Case Challenges in MS: Tailoring Therapy to Patient-Specific Characteristics

This activity is jointly provided by Global Education Group and Spire Learning.

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Program Overview

The complexity and heterogeneity of multiple sclerosis (MS) pathogenesis renders its clinical course and response to therapy highly variable, particularly among special populations. This includes patients considering pregnancy or minority patients. This necessitates optimal strategies to personalize therapy and monitor disease activity and progression in special populations.

This educational activity will review cutting-edge research on the unique considerations for prognosis, monitoring, and treatment response in special populations of MS patients. Focused attention will be given to translating research into optimized therapeutic strategies tailored to patient-specific characteristics with the goal of slowing disease progression. A compelling case study will be presented to illustrate clinically relevant challenges in disease management.
Target Audience

MS specialists, neurologists, internists, hospitalists, and nurses in MS center and hospital settings

Learning Objectives

Upon completion of this activity, learners will be better able to:

DESCRIBE the heterogeneity of the clinical and neuropathological characteristics of MS and evidence-based strategies to monitor disease progression and treatment failure

EVALUATE best practices in the use of disease-modifying therapies in special populations with MS
Physician Accreditation Statement

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For information about the accreditation of this program, please contact Global at 303-395-1782 or inquire@globaleducationgroup.com
Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer’s product information, and comparison with recommendations of other authorities.

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Ashley Marostica, RN, MSN; Andrea Funk; Liddy Knight: No relevant financial relationships with any commercial interests.

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Levels of Evidence

Levels of evidence are provided for any patient care recommendations made during this presentation.

**Level A (randomized controlled trial/meta-analysis):** High-quality, randomized controlled trial (RCT) that considers all important outcomes. High-quality meta-analysis (quantitative systematic review) using comprehensive search strategies

**Level B (other evidence):** A well-designed, nonrandomized clinical trial. A nonquantitative systematic review with appropriate search strategies and well-substantiated conclusions. Includes lower-quality RCTs, clinical cohort studies and case-controlled studies with nonbiased selection of study participants and consistent findings. Other evidence, such as high-quality, historical, uncontrolled studies, or well-designed epidemiologic studies with compelling findings, is also included

**Level C (consensus/expert opinion):** Consensus viewpoint or expert opinion

Each rating is applied to a single reference in the presentation, not the entire body of evidence on the topic.

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Faculty Presenter

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Multiple Sclerosis Overview

- Immune-mediated disease of the central nervous system that is associated with inflammation, demyelination, axonal loss, and neurodegeneration
- Primary etiology unknown, but likely multifactorial
- Risk factors: low vitamin D, smoking, overweight/obesity, environmental exposures, etc

Epidemiology

- Newly diagnosed: ~200 people per week
- Most common cause of nontraumatic disability in 18- to 60-year-old population
- Female predominance with peak incidence between 20 and 40 years old
- Incidence may be highest among African American women
- 58% of neurologists treat 2 or more pregnant patients per year
Diagnosis of MS

- Based on clinical history, neurologic exam, MRI, paraclinical tests, and exclusion of other possible causes
- Can diagnose MS after a single attack with 2010 McDonald criteria and 2017 criteria will expand this


Clinical Courses of MS: Classification

- What is the pattern of disease?
  - Once patients are diagnosed with MS, defining their MS subtype is critical

- Why define the clinical course?
  - It may help to:
    - Guide treatment choices
    - Guide communication between the clinician and patient and help to set more appropriate and realistic expectations

MS Disease Subtypes

- Clinically isolated syndrome (CIS)
  - Active
  - Not active

- Relapsing-remitting MS (80%–85%)
  - Active
  - Not active

- Primary progressive MS (10%–15%)
  - Active and with progression
  - Active but without progression
  - Not active but with progression
  - Not active and without progression (stable disease)

- Progressive disease

Not active = Inflammatory activity measured by clinical relapses and/or MRI activity.
Progression = Measured by clinical evaluation.
Radiologically isolated syndrome not included

Initial Presentation
Case Study – Beth

- An otherwise healthy 28-year-old African American female school teacher presents with a complaint of progressive double vision and unsteady gait over 1 week
- Upon further questioning, she had an episode of left lower extremity weakness earlier this year while training for a 5K run
- Past medical, surgical, and family histories are unremarkable
- Social history only remarkable for occasional alcohol on weekends. Not a smoker
- Physical examination, including detailed neurologic examination, is significant for left internuclear ophthalmoparesis, ataxia of the left upper extremity, spastic weakness of the left lower extremity, and diminished vibratory perception in both feet

Initial Presentation – Beth

- MRI of the brain and spine reveals an enhancing lesion in left pons, non-enhancing right pontine lesion, with additional non-enhancing lesions in corpus callosum, and in cervical and thoracic spinal cord
- Lumbar puncture revealed 5 unique oligoclonal bands and is otherwise normal
- Serologic studies reveal no other etiologies for her symptoms

Typical MRI Features in MS

- Periventricular
- Corpus callosum and juxtacortical
- Spine lesions

Images courtesy of Dr. Scott Newsome, DO
Follow-up Case Study – Beth

- She was diagnosed with relapsing-remitting MS and treated with pulse steroids for her acute relapse
- Following steroids, her double vision resolved but she still had gait ataxia and spasticity

Factors Associated With More Aggressive MS

<table>
<thead>
<tr>
<th>Clinical factors</th>
<th>Paraclinical factors</th>
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<tbody>
<tr>
<td>Male gender</td>
<td>MRI high lesion burden at presentation</td>
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<tr>
<td>Older age at onset</td>
<td>Two gadolinium-enhancing/new T2 lesions or more than two T1 hypointense lesions*</td>
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<tr>
<td>African American*</td>
<td>Two spinal cord lesions*</td>
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<tr>
<td>Motor involvement</td>
<td>Brain atrophy*</td>
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<td>Cerebellar involvement</td>
<td>Low vitamin D</td>
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<td>Sphincter involvement</td>
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<td>Frequent relapses</td>
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<td>Poor recovery from relapses</td>
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<td>Multifocal involvement at onset</td>
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Demographic Characteristics Inform Relapse Frequency

- N=330 patients; seen within the first year of disease onset to determine predictors of having a second MS relapse within the first year of onset
  => younger age and non-white race strong predictors
- These results are relevant since African Americans appear to be at higher risk of long-term disability over time, and some studies suggest an earlier age at diagnosis is associated with an earlier age of disability

Relapse-free survival curves by age (a), race (b)


African Americans (AA) with MS have more disease activity than Caucasians

- Greater pyramidal dysfunction in early disease
- More cerebellar symptoms
- Higher likelihood of transverse myelitis
- More with PPMS
- Higher EDSS at diagnosis
- Higher median MS Severity Score
- Higher risk of cane dependency/shorter time to cane
- Overall lesion burden and lesion volume is greater in AA compared to similar non AA cohort
- Greater tissue damage as measured by MTR
- Accelerated retinal damage and vision loss in AA compared to Caucasians
- Poorer response to interferon agents
  - Increased annualized relapse rate
  - Fewer exacerbation free
- Better disease control on natalizumab
  - Fewer relapses and less brain lesions

PPMS, primary progressive multiple sclerosis; EDSS, Expanded Disability Status Scale; MTR, magnetization transfer ratio
**Follow-up Case Study – Beth**

- She was started on an MS disease-modifying therapy (DMT) which she tolerated and had strict compliance to.

- Unfortunately, 8 months out from starting her DMT she experienced another relapse consisting of progressive right sided weakness and urinary urgency.
  
  => What could be considered suboptimal treatment response:
  - Clinical evidence of disease activity
    - ≥2 relapses within 1 year
    - One significant relapse in the past year
  - Concerning levels of MRI activity
    - Significant MRI changes at 1 year in the absence of clinical symptoms
    - Continued MRI activity on serial MRIs

- Following another round of steroids and physical therapy, she was interested in stopping therapy to pursue pregnancy.

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**Pregnancy in MS**

- Pregnancy is a relatively protected time for people with MS (2nd and 3rd trimester).

- Majority of DMTs need to have wash out before pursuing pregnancy.

- Gonadotropin-releasing hormone (GnRH) agonists may provoke relapses (activate immune system) while GnRH antagonists or recombinant gonadotropins do not affect MS relapse rates.

- Postpartum MS disease activity correlates with pre-pregnancy disease activity.

- Breastfeeding data mixed.

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Summary

- MS is a common, chronic demyelinating disease of the central nervous system that usually presents in prime of life.
- The ability to diagnose and treat MS has improved greatly over the past 20 years.
- An aggressive or highly active course can occur at onset or arise later in disease course.
- It is important to recognize clinical and paraclinical features of a highly active course since a more aggressive treatment approach may be warranted.
- Identifying optimal therapeutic strategies relative to patient-specific characteristics and desires is key.