Objectives

- Emphasize the importance and frequency of central nervous system (CNS) inflammatory demyelinating disorders, with an emphasis on multiple sclerosis (MS)
- Provide an overview of the most common symptoms and signs seen in multiple sclerosis
- Present diagnostic criteria for multiple sclerosis
- Outline therapeutic management of multiple sclerosis
- Briefly discuss some less common CNS inflammatory diseases or syndromes

Characteristics and Definition of MS

- MS is an inflammatory demyelinating disorder of the CNS
- The cause of demyelination is not known and may be autoimmune
- Clinical diagnosis requires evidence of two neurological events that localize to the CNS that are separated in space and time
- The pathological hallmark of the disease is a demyelinating plaque/lesion

Epidemiology

- Predominantly females (2:1)
- Between the ages of 15-45 years
- There are over 350,000 patients in the USA, prevalence ~50/100,000
- With some exceptions there is greater incidence of MS at higher latitudes
- First degree relative increases risk 25-50 fold

Incidence of Multiple Sclerosis
Clinical Categories of MS

- Relapsing remitting
- Secondary progressive
- Primary progressive
- Progressive relapsing

Pathology

The hallmark of MS is the MS plaque, which represent areas of myelin destruction with attendant axonal loss.

1. Primary damage to myelin
   I. Antibodies, complement and immune cells
   II. Immune cells only
2. Oligodendrocyte death (primary oligodendrogliopathy)

Pathophysiology

- Demyelinated plaque: well demarcated, hypocellular, myelin loss with relative preservation of axons.
- Perivascular lymphocytes, astrocytic-glial scars.
- Plaques can occur anywhere although they are more prominent in periventricular regions, grey-white junction and the cervical region of spinal cord
- Demyelination and axonal loss leads to loss of saltatory conduction and motor and sensory deficits

What is the Uthoff’s phenomenon?

Diagnostic Criteria

- Diagnosis is clinical, and is supported by attendant laboratory and radiological studies

How is MS Diagnosed?

The diagnosis of MS is based on clinical grounds. In individual who do not meet the clinical criteria of dissemination of lesions in space and time, the diagnosis may be made with MRI, spinal fluid and electrodiagnostic studies. The McDonald criteria is now the standard for diagnosis of definite MS.
Diagnosis of MS

<table>
<thead>
<tr>
<th>Test or exam</th>
<th>First clinical episode</th>
<th>Subsequent clinical episode</th>
<th>Paraclinical data</th>
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<tbody>
<tr>
<td>MRI</td>
<td>Lesion, demyelination,</td>
<td>New lesion, demyelination</td>
<td>Not required</td>
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<td></td>
<td>optic nerve</td>
<td>optic nerve</td>
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<td>CSF</td>
<td>Normal</td>
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<td>Oligoclonal bands</td>
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<td>Telangiectatic veins</td>
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<td>Visual evoked potentials</td>
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<td>MRI brain ± spinal cord</td>
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What is an “attack” in MS?

- Change in neurological function persisting for more than 24 hours
- Most common changes are visual loss (lesion in optic N) and ascending parasthesias (lesion in spinal cord)
- Episodes last on average for 6-12 weeks

What is NOT an “attack” in MS?

- Change in neurological function due to an underlying infection/fever also called as a pseudo-relapse
- Most common infections are UTIs and URIs
- Paroxysmal symptoms including pain, spasms, or fatigable weakness are not exacerbations

What is Lhermitte’s phenomenon?

What is internuclear ophthalmoplegia?

Case

A previously healthy 24-year-old female is referred for a second opinion because 10 weeks before she had an episode of blurred vision on the left eye and numbness, mild imbalance, and tingling and numbness in both legs. The vision disturbance resolved in 12 days, while the numbness resolved in about 4 weeks. The ophthalmologist who saw her during her episode found 20/100 vision on the left eye no papilledema. The neurological examination eight weeks after the episode was normal.

- How would you work her up?

Laboratory Findings

- There is no diagnostic test for MS, but there are some characteristics clinical findings
  - Increased IgG synthesis rate (IgG index)
  - Oligoclonal bands (in-situ antibodies production)
  - Visual evoked potentials
  - MRI brain (± spinal cord)
What does this MR-FLAIR show?

MR Images of MS

Gd enhancement

Brain atrophy (shrinkage)

T1 “black hole”

Spinal cord lesion

What other illnesses are in the differential diagnosis for MS?

Worth thinking about...

- Systemic autoimmune diseases with CNS involvement; these include, CNS lupus, Sjogrens syndrome, anti phospholipid antibody syndrome
- CNS sarcoidosis
- Devic’s disease
- Infectious myelopathies (HTLV-1 myelopathy)
- Post infectious autoimmune syndromes
- CNS lyme disease, HTLV-1 myelopathy
- Metabolic disorders (Vit B12 deficiency)
- Compressive myelopathies
- Mitochondrial disorders
- Behcet’s disease
- ... hence consider:
  - ANA, B12, CBC, ESR, serology for HIV, HTLV1, syphilis, Lyme; CXR, pathergy test, among others.

Therapy, acute attack

- Methylprednisolone (500-1000 MG) IV for 3-5 days
- Prednisone taper?
- PLEX

Case

26 year old female, previously healthy. Develops episodes of severe, brief right facial pain, that is triggered by talking and tooth brushing. Six months ago she had left optic neuritis, with complete resolution of symptoms.

- What are the diagnostic considerations?
- How would you manage her symptoms?
Therapy, symptomatic therapy

- Oxybutinin (Ditropan), propantheline, tolterodine (Detrol), intermittent bladder cath
- Baclofen, botulinum – spasticity
- Amantadine - fatigue
- Tricyclic drugs – depression, pain, emotional incontinence
- Physical, occupational, speech therapy

Therapy, disease modifying agents

- Interferon 1a (Avonex and Rebif), weekly IM injections and 3X/week SC injections; slows accumulation of disability
- Interferon 1b (Betaseron), SQ injections QOD, reduces frequency of relapses; MRI is improved
- Glatiramer acetate (Copaxone), SQ injections QD, reduces frequency of relapses
- Mitoxantrone
- IVIG
- Others: cyclophosphamide, azathioprine, methotrexate and mycophenolate

Case

A 32 year old white female presents with multiple attacks of eye pain with movements of her eyes and right eye vision impairment starting about 4 years ago at which time she was diagnosed with optic neuritis. The episodes generally last only 1-2 weeks and then disappear with apparently complete recovery. In the past 6-9 months she has had several episodes of urinary incontinence resulting in bed-wetting. Physical exam reveals nystagmus, right papilledema with decreased visual acuity. DTRs are 3/4 on the right side, sensory exam is normal. She exhibits spastic gait.

- What work up would you suggest?
- What therapies would you consider for the acute attacks?
- Any ideas for long-term management?

Additional MS Symptoms

- Fatigue
- Trigeminal neuralgia

Support

- National Multiple Sclerosis Society – nmss.org
- Multiple sclerosis Association of America – msaa.com

What is Neuromyelitis Optica?
Neuromyelitis Optica (Devic’s)

- Uncommon
- Association of optic neuropathy and autoimmune(?) myelopathy
- Age 27 years (range 1-73), predominantly women
- May respond to IV steroids, otherwise supportive therapy
- Prognosis tends to be poor

Other Demyelinating Diseases

- Balo’s concentric sclerosis
- Acute disseminated encephalomyelitis (ADEM)
- Marburg’s variant
- Monophasic syndromes
  - Optic neuritis
  - Acute transverse myelitis
  - Acute inflammatory brainstem syndromes

Questions?

Comments