GULLAIN
BARRE’S SYNDROME AND VARIANTS

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Guillain Barre Syndrome

• Acute monophasic immune mediated neuropathy

• Most common cause of acute flaccid paralysis.
  • waldrop and olliver - 1834

• Jean-Baptiste Occtave Landry

• “Acute ascending paralysis”-1859

• Guillain,Barre&Strohl-1916
Guillain Barre Syndrome

• “Guillain Barre syndrome: the need for exact diagnostic criteria”-Osler and Siddel-1960

• Swine flu influenza vaccination programme-1976

• NINCDS Criteria

• GBS-A heterogenous disorder

• Variants of GBS-15-18%
Pathology

- Endoneural perivascular (mainly perivenous) lymphocytic infiltrates
- Segmental demyelination and variable degree of wallerian degeneration
- Cellular infiltrates scattered cranial nerves, ventral and dorsal spinal roots, dorsal root ganglion and the entire length of peripheral nerves
- Swelling of nerve roots at the site of dural exit
- Occasionally inflammatory process with primary axonal damage rather than demyelination (Honovar et al)
Pathogenesis and etiology

- cell-mediated immunological reaction directed against peripheral nerves
- Brostoff and colleagues suggested that the antigen in this reaction is a basic protein (p2) found only in peripheral nerve myelin
- Complement also to be a necessary factor in the initial attack on myelin
• Anti GQ1b found in almost all patients with ophthalmoplegia

• One fifth of patients have anti Gm1 antibodies early in their course, corresponding in most instances to a predominantly motor presentation

• Highest titres being associated in some cases that follow campylobacter infections

• Antibodies directed against GD1a or GT1b are associated in some cases with pharyngeal-brachial-cervical variant
NINCDS Criteria

• **Features Required for the Diagnosis.**
  
  i) Progressive motor weakness of more than one limb.
  
  ii) Areflexia
  
  iii) Disease course < 4 weeks

• **Features strongly supportive of diagnosis**

  A. Clinical features
  B. CSF Features
  C. Electrodiagnostic features
CLINICAL FEATURES:
i) Progression
ii) Relative symmetry
iii) Mild sensory symptoms or signs
iv) Cranial nerve involvement.
v) Recovery
vi) Autonomic dysfunction
vii) Absence of fever at the onset
NINCDS Criteria

• Features casting doubt on the Diagnosis
  • Marked persistent asymmetry of weakness
  • Persistent bladder or bowel dysfunction
  • Bladder or bowel dysfunction at onset
  • More than 50 cells/mm³ in CSF
  • Presence of polymorphonuclear cells in CSF
  • Persistent diminished reflexes
NINCDS Criteria

• **Features that rule out the diagnosis**
  - Abnormal porphyrin metabolism
  - Recent diphtheria
  - Lead neuropathy
  - A purely sensory syndrome
  - Diagnosis of Botulism, Poliomyelitis, Myasthenia gravis or Toxic neuropathy
Key diagnostic criteria and Brighton case definitions for Guillain-Barré syndrome

Level of diagnostic certainty

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td>Bilateral and flaccid weakness of limbs</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
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<tr>
<td>Decreased or absent deep tendon reflexes in weak limbs</td>
<td>+</td>
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<td>+</td>
<td>+/−</td>
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<tr>
<td>Monophasic course and time between onset-nadir 12 h to 28 days</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/−</td>
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<tr>
<td>CSF cell count &lt;50/μl</td>
<td>+</td>
<td>+a</td>
<td>−</td>
<td>+/−</td>
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<tr>
<td>CSF protein concentration &gt; normal value</td>
<td>+</td>
<td>+/−a</td>
<td>−</td>
<td>+/−</td>
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<tr>
<td>NCS findings consistent with one of the subtypes of GBS</td>
<td>+</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
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<tr>
<td>Absence of alternative diagnosis for weakness</td>
<td>+</td>
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a If CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis Guillain-Barré syndrome
When to suspect variants of GBS?

- Fever at the onset of neuritic symptoms
- Severe sensory loss with pain
- Progression beyond four weeks
- CNS involvement
- Sensory level
- Very poor recovery
Classification of GBS variants

• Topographic

• Clinical course

• Fibre Type

• Pathological
VARIANTS OF GBS

TOPOGRAPHIC
- i) Miller Fisher Syndrome
- ii) Pharyngo cervico brachial weakness
- iii) Paraparetic
- iv) Unusual forms

FIBRE
- i) pure motor
  - ii) pure sensory
  - iii) dysautonomia

PATHOLOGICAL
- axonal

CLINICAL
- i) recurrent
  - ii) SADP
Miller Fisher syndrome

- Miller Fisher-1956
- 5% of all cases with GBS
- Classical triad
- Most common trigger-C. Jejuni infection
- IgG Antibodies to GQ1b ganglioside
MFS-Clinical features

- Diplopia - most common initial symptom
- Ophthalmoplegia - Asymmetrical or symmetrical
- Eyeballs become frozen
- Pupillary dysfunction - Rare
- Ptosis - varying degrees.
• Ataxia-usually on 3\textsuperscript{rd} or 4\textsuperscript{th} day.

• Has dysmetric quality of cerebellar ataxia.

• No nystagmus or dysarthria

• Facial and limb paresthesia-1/3 cases

• Facial or proximal muscle weakness-1/3

• Hyporeflexia/Areflexia-Usually end of first week.
MFS v/s Bickerstaff Encephalitis

• BBE-? Variant of MFS with a central involvement
  • Ataxia
  • Ophthalmoplegia
  • Areflexia
  • Drowsiness (CNS involvement)
  • Extensor plantar response (long tract involvement)
  • Hemisensory loss

• AntiGQ1b antibody
Pharyngeal Cervical Brachial weakness

- Symptoms remain confined to cranial, cervical and shoulder muscles

- Areflexia of upper limbs.

- Normal power and reflexes in legs.

- Electrophysiological abnormalities confined to UL.

- Antibodies against gangliosides GT1a & GD1a.
PARAPARETIC FORM

• Disease confined to legs.

• Areflexia, radicular pain is common.

• Sparing of upper limbs, cranial nerves and sphincters.

• Electrophysiological findings confined to lower limbs.

• CSF-Albuminocytological dissociation.
Unusual Topographic variants

• Purely facial or oculomotor form.

• Facial diplegia with distal limb paresthesia.

• Abducent nerve palsy with distal paresthesia.

• Severe ptosis without ophthalmoplegia.

• Bilateral foot drop with upper limb paresthesias.

• Acute ataxia without ophthalmoplegia.
PATHOLOGICAL VARIANT
AXONAL FORM

• Feasby et al-1986

• Patients present with fulminant onset, severe paralysis and poor recovery

• Campylobacter jejuni infection-Anti GD1a antibodies

• Pathology-severe axonal degeneration

• Electrophysiology- characteristic
AMAN (Acute Motor Axonal Neuropathy)

- Mckhann et al-90 pts with AFP from Northern China.
- Children from rural areas of China.
- “Chinese paralytic syndrome”
- Peak incidence was in summer.
- Serological evidence of C.Jejuni infection.
- Autopsy-Motor nerve degeneration without inflammation.
• Spinal cord - extensive abnormalities of anterior horn cell.

• Extensive wallerian like degeneration of motor nerve roots & motor fibers of peripheral nerves.

• Lymphocytic infiltrates, perivascular cuffing and demyelination - absent.
AMAN-Diagnostic criteria

- Symmetric motor weakness in all four limbs.
- Absence of paresthesias or sensory loss.
- Areflexia by one week.
- Progression of weakness by one day to three weeks.
AMAN-Diagnostic criteria

- CSF-Albuminocytological dissociation
- Abnormalities of F waves in at least two limbs, or motor conduction block, or slowing.
- Normal sensory nerve potential
ASAN (Acute Sensory Axonal Neuropathy)

- Paresthesia in the feet and hands.
- Absence of weakness.
- Areflexia involving all four limbs
- Distally diminished sensation mainly vibration/joint position sense.
- Progression over days to one month.
- Ataxia, paresthesia, distal areflexia, profound loss of position sense, no motor weakness.
- Improvement by 2-4 month.
• High CSF protein within 3wks of onset.
• Severe sensory conduction abnormalities.
• Minimal motor conduction
• Autopsy studies-Inflammation and degeneration of dorsal root ganglia, dorsal roots and posterior column in spinal cord.
• Antibodies to ganglioside GD1b & GD3 in serum
• Electrophysiology-severe sensory neuropathy with minimal or no motorfiber involvement.
• Sural nerve biopsy-loss of both large and small fibers.
AMSAN (Acute Motor Sensory Axonal Neuropathy)

- Acute quadriparesis, areflexia, distal sensory loss, respiratory insufficiency

- Diffuse axonal degeneration without demyelination

- CSF analysis – increased protein

- EDX – loss of motor and sensory potentials with diffuse denervation

- Incomplete recovery
FIBRE VARIANTS

Pure Motor

- Acute, progressive, symmetric limb weakness, no sensory loss and areflexia.

- Normal cranial nerve function, sphincter.

- Elevated anti – GM1 titers.

- CSF protein is elevated.

- EDX – both axonal and demyelination features.
Pure Sensory variants

- Rapid onset of large fibers sensory loss
- sensory ataxia.
- Positive rhomberg’s sign and pseudoathetosis.
- Small fiber sensory function is normal.
- Sensory dysfunction may involve face.
- CSF protein is elevated.
- EDX – large sensory fiber demyelination.
Pure Dysautonomia

- Young and associates-Reported a syndrome that resembles in pure form, the autonomic component of severe acute GBS.

- Clinical features
  - Hypertension
  - Orthostatic hypotension
  - Vomiting
  - Diarrhoea or constipation
  - Paralytic ileus
  - Sweating disturbance
  - Cardiac arrhythmias
• Involvement of myelinated portions of autonomic nervous system
  – Sympathetic white rami communicans
  – Vagus nerve, splanchnic nerves

• Demyelination, axonal degeneration, loss of unmyelinated fibers
• Progressive sympathetic and parasympathetic dysfunction over 1-3 wks

• No motor weakness, sensory disturbances, ataxia or opthalmoplegia.

• Areflexia or hyporeflexia by 1 week

• Improvement in some autonomic dysfunction by 2-4 months

• CSF - albuminocytological dissociation

• Normal motor conduction and abnormal sensory conduction studies.
Management

- Plasma exchange
- Immunoglobulins
- Supportive Treatment.
  - Alternate eye patching
  - Corneal care
  - Physical therapy
  - Gait training
General Medical Care

- In severe cases respiratory assistance assiduous nursing are paramount
- One quarter of patients may require mechanical ventilation
- Measurement of maximal inspiratory force and expiratory vital capacity suffices for the bedside estimation of diaphagmatic strength and respiratory function
• hypotension due to dysautonomia
• hypertension managed by short acting and titratable antihypertensive
• prevent electrolyte imbalances, pulmonary embolism
• physical therapy
Plasma exchange and immune Globulin

- Advised regimen of plasma exchange removes a total of 200 to 250 ml/kg of plasma in 4-6 treatments on alternate days
- Replacement of fluid is saline combined with 5% albumin
- IVIg (0.4g/kg per day for 5 consecutive days)
Major clinical trials in treatment of gullian-Barr'e syndrome

- GBS study Group
- French Coop Group
- Dutch GB study group
- Plasma Exchange/sandaglobulin GBS trial
Recurrent GBS

• GBS—Essentially a monophasic illness.
• 10-25% pts—Relapses.
• Predisposing factors
  • Early plasmapheresis
  • Infections
  • Vigourous physiotherapy
Prognosis

- Approximately 85% achieve full functional recovery within several months to a year
- Mortality is <5% in optimal settings
- Death usually results from secondary pulmonary complications
Conclusions

• Early diagnosis is important
• Therapeutic intervention.
• Neuropathies and antiglycolipid antibodies
• Many key issues remains unresolved
• Scope for targetted immunotherapy.
THANK YOU