GULLAIN BARRE'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

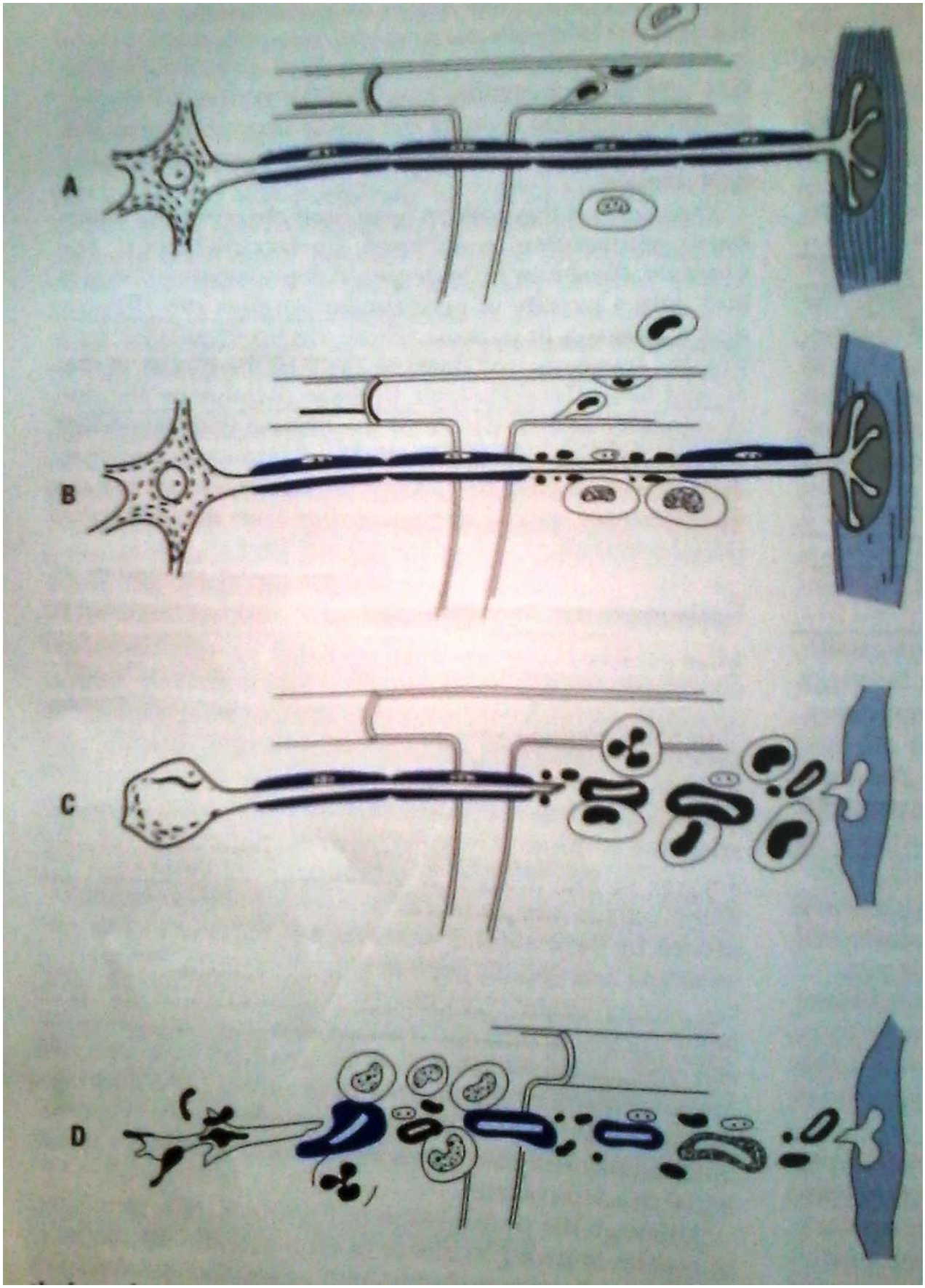
- Guillain,Barre&Strohl-1916

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 scatterd cranial nerves, ventral and dorsal spinal roots, dorsal root ganglion and the entire length of perpheral nerves
- Swelling of nerve roots at the site of dural exit
- Ocassionaly inflammatory process with primary axonal damage rather than demyelination(Honovar et al)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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/mm^3 in CSF
  - Presence of polymorphonuclear cells in CSF
  - Persistent diminished reflexs

NINCDS Critera

- **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

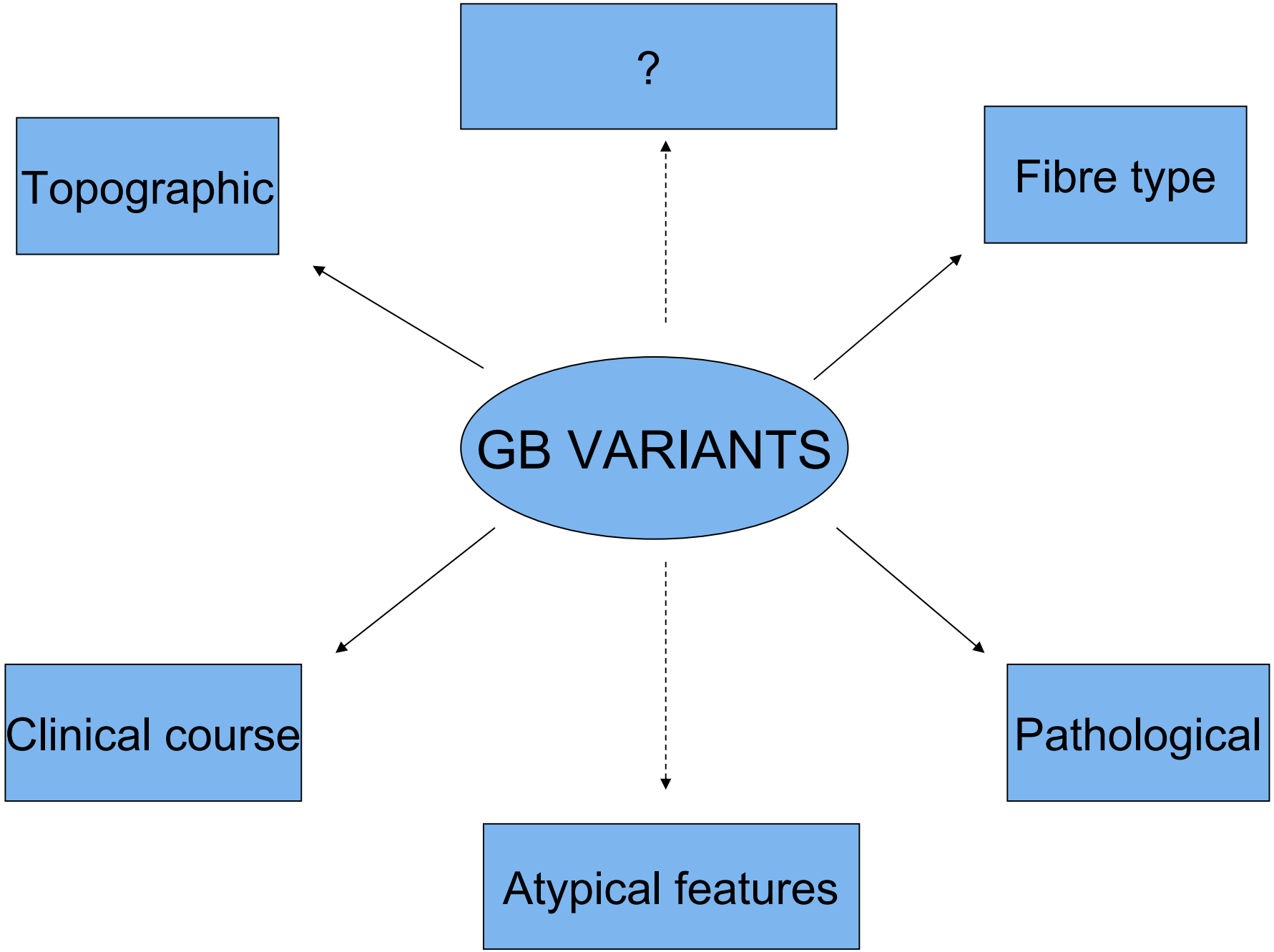
Level of diagnostic certainty

Diagnostic criteria	1	2	3	4
Bilateral and flaccid weakness of limbs	+	+	+	+/−
Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/−
Monophasic course and time between onset-nadir 12 h to 28 days	+	+	+	+/−
CSF cell count <50/μl	+	+a	−	+/−
CSF protein concentration > normal value	+	+/−a	−	+/−
NCS findings consistent with one of the subtypes of GBS	+	+/−	−	+/−
Absence of alternative diagnosis for weakness	+	+	+	+

a If CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis Guillain-Barré syndrome

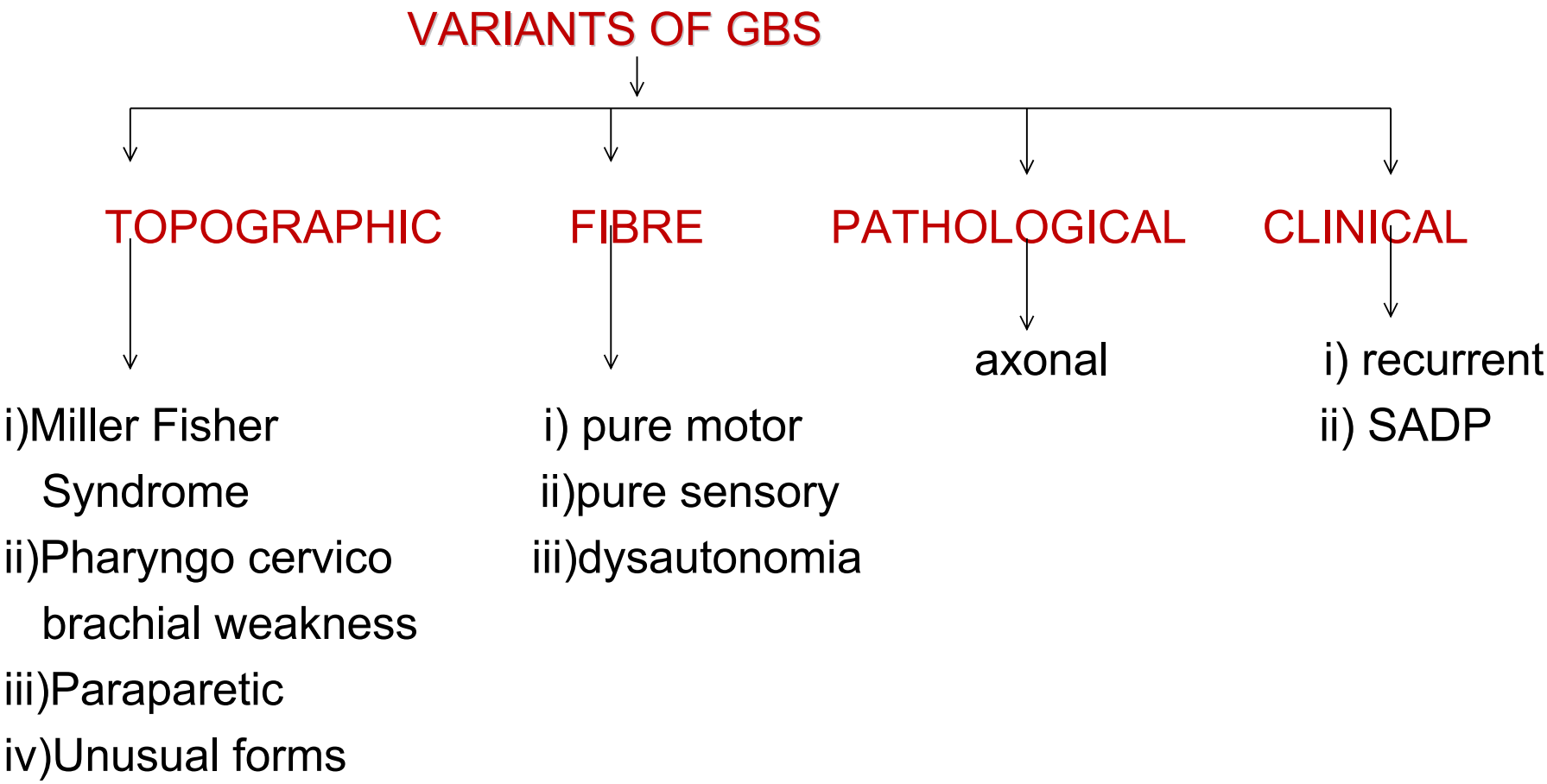
When to suspect variants of GBS?

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


?
Topographic
Fibre type
GB VARIANTS
Clinical course
Pathological
Atypical features

Classification of GBS variants

- Topographic
- Clinical course
- Fibre Type
- Pathological


VARIANTS OF GBS
TOPOGRAPHIC
FIBRE
PATHOLOGICAL
CLINICAL
i)Miller Fisher Syndrome
ii)Pharyngo cervico brachial weakness
iii)Paraparetic
iv)Unusual forms
i) pure motor
ii)pure sensory
iii)dysautonomia
axonal
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
- Opthalmoplegia -Asymmetrical or symmetrical
- Eyeballs become frozen
- Pupillary dysfunction-Rare
- Ptosis-varying degrees.

- Ataxia-usually on 3rd or 4th 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
  - Opthalmoplegia
  - Areflexia
  - Drowziness(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 opthalmoplegia.
- 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 insuffiency
- 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 protien 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 1week
- Improvement in some autonomic dysfunction by 2-4 months
- CSF - albuminocytological dissociation
- Normal motor conductions 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

- Adviced regimen of plasma exchange removes a total of 200 to 250 ml/kg of plasma in 4-6 treatments on alternate days
- Replacemement 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