MRI in Differential Diagnosis

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DISCLOSURES

• Speaking, consulting, and/or advisory boards for Genzyme, Novartis, Bayer, and Teva.
• Institutional research support from Avanir, Biogen, Novartis, Roche, Teva.
OUTLINE

• Introduction to MRI
  • T1/T2/FLAIR/gado – what does it mean?
• Typical MRI findings in MS
• Differential diagnosis of MS on MRI
• Case studies
  • Common and uncommon MS mimics
  • MS spectrum on MRI

MRI: TYPES OF IMAGING

• T1: good for brain anatomy
• T2: highlights pathology
• Fluid Attenuated Inversion Recovery (FLAIR): suppresses CSF signal
• T1 + gado: shows BBB breakdown
MRI: T1 IMAGING

TYPICAL MS: T1 BLACK HOLES
MRI: T2 Imaging

Typical MS: Axial FLAIR
TYPICAL MS: SAGITTAL FLAIR

SPINAL CORD MRI
MRI IN DIAGNOSIS:

- Periventricular, ovoid lesions
- Cerebellum frequently involved
- Corpus callosum lesions common
- Cortical lesions poorly seen on MRI
- MRI is highly variable

MRI IN MS DIAGNOSIS

<table>
<thead>
<tr>
<th>TABLE 1: 2010 McDonald MRI Criteria for Demonstration of DIS</th>
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<tbody>
<tr>
<td>DIS Can Be Demonstrated by ≥1 T2 Lesion* in at least 2 of 4 Areas of the CNS:</td>
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<tr>
<td>- Periventricular</td>
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<tr>
<td>- Juxtacortical</td>
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<tr>
<td>- Infratentorial</td>
</tr>
<tr>
<td>- Spinal cord†</td>
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<tr>
<td>Based on Swanson et al 2006, 2007.25,27</td>
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<tr>
<td>*Gadolinium enhancement of lesions is not required for DIS.</td>
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<td>†If a subject has a brainstorm or spinal cord syndrome, the symptomatic lesions are excluded from the Criteria and do not contribute to lesion count.</td>
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<td>MRI = magnetic resonance imaging; DIS = lesion dissemination in space; CNS = central nervous system.</td>
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<table>
<thead>
<tr>
<th>TABLE 2: 2010 McDonald MRI Criteria for Demonstration of DIT</th>
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<tr>
<td>DIT Can Be Demonstrated by:</td>
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<tr>
<td>1. A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI</td>
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<td>2. Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time</td>
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<tr>
<td>Based on Montalban et al 2010.24</td>
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<tr>
<td>MRI = magnetic resonance imaging; DIT = lesion dissemination in time.</td>
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## Differential Diagnosis of MS

**MS forms and mimics**
- Neuromyelitis optica
- ADEM
- Balo’s concentric sclerosis
- Marburg variant

**Autoimmune disease**
- Systemic lupus erythematosus
- Sjögren’s syndrome
- Antiphospholipid antibody syndrome
- Behcet’s disease
- Neurosarcoid

**Infectious**
- HIV and HTLV
- Herpes viruses
- VZV
- JC virus
- Measles virus
- Toxoplasmosis
- Histoplasmosis
- Syphilis

**Genetic**
- Adrenoleukodystrophy
- Leber’s optic atrophy
- Mitochondrial diseases
- CADASIL

**Other**
- B12 deficiency
- Complicated migraine
- Nonspecific WM lesions
- SVID

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### MS Mimics on MRI
NONSPECIFIC WM LESIONS

- 32 yo diagnosed with MS in 2006
  - MRI done for recurrent headache
  - Pain in multiple locations refractory to treatment
- Cervical and thoracic spine MRI: normal
- Lumbar puncture
  - No cells, normal protein, no oligoclonal bands
- Labs for other conditions normal
  - B12, ESR, ANA, SSA/B, ACE level

MRI: NONSPECIFIC WM LESIONS
NEUROMYELITIS OPTICA

- 30 yo African-American woman with a history of optic neuritis and lupus since 2003
- Treated with Avonex and azathioprine
- Did very well and stopped treatment and no follow-up for years
NEUROMYELITIS OPTICA

• Presented with confusion in 2011
• Lumbar puncture done with 5 WBC, no oligoclonal bands
• Tested positive for NMO antibody
• Treated with plasmapheresis and monoclonal antibody

NEUROMYELITIS OPTICA: BRAIN MRI
NEUROMYELITIS OPTICA

- MRI brain variable, often few lesions initially
- Spinal cord MRI with longitudinally extensive lesion (3 segments)
- NMO-IgG seropositive status
- NMOSD may show variability

NEUROSARCOID: HISTORY

- 63 yo woman presents with recent MS diagnosis
  - Symptoms include vertigo, dragging right leg
  - LE pain and fatigue began many years ago

- MRI suspicious for demyelinating disease

- Lumbar puncture: many white cells (120), elevated protein, low glucose, and positive oligoclonal bands
NEUROSARCOID: MRI

[Images of MRI scans showing brain structures]
NEUROSARCOID: FOLLOW-UP

• Extensive infectious disease workup was negative
• Meningeal biopsy normal
• Diagnosed with neurosarcoid
  • Autoimmune systemic inflammatory condition
  • Lesions may mimic MS
    • Often leads to meningeal enhancement
    • Optic chiasm and nerves often affected
    • May involve spinal cord lesions
• Patient stable on TNF-alpha blocker
• Skin lesions 5 years later – biopsied with evidence of sarcoid
SKIN LESION

DIAGNOSIS

• Headaches and pain without relapses uncommon
• Typically lumbar puncture shows <50 WBCs
• Typical pattern of lesions can be seen in MS and in other conditions
• Continue evaluating for other possibilities when MS diagnosis is uncertain
MS Spectrum on MRI

RIS: MS ON MRI WITHOUT SYMPTOMS

Table 1

Proposed diagnostic criteria for the radiologically isolated syndrome

1. The presence of Incidentally identified CNS white matter anomalies meeting the following MRI criteria:
   - Ovoid, well-circumscribed, and homogeneous foci with or without involvement of the corpus callosum
   - T2 hyperintensities measuring >3 mm and fulfilling Barkhof's criteria (at least 3 out of 4) for dissemination in space
   - CNS white matter anomalies not consistent with a vascular pattern

RIS: CASE EXAMPLE

- 16 yo female
- Identical twin
- Sister diagnosed with MS after multiple symptoms and MRI with changes consistent with MS
- Twin in NIH study and MRI done annually
- Report of minor MRI changes on recent research MRI

RIS: MRI
ESTABLISHED MS: TYPICAL MRI

RISKS FOR AGGRESSIVE DISEASE

- More relapses in first 2 years
- Male gender
- Spinal cord disease
- Number of T2 lesions at baseline
- Enhancing lesions on therapy

Coret, F et al. Multiple Sclerosis: 16(8) 935-941
AGGRESSIVE MS
Tumefactive MS

- Lesions larger than 2 cm
- May have edema, mass effect
- Enhancement typical
- 70% with MS at follow-up
- Median time to next event was 4.9 years
- Younger patients had more relapsing disease

TUMEFACTIVE MS

MRI lesions after one year predict future disability

Why MRI matters in treatment

Patients taking any interferon  
MRI done after one year  
Patients followed for EDSS up to 4 years

MRI lesions after one year predict future disability

<table>
<thead>
<tr>
<th>No. of New Lesions</th>
<th>Patients with Worsening Disability (%)</th>
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<tr>
<td>0</td>
<td>5%</td>
</tr>
<tr>
<td>1</td>
<td>54%</td>
</tr>
<tr>
<td>2</td>
<td>73%</td>
</tr>
<tr>
<td>≥3</td>
<td>83%</td>
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Most lesions are clinically silent. MRI can show whether a medication is working. MRI recommended 6 months after medication change.

CASE I: STRAIGHTFORWARD

• 46 yo male
  • Noted red desaturation 6 years ago
  • Diagnosed 4 years ago after vertigo
• Started a DMT
• Full recovery from initial symptoms
• No further relapses
• No change on MRI
CASE I: POOR PROGNOSIS?

• Male
• Had spinal cord lesions at diagnosis and diagnosed with brainstem syndrome
• Despite some risk factors, no progression or relapses on first-line therapy

CASE II: MORE COMPLICATED

• 30 yo male
• Diagnosed after one week of bilateral hand weakness and numbness in his feet with L’hermitte’s sign
• History of optic neuritis in the right eye 5 years previously
INITIAL MRI AT DIAGNOSIS

INITIAL SPINAL CORD MRI
TREATMENT HISTORY

• Started on a DMT but multiple steroid courses in the first year
• Switched to a second DMT, but MRI 6 months later showed multiple enhancing lesions
• Switched to another therapy and had good clinical response, but changed medications due to concern about risk

TREATMENT HISTORY

• On his 4th DMT, he again had breakthrough disease
• Changed to another medication, and again had significant breakthrough disease
• Now on his 6th DMT
• Recent MRI with additional breakthrough
BRAIN MRI ON 5TH DMT

BRAIN MRI ON 5TH DMT
MRI IN MONITORING

• It is easier to prevent than repair
• Gd+ lesions predict poor outcome
• MRI lesions 5-10 times more common than symptoms
• MRI 6 months after change of therapy to assess effectiveness
• Consider alternatives if active disease

CONCLUDING THOUGHTS

• MRI is a useful tool in diagnosis
  • There are many non-MS causes of WM lesions

• MRI can be useful in monitoring MS on treatment
  • New T2 lesions or enhancing lesions indicate disease activity
  • Disease activity predicts poor prognosis over time

• Initial MRI can help with treatment decisions
  • More aggressive MS may need more aggressive therapy
  • Spinal cord lesions, large lesion volume, and black holes indicate worse prognosis
QUESTIONS?