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Updates in Multiple Sclerosis

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Review the role of MRI of the brain and spinal cord in the routine diagnosis and management of Multiple Sclerosis (MS).
Identify prognostic indicators of disease severity and progression in patients with MS.
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Disclosures

- **Research/Grants**: Biogen; Genzyme; Novartis; Sun Pharma; MedImmune; Actelion; Mallinckrodt; EMD Serono; Genentech

- **Speakers Bureau**: Biogen; Pfizer; EMD Serono; Genzyme; Teva Neuroscience; Mallinckrodt; Acorda

- **Consultant**: Biogen; Genzyme; Teva Neuroscience; Pfizer
Case Study

- **HPI:**
  - 30 year-old man presents with 2-week history of right leg weakness and fatigue. Denies previous neurologic symptoms.

- **PMH:**
  - None

- **Social History:**
  - Works as nurse, denies toxic habits

- **Family History:**
  - Sister has MS

- **ROS:**
  - Otherwise negative
### Case Study (cont.)

<table>
<thead>
<tr>
<th>Mental status:</th>
<th>Reflexes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>– MMSE 26/30 with noted impairments in attention and delayed recall</td>
<td>– Brisk throughout</td>
</tr>
<tr>
<td>– Intact</td>
<td>– Plantar extensor bilaterally</td>
</tr>
<tr>
<td><strong>Cranial nerves 2-12:</strong></td>
<td><strong>Cerebellar/Gait:</strong></td>
</tr>
<tr>
<td>– Intact</td>
<td>– Intact with mild difficulty on tandem due to weakness</td>
</tr>
<tr>
<td><strong>Motor:</strong></td>
<td><strong>Sensory</strong></td>
</tr>
<tr>
<td>– Tone/bulk normal</td>
<td>– Lhermitte’s sign present</td>
</tr>
<tr>
<td>– Weakness RLE</td>
<td>– + Rhomberg</td>
</tr>
</tbody>
</table>
Case Study (cont.)

- Differential diagnosis?

- What testing is needed?
  - Serologic studies
  - Evoked potentials
  - CSF analysis
  - MRI brain
  - MRI spinal cord
Case Study (cont.)

- Thoughts on MRI?
- Does CSF analysis have to be completed for diagnosis confirmation?
- Diagnosis: Relapsing Remitting MS (RRMS)
  - Patient started on injectable DMT
  - 6 months later, he had residual RLE weakness but developed over 1 week bilateral LE numbness/weakness, balance difficulties
  - MRIs showed…
Case Study (cont.)

● What is the role of MRI in the long-term management of MS patients?

● Would you change DMT at this point?

● If so, what therapies should be considered?
Poor Prognostic Indicators in RRMS

- High relapse rate during first 2 years of disease onset\(^1,2\)
- Incomplete recovery and short interval between first 2 exacerbations\(^1-5\)
- Greater lesion burden on MRI at time of diagnosis\(^6\)

## Prognostic Indicators of Disease Severity and Progression in MS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Prognostic Factors</th>
<th>Predictors of Increased Disease Severity and/or Conversion to MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Gender</td>
<td>• Male gender</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>• Late age at onset</td>
</tr>
<tr>
<td>Clinical features(^1)</td>
<td>Symptoms</td>
<td>• Polysymptomatic onset</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Motor, cerebellar, and sphincter involvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Incomplete recovery after onset</td>
</tr>
<tr>
<td></td>
<td>Relapse and disease course</td>
<td>• Frequent early relapses, short intervals between relapses, cognitive impairment and moderate disability at onset</td>
</tr>
<tr>
<td>MRI(^1,2)</td>
<td>Lesion load and brain atrophy at disease onset</td>
<td>• Increased T(_2) lesion number and volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increased Gd-enhancing lesion number and volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increased T(_1) lesion number and volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Extensive white and gray matter atrophy</td>
</tr>
<tr>
<td></td>
<td>Site of lesions</td>
<td>• Lesions in the infratentorial regions of the brain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Atrophy in the upper cervical area of the spinal cord</td>
</tr>
<tr>
<td>Biological markers</td>
<td>CSF markers</td>
<td>• Presence of IgG or IgM oligoclonal bands</td>
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<tr>
<td></td>
<td></td>
<td>• Elevated levels of SCF proteins: Tau, Nf (heavy and light), glial fibrillary acidic protein or CSCL 13</td>
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<tr>
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<td></td>
<td>• Reduced levels of N-acetylaspartate</td>
</tr>
</tbody>
</table>

Clinical Connections

- There are many diseases/conditions that can cause white matter lesions in the central nervous system, making the accurate diagnosis of MS difficult at times.

- MRI has become the most important para-clinical tool for both diagnosis and ongoing management of MS.

- Increasing evidence of prognostic indicators has allowed for individualized approaches to MS clinical management.
Call to Action

- Utilize MRIs of the brain and spinal cord to optimize the long-term management of patients with MS
- Identify prognostic indicators of disease progression and severity in MS in order to develop patient-centered treatment paradigms