GUILLIAN BARRE SYNDROME

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Neuromuscular weakness in the Intensive Care Unit

- Neuromuscular weakness is a common occurrence in patients who are critically ill
- Developing in ≥ 25 % of patients who are in the ICU

Weakness Patients in the Intensive Care Unit

- Established neuromuscular weakness as an important complication of critical illness in the ICU.

Weakness Patients in the Intensive Care Unit

- Patients with neuromuscular weakness characterized it as axonal motor and sensory neuropathy and distinguished it from acute neuropathy of Guillain-Barre syndrome.

Weakness Patients in the Intensive Care Unit

- These İllnesses;
  - Critical illness myopathy
  - Critical illness polyneuropathy
  - Combined critical illness myopathy and polyneuropathy
  - Prolonged neuromuscular junction blockade

Weakness Patients in the Intensive Care Unit

- In a critically ill patient who develops flaccid generalized weakness
- Differential diagnosis;
  - critical illness myopathy
  - critical illness polyneuropathy
  - combination of the two.
  - prolonged neuromuscular junction blockade

Weakness Patients in the Intensive Care Unit

- Other acute and subacute myopathies can occur in critically ill patients such as;
  - Rhabdomyolysis
  - Cachectic myopathy
  - **Guillain-Barre syndrome**

Guillain-Barre syndrome (GBS)

- The acute immune-mediated polyneuropathies are classified under the eponym Guillain-Barre syndrome.
- GBS is an acute monophasic paralyzing illness, usually provoked by a preceding infection.
- GBS occurs world-wide and all age groups are affected.

Pathophysiology

- Usually postinfectious (Campylobacter, CMV, EBV, HIV)
- A small percentage of patients develop GBS after another triggering event such as immunization, surgery, trauma etc.
- GBS is thought to result from an immune response to a preceding infection that cross-reacts with peripheral nerve components because of molecular mimicry.

Pathophysiology

- The immune response can be directed towards the myelin or the axon of peripheral nerve, resulting in demyelinating and axonal forms of GBS
- Result: defects in the propagation of electrical nerve impulses, with eventual conduction block and flaccid paralysis

Clinical Features

- Progressive, fairly symmetric muscle weakness accompanied by absent or depressed deep tendon reflexes.
- The weakness can vary from mild difficulty with walking to nearly complete paralysis of all extremity, facial, respiratory and bulbar muscles

Clinical Features

- Progressive, fairly symmetric muscle weakness
  - Typically starts in proximal legs
  - It begins in the arms or facial muscles in about 10 percent of patients
  - 10-30 % Severe respiratory muscle weakness
  - 50 % oropharyngeal weakness

Clinical Features

- Oculomotor weakness (15 %)
- Paresthesias in the hands and feet accompany the weakness (more than 80 %)
- Pain, typically located in the back and extremities (during the acute phase 66 %)

Clinical Features

- Dysautonomia occurs in 70 percent of patients
  - Tachycardia (the most common)
  - Urinary retention
  - Hypertension/hypotension
  - Bradycardia,
  - Ileus

Diagnosis

- The typical finding; elevated cerebrospinal fluid (CSF) protein with a normal white blood cell count (*albuminocytologic dissociation*)
- Clinical neurophysiology studies (ie, electromyography and nerve conduction studies) show evidence of an acute polyneuropathy

Diagnosis

- Glycolipid antibodies may be associated with different forms or aspects of GBS

GBS Variants

- GBS is a heterogeneous syndrome with several variant forms.
- Each form of GBS has distinguishing clinical, pathophysiologic, and pathologic features.

Acute inflammatory demyelinating polyneuropathy (AIDP)

- The most common form in the US and Europe (85-90 %)
- Progressive, fairly symmetric muscle weakness accompanied by absent or depressed deep tendon reflexes.

Acute inflammatory demyelinating polyneuropathy (AIDP)

- Immune reactions directed against epitopes in Schwann cell surface membrane or myelin
- Inflammatory demyelination is thought to start at the level of the nerve roots
- Result: muscle weakness
- Remyelination occurs several weeks to months

Acute inflammatory demyelinating polyneuropathy (AIDP)

- clinical neurophysiology studies:
  - prolonged or absent F waves and absent H reflexes
  - İt reflects demyelination at the level of the nerve roots
- conduction studies: slowed conduction velocities after the third or fourth week
- EMG of weak muscles shows reduced recruitment

Acute motor axonal neuropathy

- An acute axonal form of GBS is AMAN.
- Most cases are preceded by Campylobacter jejuni infection.
- Clinically;
  - deep tendon reflexes are occasionally preserved
  - Sensory nerves are not affected.
- Other clinical features and recovery of AMAN similar to those of AIDP.

Acute motor axonal neuropathy

- There is;
  - Selective involvement of motor nerves
  - No sensory nerve involvement
  - No peripheral nerve demyelination.
  - No significant slowing of conduction velocities

Acute motor axonal neuropathy

- There are antibodies (GM1, GD1a, GalNac-GD1a, and GD1b) to the gangliosides of peripheral nerve axons
- These anti-ganglioside antibodies can be induced by Campylobacter jejuni infection.
- Result: axonal nerve damage without significant axonal degeneration

Acute motor and sensory axonal neuropathy (AMSAN)

- It is severe form of AMAN
- Sensory and motor fibers are affected with marked axonal degeneration
- Clinically, AMSAN has more sensory symptoms.
- Pathology: axonal lesions of both motor and sensory nerve fibers.

Miller Fisher syndrome

- The typical presentation:
  - ophthalmoplegia with ataxia and areflexia
- 1/4 of patients will develop some extremity weakness
- Incomplete forms;
  - include acute ophthalmoplegia without ataxia,
  - acute ataxic neuropathy without ophthalmoplegia

Miller Fisher syndrome

- Clinical neurophysiology studies:
  - reduced or absent sensory responses without slowing of sensory conduction velocities.
  - When there is associated weakness, the motor nerve conduction
- abnormalities of AIDP may be present

Bickerstaff encephalitis

- This is variant of GBS and characterized by;
- encephalopathy
- hyperreflexia
- ophthalmoplegia and ataxia. (like Miller Fisher syndrome)

Pharyngeal-cervical-brachial weakness

- Another variant of GBS
- Characterized by;
  - acute weakness of the oropharyngeal, neck, and shoulder muscles with swallowing dysfunction
  - May be facial weakness

Other variants

- Acute pandysautonomia
- Pure sensory GBS,
- Facial diplegia and distal limb paresthesia
- Sixth nerve palsy and distal paresthesia
- Bilateral lumbar radiculopathy

Diagnosis

- Clinical presentation of GBS is important
  - Progressive
  - Mostly symmetric muscle weakness
  - absent or depressed deep tendon reflexes
- It is confirmed
  - cerebrospinal fluid (CSF)
  - Clinical neurophysiology studies

CSF

- Elevated CSF protein with a normal CSF white blood cell count.
- This finding, known as albuminocytologic dissociation (50-66 % positive in the first week)
- Normal CSF protein is found if it is tested earlier than one week. (30-50 %)

CSF cell count

- Typically normal
- Some times mildly elevated

Neurophysiological studies

- Performed to confirm the diagnosis of GBS
- Give some information about prognosis.
  - Nerve conduction studies (NCS)
  - Electromyography (EMG)

Neurophysiological studies

- Some times the diagnosis of GBS and
- Differential diagnosis can be difficult.
  - acute motor axonal neuropathy (AMAN)
  - acute motor and sensory axonal neuropathy (AMSAN)
  - acute inflammatory demyelinating polyneuropathy (AIDP)
- Serial neurophysiological studies are frequently helpful.

Antibodies

- Immune reactions directed against Schwann cell surface membrane or myelin
- limited clinical utility

Antibodies

- Currently, laboratory testing for antibodies to glycolipids other than GQ1b is not performed routinely because of limited clinical utility.

Diagnostic features

- Progressive weakness of more than one limb
  - from minimal weakness to total paralysis
- Areflexia.
  - universal areflexia is typical
  - distal areflexia with hyporeflexia at the knees and biceps will suffice if other features are consistent

Supportive features

- Progression of symptoms over days to four weeks
- Relative symmetry
- Mild sensory symptoms or signs
- Cranial nerve involvement, especially bilateral facial nerve weakness
- Recovery starting two to four weeks after progression halts
- Autonomic dysfunction
- No fever at the onset
- Elevated protein in CSF with a cell count <10/mm3
- Electrodiagnostic abnormalities consistent with GBS

Differential diagnosis

- Cerebral
  - Bilateral strokes
  - Psychogenic symptoms
- Cerebellar
  - Acute cerebellar ataxia syndromes
  - Posterior fossa structural lesion

Differential diagnosis

- Spinal
  - Compressive myelopathy
  - Transverse myelitis
  - Anterior spinal artery syndrome
  - Poliomyelitis
  - Other infectious causes of acute myelitis (eg, West Nile virus, coxsackieviruses, echoviruses)

Differential diagnosis

- Peripheral nervous system
  - Toxic neuropathy (drugs, toxins)
  - Critical care neuropathy
  - Diphtheria
  - Tick paralysis
  - Porphyria
  - Lyme disease
  - Vasculitis

Differential diagnosis

- Neuromuscular junction
  - Botulism
  - Myasthenia gravis
  - Neuromuscular blocking agents
- Muscle disease
  - Acute viral myositis
  - Acute inflammatory myopathies
  - Metabolic myopathies (hypo/hyperkalemic)
  - Periodic paralysis

Treatment

- Supportive care is important
- due to autonomic dysfunction
  - Patients need intensive care unit (ICU) monitoring
    - Respiratory
    - Cardiac
    - hemodynamic.
- Less severely affected patients can be managed in intermediate care units

Treatment

- Respiratory failure 15-30 %
- due to bulbar dysfunction
  - swallowing problems
  - inability to clear secretions
- If Patients need ventilatory support
  - Succinylcholine should be avoided
  - Forced vital capacity <20 mL/kg
  - Maximum inspiratory pressure <30 cmH2O
  - Maximum expiratory pressure <40 cmH2O

Treatment

- predictors of respiratory failure*
  - Time of onset to admission less than seven days
  - Inability to cough
  - Inability to stand
  - Inability to lift the elbows
  - Inability to lift the head
  - Liver enzyme increases

*Sharshar T et all. Early predictors of mechanical ventilation in Guillain-Barrésyndrome. Crit Care Med. 2003;31(1):278.

Cardiovascular management

- Cardiovascular monitoring
  - İt should be instituted at time of admission
- Intraarterial monitoring
  - İt should be instituted in the presence of significant blood pressure fluctuations
  - Both paroxysmal hypertension and orthostatic hypotension are frequent

Cardiovascular management

- Hypotension;
  - treated with fluids
  - low-dose phenylephrine
- Hypertension (severe HT, MAP>125)
  - Labetalol
  - Esmolol
  - nitroprusside

Arrhythmias

- Sustained sinus tachycardia
  - requires no treatment
- bradycardia and asystole may be seen
- Others
  - atrial fibrillation
  - Atrialflutter
  - paroxysmal tachycardia
  - ventricular tachycardia
  - elevated or depressed ST segments
  - flat or inverted T waves

- Bowel and bladder care
  - Additional autonomic problems include adynamic ileus and urinary retention.
  - Daily abdominal auscultation to monitor for bowel silence

Pain control

- Neuropathic pain occurs (40-50 %)
- Gabapentin or carbamazepine
  - may be used to control of pain during the acute phase
- NSAIDS do not provide adequate pain relief
- Appropriate narcotic analgesics may be used
  - careful monitoring for adverse effects

Rehabilitation

- Acute-phase rehabilitation
  - individualized program of gentle strengthening
    - Isometric
    - Isotonic
    - Isokinetic
    - manual resistive and progressive resistive exercises
- After the acute phase, disabled patients should be treated by a multidisciplinary rehabilitation team.

Disease Modifying Treatment

- The main modalities of therapy for GBS
  - plasma exchange (plasmapheresis)
    - Plasmapheresis is thought to remove circulating antibodies, complement, and soluble biological response modifiers.
  - administration of intravenous immune globulin (IVIG)

- IVIG
  - mechanism of action is unknown
    - providing anti-idiotypic antibodies
    - modulating expression and function of Fc receptors
    - interfering with activation complement

Other therapies

- Glucocorticoids
- Interferon-beta has been reported to be beneficial in individual cases

Choice of therapy

- Guidelines from the American Academy of Neurology (AAN)
  - Treatment with plasma exchange or IVIG hastens recovery from GBS
  - The beneficial effects of plasma exchange and IVIG are equivalent
  - Combining the two treatments is not beneficial
  - Glucocorticoid treatment alone is not beneficial

Prognostic factors

- Poor prognosis for recovery from GBS
  - Older age
  - Rapid onset (less than seven days) prior to presentation
  - Severe muscle weakness on admission
  - Need for ventilatory support
  - An average distal motor response amplitude reduction to <20 percent of normal
  - Preceding diarrheal illness

Thank you