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Financial Disclosure

- *Dr. Edmundson has received consulting fees from Alexion*
Warning

Videotaping or taking pictures of the slides associated with this presentation is prohibited. The information on the slides is copyrighted and cannot be used without permission and author attribution.
A 32-year-old man presented to the emergency department with several days of progressive numbness and weakness.

- 3 weeks prior, he had symptoms of a diarrheal illness that resolved without intervention. 5 days prior he noticed low back aching and tingling/numbness in his toes, which spread to involve the arms and legs. 3 days prior he began tripping as he went up stairs and on presentation to the ER he was unable to walk unassisted.
Rapidly Progressive Weakness

A 32-year-old man presented to the emergency department with several days of progressive numbness and weakness.

- Neurologic examination was notable for weakness of eye closure, arm and leg weakness most pronounced in the distal legs, diffuse areflexia and reduced sensation distal to the elbows and groin bilaterally.

- Lumbar puncture:
  - CSF glucose 65 (normal), protein 98 (elevated), RBCs 2, WBCs 0

- Nerve conduction studies:
  - Non-length-dependent neuropathy with features of acquired demyelination.
Guillain-Barré Syndrome

A group of acute immune-mediated disorders of the peripheral nerves and/or nerve roots typically characterized by:

- Acute, areflexic paralysis and sensory changes
- A monophasic course with nadir within 4 weeks of onset
- Cytoalbuminologic dissociation in the cerebrospinal fluid

Clinical Presentation – Classic GBS

Bilateral, progressive symptoms over hours to days

• Motor: Ascending weakness, facial palsies, respiratory insufficiency

• Sensory: Ascending paresthesias, numbness, limb pain, low back pain

• Reflexes: Generalized hyporeflexia or areflexia

• Autonomic dysfunction: GI dysmotility, arrhythmias and fluctuations in blood pressure
Pathogenesis

- Two-thirds of GBS cases are preceded by infection.

- Associated infectious agents include:
  - *Campylobacter jejuni*
  - *Mycoplasma pneumoniae*
  - Cytomegalovirus
  - Epstein-Barr virus
  - Varicella-Zoster virus
  - Zika virus

- Regarding vaccines:
  - Influenza vaccination may have an overall protective effect in preventing GBS\(^1\)
  - There is no contraindication to vaccination in GBS patients after roughly 3 months\(^2\)

Pathogenesis

Molecular Mimicry:

• Similarities exist between antigenic molecules on pathogens and molecules found in myelin or nerve axons

• Immune recognition of pathogenic antigens results in an autoimmune reaction against the nerve/myelin
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GBS Subtypes

• Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

• Axonal Variants
  o Acute Motor Axonal Neuropathy (AMAN)
  o Acute Motor and Sensory Axonal Neuropathy (AMSAN)
  o These variants carry a poorer prognosis for recovery

• Anti-GQ1b-Associated Disorders
  o Miller Fisher Syndrome (MFS): Ataxia, ophthalmoplegia and areflexia
  o Bickerstaff encephalitis: Ataxia, ophthalmoplegia and encephalitis
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## Subtypes and variants

<table>
<thead>
<tr>
<th>Subtype</th>
<th>IgG autoantibodies to</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guillain–Barré syndrome</strong></td>
<td></td>
</tr>
<tr>
<td>Acute inflammatory demyelinating polyneuropathy</td>
<td>None</td>
</tr>
<tr>
<td>Facial variant: Facial diplegia and paresthesia</td>
<td>None</td>
</tr>
<tr>
<td>Acute motor axonal neuropathy</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>More and less extensive forms</td>
<td></td>
</tr>
<tr>
<td>Acute motor–sensory axonal neuropathy</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>Acute motor-conduction-block neuropathy</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>Pharyngeal–cervical–brachial weakness</td>
<td>GT1a &gt; GQ1b &gt; GD1a</td>
</tr>
<tr>
<td><strong>Miller Fisher syndrome</strong></td>
<td></td>
</tr>
<tr>
<td>Incomplete forms</td>
<td></td>
</tr>
<tr>
<td>Acute ophthalmoparesis (without ataxia)</td>
<td>GQ1b, GT1a</td>
</tr>
<tr>
<td>Acute ataxic neuropathy (without ophthalmoplegia)</td>
<td>GQ1b, GT1a</td>
</tr>
<tr>
<td>CNS variant: Bickerstaff’s brain-stem encephalitis</td>
<td>GQ1b, GT1a</td>
</tr>
</tbody>
</table>

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Epidemiology

- 1-2 cases per 100,000 person-years in the US and Europe\(^1\)

- AIDP accounts for up to 90% of cases in the North America\(^2\)

- Axonal variants are more common in Northern China\(^3\)

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Complement Deposition in Early AIDP

Hafer-Macko et al. (1996)
Diagnostics

Careful Physical Examination

• Cranial Nerves
• Sensation
• Strength
• Reflexes

Diagnostics

Nerve Conduction Studies (NCS):

- NCS can be normal early and develop over weeks¹
- Serial NCS are often done, but may not change the subtyping of GBS²

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AIDP Electrodiagnostic Features

Motor NCS
- Increased distal latencies
- Conduction block
- Temporal dispersion
- Slowing of nerve conduction velocities (usually not seen until the third or fourth week)
AIDP Electrodiagnostic Features

Sensory NCS
• “Sural Sparing” pattern – in AIDP or axonal variants
• Absent responses or slowed conduction velocities.

Late Responses (earliest feature in AIDP)
• Prolonged or absent F waves
• Absent H reflexes

Needle EMG
• Reduced recruitment in weak muscles.
• Fibs/PSWs after weeks IF there has been axon loss.
Axonal Variant EDx Features

AMSAN:
• No demyelination
• Motor and sensory responses severely reduced or absent
• F waves may be absent (not significantly prolonged)
• Denervation on needle study after weeks

AMAN:
• No sensory nerve involvement or demyelination
• Motor amplitudes may be reduced
• F waves may be absent (not significantly prolonged)
• Denervation in needle study after weeks
Proposed GBS EDx Criteria

- Decreased CMAP amplitude
- Prolonged distal motor latency
- Decreased motor conduction velocity
- Temporal dispersion (increased duration of more than 30% compared to the distal)
- Conduction block (decrease of more than 50% in proximal CMAP compared to distal without an increase on duration of more than 30%)
- Prolonged F latency

Diagnostics

Lumbar Puncture

- CSF cytoalbuminologic dissociation = elevated protein with normal white blood cells
- Cytoalbuminologic dissociation is present in 50% of GBS patients in the first week after onset, but 70-90% 2 weeks after onset \(^1,^2\)
- CSF Pleocytosis may indicate disease mimics: lymphoma, sarcoidosis, Lyme, West Nile Virus
- CSF Pleocytosis is also present in some GBS patients with HIV

Consider MRI:
- Assess for cauda equina syndrome or other compressive lesion of the spinal nerve roots

Consider serum antibodies:
- Particularly to GQ1b in suspected MFS and Bickerstaff
Management – Respiratory

GBS patient require admission for close monitoring of respiratory status

- Roughly 30% of GBS patients require mechanical ventilation

- Elective intubation is preferred over emergent intubation

- Hypoxemia and hypercarbia are late signs of neuromuscular respiratory weakness

Management – Respiratory

Frequently Check:
- Vital Capacity (VC)
- Maximal Inspiratory Pressure (MIP), also know as Negative Inspiratory Force (NIF)
- Maximal Expiratory Pressure (MEP)

“20/30/40 rule”, intubate when\(^1\):
- Vital Capacity is <20ml/kg (i.e. <1.4L in a 70kg person)
- MIP/NIF is less negative than -30cm H\(_2\)O
- MEP is <40cm H\(_2\)O
- >30% decline in any of these parameters

Management – Respiratory

Single Breath Count (SBC)¹

- Each 10 digits counted on a single breath corresponds with ~1L VC
- Demonstrated in patients with myasthenia gravis
- Useful when formal VC/MIP/MEP aren’t available

Patients with GBS should be treated with Intravenous Immunoglobulin (IVIG) or plasmapheresis (PLEX)

- IVIG and PLEX are equally effective in GBS\(^1,2\)
- Choice of IVIG 2gm/kg over 5 days v. PLEX 4-6 exchanges over 8-10 days
- Treatment should be initiated as soon as there is a clinical diagnosis
- IVIG v. PLEX depends on: institutional availability and patient comorbidities
  - Avoid IVIG in: renal failure, hypercoagulable states, IgA deficiency
  - Avoid PLEX in: sepsis due to hemodynamic changes and bacterial colonization of catheter

Treatment-Related Fluctuation v. CIDP

Course of Untreated GBS

GBS Treated

Early Treatment-Related Fluctuations

CIDP

4 weeks

4 weeks
When does AIDP become CIDP?

Consider Maintenance Treatment for CIDP (corticosteroids, chronic IVIG) When:

- There is clinical deterioration after 8 weeks from onset
- When deterioration occurs 3 times or more.

Suggestive features of CIDP:

- Patient remains able to walk independently
- Patient has no cranial nerve dysfunction
- Electrophysiologic features likely to be compatible with CIDP
Ancillary Supportive Care

• Monitor/Treat Dysautonomia:
  o Cardiac monitoring for arrhythmias
  o Blood pressure management
  o GI dysmotility and urinary retention

• Proactively Address Immobility and Associated Comorbidities
  o Early physical and occupational therapy
  o DVT Prophylaxis
  o Careful skin care to avoid decubitus ulcers

• Pain Management
  o Neuropathic agents (gabapentin, pregabalin, low dose tricyclic antidepressants)
  o Avoid long-term opioid use
Prognosis

• Mortality in Europe and North America is 3-7%, often due to respiratory complications or autonomic dysfunction¹

• Nearly 90% experience full recovery or only minor residual deficits², though recovery may be slow and 20% remain unable to walk unassisted at 6 months³

• Axonal variants may have a more protracted course and slower, incomplete improvement⁴

Follow Up on Our Case

A 32-year-old man with several days of progressive numbness and weakness. Areflexia, weakness and numbness on exam. Cytoalbuminologic dissociation in CSF. Acquired, demyelinating neuropathy on NCS.

- Diagnosed with AIDP
- Treated with 5 days of IVIG (0.4gm/kg daily for 5 days)
- Treated with gabapentin for burning leg pain
- Respiratory function was closely monitored and was stable over a week
- Transferred to rehab after 10 days
- On evaluation 3 months later, he had regained most of his strength and returned to work
- He continue to experience mild, intermittent tingling in the feet
Summary

• Guillain-Barré Syndrome refers to a group of monophasic, immune-mediated polyneuropathies/polyradiculoneuropathies, typically characterized by rapidly progressive areflexic paralysis and sensory symptoms.

• Key diagnostic tests include NCS and lumbar puncture for cytoalbuminologic dissociation.

• Management includes treatment with IVIG or PLEX and close respiratory function monitoring.

• Prognosis is good in most patients.
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