MULTIPLE SCLEROSIS
Update

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Disclosures

• I do not have any disclosures.

Multiple Sclerosis

• Most common demyelinating disease of the CNS
  – > 90% affected prior to age 55
  – < 5% diagnosed before the age of 14
• Multifocal with lesions of different ages, time and site
• Relapsing and remitting (80%) vs progressive course (15%), focal single lesion (<5%)

• Classification:
  – Classic (Charcot type)
  – Acute (Marburg type)
  – Concentric sclerosis (Balo’s type). Very rare
  – Schilder’s disease – occurs in children, extensive demyelination, acute, can be remitting, responds to steroids.
Jean Martin Charcot (1825-1893)

Who gets MS?

Each week, about 200 Americans are diagnosed with MS.1

Most people are diagnosed between the ages of 20 and 50 (average age, 31-33).1,2

More than twice as many women have MS as men.1

MS is more common in Caucasians, especially those of northern European descent.1

2. MS Network. Who Gets MS? Available at: www.ms-network.com

MS: Magnitude of the Problem

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### Epidemiology of MS

- Individuals who migrate to high risk area before age 10 have a high risk for disease
- Individuals who migrate to low risk area before age 10 assume a low risk for disease
- Individuals who migrate after the age of 10 assume the risk of the area in which they spent their first 10 years

### Birth Month and Risk of MS

- N = 17,874 Canadian patients with MS
- Significantly fewer patients with MS were born in November ($p=0.009$) and more were born in May ($p<0.0001$) compared with other months
- Vitamin D influences the expression of HLA-DRB1*15

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**Potential Triggers for Multiple Sclerosis**

- Infectious agent
- Abnormal immunologic response
- Genetic predisposition
- Environmental factors

MS = multiple sclerosis

Genetic Prevalence of MS

- In a recent genome wide transcription analysis for MS, 48 new genetic variants were identified
- Of interest most genes reverted back during pregnancy.

(Nature Genetics, September 2013)

Genetic Prevalence of MS

- 10 X increase for MS if direct relative affected
- Siblings of an affected person have a 2-5% risk of developing MS.
- Higher prevalence in identical twins
- Variability in severity of disease in twins and affected relatives

EBV and Children

- Children with MS demonstrate abnormally increased rates of EBV viral reactivation and a broader range of genetic variants, suggesting a selective impairment in their immunologic control of EBV.

Yea, C (AAN, Oct 15, 2013)
Update on IM and MS

• Research on EBV has continued to evolve.

• Latest findings shows that it is unlikely any of the studied polymorphisms contribute to explaining association between anti-EBNA1 Ab titer or history of IM and MS.

Simon, KC (Multiple Sclerosis and Related Disorders, 2015)
MR Imaging in MS

- Gd enhancement
- T2 lesion
- Brain atrophy (shrinkage)
- T1 “black hole”
- Spinal cord lesion
47 year old female; RN
MRI Findings in the Diagnosis of MS

<table>
<thead>
<tr>
<th>MRI Findings Supporting the Diagnosis of MS</th>
<th>MRI Findings cautioning against the Diagnosis of MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Lesion size &gt; 5 mm in diameter</td>
<td>• Lesion size smaller, many or all ≤ 5 mm in diameter</td>
</tr>
<tr>
<td>• Lesion shape – ovoid or oval</td>
<td>• Lesion shape – linear, punctate, comma, subtle</td>
</tr>
<tr>
<td>• Lesion location</td>
<td>• Lesion location – lack of periventricular involvement</td>
</tr>
<tr>
<td>– Periventricular, perivenular (Dawson’s fingers), juxtacortical, corpus callosum, intratentorial, spinal cord</td>
<td>• Meningeal/basilar enhancement</td>
</tr>
<tr>
<td>• Homogeneous or open ring-enhancing</td>
<td>• Normal scan of brain and spinal cord</td>
</tr>
<tr>
<td>• Presence of T1 black holes</td>
<td></td>
</tr>
</tbody>
</table>

- Oligoclonal bands are more sensitive and specific (90-95%).
- IgG index or IgG synthesis are sensitive and specific (70-75%).
### Differential Diagnosis of MS

- **Inflammatory diseases**
  - SLE
  - Sjogren’s disease
  - Behcet’s disease
  - Polyarteritis nodosa
  - Granulomatous angitis
  - Sarcoidosis
  - Panencephalitic encephalomyelitis
- **Infectious diseases**
  - Lyme disease
  - HIV
  - PML
  - Neurosyphilis
  - Hashimoto Thyroiditis
  - Leber’s Optic Atrophy
- **Disease of myelin**
  - ALD
  - ADEM
  - Central pontine myelinolysis
- **Vascular**
  - Lacunes
  - Embolic
  - CADASIL
  - Stroke due to APLA
- **Miscellaneous**
  - Spinocerebellar disorders
  - Cerebral spongiosis
  - Arnold-Chiari malformation
  - Syrinx
  - Vitamin B12 deficiency
  - Leber’s Optic Atrophy

### Clinical Presentations of MS

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### Multiple Sclerosis: Common Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder symptoms</td>
<td>90</td>
</tr>
<tr>
<td>Fatigue</td>
<td>80</td>
</tr>
<tr>
<td>Spasticity</td>
<td>70</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>64</td>
</tr>
<tr>
<td>Pain</td>
<td>62</td>
</tr>
<tr>
<td>Cognitive dysfunction</td>
<td>50 in 15 yrs, 90 in 25 yrs</td>
</tr>
<tr>
<td>Depression</td>
<td>50</td>
</tr>
<tr>
<td>Bowel dysfunction</td>
<td>40</td>
</tr>
</tbody>
</table>


### Fatigue in MS

- Probably the single most common symptom shared by patients with MS
  - Reported > 75% of patients
  - In 30% of patients, it occurs before other symptoms of the disease
- In many patients, fatigue is the most disabling symptom and one of the most common reasons for retirement due to disability

### Depression and Multiple Sclerosis

- Does MS cause depression?
- Does the therapy for MS (specifically IFN) cause depression?
- How is depression best managed?
Cognitive Impairment in Untreated MS

• Occurs in approximately half of all people with MS

• Often under recognized or misdiagnosed as depression, stress, or personality disorder

• Impairs daily functioning of people with MS

• Leading cause of unemployment in persons with MS

Mesenchymal Stem Cells as a Treatment for MS

• Mesenchymal stem cells (MSCs) could reduce inflammatory lesions in patients with MS.

• MSCs can be derived from bone marrow or placenta.

(Acta Biom, Summer 2014)
Complementary & Alternative Medicine in MS

• The guidelines demonstrate that even though there are multiple CAM therapies, there is little evidence that most of them are effectively treating MS.

(Neurology Today, 2014)

• Functional brain abnormalities linked to cognitive impairments in MS patients who use Marijuana

• Medical Marijuana does not appear to have curative effects on any neurologic condition, but it may ameliorate unwanted symptoms and ease suffering.

Hurley (Neurology Today, 2014)
Fife (AAN, 2015)

Vitamin D

• Vitamin D is a protective factor in MS

• For every 10 ng/mL increase in Vitamin D levels in patients with MS, their EDSS scores were 0.05 points lower.

• Recommended Vitamin D levels of 50-80 ng/mL.

Otto, A (Clinical Neurology News, June 2012)
Additional CAM Therapies

- Ginkgo biloba
- Ginseng
- Omega-3 fatty acid (anti-inflammatory)
- Omega-6 fatty acid (pro-inflammatory)

Medical Management During Pregnancy, Delivery, and Postpartum

- None of the disease-modifying medications are approved for use during pregnancy.
- The disease-modifying drugs are also not recommended for use during breastfeeding.
- Women with MS usually do not need special gynecologic care during pregnancy, labor and delivery.

Conclusion

- MS is the most common demyelinating disease of the CNS.
- Relapsing remitting (80%), Progressive (15%), Focal Single Lesion (< 5%)
- 200 Americans (primary between ages 20-50) diagnosed weekly with MS.
- More than twice as many women have MS than men.
- Less than 10% of all MS patients are younger than age 18.
- 10% increase for MS if direct relative affected.
Conclusion (con’t)

• Correlation between EBNA-1 IgG and gadolinium enhancing lesions in MS disease activity.

• Patients need to undergo an MRI and CSF for oligoclonal bands and IgG index/synthesis.

• Diagnosing MS is still a clinical diagnosis (no single diagnostic laboratory test).

Conclusion (con’t)

• Common symptoms include neurogenic bladder, fatigue, spasticity, sexual dysfunction, pain, cognitive dysfunction, and depression.

• There are several different types of injectable and oral medications for treatment.

Take Home Message

Patients do not care about how much you know. What they want to know is how much you care!
Thank you!

Q & A