Neuromuscular Diseases

Numbness + weakness could for once be the interesting chart in the rack

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Objectives

• To help you determine when to take vague complaints such as weakness and numbness seriously
• Ensure you get all the inservice exam questions on neuromuscular diseases correct
• Provide you with the differences in history and examination that can lead you to the correct diagnosis
Case #1

• 40-year-old African American female presented to ED with a 2 month history of worsening generalized weakness, dyspnea, and that progressively worsens throughout the day. Has been to her PCP multiple times and diagnosed with chronic fatigue
Differential?

- Myasthenic Gravis
- Anticholinesterase Overdose
- Guillain-Barre
- Transverse Myelitis
- Lambert-Eaton Myasthenic Syndrome
- Botulism
- Neuroparalytic envemonation (e.g. tick or snake bite)
- Drug Induced Myasthenic Syndrome
- Multiple Sclerosis
- Vitamin B12, E, or copper deficiency
Myasthenia Gravis

- Myasthenia gravis (MG) is an autoimmune disorder affecting neuromuscular transmission, leading to generalized or localized weakness characterized by fatigability.
- It is the most common disorder of the neuromuscular junction.
  - Prevalence: 20/100,000 in United States
Myasthenia Gravis

• Most common form characterized by antibodies against post-synaptic acetylcholine receptors

• Second group characterized by autoantibodies against muscle specific tyrosine kinase (MuSK)
  o Typically more severe

• A third group of patients has antibodies to neither AChR nor MuSK, and these patients are considered seronegative.
Symptoms

- Fluctuating skeletal muscle weakness with muscle fatigue
  - Usually worse in the evening or after exercise
- Ptosis and/or diplopia initial symptom in >50%
- Weakness with prolonged chewing
- Dropped head syndrome
- Respiratory weakness
Diagnosis

- **Tensilon (edrophonium test)**
- **Ice Test**
- **SeroLogic testing: Ach-R Ab, MuSK-Ab**
  - Titers correlate poorly with disease severity
- **Repetitive nerve stimulation**
  - Progressive decline in compound muscle action potential (CMAP)
  - Positive if decrement >10%
Ice Pack Test

Myasthenic Crisis

- Complication of Myasthenia Gravis characterized by worsening muscle weakness, resulting in respiratory failure

- Often diagnosed by:
  - Vital capacity (VC) <1L (20-25mL/kg)
  - Negative inspiratory force (NIF) <-20cm H2O
  - Positive expiratory force (PEF) <40cm H2O


Myasthenic Crisis

- 15-20% of MG patients have at least one crisis in their lives
- Median time to the first crisis from onset of MG is 8-12 months
  - May be the initial presentation in 1/5 MG patients
- Bimodal Distribution
  - Early peak, <55yo, women 4:1
  - Later peak, >55yo, affects men and women 1:1

Precipitants

- α-Interferon
- Abx (AMG, ampicillin, macrolides, cipro...)
- Antiepileptics
- β-Blockers
- Ca Channel blockers
- Contrast media

- Infection
- Physical stress
- Aspiration pneumononitis
- Pregnancy
- Sleep deprivation
- Surgery
- Emotional stress
- Pain
- Temperature extremes
Management

- Over 20% require intubation in the ED
  - Succinylcholine is less potent
  - Nondepolarizing agents have increased potency
- Noninvasive Positive-Pressure Ventilation (NPPV)
  - Reduces the need for intubation
  - PCO2 > 50 mmHG at baseline is predictor of failure

Management

Intravenous Immunoglobulin (IVIg)

- 1.2-2 g/kg over 2-5d
- Improvement in 4-5d
- Contraindications
  - IgA deficiency
- Serious Complications
  - Aseptic meningitis, arrhythmias, thrombocytopenia, thrombotic events, ATN, anaphylaxis

Plasma Exchange

- One exchange every other day over 10d
- Improvement in 2d
- Contraindications
  - Hemodynamic instability, unstable coronary diseases, internal bleeding
- Serious Complications
  - Hemodynamic instability, arrhythmias, myocardial infarction, hemolysis, catheter related

Management

- Anticholinesterase inhibitors should be temporarily stopped
  - Avoid excessive secretions in resp failure
- Corticosteroids
  - 1-1.5 mg/kg/d
  - May initially worsen symptoms in 9-75%
  - Begins working after 2wks
- Thymectomy
  - Thymus tumors in 15-32% of people with myasthenic crisis

St Johns, MI
Case #2

- 29yo male had a 1wk history of diarrhea 5wks ago. Presents with a 2 day history of ascending weakness beginning in his legs
- On examination his leg strength is 1/5 and his knees are areflexic
Guillain–Barré Syndrome

• Heterogenous group of disorders characterized by acute polyneuropathy, affecting the peripheral nervous system
Subtypes

- **Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)**
  - Most common
- **Acute motor axonal neuropathy (AMAN)**
  - Purely motor
- **Acute motor and sensory axonal neuropathy (AMSAN)**
  - Sensory + motor
- **Fisher’s Syndrome**
  - Triad of acute ophalmoplegia, ataxia, and areflexia

Guillain–Barré Syndrome

- **Preceding infections**
  - Campylobacter jejuni, Cytomegalovirus, Epstein-Barr virus, Mycoplasma pneumonia, Haemophilus influenza

- **Pathogenesis**
  - Activated macrophages target antigens on Schwann cells, nodes of Ranvier, or myelin sheath

Symptoms

• First symptoms usually pain, numbness, parathesia, or weakness in limbs
• Stereotypically an ascending paralysis beginning in hands or feet
• Infants: inability suck and swallow, floppy neck, generalized flaccidity
• 25% develop respiratory weakness requiring mechanical ventilation
• Autonomic involvement common
Diagnosis

- CSF Findings: elevated protein
- Electromyography & nerve conduction studies
  - Early electrodiagnostic studies abnormal in >85%
  - Motor studies abnormal earliest
Management

- Airway support
- Cardiac monitoring
- Plasma exchange (gold standard)
- IVIg
- Corticosteroids not recommended

Prognosis

- Between 4-15% dies
- Up to 20% are disabled after 1 yr despite treatment
- Outcome worse in elderly
- In children recovery is more rapid and complete
St Johns, MI
Case #3

- 35yo female awoke with dry mouth and blurred vision which rapidly progressed over the next 2hrs to include diplopia, dysphagia, and bilateral arm weakness
- Earlier there was unrelated 20yo male who presented with similar symptoms, was immediately intubated, cause undetermined.
- Both ate at the same Italian restaurant 3 days ago
- Vital signs normal, sensation intact
Botulism

• A rare naturally occurring disease caused by exposure to botulism
• Botulism is a sporulating, obligate anaerobic, gram-positive bacillus, ubiquitous to soil and aquatic sediment
Botulism

- Foodborne botulism
- Infant intestinal botulism
- Adult intestinal toxemia
- Wound
- Inhalation
- Iatrogenic


Pathogenesis

- 7 immunologically distinct toxins (A-G)
Symptoms

• First nausea + vomiting
• All forms produce syndrome of symmetrical cranial nerve palsies followed by descending, symmetric flaccid paralysis of voluntary muscles
• Sensory system + intellectual function unaffected
Diagnosis

• History and examination
  o 2 or more cases with similar symptoms pathognomonic

• Serum, stool, and any left over suspect food tested for presence of toxin

• C. botulinum culture

• Bioassay
• Call public health department if suspected
• Human-derived botulinum immune globulin
• Equine-derived botulinum antitoxin
• Guanidine hydrochloride
• 3,4 Diaminopyrididine
• Plasmapharesis

Prognosis

- Untreated mortality 40-50%
- Current mortality 3-5%
- With intensive care survival near 100% with or without antitoxin


Case #4

• 45yo female with no PMHx presented to her PCP 2 day prior for urinary retention, 1 liter was drained and she was discharged home with antibiotics for a UTI, since that time she has developed an ascending numbness that began in her legs and moved up to her waist
Acute Transverse Myelitis

- Is a medical emergency
- Focal inflammation of spinal cord of different etiologies
- Progressive inflammation of the spinal cord over minute, hours, days, or even weeks
- Incidence: 4.6/million/year

Fig. 54. Cell columns and tracts of the human spinal cord

Dorsal (posterior) columns (Sensations from same side of body)
- Cuneate fasciculus (Discriminative touch and proprioception, upper limb)
- Gracile fasciculus (Discriminative touch, lower limb)

Dorsal spinocerebellar tract (Proprioception; lower limb, same side)

Nucleus proprius of dorsal horn (Origin of contralateral spinothalamic tract)

Ventral spinocerebellar tract (Proprioception, both lower limbs)

Spinothalamic tract (Simple touch, pain and temperature, opposite side of body)

Lateral corticospinal (pyramidal) tract (From contralateral cerebral cortex; skilled and willed movements, same side of body)

Lateral horn (Origin of preganglionic sympathetic fibers; in segments T1 to L2)

Nucleus thoracicus (Origin of dorsal spinocerebellar tract; in segments T1 to L3)

Vestibulospinal tract (Uncrossed; stimulates extensors of trunk and lower limb, and flexors of upper limb)

Reticulospinal fibers (Crossed and uncrossed; unskilled and involuntary movements)

Limb muscles

Trunk muscles

Motor neurons in ventral horn
Pathogenesis

- Inflammatory infiltrates $\rightarrow$ cytokines $\rightarrow$ demyelination $\rightarrow$ inhibition of signal propagation $\rightarrow$ neurological deficits
Pathogenesis

Symptoms are mediated by various pathogenic processes

- Inflammation
- Demyelination
- Axon transection

- Reversible
- Moderately reversible
- Marginally reversible

Symptoms

• Bladder dysfunction (>99%)
• Lower limb parathesias (80-95%)
• Paraparesis (50%)
• Back pain (30-50%)
• Sensory level (e.g. band-like sensation/pressure around abdomen or chest) (80%)
Diagnosis

- Hyperintense lesions on MRI (75%)
- CSF: elevated protein (50%), oligoclonal bands
- May see oligoclonal bands if multiple sclerosis
A 9-year-old boy suddenly developed flaccid tetraparesis with respiratory insufficiency and refractory hiccups. MRI showed Longitudinal extensive transverse myelitis (LETM) in the anterior part of the cord. CSF was normal, biochemical parameters and immunological work up were unremarkable. After corticosteroid treatment and plasmapheresis he was better, there was no more need for ventilation, and he was partially able to move his extremities.
Management

- No randomized, double-blinded, controlled treatment trials
- Corticosteroids
- Plasmapharesis or Plasma exchange (PLEX)
- Immunomodulators
Prognosis

- Recovery usually begins within one to three months
- Some degree of persistent disability in 40%
- Significant recovery is unlikely if there is no improvement by three months
- Worse outcome if: rapid progression, spinal shock, cervical spine involvement, denervation, back pain

Metabolic Myelopathies

• Vitamin B12 Deficiency
  o Relative sudden onset spastic paraparesis
  o Impaired perception of joint position and vibration
  o Neurological symptoms may be the earliest and only sign

• Copper Deficiency
  o Malabsorption, gastric surgery, excessive zinc
  o Subacute symptoms similar to B12
Vascular Myelopathies

- **Vasculitis**
  - Polyarteritis nodosa, Behcet, giant cell arteritis

- **Systemic Hypoperfusion**
  - Arrest, aortic rupture, aortic dissection

- **Infectious**
  - Syphilitic arteritis, bacterial meningitis

- **Arise from hemorrhage, “steal” syndrome, venous congestion, embolism**
Summary

- Many neuromuscular diseases present with distinct features that can be found on a thorough history and physical examination.
- The most important theme of these diseases are early diagnosis and admission.
Thank you

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And you're getting on it

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