had a non–length-dependent pathology result. In the antibody-positive group, 43% had a positive sympathetic skin response (SSR) study versus 62% in the antibody-negative group (odds ratio=0.47). Six antibody-positive patients improved on IVIg, but 2 stopped due to side effects. Two patients improved on prednisone, and 2 had no improvement/side effects and stopped the drug.

SUMMARY/CONCLUSION: TS-HDS and FGFR3 antibodies may be present in a high proportion of cryptogenic biopsy-proven SFN cases which usually have normal SSR, suggesting lack of autonomic involvement. These cases may be responsive to immunosuppression, especially with IVIg.

Disclosures:
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THE COMBINED USE OF ELECTRODIAGNOSIS AND ULTRASOUND TO ASSESS A COMPLICATED TRAUMATIC BRACHIAL PLEXUS INJURY
Ana Moreira (São Paulo, Brazil), Jeffrey Strakowski (Powell, OH)

INTRODUCTION: Precise localization in brachial plexus injuries is challenging. Electrophysiologic measurement and anatomic visualization with ultrasound (US) are complimentary and together can dramatically improve diagnostic acumen.

CASE REPORT: A 26-year old male presented with severe right-hand weakness and partial global sensory disturbance following extraction injury. He had weakness in the right hand intrinsics (MRC grade 0) and extension and flexion of the wrist/fingers (grade 2-3), but normal strength more proximally. MRI suggested C8/T1 avulsion injury; electroneuromyography C8/T1 radiculopathies and median/radial neuropathies. Sensory responses were partially reduced in the right median, radial, and ulnar nerves, but a normal medial cutaneous nerve of the forearm response was seen. The right median motor response was absent; ulnar response was small. US showed normal right brachial plexus roots, trunks, and cords with exception of a mildly visible enlargement of T1 as it emerged from behind the first rib. Distinct abnormalities seen at the branch level of the plexus with markedly enlarged median, radial, and ulnar nerves. A stark contrast was seen in the degree of neurogenic muscle change in the mildly involved C8/T1 portions of the pectoralis, versus forearm and intrinsic hand muscles of the same myotome. Imaging helped confirm both pre- and post-ganglionic injuries and demonstrated the latter as more significant.

SUMMARY/CONCLUSION: This case demonstrates the utility of combining both electrodagnosis and US in a complicated brachial plexus injury. US provided better acumen than MRI for identifying the more distal lesions and helped confirm the basis of the EDX findings that suggested both pre- and post-ganglionic injury.
EXERCISE PROVOKATION OF STIMULATED SINGLE FIBER ELECTROMYOGRAPHY: AN ATTEMPT TO INCREASE THE DIAGNOSTIC YIELD IN MYASTHENIA GRAVIS PATIENTS
AyatAllah Farouk Hussein (Cairo, Egypt)

INTRODUCTION: Single-fiber EMG (SFEMG) provides the most useful test in patients with suspected myasthenia gravis (MG). Stimulated SFEMG (SSFEMG) is a useful, easier technique as compared to volitional SFEMG (VSFEMG). Here, the intramuscular twigs of the nerve are stimulated near the endplate zone. The jitter is calculated from the stimulus artifact and the single muscle fiber action potential. In an attempt to increase its diagnostic yield, it is performed after exercise and detects the post exercise exhaustion in the form of increased jitter and neuromuscular blocking.

OBJECTIVE: To estimate jitter values in MG patients pre and post exercise, and to detect if any prolongation of the jitter or blocking occurs.

METHODS: Twenty confirmed MG patients (12 female, 8 male; age: 28.34±10.1 years) were studied. All were diagnosed with MG through VSFEMG. SSFEMG was carried for the extensor digitorum communis muscle pre and post exercise. The parameters for evaluation were jitter, expressed as the mean consecutive difference, and presence of blocking.

RESULTS: SSFEMG prolonged jitter was found in 60% (12 patients) pre exercise and increased to 80% (18 patients) post exercise. Also, 5 patients had blocking pre exercise, while 10 patients showed blocking post exercise.

SUMMARY/CONCLUSION: Exercise provocation for SSFEMG increased the diagnostic yield in MG diagnosis.

THE DEVELOPMENT OF MYASTHENIA GRAVIS IN A PATIENT WITH FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY: CASE REPORT AND LITERATURE REVIEW
Feryal Nauman (Roanoke, VA), Muhammad Fawwad Ahmed Hussain (Roanoke, VA), Ahmet Burakgazi (Roanoke, VA)

INTRODUCTION: The coexistence of facioscapulohumeral muscle dystrophy (FSHD) and myasthenia gravis (MG) is very rare and few cases have been described in the literature.

CASE REPORT: We present the case of a 77-year-old male who was previously diagnosed with FSHD at age 50 and who came to our clinic due to the worsening of new symptoms, including double vision, ptosis, and swallowing issues, and the worsening of previous weaknesses. Along with FSHD, he was diagnosed with MG at age 74. When he was first diagnosed with FSHD, he presented with weakness of the facial muscles, proximal greater than distal muscle weakness in the upper limbs, and right greater than left weakness in the lower limbs along with gait disturbance. The diagnosis of FSHD was confirmed with genetic and EDX tests in 2002. The patient had progressive weakness and a decline in function over time. A followup visit in 2015 at a clinic revealed a remarkable decline in function. He had progressive weakness in lower greater than upper limbs and facial muscle weakness. In 2016, he developed new-onset double vision, worsening facial and neck weakness, and worsening weakness in swallowing, in addition to generalized weakness. A blood workup showed elevated acetylcholine receptor antibody levels. He showed a remarkable improvement in his symptoms with IVIg treatments.

CONCLUSION: To increase the awareness of the healthcare providers, we present a rare case of MG in a patient with FSHD, discuss the diagnostic challenges, present pre- and post-treatment findings, and provide a literature review.
CONCENTRIC NEEDLE JITTER IN CHRONIC RADICULOPATHY WITH AND WITHOUT ACTIVE DENERVATION
Joao Kouyoumdjian (Sao Jose do Rio Preto, Brazil), Felipe Faria (Sao Jose do Rio Preto, Brazil), Luis Ronchi (Sao Jose do Rio Preto, Brazil)

INTRODUCTION: Radiculopathy is a common cause for EDX evaluation, and active denervation/chronic reinnervation are useful parameters for severity.

OBJECTIVE: To prospectively study concentric needle jitter (CN-J) measurements in denervated/reinnervated muscles due to chronic radiculopathy (CR).

METHODS: CN-J was obtained from 27 selected patients (51.9% male; mean age: 51.5 years, range 36-74) through both voluntary and micro axonal intramuscular electrical activation in the same muscle that presented motor unit action potentials (MUAPs) with increased amplitude/duration and/or fibrillation and positive sharp wave potentials. The studied muscles were tibialis anterior, triceps, biceps brachii, vastus lateralis, and gastrocnemius. Spontaneous activity (SA) and MUAP amplitude were checked before jitter evaluation. In all cases, 20 and 30 apparent single fiber action potentials were taken for voluntary and electrical activation, respectively.

RESULTS: The mean consecutive difference (MCD) for voluntary activation was increased in 88.9% (mean: 50.2 μs). The MCD for electrical activation was increased in 81.5% (mean: 37.3 μs). There was a strong correlation between higher jitter values and SA (p<0.00001), but not with MUAP amplitude (r2=0.0994). The expected stimulated CN-J is expressed by the voluntary jitter/1.41 (71% lower). Here we found a mean 75% lower.

SUMMARY/CONCLUSION: CR with SA revealed high jitter values due to the immature motor axons and neuromuscular junctions. Isolated high MUAP amplitude did not correlate to the increased jitter. In CR cases with very high jitter but without SA, we had probably missed fibrillation and/or positive sharp wave potentials, or we should consider other possibilities.

COULD ANTIGANGLIOSIDE ANTIBODIES CAUSE A NEUROMUSCULAR JUNCTION DISORDER: A CASE OF ELEVATED ANTIGANGLIOSIDE ANTIBODIES IN A PARANEOPLASTIC NEUROMUSCULAR JUNCTION DISORDER
Noushin Jazebi (Galveston, TX), Ahmad Yusuf Solaiman (Galveston, TX), Xiang Fang (Galveston, TX)

INTRODUCTION/BACKGROUND: Antiganglioside-antibodies (Abs) are implicated as primary immune effectors in variants of Guillain–Barré syndrome (GBS). Besides affecting peripheral nerve axons, they may also target distal portions of motor axons including the neuromuscular junction (NMJ). It is reported that antiganglioside-Abs can bind to NMJs and thereby exert a variety of pathophysiological effects in animal models. However, it is unknown whether they can cause NMJ disease in humans. We report a rare case of NMJ-mediated weakness as a clinical manifestation of antiganglioside-Abs (Anti-G1a and GM1) in a patient with newly diagnosed lung cancer.

CASE REPORT: A 39-year-old male smoker presented with a 3-month history of progressive proximal muscle weakness, and bulbar symptoms. Neuroimaging and cerebrospinal fluid studies were normal. He responded well to initial treatment with IVIg and Mestinon® for possible myasthenia gravis. Workups—including acetylcholine receptor-Abs, anti-muscle specific kinase-Abs, and Abs to presynaptic-voltage-gated calcium channels—were negative. However, serum antiganglioside GD1a/GM1-Abs was significantly increased by 3-4 fold. NCSs/repetitive nerve stimulation showed pathological decrement of more than 10%, suggestive of a NMJ disorder. One month later, CT of the chest showed lung mass and biopsy revealed squamous cell carcinoma. This patient has been treated with monthly IVIg, and was stable at 3-month followup.

SUMMARY/CONCLUSION: We speculate that, in addition to GBS variants, antiganglioside-Abs might also be associated with NMJ dysfunction. Antiganglioside-Abs mediated NMJ disorder might present as a new paraneoplastic entity in patients with underlying lung cancer.

Noushin Jazebi, MD
Resident and Fellow Member Award Recipient
JITTER MEASUREMENT IN DISTANT MUSCLES FROM PATIENTS USING BOTULINUM TOXIN

Carla Graca (Sao Jose do Rio Preto, Brazil), Fabio Oliveira (Sao Jose do Rio Preto, Brazil), Joao Kouyoumdjian (Sao Jose do Rio Preto, Brazil)

INTRODUCTION: Botulinum toxin (BT) has been used therapeutically in the last decades. Single-fiber EMG measures jitter parameters to detect neuromuscular junction dysfunction. OBJECTIVE: To study the jitter parameters in distant muscles from the BT injection site.

METHODS: Outpatients who have BT injected their in facial and/or neck muscles, mainly for movement disorders, were recruited. Voluntary concentric needle jitter was measured in 41 patients (68.3% female; mean age: 65 years, range: 35-83) in a distant muscle, mainly extensor digitorum. Muscles with active denervation and/or chronic reinnervation were not used. T-test for 2 independent means (normal and abnormal jitter) was used to compare the following variables: time in days for jitter measurement from the last BT injection, time in days for jitter measurement from the first BT injection, total BT units used since the first injection, and age.

RESULTS: Abnormal jitter (>30 μs) was found in 7 cases (17.1%) with a mean of 35.6 μs (30.5-38.1). Normal jitter (≤30 μs) was found in 34 cases (82.9%) with a mean of 22.8 μs (17.3-29.6). There was no difference in any of the variables at a significance level of 0.05. The longest time with abnormal jitter (33 μs) from the last BT injection was 229 days.

SUMMARY/CONCLUSION: Jitter can be measured with high confidence in muscles of upper and lower limbs in cases of BT use in neck or facial muscles. To achieve the highest confidence, we suggest an 8-month interval from the last BT injection and/or anytime by increasing the upper limit of normal to 39 μs.

MYASTHENIA GRAVIS: A COHORT OF 91 CASES WITH CONCENTRIC NEEDLE JITTER

Gabriel Paiva (Sao Jose do Rio Preto, Brazil), Joao Kouyoumdjian (Sao Jose do Rio Preto, Brazil)

INTRODUCTION: Myasthenia gravis (MG) is the most frequent indication for measuring jitter for detecting neuromuscular junction dysfunction.

OBJECTIVE: To analyze antibodies (Abs), repetitive nerve stimulation (RNS), concentric needle jitter, and some epidemiological parameters in a confirmed MG cohort.

METHODS: Ninety-one patients (53.8% male; mean age: 54.7±17.9 years), 9.9% with ocular MG and 90.1% with generalized MG, were studied. Jitter was performed in extensor digitorum (62), orbicularis oculi (27), and frontalis (69), either by voluntary or stimulated activation, and results were expressed as the mean consecutive difference (MCD) and/or the percentage above individual MCD values. Abs to acetylcholine receptor (AChR) and muscle specific kinase (MuSK) were evaluated; the worst decrement values were used.

RESULTS: Mean age of onset was 44 years (females 37, males 50). Nine cases (9.9%) started after age 70. Mean time for diagnosis was 42 months. Mean disease duration was 10.4 months (range: 0.8-33.3). Two deaths occurred unrelated to MG. Some jitter parameters were abnormal in 95.1% (generalized) and 100% (ocular). Abnormal jitter was found in 1 muscle (83 cases) and 1/2 muscles (6 cases) studied; in 2 normal jitter cases, only 1 muscle was studied. AChR-Abs were abnormal in 95.5% (generalized; mean 16.9 nmol/L) and 66.7% (ocular; mean 2.4 nmol/L). MuSK-Abs were abnormal in 2.5%. RNS was abnormal in 80.5% (generalized) and 33.3% (ocular). MG crisis occurred in 23.1%. Thymectomy was performed in 51.6% (47 cases), and thymoma was found in 38.3%.

SUMMARY/CONCLUSION: Sensitivity for MG tests in all cohorts was shown to be 80.2% (RNS), 92.3% (Abs), and 95.6% (jitter).
PHENOTYPIC HETEROGENEITY IN A FAMILY WITH CONGENITAL MYASTHENIC SYNDROME  
Sandeep Devarapalli (Birmingham, AL), Kenkichi Nozaki (Birmingham, AL)

BACKGROUND: Congenital myasthenic syndromes (CMSs) are a heterogenous group of rare inherited disorders affecting neuromuscular transmission. There are more than 20 different gene mutations known to cause CMS, and SCN4A mutation is a rare cause.

CASE REPORT: A 30-year-old female with history of mild thoracic syrinx was referred to neurology at the age of 24 for back pain in the upper thoracic region. She was incidentally noted to have mild bilateral ptosis and facial weakness. On further inquiry, she reported having generalized weakness, especially in the face, and to be a slow runner and clumsy since childhood. She denied diplopia and dysphagia. Neurological examination showed mild bilateral ptosis, intact extraocular movements, facial weakness, and mild and symmetric weakness in upper and lower extremities. NCSs, needle EMG, and repetitive nerve stimulation were normal. Single-fiber EMG showed markedly prolonged jitter in the right frontalis. A genetic test for a clinical CMS diagnosis was reported to show a heterozygous variance of unknown significance in SCN4A gene (c.2662A>C, p.Lys888Gln). Further investigation disclosed her father having “lazy eyes” since childhood for which he underwent surgery. While his examination showed no weakness, it showed outward deviation of the right eye with upgaze. He claims similar “lazy eyes” in his brothers and maternal aunt. Further genetic tests in the parents of the patient showed the same variance in her father, but not in her healthy mother.

CONCLUSION: The patient has CMS with phenotypic variation in her family. The variance in the SCN4A gene may be a pathogenic mutation.

Disclosures:
Kenkichi Nozaki - Principal investigator of the clinical study organized by Catalyst Pharmaceutical. Genetic test of the patient is supported by Catalyst Pharmaceutical.

SENSITIVITY AND SPECIFICITY OF ACETYLCHOLINE RECEPTOR AUTOANTIBODY TESTING FOR MYASTHENIA GRAVIS  
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INTRODUCTION: Acetylcholine receptor (AChR) binding and modulating assays are frequently used in myasthenia gravis (MG) evaluation. How combinatorial assays and coexisting neuromuscular disorders affect accuracy in testing has not been established.

OBJECTIVE: To investigate the utility of AChR binding and modulating autoantibodies assays in myasthenia service line testing.

METHODS: Clinical and electrophysiological testing was reviewed for 360 MG-suspect patients; all underwent AChR autoantibody testing between January 1, 2012 and December 31, 2015.

RESULTS: Of 360 patients, 123 had a final clinical and electrophysiological (>10% decrement and/or positive single fiber testing) diagnosis of MG. Testing sensitivities of AChR binding and modulating autoantibodies were 92% and 90%, respectively, and 94% by either 1 or both. Within 123 confirmed MG patients, 45 had coexisting neuromuscular disorders including: peripheral neuropathy (n=20), radiculopathy (n=17), mononeuropathies (n=7), and motor neuron disease (n=1). Testing sensitivity in these 45 for AChR binding and modulating autoantibodies were 93% and 89%, and 93% by either 1 or both. Of the 237 patients ultimately confirmed as not myasthenia, 89 had electrophysiological confirmation of alternative diagnosis. Among them, false– positives totaled 11 (3 both, 6 binding, 2 modulating), translating to 10% for binding and 6% for modulating. The final diagnosis for those with false–positive results was diverse and clinically distinguishable from MG: 1 hemifacial spasm, 2 neuropathy, 4 myalgia, 1 blurred vision, 1 epilepsy, and 1 encephalopathy.

SUMMARY/CONCLUSION: Accuracy in MG autoantibody testing is best achieved by combining AChR binding and modulating testing in patients with and without coexisting neuromuscular diagnoses.

Pritikanta Paul, MBBS  
Resident and Fellow Member Award Recipient
LIKELIHOOD OF GENERALIZATION: DOES IT EVER GO AWAY?
Ritika Suri (Detroit, MI), Anirudha Rathnam (Detroit, MI), Naganand Sripathi (Detroit, MI), Kavita Grover (Detroit, MI)

INTRODUCTION/BACKGROUND: Ocular symptoms are seen at onset in 50% of patients with myasthenia gravis (MG). Generalization of symptoms occurs in up to 80% of patients, out of which the majority (up to 90%) generalize within 2 years of presentation. We present a case of delayed generalization of symptoms in a patient with ocular MG.

CASE REPORT: A 60-year-old woman developed isolated double vision and drooping of lids in 2012. She was diagnosed with acetylcholine receptor antibody positive ocular MG. She was treated with pyridostigmine with good resolution. In February 2018 (6 years after initial symptom onset), she had worsening diplopia and ptosis and was treated with prednisone. Evaluation for aggravating factors for an MG exacerbation including repeat chest CT was negative. She was successfully weaned off the prednisone in August; however, within 1 month she had worsening ocular symptoms along with new dysarthria, dysphagia, and proximal arm weakness. Prednisone was restarted with gradual upward dose titration without improvement. She required treatment with IVIg with rapid improvement of her symptoms.

SUMMARY/CONCLUSION: There are no previous reports of delayed generalization in ocular MG patients. This report highlights that generalization can rarely occur at a much later stage, as depicted in this patient where generalization occurred after 6 years. It also underlines the importance of continued followup of all MG patients including those with pure ocular MG. Further research highlighting mechanisms of late generalization of symptoms would be helpful in understanding the disease process and providing better care to patients.

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NEUROPHYSIOLOGY OF GIANT AXONAL NEUROPATHY
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INTRODUCTION: Giant axonal neuropathy (GAN) is an autosomal recessive neurodegenerative disorder affecting both peripheral and central nervous systems. It is the result of loss-of-function mutations in the GAN gene encoding gigaxonin, which regulates intermediate filament turnover. Onset of symptoms are typically at age 3-4 years, with sensory ataxia, followed by progressive length-dependent loss of motor and sensory function. Demise is frequently by the third decade due to respiratory dysfunction, though there are milder phenotypes.

OBJECTIVE: To characterize the neurophysiological function in individuals with GAN.

METHODS: Forty GAN patients were evaluated under Genetic and Physical Study of Childhood Nerve and Muscle Disorders (NCT01568658) and Electrical Impedance Myography (EIM): Exploratory Studies in Healthy People and People With Neuromuscular Disorders (NCT01900132).

RESULTS: All patients (age: 9.4±4.0 years, range: 4-21) had axonal sensorimotor neuropathies. Median compound muscle action potential (CMAP) (3.2±2.3, 9.3-0.1 mV) was present in all. Fibular CMAP recording from tibialis anterior was present in 34/37 (1.7±1.3, 0.1-5.1 mV) but the extensor digitorum brevis was in only 16/32 (0.7±1.0, 0.1-3.7 mV). Median sensory responses (19.0±24.9, 2.0-86.4 μV) were present in 16/40 but only 5/36 had sural sensory responses (13.0±4.4, 7.1-18.8 μV). Q-Sweats (n=17) in the forearm (0.30±0.46, 0.11-1.67 μL/cm2) and ankle (0.26±0.27, 0.02-0.94 μL/cm2) were low. Tilt table (n=8) did not show orthostatic changes. EIM 50 Hz phase showed an 8-muscle EIM of 7.8±2.8, 4 upper extremity-EIM of 9.3±3.3, and 4 lower extremity-EIM of 6.2±2.6.

SUMMARY/CONCLUSION: This study shows the range of severity in neurophysiological testing of GAN patients including a subset of older patients with milder findings.
COMITANT OCULAR DEVIATION IN MYASTHENIA GRAVIS
Tiffany Pike-Lee (Cuyahoga Falls, OH), Yuebing Li (Cleveland, OH), Jeremy Hill (Cleveland, OH), Gregory Kosmorsky (Cleveland, OH)

INTRODUCTION: Ocular deviation (strabismus) is often classified as being comitant or incomitant. Incomitant strabismus occurs when the degree of ocular deviation changes with directions of gaze. Comitant strabismus is equal in all gaze directions regardless of the eye used for fixation, and is usually seen in congenital or acquired disorders of brainstem or cerebellum. It is traditionally thought that myasthenia gravis (MG) is associated with incomitant strabismus. Occurrence of comitant strabismus in MG is not well established, thus the focus of our study.

OBJECTIVE: To determine occurrence of comitant strabismus in MG patients at a single tertiary center.

METHODS: This was a retrospective review of MG patients receiving detailed strabismus examination. Comitance was defined as deviations in horizontal or vertical planes varying by less than 20%.

RESULTS: Of 120 MG patients, 25.8% had generalized MG and 74.2% ocular; 61.7% were MG-treatment naïve, and 42.5% had ptosis. Strabismus testing revealed comitant strabismus in 27 (22.5%), incomitant strabismus in 28 (23.3%), and no ocular deviation in 65 (54.2%) patients. In 8 patients with comitant strabismus who had followup strabismus examination, strabismus remained comitant in 2, converted to incomitant strabismus in 1, and improved to no deviation in 5. In 11 comitant patients who had brain MRI, no abnormalities were observed in the brainstem or cerebellum region. After a mean followup duration of 2.5 years (range: 0–7), MG remained the final diagnosis in the comitant group.

SUMMARY/CONCLUSION: Comitant strabismus is common in MG patients with ocular symptoms. Its presence does not necessarily indicate a central etiology; neither excludes a MG diagnosis.

Tiffany Pike-Lee, MD
Resident and Fellow Member Award Recipient

OCULAR NON-THYMOMATOUS SEROPOSITIVE MYASTHENIA GRAVIS WITH MINIMAL DISEASE MANIFESTATIONS ASSOCIATED WITH ACQUIRED RIPPLING MUSCLE DISEASE
Karissa Gable (Hillsborough, NC), Vern Juel (Durham, NC)

INTRODUCTION/BACKGROUND: Acquired rippling muscle disease (RMD) has been reported to be associated primarily with generalized, thymomatous myasthenia gravis (MG).

OBJECTIVE: To describe 2 cases of ocular non-thymomatous seropositive MG (Myasthenia Gravis Foundation of America Class 1) with minimal manifestations and refractory RMD.

CASE REPORT: A 78-year-old man with acetylcholine receptor binding antibody (seropositive), non-thymomatous MG developed RMD symptoms 2 years prior to onset of fatigable diplopia. Caveolin-3 genetic testing was negative. He began immune suppression (IS) with mycophenolate mofetil 1000 mg twice daily with resolution of MG symptoms but without improvement of RMD. After several years, he tapered off mycophenolate mofetil due to development of leukopenia without recurrence of diplopia. His RMD symptoms persisted and remained refractory to symptomatic treatment. A 60-year-old man with seropositive, non-thymomatous MG developed RMD symptoms several months prior to onset of fatigable diplopia. Caveolin-3 genetic testing was negative. He was treated with a 4-month course of prednisone and 2 series of plasma exchange with resolution of diplopia but with persistent RMD symptoms. Symptomatic treatment for RMD produced minimal improvement.

SUMMARY/CONCLUSION: Acquired RMD is an interesting, presumably autoimmune phenomenon that may accompany MG. Most RMD/MG cases were heralded by RMD and have been associated with seropositive generalized MG with a higher than typical incidence of thymoma. These 2 cases demonstrate a spectrum of RMD that can be associated with more mild ocular MG with refractory RMD despite IS and symptomatic treatment.
USE OF SUBCUTANOUS IMMUNGLOBULIN IN A PATIENT WITH REFRACTORY MYASTHENIA GRAVIS

Jerrica Farias (Tampa, FL), Niraja Suresh (Riverview, FL), Brittany Harvey (Tampa, FL), Allison Schleutker (Tampa, FL), Natalie Tucker (Tampa, FL), Samuel Dang (Tampa, FL), Clifton Gooch (Tampa, FL), Tuan Vu (Tampa, FL)

INTRODUCTION: Myasthenia gravis (MG) is an autoimmune disorder of the neuromuscular junction resulting in ptosis, diplopia, weakness, dyspnea, dysarthria, dysphagia, and fatigue. In patients with severe impairments in function and quality of life, regular infusions of IVIg are sometimes utilized in addition to anticholinesterase inhibitors, corticosteroids, and immunosuppressants. Subcutaneous Ig (SCIg) therapy is being increasingly used in other neuromuscular disorders, but remains scarcely explored in patients with MG.

OBJECTIVE: To describe significant improvements in side effects, quality of life (measured by MG-QOL15), and activities of daily living (measured by MG-ADL) in a patient with refractory MG after transitioning from IVIg to SCIg.

CASE REPORT: We reviewed the medical record of the patient. MG-ADL and MG-QOL scores (collected routinely in MG patients at our institution) while on IVIg were compared to those obtained after switching to SCIg. The patient’s treatment regimen was otherwise unchanged.

RESULTS: After transitioning to an equivalent monthly dose of IVIg, weekly SCIg infusions provided drastic improvement in this patient’s MG-QOL15 and MG-ADL scores. The patient also had significantly fewer side effects and was able to avoid port placement.

SUMMARY/CONCLUSION: This case study suggests that some patients with refractory MG may be safely transitioned from IVIg to SCIg and such transition may improve their function and QOL.

MYASTHENIA GRAVIS AND PARKINSON’S DISEASE: CAUSATION OR CORRELATION?

Kalea Colletta (Orland Hills, IL), Jasvinder Chawla (Darien, IL), David Kvarnberg (Chicago, IL)

INTRODUCTION/BACKGROUND: Myasthenia gravis (MG) and Parkinson’s disease (PD) are seemingly unrelated diseases that rarely manifest in the same patient. MG is an autoimmune neuromuscular junction disorder, and PD is caused by dopamine loss in the substantia nigra. However, there is an increase in reported cases. Is there a link? We describe 2 patients with coincident MG and PD.

CASE REPORT: Patient 1 had positive anti-acetylcholine receptor antibodies (a-AChRAbs), single-fiber EMG, and DaTscan™. Patient 2 was diagnosed with MG elsewhere. Confirmatory antibody testing and EMG currently pending. However, examination and pharmacotherapy response are consistent with MG and PD. Both developed MG first; patient 1 within 2 years and patient 2 within 4 years.

SUMMARY/CONCLUSION: There are currently 18 reported cases of coincident MG and PD. a-AChRAbs were positive in a majority (61.1%) of cases, which questions the impact of a-AChRAbs on the central nervous system (CNS). Even though a-AChRAbs were thought to only affect peripheral muscular subunits, several studies described cross-reactivity with CNS antigens, namely neuronal AChR α9 and α7 subunits, accounting for CNS manifestations of MG. These manifestations include pain; sleep, cognitive, and autonomic dysfunction; and anosmia, which coincidentally are nearly identical to PD non-motor symptoms. Furthermore, CNS nicotinic AChR binding deficits have been described in PD patients, including the α7-subunit, which suggests further CNS insult by a-AChRAbs. Based on current research, a-AChRAbs seem to have a greater CNS impact than originally believed and may be linked to increases in coincident cases of PD and MG. Further investigation is necessary.
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THYMECTOMY IN A PEDIATRIC LRP4 POSITIVE MYASTHENIC PATIENT
Kabelo Thusang (East Lansing, MI), Amit Sachdev (Okemos, MI)

INTRODUCTION: Myasthenia gravis (MG) is an autoimmune neuromuscular junction disorder characterized by fluctuating muscle weakness. The LRP4 antibody has been associated with MG. While data are limited, the LRP4 mediated subtype is thought to be mild in terms of symptom burden. Thymectomy is a well-recognized therapy for acetylcholine receptor (AChR) associated MG. Controversy exists regarding the use of thymectomy in mild, medication-controlled versions of MG and non-AChR associated MG. We present the remarkable reduction in symptoms in a pediatric case of LRP4-associated MG following thymectomy.

CASE REPORT: We evaluated a 10-year-old girl and her mother. They presented with 2 years of ptosis, fatigue, and proximal muscle weakness. Pyridostigmine helped both patients. Both mom and daughter were found to be LRP4 positive. A CT scan of the chest showed a normal thymus in both. We recommended conservative therapy for both mom and daughter but also offered a second opinion. Both patients did well. However, the family felt strongly that they wanted to pursue aggressive management for the 10-year-old. Thymectomy was performed, and the pathology was consistent with hyperplasia of the thymus. She gradually improved.

SUMMARY/CONCLUSION: Autoantibodies against LRP4 are thought to predominantly cause a mild form of MG, where the mainstay of treatment has been symptomatic management. There is literature that recommends thymectomy for mild AChR-seropositive MG. It remains unclear if LRP4-seropositive MG should be managed with thymectomy, however this case suggests a positive outcome can occur with this management strategy.

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HETEROZYGOUS MUTATION IN CONGENITAL MYASTHENIC SYNDROME PATIENTS WITH LIMB-GIRDLE FORM OF CONGENITAL MYASTHENIA GRAVIS
Irine Siraj (Syracuse, NY), Furqan Waseem (Syracuse, NY), Amr Ewida (Syracuse, NY), Deborah Bradshaw (Syracuse, NY)

INTRODUCTION/BACKGROUND: Congenital myasthenic syndromes (CMSs) are debilitating disorders of neuromuscular junction characterized by fatigable weakness affecting limbs and oculofacial and bulbar muscles.

OBJECTIVE: To report a new heterozygous mutation a CMS with the limb-girdle form of congenital myasthenia gravis (MG).

CASE REPORT: An 11-year-old male presented with abnormal exercise-induced fatigue and difficulty running. Symptoms improved with rest. He did not experience ptosis, diplopia, dysphagia, or dysarthria. His sister was diagnosed with early-onset myasthenia. Neurological examination demonstrated progressive decrease in strength with repetitive strength testing in proximal muscles. Edrophonium improved his symptoms. Anti-acetylcholine receptor and anti-muscle specific kinase antibodies were absent. Repetitive stimulation studies demonstrated a percent decrement at 3 Hz. Muscle biopsy demonstrated type 1 fiber predominance with tubular aggregates. He was diagnosis with limb-girdle congenital MG. Pyridostigmine significantly improved his symptoms. At 5 years of age, genetic testing demonstrated heterozygosity for 3 variants on a CMS sequencing panel. Two in the GFPT1 gene, c.1831A>T, c.*22C>A, and 1 in SCN4A, c.4605G>A. His sister also possessed the c.1831A>T variant.

SUMMARY/CONCLUSION: CMSs are a group of diverse disorders linked by abnormal signal transmission at the motor endplate. Understanding disease pathophysiology can be interrogated by appropriate electrophysiologic and biochemical studies. In the absence of such clues, exome sequencing is useful for finding the disease gene. Our patients were heterozygous for GFPT1 c.1831A>T, a new variant of the limb-girdle type of CMS. This variant had not been reported previously. Most CMSs are treatable.
Abstracts

AN EXCEPTIONAL CASE OF A METASTATIC HIGH GRADE ASTROCYTOMA TO THE SPINAL CORD MIMICKING GUILLAIN–BARRÉ SYNDROME AT PRESENTATION
Dina Dababneh (Saint Louis, MO), Kevin Yeboah (Saint Louis, MO) Jafar Kafaie (Saint Louis, MO)

INTRODUCTION/BACKGROUND: Astrocytoma are slow-growing tumors in the brain where they rarely metastasize. Here, we describe an extremely rare case of metastatic spinal astrocytoma presenting with acute onset of ascending lower extremity weakness mimicking Guillain–Barré syndrome (GBS).

CASE REPORT: A 36-year-old male with history of a grade 2 astrocytoma with resection and radiotherapy, hypertension, type 2 diabetes, and hyperlipidemia presented with acute onset lower extremity weakness which had been static for 10 days. He reported recent influenza vaccination a few days prior to symptom onset, paresthesia in extremities and upper chest, and intermittent urinary incontinence. He denied double vision, dysphagia, or shortness of breath. Examination showed normal mental status, cranial nerves, language, and speech. Muscle strength was full in upper extremities and 0/5 in both lower extremities proximal and distally; deep tendon reflexes were absent on the left ankle and intact elsewhere. No sensory level was noted, and cerebellar examination was intact. Lumbar puncture, performed for GBS concerns, was unremarkable. Cytology was normal; needle EMG/NCSs were inconsistent with GBS. MRI of the thoracic and lumbar spines showed leptomeningeal carcinomatosis. Positron emission tomography showed increased fluorodeoxyglucose activity in the spinal column, pelvic bones, and splenic flexure of the colon. Final diagnosis was consistent with high grade astrocytoma causing spinal cord compression. Patient was on chemotherapy in addition to corticosteroids.

SUMMARY/CONCLUSION: Despite being extremely rare, infiltrative astrocytoma can still metastasize to the spinal cord and present with new onset lower extremity weakness mimicking GBS. A treatment decision should be urgently made to prevent clinical deterioration and subsequent death.

STAGED HEALING OF WRIST TENDONITIS FOLLOWING CMED® TREATMENT
Roger Coletti (Lewes, DE)

INTRODUCTION: CMED® (Coletti Method EMG Chemodenervation) denervation treatment (previously described, also see CMED.info) of chronic muscle spasm of forearm muscles with associated wrist tendonitis follows a different pattern of recovery from most other muscles in chronic spasm. The associated muscle spasm and wrist pain is generally considered referred pain or isolated tendonitis.

OBJECTIVE: To identify underlying pathophysiologic.

METHODS: Initial response to treatment and self-reporting of pain relief in the week following treatment was compared to patients without associated wrist tendonitis.

RESULTS: Patients with forearm pain secondary to chronic muscle spasm without tendonitis reported initial relief of pretreatment pain and 2-5 days of local mild injection site discomfort without recurrence of the presenting pain. Patients with chronic muscle spasm and associated wrist tendonitis reported predominant relief of pretreatment wrist pain associated with motion or stress but typically required 3 days before the wrist motion associated pain fully resolved. Injection site discomfort for 3-5 days was also noted.

SUMMARY/CONCLUSION: Complete relief of wrist tendonitis associated with forearm chronic muscle spasm appears to be time dependent. It is postulated that the tendonitis was the result of the chronic muscle spasm pull on the tendon and that resolution of the chronic muscle spasm pull allowed the tendon to recover. It was notable that 1 patient had undergone steroid injections of the wrist tendon with only temporary relief but attained long standing relief after the associated chronic muscle spasm was resolved following CMED® treatment. In contrast to the concept of referred pain, this appears to represent tendinopathy secondary to chronic muscle spasm.

Disclosures:
Dr. Coletti- Inventor of CMED®

Abstracts
NON-SKELETAL ETIOLOGY OF FOOT DROP WITH THERAPEUTIC REVERSAL

Roger Coletti (Lewes, DE)

INTRODUCTION: Foot drop has been long considered the result of neural foraminal compression or spinal stenosis. Therapeutic intervention has focused on epidural injections or laminectomy.

OBJECTIVE: To identify potential etiology of successful cases of foot drop reversal with non-skeletal interventions.

METHODS: CMECD® (Coletti Method EMG Chemodenervation) denervation procedure (previously described, see also CMECD.info) was performed on 4 cases of foot drop lasting from 3 months to 4 years. Outcomes were classified as immediate, progressive, or delayed. Injection was performed of the ipsilateral erector spine at the level of the lower lumbar vertebrae, typically at sites of discomfort on manual focused compression.

RESULTS: An immediate reversal was seen with a case of 3 month foot drop duration. An immediate improvement with full recovery was noted in a case with 6 months of foot drop. An improvement but not full reversal was seen in a case 2.5 years post laminectomy. Minimal initial with complete progressive recovery was seen after 6 months, including return of knee-jerk reflex, with 4 years of foot drop.

SUMMARY/CONCLUSION: Various responses of non-skeletal muscular intervention indicate that non-skeletal etiologies exist and may be caused by and responsive to treatment of chronic muscle spasm. Time frames of response appear to coincide with the duration of the presenting symptom although at least some immediate response was present in all cases. Nerve recovery with release of compression is known to vary with the extent of nerve injury. Current findings suggest that nerve compression muscular non-skeletal etiologies of foot drop exist and may be potentially treated with therapies to resolve chronic muscle spasm.

Disclosures:
Dr. Coletti- Inventor of CMECD®

PATTERN OF RECOVERY OF ACQUIRED CHRONIC MUSCLE SPASM CONSISTENT WITH ISCHEMIC INJURY MODEL

Roger Coletti (Lewes, DE)

INTRODUCTION: It is known that the blood supply of cardiac muscle is lessened by cardiac contraction. Flow is significantly less in systole than diastole even though the perfusion pressure is higher in systole. Prior unpublished work by this author demonstrated that with a weakening of the force of contraction, predominant cardiac flow occurred in systole. Microvascular supply of skeletal and cardiac muscle are similar. High heart rates that can occur with atrial fibrillation with near constant contraction can lead to cardiac dysfunction and muscle injury that slowly recovers over a 1-2 month period. Skeletal muscle in chronic spasm has been shown to have a depleted number of mitochondria that normalize with relief of the chronic spasm.

OBJECTIVE: To record patterns of clinical recovery of chronic muscle spasm to find potential consistency with an ischemic injury model.

METHODS: Muscles identified with acquired chronic muscle spasm by needle EMG, according to criteria previously described, were treated with the CMECD® (Coletti Method EMG Chemodenervation) procedure.

RESULTS: Relief of pain occurred early but the capacity of the muscle to perform work, without return to spasm, gradually increased. The severity and extent of the spasm appeared to correlate with the length of time to full recovery, noted to occur within a 2 month span.

SUMMARY/CONCLUSION: Clinical findings are supportive of an ischemic injury model of chronic muscle spasm. Expectations of full recovery and physical therapy interventions should be informed by consideration of this model. Assessment of treatment success or failure viewed within the context of this model may improve treatment outcomes.

Disclosures:
Dr. Coletti- Inventor of CMECD®
CO-OCCURRENCE OF OCULAR MYASTHENIA GRAVIS AND CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY

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INTRODUCTION: The concomitant association of myasthenia gravis (MG) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) has been sporadically reported. We present a case of a middle-aged man with this rare association.

OBJECTIVE: To report a case with co-occurrence of two autoimmune neuromuscular disorders.

METHODS: Case report

RESULTS: A 43-year-old man with history of diabetes mellitus, initially presented in 1989 with ocular symptoms of double vision and drooping of eyelids. He had no other reported weakness. His testing was positive for acetylcholine receptor antibodies. He was treated with pyridostigmine without relief, requiring initiation of prednisone and was maintained on 10-15 mg per day. Approximately 16 years later, he began having progressive foot drop on both sides and examination was consistent with absent reflexes and distal motor and sensory deficits. Nerve conductions and electromyography was consistent with acquired sensorimotor peripheral demyelinating polyneuropathy. Monoclonal protein evaluation showed IgG lambda monoclonal protein. He was started on Intravenous Immunoglobulin treatments with subsequent improvement in his CIDP and MG symptoms. In 2015, he had increased weight loss, developed anemia and renal failure and was diagnosed with IgG lambda multiple myeloma. He received chemotherapy with Bortezomib and dexamethasone with improvement in the myeloma, however, chemotherapy was stopped due to painful neuropathy.

SUMMARY/ CONCLUSION: Myasthenia gravis and CIDP are different autoimmune disorders with distinct immune mechanisms. Given that this association is so rare, physicians need to be cognizant of this co-occurrence as it can influence management in these patients.
INTRODUCTION: AChR and MuSK antibodies are found in 90% of generalized MG patients. In some double negative MG (DNMG) patients, LR4 and Agrin antibodies were detected. These antibodies were demonstrated to produce experimental autoimmune MG (EAMG) in mice and have been postulated to cause MG in humans. However, little is known regarding the incidence and clinical features of these patients.

OBJECTIVE: We studied the prevalence and clinical characteristics of LR4 and Agrin antibody-positive DNMG.

METHODS: DNMG patients at 16 U.S. sites were tested by ELISA for LR4 and Agrin antibodies, and clinical data was collected. Study patients must have had an abnormal SFEMG or repetitive nerve stimulation study, have clinical symptoms of MG, and not have recent IVIG, rituximab or plasmapheresis.

RESULTS: Of 182 DNMG patients, 12.6% (23) were positive for LR4 antibodies and 13.7% (25) were positive for Agrin antibodies. Twenty-two of these patients (12.1% of the total) were positive for both LR4 and Agrin antibodies. LR4/Agrin antibody positive patients were predominantly female (62%) and had an average age at sample draw of 55 (standard deviation 13.2). Initially 50% (13) had ocular symptoms only. MGFA classification of patients’ worst symptoms were: I (11.5%), II (42.3%), III (30.8%), IV (11.5%) and V (3.9%). Most patients’ symptoms were controlled with standard therapies. With treatment, 92.3% of patients were classified as either Class I or II.

SUMMARY/ CONCLUSION: Fourteen percent of DNMG patients had antibodies to either LR4 or Agrin. Eighty-eight percent of patients developed generalized MG. Most patients with therapy attained minimal manifestation status or better.

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MYASTHENIA GRAVIS PATIENT AND PHYSICIAN OPINIONS ABOUT IMMUNOSUPPRESSANT DOSE REDUCTION

INTRODUCTION: International MG Consensus Guidelines define successful MG treatments as those that result in minimal disease manifestations or remission with no more than minimal adverse events (AE). 1. In an effort to reduce risk of immunosuppressant (IS) exposure AEs, e.g. opportunistic infections and malignancies 2-9 to reduce burden to patients and the health care system, the guidelines also recommend decreasing IS dose in MG patients with prolonged clinical stability. 1, 10. However, IS dose reduction could also increase patient risk for clinical relapse.

OBJECTIVE: Define MG physician and MG patient opinions about IS dose reduction strategies to inform design of clinical trial of IS dose reduction in MG patients with prolonged disease stability.

METHODS: Online surveys of MG patients and MG physician experts identified from Myasthenia Gravis Foundation of America database.

RESULTS: 84% of MG patients (n=285) and 100% of physicians (n=45) in our recent national survey were concerned about long-term IS associated AEs, especially cancers. Although 98% of the MG patients felt it is important to consider medication reduction, 55% had concerns including: MG relapse (92%), hospitalization (60%), and uncertainty about the future (56%). 93% of physicians were also concerned about IS dose reductions. Presented with an estimated 12% serious relapse rate with IS dose reduction, 75% of patients would be willing to enroll in a randomized IS dose reduction clinical trial.

SUMMARY/ CONCLUSION: Physicians and patients are concerned about long-term IS exposure. Although both groups favor considering IS dose reduction, they are also concerned about potential negative sequelae of IS dose reduction.
ZILUCOPLAN, A SELF-ADMINISTERED SUBCUTANEOUS PEPTIDE INHIBITOR OF COMPLEMENT COMPONENT 5 (C5) FOR THE TREATMENT OF GENERALIZED MYASTHENIA GRAVIS: PHASE 2 RESULTS

James Howard (Chapel Hill, NC), Richard Nowak (New Haven, CT), Gil Wolfe (Buffalo, NY), Michael Benatar (Miami, FL), Petra Duda (Cambridge, MA), James MacDougall (Cambridge, MA), Ramin Farzaneh-Far (Cambridge, MA), Henry Kaminski (Washington, DC)

INTRODUCTION: In anti-acetylcholine receptor positive (AChR-Ab+) generalized myasthenia gravis (gMG), autoantibodies activate the classical complement pathway and trigger complement-mediated damage to the neuromuscular junction. Zilucoplan inhibits the cleavage of C5, thereby preventing the formation of the terminal complement complex.

OBJECTIVE: This randomized, double-blind, placebo-controlled Phase 2 study was conducted to evaluate the safety, tolerability, and efficacy of zilucoplan in AChR-Ab+ gMG patients with a Quantitative Myasthenia Gravis (QMG) score ≥12, regardless of prior treatment history.

METHODS: The primary and key secondary endpoints were change in QMG and MG Activities of Daily Living (MG-ADL) scores from baseline to week 12. MG Quality of Life and MG Composite scores were also assessed.

RESULTS: Forty-four patients were randomized 1:1:1 to placebo, zilucoplan 0.1 mg/kg, or zilucoplan 0.3 mg/kg self-administered subcutaneously daily over 12 weeks. Clinically meaningful and statistically significant reductions in mean QMG (6 points) and MG-ADL (3.4 points) were observed in the zilucoplan 0.3 mg/kg treatment group (placebo-corrected changes: -2.8; p=0.05 (QMG) and -2.3; p=0.04 (MG-ADL)). Rescue therapy (IVIg or plasma exchange) was required in 3/15 subjects in the placebo arm, 1/15 in the 0.1 mg/kg zilucoplan arm, and 0/14 in the 0.3 mg/kg zilucoplan arm. Zilucoplan was observed to have a favorable safety and tolerability profile, consistent with prior trials. Additional data on Phase 2, including the open-label long-term extension, and the Phase 3 design will be presented.

SUMMARY/CONCLUSION: These results support the further evaluation of zilucoplan in a registrational Phase 3 trial and its potential therapeutic role in a broader spectrum of patients with gMG.

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MINIMAL MANIFESTATIONS OF STATUS AND PREDNISONE WITHDRAWAL IN THE MGTX TRIAL
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INTRODUCTION/ OBJECTIVE: To examine whether sustained minimal manifestation status (MMS) with complete withdrawal of prednisone is better achieved in thymectomized myasthenia gravis (MG) patients.

METHODS: This study is a post hoc analysis of data from the randomized trial of thymectomy in myasthenia gravis (MGTX). MGTX was a multicenter, randomized, rater-blinded 3-year trial that was followed by a voluntary 2-year extension for patients with acetylcholine receptor (AChR) antibody positive MG without thymoma. Patients were randomized 1:1 to thymectomy plus prednisone versus prednisone alone. Participants were age 18-65 years at enrollment with disease duration less than 5 years. All patients received oral prednisone titrated up to 100mg on alternate-days until they achieved MMS, which prompted a standardized prednisone taper. The achievement rate of sustained MMS (no symptoms of MG for 6 months) with complete withdrawal of prednisone was compared between the thymectomy plus prednisone and prednisone alone groups.

RESULTS: MG patients in the thymectomy plus prednisone group achieved sustained MMS with complete withdrawal of prednisone more frequently (64% vs 38%) and quickly compared to the prednisone alone group (median time 30 months vs not achieved, P<0.001) over the 5-year study period. Prednisone associated adverse symptoms were more frequent in the prednisone alone group and distress level increased with higher doses of prednisone.

SUMMARY/CONCLUSIONS: Thymectomy benefits MG patients by increasing the likelihood of achieving sustained MMS with complete withdrawal of prednisone. This study provides Class II evidence that thymectomy plus prednisone is superior to prednisone alone in the treatment of AChR-antibody positive MG patients.
generalized MG patients without thymoma.

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RETROSPECTIVE LONGITUDINAL ASSESSMENT OF MG-ADL SCORE WITH TREATMENT OF MYASTHENIA GRAVIS

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INTRODUCTION: The MG-ADL scale is a validated eight-item questionnaire which assesses the symptoms and correlates well with functional impairment from myasthenia gravis (MG). A two-point change in the MG-ADL is clinically meaningful, with higher scores indicating worse function. Patient reported outcome measures such as MG-ADL have been utilized frequently as an outcome measure in MG research. More recently these have been used in routine clinical care.

OBJECTIVE: To assess the feasibility of retrospectively extracting the Myasthenia Gravis Activities of Daily Living (MG-ADL) score from the electronic medical record (EMR) for purposes of monitoring clinical status of populations of MG patients.

METHODS: MG-ADL scores are routinely obtained and inserted in the documentation flowsheet of the EMR at clinic visits for MG patients in the KUMC neuromuscular clinics. At each clinic visit where MG-ADL scores were obtained we abstracted MG-ADL values, demographics, serology, and interventions received. Descriptive statistics were used to define baseline characteristics and analyze the data.

RESULTS: Data abstraction yielded 845 MG-ADL scores for 334 patients. Data for 61 subjects in which the initial visit was identified was used for analysis. The median age at first encounter was 66 years and 34.4% were female. The median MG-ADL score at the first visit was 7. Median MG-ADL scores at 3, 6, 9, and 12 months were 6, 4, 6, and 4.

SUMMARY/CONCLUSION: It is feasible to extract MG-ADL scores from our EMR. Median MG-ADL scores suggest that overall most cases of MG remain stable or improve over more than 1 year.

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SURVIVIN IS A NEGATIVE REGULATOR OF APOPTOSIS IN MYASTHENIA GRAVIS: A HUMAN AND ANIMAL MODEL STUDY
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INTRODUCTION: Myasthenia gravis (MG) is caused by autoantibodies directed against the neuromuscular junction, with the majority of patients expressing antibodies to acetylcholine receptor (AChR). Autoreactive cells that produce the disease evade the immune checkpoints by an unknown mechanism. Survivin is a member of the inhibitor of apoptosis family and known to be expressed in circulating lymphocytes from MG patients. Survivin expression may be part of a mechanism that inhibits the apoptosis of autoreactive B cells in MG.

OBJECTIVE: To assess the role of survivin in myasthenia gravis

METHODS: The peripheral blood mononuclear cells were obtained from MG patients and non-autoimmune controls and stained with anti-human CD45, T cell marker (CD4), B cell marker (CD20), and anti-Survivin. The extracellular or intracellular survivin expression on human CD20+ or CD4+ lymphocytes were viewed by using BD Celesta analyzer followed by FlowJo software. To target survivin, a monoclonal antibody was developed against survivin peptide (SVN53-67/M57). For the animal model, EAMG was induced and mice stratified into three treatment groups (PBS, anti-Survivin 20 mcg and 100 mcg). EAMG mice were assessed for disease severity, AChR-specific antibody production, and expression of survivin in splenocyte population.

RESULTS: Significantly higher percentage of CD4- CD20+ human B cells showed intracellular survivin expression in MG patients compared to controls. In the animal model of MG, antibody to survivin treatment improved disease severity, reduced AChR-specific antibody titers, and decreased survivin expression in CD3- CD19+ splenic B cells compared to PBS controls.

SUMMARY/CONCLUSION: Targeting survivin–expressing B cells for elimination may be an effective therapeutic approach.

CONGENITAL MYASTHENIC SYNDROMES: A CLINICAL, ELECTROPHYSIOLOGICAL, AND GENETIC REVIEW
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INTRODUCTION: The congenital myasthenic syndromes (CMS) are a group of heterogeneous genetic disorders. Clinical, electrophysiological, and genetic studies on pre-synaptic, synaptic, and post-synaptic subtypes of CMS are limited.

OBJECTIVE: To study a clinical, electrophysiological, and genetic profile of CMS.

METHODS: Retrospective study of genetically confirmed CMS patients (CHRNE n=5, CHAT deficiency, n=4, PLEC n=3, Dok7 n=1) at a tertiary care Children's hospital from 2013 to 2019. Demographic data, signs, symptoms, electrophysiological data, and treatment strategy were recorded. Descriptive statistics were used.

RESULTS: Thirteen children (7 girls) mean age 7.6±5.5 years (range 1.5-21 years) with symptom onset at mean age 10.5±11.8 months (range 0-36 months). Genetic confirmation mean age 33.3±37.3 months (range 3 months-11.5 years) with 69% (n=9) post- and 31% (n=4) pre-synaptic defects. Mean delay of diagnosis 22.7±30.0 months (range 1 month-8.5 years). All children (n=13) had fatigue. Ninety two percent (n=12) had proximal muscle weakness, ptosis, and feeding difficulty. Seventy seven percent (n=10) had cognitive/behavioral problems and 70% (n=9) had apnea episodes. Thirty percent (n=4) underwent gastrostomy and 23% (n=3) had tracheostomy. Orbicularis oculi stimulated jitter analysis in twelve children showed mean mean jitter 50.4±19.2 µs (range 25-86 µs, normal ≤26 µs) and 30.3±26.2 % blocking (range 0-77%). All patients received pyridostigmine, 54% (n=7) 3,4-Diaminopyridine (3,4-DAP), 38% (n=5) liquid albuterol, and 8% (n=1) ephedrine.

SUMMARY/CONCLUSION: CMS is rare with no sex predilection. Delay in diagnosis was common. CHRNE and CHAT deficiency were the two most common genetic defects in our cohort. Majority of subjects required polypharmacy, with pyridostigmine and 3,4-DAP most commonly used.
LONG-TERM EFFICACY OF ECULIZUMAB IN REFRACTORY GENERALIZED MYASTHENIA GRAVIS: RESPONDER ANALYSES
James Howard (Chapel Hill, NC), Chaﬁc Karam (Portland, OR), Marcus Younitz (Boston, MA), Fanny O’Brien (Boston, MA), Tahseen Mozaffar (Irvine, CA)

INTRODUCTION: The 6-month double-blind placebo-controlled REGAIN study (NCT01997229) and its open-label extension (OLE; NCT02301624) demonstrated the sustained effectiveness of the terminal complement inhibitor eculizumab in adult patients with anti-acetylcholine receptor antibody-positive refractory generalized myasthenia gravis (gMG).

OBJECTIVE: To analyze response profiles in REGAIN and its OLE.

METHODS: The analysis was conducted using Myasthenia Gravis–Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores recorded during REGAIN and its OLE. Early/late responses were defined as improvement in MG-ADL score (≥3 points) or QMG score (≥5 points) occurring at ≤12/>12 weeks, respectively, after baseline (eculizumab initiation).

RESULTS: The analysis included 98 patients. By Week 12 and OLE end, MG-ADL response had been achieved at some point by 67.3% and 84.7% of patients, respectively; QMG response by 56.1% and 71.4%, respectively. Response was observed over multiple consecutive assessments for the vast majority of patients. At Week 130, the least-squares mean (LSM) percentage changes from baseline in MG-ADL score were -61.9% and -47.5% in early and late MG-ADL responders, respectively; the LSM percentage changes from baseline in QMG score were -40.8% and -55.5% in early and late QMG responders, respectively (all p<0.0001).

Signiﬁcant baseline differences between early versus late QMG responders were seen for mean duration of MG (10.46 versus 5.46 years, respectively; p=0.0002) and mean QMG score (18.6 versus 15.1, respectively; p=0.0223).

CONCLUSION: The findings suggest that although most patients with refractory gMG will achieve clinical response (assessed by MG-ADL or QMG scores) by Week 12 of eculizumab treatment, responses can be observed with longer-term treatment.

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EFGARTIGIMOD IN MYASTHENIA GRAVIS: UPDATE ON CLINICAL DEVELOPMENT AND PHASE 3 ADAPT STUDY
Peter Ulrichts (Boston, MA), Antonio Guglietta (Ghent, Belgium), Jon Beauchamp (Boston, MA), Hans de Haard (Ghent, Belgium), Wim Parys (Ghent, Belgium)

INTRODUCTION: Myasthenia Gravis (MG) is mediated by pathogenic IgG autoantibodies causing receptor blockade, accelerated receptor degradation and complement activation. The neonatal Fc receptor (FcRn) recycles IgG, rescuing it from degradation, extending IgG autoantibody half-life. Blocking FcRn function, to reduce IgG autoantibody levels, is a logical potential therapeutic approach for MG. Efgartigimod is a human IgG1 antibody Fc-fragment, a natural ligand of FcRn, engineered for increased, pH-dependent, FcRn affinity. Efgartigimod outcompetes endogenous IgG binding, preventing recycling, increasing IgG degradation.

OBJECTIVE: Present data from efgartigimod phase 1/2 studies.

METHODS: Efgartigimod at doses ≥10mg/kg IV has been administered to >115 subjects in healthy volunteer and three autoimmune disease studies (prior to phase 3 MG study).

RESULTS: Efgartigimod results in targeted reduction of all IgG subtypes without impacting levels of other immunoglobulin isotypes or albumin. It has been well tolerated, with no safety signals or increased risk of infection observed. In a Phase 2 MG study patients received a cycle of 4 weekly IV infusions of 10mg/kg efgartigimod, or placebo (n=24). Efgartigimod resulted in clinically meaningful and sustained improvements in symptoms, consistent across four MG scales. 75% of efgartigimod patients achieved ≥2-point reduction in MG-ADL for ≥6 consecutive weeks versus 25% for placebo (p=0.039). At end of study, 8 weeks after last dose, 6/12 efgartigimod patients maintained clinically meaningful improvement of MG-ADL score, the effect persisting beyond IgG reduction. Additional pharmacodynamic, safety and efficacy data will be presented.

SUMMARY/ CONCLUSION: The global phase 3 ADAPT MG study is ongoing, recruiting 150 AChR, MuSK, LRP4-antibody positive and seronegative patients.

Disclosures: Peter Ulrichts, Antonio Guglietta, Jon Beauchamp, Hans de Haard, Wim Parys - Employee of the company developing the drug and who is the sponsor of clinical trials described.
LAMBERT-EATON MYASTHENIC SYNDROME IN THE SETTING OF IMMUNE CHECKPOINT INHIBITOR TREATMENT OF SMALL CELL LUNG CANCER

Nadim Jiwa (Boston, MA), Mary Jane Lim-Fat (Boston, MA), Ugonna Chukwueke (Boston, MA), Jacob Sands (Boston, MA), Christopher Doughty (Boston, MA)

INTRODUCTION: Treatment with immune checkpoint inhibitors (ICIs) for cancer may result in neuromuscular immune related adverse events (irAEs). To our knowledge, Lambert-Eaton Myasthenic Syndrome (LEMS) in patients treated with ICIs has been seldom described.

OBJECTIVE: To report the clinical course of LEMS in the context of treatment with nivolumab.

CASE: A 77-year-old man with small cell lung cancer (SCLC) treated with partial lobectomy followed by carboplatin and etoposide noticed progressive leg weakness after completion of chemotherapy. This was associated with new xerostomia. Weakness plateaued after 2 months, at which point he was ambulating independently, so no work-up was performed at that time. He was subsequently found to have metastatic disease and started nivolumab. Within 4 weeks of his first infusion, he developed progressive proximal>distal lower extremity weakness and required a walker. Examination after his fourth infusion demonstrated proximal and distal weakness in his lower extremities, distal sensory loss, and facilitation of reflexes. EDX showed evidence of both an axonal polyneuropathy and a presynaptic disorder of neuromuscular transmission. Antibodies to P/Q-type Voltage-Gated Calcium Channel (VGCC) returned positive, confirming the diagnosis of LEMS. Nivolumab was stopped and pyridostigmine 30mg TID was started. Within 4 weeks, his strength improved, he resumed independent ambulation, and pyridostigmine was stopped.

SUMMARY/ CONCLUSION: LEMS, a known paraneoplastic consequence of SCLC, may worsen with ICI treatment. Our patient achieved meaningful improvement simply by holding the ICI and starting pyridostigmine. This suggests that patients with mild symptoms may not need immunomodulatory therapy such as corticosteroids and may help guide management of similar patients.

EVALUATION OF MEDICATIONS IMPLICATED IN PROMOTING MYASTHENIA GRAVIS (MG) EXACERBATION FACT OR FICTION

George Small (Pittsburgh, PA), Mohammad Ali (Wexford, PA), Carol Schramke (Pittsburgh, USA)

INTRODUCTION: The Myasthenia Gravis Foundation of America (MGFA) lists multiple medications as relatively contraindicated (RCMS) in MG patients. Evidence of increased exacerbation risk associated with using these medications may be unclear. If only questionably associated with exacerbation, treatment delay with such therapies may promote unnecessary morbidity and mortality.

OBJECTIVE/METHODS: 100 clinical records of electrically or serologically confirmed MG patients over a 3 year period were reviewed. We defined an exacerbation as MGFA stage worsening by 2 grades, defined in patients who did and did not report receiving RCMS. Chi Square tests were utilized to examine increased exacerbation risk in patients treated with any RCM, particularly beta blockers (BBs) and certain antibiotics.

RESULTS/CONCLUSIONS: 67 patients reported taking a RCM. 25 (37%) had exacerbations, compared to 15/33 (46%) who did not take a RCM. Of the 36 on BBs, 16 (44%) suffered an exacerbation, compared to 24/64 (38%) not taking BBs. Of 14 patients on contraindicated antibiotics, 3 (21%) suffered an exacerbation, compared to 37/86 experiencing an exacerbation not taking contraindicated antibiotics. None of the differences were statistically significant. Human case reporting and animal studies have resulted in recommendations for caution in exposing MG patients to medications thought to promote MG exacerbation. Unfortunately, withholding useful medications for other conditions in MG patients may have severe negative consequences. Our data suggest the risk of exacerbation may not be higher when using these medications.
THYMECTOMY IN SEROPOSITIVE MYASTHENIA GRAVIS IN A QUATERNARY NEUROMUSCULAR DIVISION BEFORE AND AFTER PUBLICATION OF THE MGTX STUDY

Constantine Farmakidis (Mission Hills, KS), Matthew Varon (Kansas City, KS), Suzanne Hunt (Kansas City, Kansas), Mamatha Pasnoor (Kansas City, KS), Omar Jawdat (Lenexa, KS), Gary Gronseth (Kansas City, KS), Richard Barohn (Kansas City, KS), Mazen Dimachkie (Kansas City, KS)

INTRODUCTION: The MGTX study demonstrated that thymectomy leads to reduced disease severity in seropositive (AChRab+) generalized myasthenia gravis (MG). Higher rates of, and earlier thymectomy, may improve outcomes in seropositive MG.

OBJECTIVE: To determine if there has been increased emphasis in patient counseling and use of thymectomy in seropositive MG patients in our academic practice, as may be expected following publication of MGTX.

METHODS: This is a single center retrospective study of generalized seropositive MG patients without thymectomy contraindications. The rates of documented thymectomy counseling, thoracic surgery referral, and thymectomy were compared in new patients seen in the 30-month epochs immediately before and after publication of MGTX in 2016.

RESULTS: 400 adult patients were identified in the HERON database with first encounters including MG codes during both epochs. After excluding patients with contraindications for thymectomy, 41 patients remained. The rate of thymectomy in the before MGTX epoch was 7 per 24 (29.2%). The rate of thymectomy in the after epoch was 9 per 17 (52.9%). This equates to a risk difference of 23.7% (95% CI -5.9% to 49.1%). Rates of documented thymectomy counseling and surgical referral were similar between the two epochs.

SUMMARY/ CONCLUSION: The thymectomy rate was higher in the post MGTX epoch, but the difference did not reach statistical significance. An increase in the use of thymectomy in seropositive MG may or may not be taking place nationally. This is an important question as it could shape future recommendations for optimal care delivery for non-thymomatosus MG at the population level.

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Mazen Dimachkie - Consultant or on the speaker’s bureau for Alnylam, Audentes, Biomarin, Catalyst, CSL-Behring, Genzyme, Mallinckrodt, Momenta, Novartis, NuFactor, Octapharma, RMS Medical, Sanofi, Shire and Terumo. Grants from Alexion, Alynlam, Amicus, Biomarin, Bristol-Myers Squibb, Catalyst, CSL-Beirng, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, MDA, NIH, Novartis, Genzyme, Octapharma, UCB Biopharma, Viromed and TMA. None of these activities present a conflict with this project.

NATURAL COURSE AND TREATMENT OF ACHR-MG CONVERTED TO MUSK-MG OR DP-MG IN CHILDREN: 2 CASE REPORTS AND LITERATURE REVIEW

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INTRODUCTION: Anti-muscle-specific tyrosine kinase antibody (MuSK-Ab) is the second most common autoantibody in myasthenia gravis. MuSK-Ab and anti-acetylcholine receptor antibody (AChR-Ab) can coexist in a few patients.

OBJECTIVE: To explore the clinical features and possible mechanism of conversion of AChR-MG to MuSK-MG or DP-MG.

METHODS: We report two children MG patients with AChR-Ab (AChR-MG) who converted to double antibody positive MG (DP-MG) or MuSK-Ab positive MG (MuSK-MG). We also conducted a literature review to find similar cases.

RESULTS: We found six similar cases through literature searches via online databases. Including our two patients, there were a total of eight patients in this study. Six female and two male. The average age of onset was 7.25±5.95 years, and the median age of onset was 5.5 years. Four AChR-MG patients converted to DP-MG in their natural course of disease, and one of them converted to MuSK-MG after converting to DP-MG; two AChR-MG patients converted to MuSK-MG after thymectomy. Two AChR-MG patients converted to DP-MG after thymectomy.

SUMMARY/ CONCLUSION: AChR-MG can convert to MuSK-MG or DP-MG under certain conditions. We speculate that this conversion is the two courses of MG. These two courses may occur in succession or overlap. Female AChR-MG patients are prone to conversion. After appearing with MuSK-Ab, they show the characteristics of MuSK-MG. These patients respond poorly to cholinesterase inhibitors and well to corticosteroids. During myasthenic crisis, plasma exchange can bring satisfactory effects.
THE ADVERSE EVENT UNIT (AEU): A NOVEL METRIC TO MEASURE THE BURDEN OF TREATMENT ADVERSE EVENTS
Michael Hehir (South Burlington, VT), Mark Conaway (Charlottesville, VA), Eric Clark (Burlington, VT), Denise Aronzon (Burlington, VT), Noah Koh (Charlotte, VT), Amanda Koh (Burlington, VT), Katherine Razhansky (Charleston, SC), Reza Sadjadi (Boston, MA). Eduardo De Sousa (Moore, OK), Ted Burns (Charlottesville, VA)

INTRODUCTION: There is increasing emphasis on treatment burden in neurology to better understand treatment comparative efficacy. We remain without a practical, easy to administer and interpret metric to measure adverse event (AE) burden that facilitates comparison of medications within and across different classes based on AE burden alone. AEs negatively impact patient quality of life and treatment adherence.

OBJECTIVE: Design a physician and patient derived tool, the Adverse Event Unit (AEU), to improve AE burden measurement.

METHODS: Online survey administered to internal medicine, neurology, and pediatric physicians to assign value to 73 AE categories chosen from the Common Terminology Criteria of Adverse Events (CTCAE) relevant to neurologic disorder treatments. Online forced choice survey of non-physician, potential patients, to weight the severity of the same AE categories. Physician and non-physician data combined to assign value to the AEU.

RESULTS: 363 physicians rated the 73 AE categories derived from CTCAE. 660 non-physicians completed forced choice experiments comparing AEs. The newly created AEU provides 0 – 10, weighted values for the AE categories studied that differ from the ordinal 1-4 CTCAE scale. For example, CTCAE severe diabetes (category 4) is assigned an AEU score of 9. Although non-physician input changed physician assigned AEU values, there was general agreement among physicians and non-physicians about the severity of AEs.

SUMMARY/ CONCLUSION: The AEU has great promise to be a useful, practical tool to add precision to the measurement of AE burden in the clinic and in comparative efficacy research. AEU utility will be assessed in planned clinical trials.

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Eduardo De Sousa - Speaker bureau for Alexion and CSL Behring.

A RANDOMIZED, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFECT OF AMIFAMPRIDINE PHOSPHATE IN PATIENTS WITH MUSK ANTIBODY POSITIVE MYASTHENIA GRAVIS
Stanley Iyadurai (Coral Gables, FL), Christian Buettner (Greensboro, NC)

INTRODUCTION: Myasthenia gravis (MG) is a rare, debilitating, acquired autoimmune disease of the neuromuscular junction (NMJ). The main proteins affected are acetylcholine receptor (AChR) and muscle-specific receptor tyrosine kinase (MuSK). MuSK-MG is a disease characterized by a predominance in females, earlier onset than other AChR-MG, prominent bulbar involvement, more severe clinical condition, and significant resistance to treatment. Although many patients with MuSK-MG are treated with anticholinesterase inhibitors or immunosuppressants, they do not respond well to such treatments. Hence, MuSK-MG patients may continue to have marked generalized weakness and bulbar signs and symptoms of the disease. In these patients, the search for alternative treatment strategies targeting different pathophysiologic aspects of the disease is a medical need.

OBJECTIVE: The purpose of this study is to evaluate the safety, tolerability, and efficacy of amifampridine phosphate in patients with MuSK-MG, and a sample of AChR-MG patients.

METHODS: This randomized, double-blind, placebo-controlled, parallel group, outpatient study is planned to include approximately 60 MuSK-MG patients and 10 AChR-MG patients. The planned duration of participation for each patient is at least 38 days, excluding the screening period, which can last up to 14 days. After the open-label run-in the patient must show ≥2-point improvement in MG-ADL score to be randomized. The randomization period consists of 10 days of amifampridine or placebo.

RESULTS: Primary endpoint efficacy of the MuSK-MG group will be analyzed as the change in MG-ADL from baseline (Day 0) using the Wilcoxon-Mann-Whitney Rank sum test.

SUMMARY/CONCLUSION: This study is open with 29 patients enrolled at the time of submission.

Disclosures:
Stanley Iyadurai, Christian Buettner – Employees and stockholders of Catalyst.
ORIGINS AND CHARACTERISTICS OF AUTOANTIBODY-PRODUCING B CELLS IN MYASTHENIA GRAVIS
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INTRODUCTION: Pathogenic autoantibodies that recognize muscle-specific tyrosine kinase (MuSK) are present in some patients with myasthenia gravis (MG). The B cells which produce these autoantibodies evade counterselection, which occurs when B cell tolerance checkpoints are not functioning properly. The recent isolation of the rare human B cells, which produce pathogenic autoantibodies, provides a novel opportunity to advance the understanding of MuSK-specific B cell development.

OBJECTIVE: To gain insight into the details of MuSK MG B cell development.

METHODS: We isolated MG patient-derived B cell populations that express MuSK autoantibodies. Human recombinant MuSK monoclonal autoantibodies (mAbs) were then produced from these cells as a means to further investigate both their characteristics and origin.

RESULTS: The mAbs and monomeric antigen-binding fragments (Fabs) bound specifically to MuSK in a live cell-based assay, effectively interrupted agrin-induced clustering of the acetylcholine receptor and altered MuSK phosphorylation patterns. The Fabs bound to their antigen target with exceptionally high affinity. Further empirical evidence was acquired, which suggests that the B cells producing these autoantibodies emerge from a defectively governed developing B cell repertoire.

SUMMARY/CONCLUSION: This study provides new details regarding the characteristics of human MuSK autoantibodies and how they relate to their pathogenic capacity. The data further provide a speculative mechanism for their development from an aberrantly formed naïve repertoire that materializes in the presence of B cell tolerance checkpoint defects.

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Miriam Fichtner - Supported by a Scientific Progress – Immunoglobulins in Neurology program awarded by Grifols.

PROMISE-MG: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY OF THE COMPARATIVE EFFECTIVENESS OF TREATMENTS FOR MYASTHENIA GRAVIS: PRELIMINARY RESULTS
Pushpa Narayanawami (Boston, MA), Donald Sanders (Durham, NC), Jeffrey Goptill (Durham, NC), Fan Li (Durham, North Carolina), Rishi Desai (Boston, MA), Jurgen Venitz (Richmond, VA), Kathleen Bibeau (Renton, WA), Andrew Krueger (Summerfield, NC), PROMISE-MG Study group (multicenter)

INTRODUCTION: PROMISE-MG is an ongoing, multicenter (US/Canada) prospective, real-world, observational comparative effectiveness study of treatments for MG.

OBJECTIVE: To present baseline data of enrolled subjects.

METHODS: All de-identified subject data are entered into a central REDCap database. We analyzed data from the initial study visit of enrolled subjects using descriptive statistics. We used Pearson correlation to measure the relationship between outcome measures.

RESULTS: One hundred and sixty six patients are enrolled (75% of projected); mean age 65 (20-90) years, 61% male, 93% Caucasian. Average age at disease onset was 64±14 years (females 61±17, males 66±11). Fifty-nine percent were generalized (females 69%, males 53%), MGFA class: 1 (40%), 2 (37%), 3 (21%) 4/5 (2%). Mean disease duration was 1.3±2.5 years; 76% were AChR-Ab positive, 6% MuSK-Ab positive. Imaging revealed normal/involuted thymus in 87%, thymoma in 7%. At the initial visit, over half were on pyridostigmine and treatment was started/changed in 74% (77% pyridostigmine, 12% corticosteroids). Mean outcome measure scores at baseline were: MGQOL15r 10.9±8.2, MG Composite (MGC) 8.6±6.3, MG-MMT 8.3±6.8, MG-ADL 5.5±3.3. Correlations between outcome measures were moderate (0.54 to 0.68, MG-QOL15r vs. MGC, MG-MMT, MG-ADL; MG-QOL15r vs. MG-MMT), all p<0.0001.

SUMMARY/CONCLUSION: The subjects in PROMISE-MG are predominantly male with disease onset in the 7th decade; 7% had thymoma. There was moderate correlation between the patient reported measures (MG-ADL, MGQOL15r); MGQOL15r correlated moderately with the other measures. The highest correlation was between MGC and MG-ADL.

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Rishi Desai - Served as PI for research grants from Bayer, Novartis, and Vertex to Brigham and Women’s Hospital for unrelated projects.
Andrew Krueger – Stock options CVS Health.
SENSITIVITY OF NEUROPHYSIOLOGIC TESTS REGARDING THE NEUROMUSCULAR JUNCTION IN PATIENTS WITH CONGENITAL MYASTHENIC SYNDROMES

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INTRODUCTION: Congenital Myasthenic Syndromes (CMS) are rare inherited disorders of the neuromuscular junction, and oftentimes are misdiagnosed for many years. The combination of modern genetic tests and classic neurophysiological techniques are the best scenario for early diagnosis in this group of patients.

OBJECTIVE: To study the physiology of the neuromuscular junction in patients with CMS with the combination of two neurophysiological techniques: low frequency repetitive stimulation (RS) and jitter analysis using disposable concentric needle electrodes (CNE).

METHODS: We selected 18 subjects (mean age 30.1 years) with CMS. The genetic profile of the group was: CHRNE gene mutation was found in eleven patients; RAPSN, COLQ and DOK-7 gene mutation were present in two patients, each; and a new COL13A1 gene mutation was detected in one subject. In all patients, we performed low frequency repetitive stimulation (RS) in at least six different muscles and collected 20 apparent single fiber action potential pairs during minimal voluntary activation of orbicular oculi muscle (OOM) using disposable CNE.

RESULTS: The combined neurophysiological techniques were positive in all patients, with at least one positive test in each of the 18 patients. 15 of them (83.3%) had both tests positive. RS was normal in only one RAPSN and one CHRNE patients (88.8% of sensitivity) and CNE Voluntary Jitter was normal in only one DOK-7 subject (94.4% of sensitivity).

SUMMARY/CONCLUSION: RS and Jitter analysis using CNE voluntary activation of OOM are very sensitive neurophysiological tests for patients with CMS, especially when used in combination.

PHENOTYPIC VARIATION BETWEEN EARLY ONSET AND LATE ONSET MYASTHENIA GRAVIS

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INTRODUCTION: Myasthenia gravis (MG) phenotype and pattern of progression may be related to age of onset. Differences in phenotype may influence treatment decisions and prognosis. Published series of MG phenotype in late onset MG (LOMG) patients are mixed with reports of both more and less severe phenotypes when compared to patients with early onset MG (EOMG).

OBJECTIVE: Define the phenotypes of LOMG and EOMG in large cohort of MG patients.

METHODS: Retrospective review of all MG patients seen at a tertiary neuromuscular center between 2003 to 2017. Patients with congenital and checkpoint inhibitor MG were excluded from analysis. The primary outcome is the worst median Myasthenia Gravis Foundation of America Clinical Classification (MGFA-CC) in the course of each patients disease course. The MGFA-CC will be compared between EOMG (age ≤ 59 years) and LOMG (age ≥ 60 years) patients. Secondary outcomes include: MGFA Post-intervention status (PIS) at final visit, MG Status and Treatment Intensity Score at final visit, antibody status, thymus pathology, number of myasthenia exacerbations, number and type of immunosuppressant treatments during illness course, and dose of immunosuppressants at time of last visit.

RESULTS: Records from 551 MG patients (EOMG n = 182 and LOMG n = 369) will be reviewed for this study.

SUMMARY/CONCLUSION: We will report the clinical phenotype of a cohort of MG patients that includes a large percentage of LOMG (67%) patients in an effort to better understand differences between EOMG and LOMG. We believe the final results will have both implications for prognosis and treatment decisions.
IN-DEPTH IMMUNE PROFILING OF TREATMENT-NAÏVE MYASTHENIA GRAVIS PATIENTS
Melissa Russo (Durham, NC), James Howard (Chapel Hill, NC), Doug Emmett (Durham, NC) Manisha Chopra (Chapel Hill, NC), Petra Duda (Cambridge, MA), Alonso Ricardo (Cambridge, MA), Simon Read (Cambridge, MA), John Yi (Durham, NC), Jeffrey Guptill (Durham, NC)

INTRODUCTION: Biomarkers in myasthenia gravis (MG) are limited and remain a critical unmet need in the field. Electrophysiological studies, such as single-fiber electromyography, are time-consuming, invasive, require specialized expertise, and have limited availability.

OBJECTIVE: Our goal was to identify an immune signature that discriminated treatment-naïve MG patients from healthy controls and could serve as a baseline prior to immunotherapy. We performed comprehensive immune analysis using high-dimensional flow cytometry and multiplex cytokine assays.

METHODS: Peripheral blood mononuclear cells from 24 treatment-naïve MG patients and 23 age- and sex-matched healthy controls were stained using a 28-color flow cytometry panel that identifies and phenotypes immune subsets. Circulating proteins were detected in the plasma using a Th17 Premixed 25-plex magnetic multiplex panel.

RESULTS: CD4 and CD8 T cells in treatment-naïve MG patients exhibited an activated phenotype with increased frequencies of central memory and effector T cells, along with enhanced expression of activation markers ICOS and CTLA-4 for CD4 T cells and EOMES, Tbet, PD-1, and TGIT for CD8 T cells. Compared to healthy subjects, MG patients had significant increases in peripheral GM-CSF, IL-10, IL-15 (all p<0.01), IFN-gamma, IL-1beta, IL-5, and IL-28A (all p<0.05). In contrast, Th2 related cytokines, including IL-13, IL-9, IL-4, IL-6, IL-25, IL-27, and TNF-beta were decreased in MG patients compared with healthy subjects.

SUMMARY/CONCLUSION: Immune profiling revealed a distinct immune signature in treatment-naïve MG patients as compared to healthy controls. Future analyses will focus on immune signature changes in response to immunotherapy to elucidate mechanisms of action and yield predictors of response.

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RITUXIMAB IN PATIENTS WITH MODERATE TO SEVERE MYASTHENIA GRAVIS: A SUBGROUP ANALYSIS OF THE BEATMG STUDY
Richard Nowak (New Haven, CT), Christopher Coffey (Iowa City, IA), Jonathan Goldstein (New York, NY), Jon Yankey (Iowa City, IA), Liz Uribe (Iowa City, IA), Mazen Dimachkie (Kansas City, KS), Michael Benatar (Miami, FL), Gil Wolfe (Buffalo, NY), Ted Burns (Charlottesville, VA), Kevin O’Connor (New Haven, CT), Robin Conway (Bethesda, MD), John Kissel (Columbus, OH), David Haftar (New Haven, CT), Merit Cudkowicz (Charlestown, MA), Richard Barohn (Kansas City, KS)

INTRODUCTION: The objective of the BeatMG study, a randomized, double-blind, placebo-controlled, phase 2 trial, was to determine whether rituximab was safe/beneficial for AChR antibody-positive generalized myasthenia gravis (MG). The primary outcome was a measure of steroid-sparing effect, defined as proportion of participants achieving ≥75% reduction in mean daily prednisone dose and with clinical improvement or no worsening. While rituximab was safe, the primary futility outcome was achieved in a predominately mild disease cohort.

OBJECTIVE/METHODS: In a post-hoc subgroup analysis, we explored the effect of rituximab in 20 patients (10 rituximab, 10 placebo) with moderate-severe disease (MGFA class III-IV) at baseline.

RESULTS: The primary outcome was achieved by 60% vs 50% of participants in the rituximab and placebo groups, respectively. While primary endpoint success was the same in the rituximab group but lower in the placebo group than in BeatMG, this was not significant. The key secondary endpoints were change from baseline to week 52 in Quantitative MG (QMG) and MG Composite (MGC) scores. Mean change in QMG and MGC were -3.9 vs -0.5 and -7.0 vs -4.8 for rituximab and placebo groups, respectively.

SUMMARY/CONCLUSION: These data suggest that we cannot exclude rituximab treatment effect on successful steroid taper and directionally favorable clinical improvement in moderate-severe AChR antibody-positive generalized MG. Caution is required as this is a post-hoc subgroup analysis without adequate power to make firm conclusions. Further study of the B-cell depletion response is critical for development of patient-tailored treatment paradigms. Additional data on further subgroup analyses will be presented.

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HAND MYASTHENIA IN A PATIENT WITH POSITIVE ACETYLCHOLINE RECEPTOR ANTIBODIES
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INTRODUCTION: A small percentage of patients with a confirmed diagnosis of myasthenia gravis (MG) have distal extremity weakness exceeding proximal weakness. However, unilateral distal weakness as a sole manifestation of MG is very rare.

OBJECTIVE: To describe a patient with mild ocular and generalized seropositive MG, who developed an unusual focal recurrence of MG involving only flexor muscles of the right hand.

METHODS: Clinical and electrodiagnostic evaluation.

RESULTS: A 56-year old man, who achieved a complete remission of MG after thymectomy and treatment with prednisone at high dose followed by slow tapering, developed weakness and fatigability of intrinsic muscles of the right hand three years after the original treatment. Symptoms were initially attributed to a carpal tunnel syndrome. However, an EMG study showed that the motor distal latency in the right median nerve was not prolonged and repetitive stimulation of the median nerve at 2 Hz was abnormal indicating failure of neuromuscular transmission. The recording from the abductor pollicis brevis muscle showed a decrement of compound muscle action potential amplitudes of 16% during the period of post-exercise exhaustion. Repetitive stimulation of the right spinal accessory nerve was normal.

SUMMARY/CONCLUSION: Unilateral hand weakness can present several years after the onset of MG in spite of a successful treatment of the presenting symptoms. It is unclear whether this constitutes an exacerbation of MG or represents a separate manifestation of the original disease with a different pathogenic mechanism.
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