PERIPHERAL NERVE AUTOIMMUNE DISORDERS OUTLINE

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Myasthenia Gravis

- An acquired disorder of fatiguable weakness
- Prominent effects on ocular and bulbar muscles
- Risk of thymoma (10%)
- Electrophysiology testing

Repetitive stimulation showing decrement at low frequencies
Single fiber showing increased jitter

- Antibody testing

AchR
MUSK
LRP4 (low-density lipoprotein receptor-related protein 4) * newer antigen
Agrin * still undergoing evaluation

- The MGTX trial (N Engl J Med. 2016 Aug 11; 375(6): 511–522.)
  - Thymectomy has long been used in patients with severe generalized MG
  - 2017 MGTX trial randomized 126 patients (18-65 years of age) to thymectomy or not
  - Thymectomy group had lower prednisone requirement, lower use of azathioprine, and significantly fewer admissions for crisis
  - ** It is not clear how this result will affect practice as newer immune therapies come into wider use.
- Emerging therapies for MG: Rituximab
  - Monoclonal antibody for depleting B cells
  - Retrospective data supports efficacy in refractory MG
  - Open labeled study also supports use in MG
- Methotrexate: A randomized 12 month trial of methotrexate showed no steroid sparing effect (Neurology 2016 Jul 5;87(1):57-64)

Lambert-Eaton Myasthenic Syndrome (LEMS

- Insidious disease of fatiguable weakness
- Often appears like a chronic myopathy
- Facilitation of strength with exercise
- On EMG very low amplitude CMAPs facilitate with exercise or high frequency rep stim (they also show decrement with low frequency rep stim)
- Autonomic symptoms
- VGCC antibodies (85%)
- Risk of lung cancer

Sensory Neuronopathy

- Direct damage to dorsal root ganglia neurons

- Progressive sensory loss
- Often painless
- Severe sensory ataxia
- Diverse causes (B6, cisplatin, Sjogren's, Lupus)
- Paraneoplastic causes include Hu, CV2

High risk of lung cancer

CIDP

- A chronic autoimmune demyelinating neuropathy
- Presumed to be mediated by autoantibodies to peripheral nerve
- Patients may have diverse phenotypes

mild/severe
Motor/sensory
Responsive/refractory to therapies
Symmetric/asymmetric

- True antigens largely unknown
- Emerging protein autoantigens in CIDP

NF155, NF186, Gliomedin, Contactin, Caspr2, Caspr2, etc.
NF155 and Contactin antibodies
are predominately IgG4
May define subsets of CIDP refractory to IVIg but responsive to rituximab (Neurol Neuroimmunol Neuroinflamm 2015;2:e149)
CIDP may soon be divided into sub-diseases based on pathogenic mechanism and have mechanism-specific treatments

POEMS syndrome

- Polyneuropathy, organomegaly, endocrinopathy, m-spike, skin changes
- A paraneoplastic neuropathy associated with osteosclerotic myeloma or Castelman's disease
- IgG lambda is the most common paraprotein
- Presentation may initially be identical to CIDP with only subtle or no findings in other organ systems
- Evaluation
    - Screen all patients with suspected CIDP for a paraprotein (serum and urine immunofixation)
    - Skeletal x-ray survey
    - Consider VEGF test if strong suspicion
    - When evaluating a new CIDP patient, look for signs of edema, papilledema, endocrinopathy, cardiomegaly, etc.
- Treatment
    - Work in conjunction with a hematologist/oncologist
    - Solitary osteosclerotic lesions may be excellent targets for radiotherapy
    - More widespread disease → chemotherapy may be the primary modality and may limit other immune therapy options; may require bone marrow transplant
    - IVIG, steroids unlikely to be effective (so consider POEMS again when facing treatment-resistant CIDP)

Isaacs Syndrome (acquired neuromyotonia)

- acquired disorder of peripheral nerve hyperexcitability
- Cramps, spasms, fasciculations, rigidity, hyperhydrosis
- Linked to myasthenia gravis
- Linked to thymoma
- Closely related Morvan Syndrome (also have encephalitis, sleep disorder)
- Subset with Caspr2 antibodies but true antigens largely unknown

Autoimmune Autonomic Neuropathy

- A severe, acquired pan-dysautonomia

Fixed or sluggish pupils
Anhydrosis
Severe orthostasis
Severe gastrointestinal immobility
Sexual dysfunction
Urinary dysfunction

- Ganglionic AchR antibodies

Target the types of acetylcholine receptors present in autonomic ganglia (α3β4 subunits)
Found in half of patient with AAN (the other half have no known mechanism)
Test prone to low titer false positives
Risk of thymoma (esp in overlap with regular myasthenia gravis, AchR antibodies)
10-30% risk of adenocarcinoma even in those without the neurological disease

Paraneoplastic enteric neuropathy

- A subset of patients with anti-Hu have severe involvement of enteric neurons
- Gastroparesis is the primary phenotype
- May co-exist with sensory neuronopathy or other anti-Hu manifestations
- Risk of small cell lung cancer may be similar to other anti-Hu patients