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The Role of MRI in Multiple Sclerosis

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Meet our patient WM

- 49yoF presents to Multiple Sclerosis Clinic for follow-up regarding worsening symptoms of progressive weakness in left upper and lower extremities

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First, a Review of WM's Clinical History

- 1984: Acute onset bilateral **visual field defects** – treated with steroids w/ full recovery but no further workup for diagnosis
- 1984-2001: In retrospect, patient had 17 years of intermittent visual symptoms without seeking medical attention
- August 2001: Diagnosis of MS after numbness in upper and lower extremities – start of Avonex therapy
- 2002-2003: Decline in vision, cognition (memory, concentration, calculations), balance (multiple falls); lower extremity pain and spasticity; fluctuation in severity with time

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Review of WM's Clinical History

- 2003-2006: Progressive symptoms, including left facial nerve palsy, diplopia, bladder incontinence, visual defects and exotropia, lower extremity weakness leading to multiple falls, pain, spasticity, depression, mood lability, fatigue, psychiatric hospitalization for suicidal ideation
- 2003-2006: Multiple therapies: frequent IV methylprednisilone, Avonex and Rebif trials
- 2003-2004: MRI shows no GAD enhancing lesions but multiple foci of T2 lesions in brainstem, cerebellum, and periventricular white matter

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A Review of Multiple Sclerosis

- Most common autoimmune inflammatory demyelinating disease of the CNS
- Age of onset 20-40 years old
- Wide variation in prevalence geographically: ~0.1% in U.S.
- More common in Caucasians of European descent
- F:M ratio 2-3:1

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MS Typical Clinical Presentation

- **Young adult with 2 or more clinically distinct episodes of CNS dysfunction with at least partial resolution**
- **Common symptoms:**
  - **Sensory deficits (vibration, proprioception, pain, light touch) primarily in extremities, less often in face; Lhermitte's phenomenon (electric shock sensation on flexion of neck)**
  - **Visual loss**
  - **Motor symptoms (paraparesis, paraplegia, weakness, spasticity)**
  - **Unilateral eye pain accentuated by ocular movement (optic neuritis)**
  - **Diplopia**
  - **Gait disturbance**
  - **Vertigo**
  - **Bladder/bowel/sexual dysfunction**
  - **Limb ataxia**
  - **Pain**
  - **Other (Fatigue, depression, cognitive dysfunction, epilepsy)**

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Patterns of Clinical Presentation

- Relapsing-remitting – clearly defined relapses with partial to full recovery; no progression between relapses (80-95% at onset)
- Secondary progressive – Initial RRMS followed by slow progression with or without occasional relapses and minor remissions; develops in 80% of RRMS patients
- Primary progressive – Progression from onset with occasional plateaus and occasional minor improvements; no acute attacks
- Progressive relapsing – Progression from onset with clear acute relapses, with or without partial remission

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Typical Clinical Presentation

Suggestive of MS

- Relapses and remissions
- Onset between age 15-50
- Optic neuritis
- Lhermitte's sign
- Internuclear opthalmoplegia
- Fatigue
- Uhthoff's phenomenon

Not Suggestive of MS

- Steady progression
- Onset <10 or >50
- Cortical deficits (aphasia, apraxia, alexia, neglect)
- Rigidity, sustained dystonia
- Convulsions
- Early dementia
- Deficit developing within minutes

Review of Multiple Sclerosis

- Prognosis
  - Highly variable; median time from disease onset to need for walking cane – 27.9 years
- Treatment
  - Exacerbations – Corticosteroid injections
  - Immunomodulation
    - Avonex – Interferon B-1a IM injection
    - Betaseron – Interferon B-1b SC injection
    - Rebif – Interferon B-1a SC injection
    - Copaxone (Glatiramer acetate) – antigenically similar to myelin basic protein; competes with myelin for T cells
    - Tysabri (Natalizumab) – recombinant monoclonal Ab against alpha-4- integrins

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Diagnosis of MS – Role of Imaging

- Until early 1980's, MS lesions were often undetectable on imaging; CT often normal
- Diagnosis remained purely clinical until 1983 – Poser criteria allowed for paraclinical signs (MRI, CSF abnormalities, evoked potential tests)
- 2001 – McDonald criteria – focused specifically on use of MRI to aid diagnosis – based on objective evidence of "dissemination in space" (multiple lesions) and "dissemination in time" (multiple attacks)

Diagnosis of MS – Role of Imaging

- McDonald criteria revised in 2005
  - MRI findings less stringent to meet criteria of "dissemination in time"
  - Spinal cord lesions have more weight in determining "dissemination in space"
  - Diagnosis of primary progressive multiple sclerosis no longer requires abnormal CSF findings; can be made with clinical picture and MRI findings alone

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McDonald Criteria for MS

CLINICAL PRESENTATION	ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS
2 or more attacks; objective clinical evidence of 2 or more lesions	• None
2 or more attacks; objective clinical evidence of 1 lesion	• Dissemination in space, demonstrated by: - MRI OR - 2 or more MRI detected lesions consistent with MS plus positive CSF OR - Await further clinical attack implicating a different site
1 attack; objective clinical evidence of 2 or more lesions	• Dissemination in time, demonstrated by: - MRI OR - Second clinical attack
1 attack; objective clinical evidence of 1 lesion (monosymptomatic presentation; clinically isolated syndrome)	• Dissemination in space, demonstrated by: - MRI OR - 2 or more MRI-detected lesions consistent with MS plus positive CSF **AND** • Dissemination in time, demonstrated by: - MRI OR - Second clinical attack

Polman et al. *Ann Neuro* 2005

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McDonald Criteria for Primary Progressive MS

CLINICAL PRESENTATION	ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS
Insidious neurological progression suggestive of MS	• One year of disease progression (retrospectively or prospectively determined) **AND** • Two out of three of the following: a. Positive brain MRI (9 T2 lesions or 4 or more T2 lesions with positive visual evoked potentials) b. Positive spinal cord MRI (two or more focal T2 lesions) c. Positive CSF

Polman et al. *Ann Neuro* 2005

MRI Findings in MS

- We will see that our patient WM presents with many of the classic MRI findings of MS
- Importantly, the location of lesions do not always correlate with clinical symptoms

MRI Findings in MS

- Characteristic lesion – cerebral or spinal plaque
  - Discrete region of demyelination
  - Perivascular infiltration of lymphocytes and macrophages
  - Perivascular and interstitial edema
- Typically found in periventricular region, corpus callosum, centrum semiovale, and less frequently in deep white matter and basal ganglia
- Hypointense or isointense on T1-weighted images (T1WI)
- Hyperintense on proton density and T2-weighted images (T2WI)

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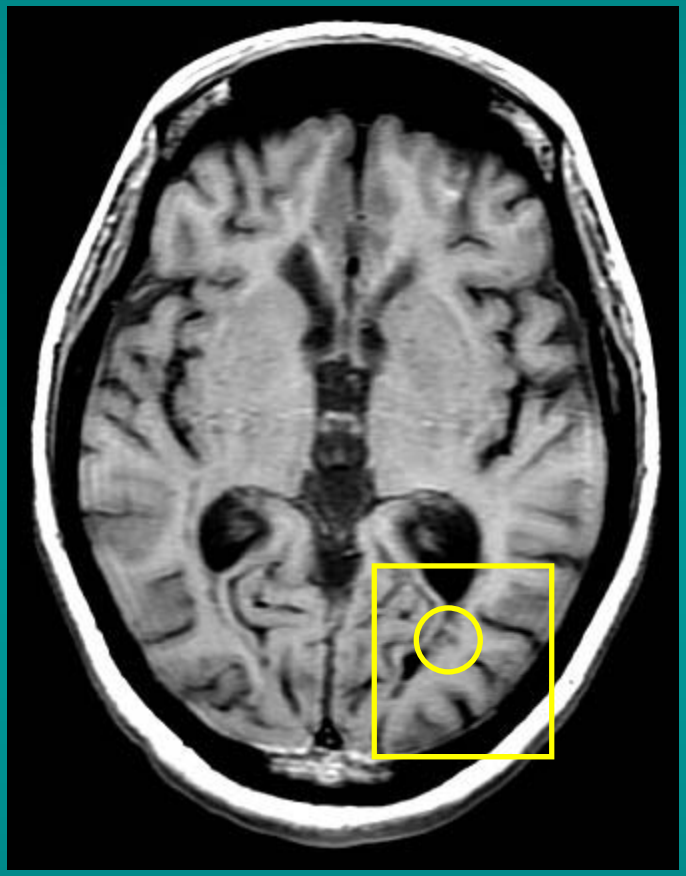
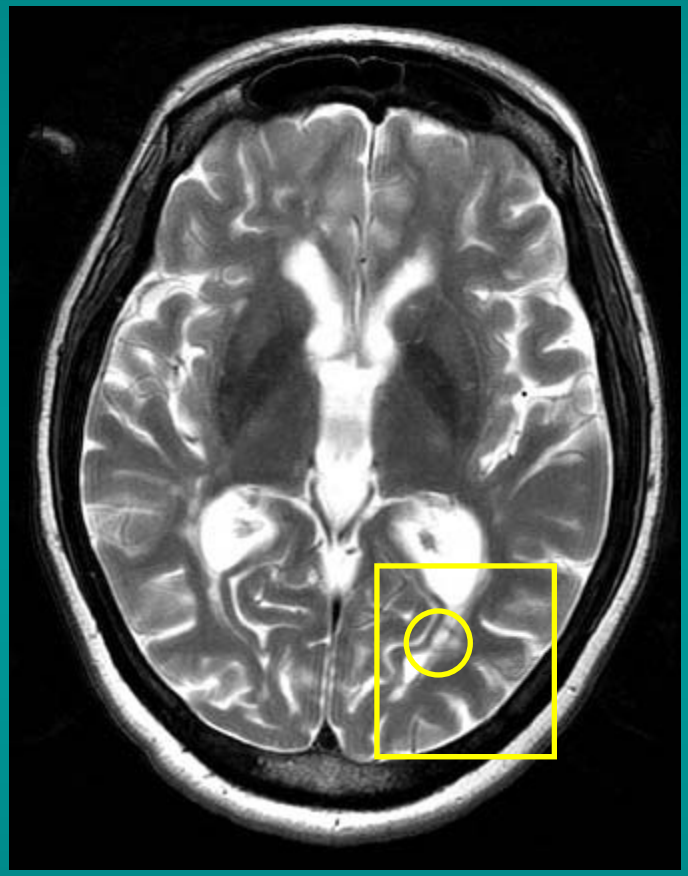
MRI Sequences for our patient WM



T1WI – hypointense lesion
Patient WM
Axial View



T2WI – hyperintense lesion
Patient WM
Axial View

Images Courtesy of Dr. Peri, BIDMC

Fluid-Attenuated Inversion Recovery (FLAIR) Suppresses CSF in T2WI

- FLAIR sequence allows for better contrast of lesions with CSF
- Especially useful for periventricular lesions
- Standard sequence used for viewing brain lesions of MS

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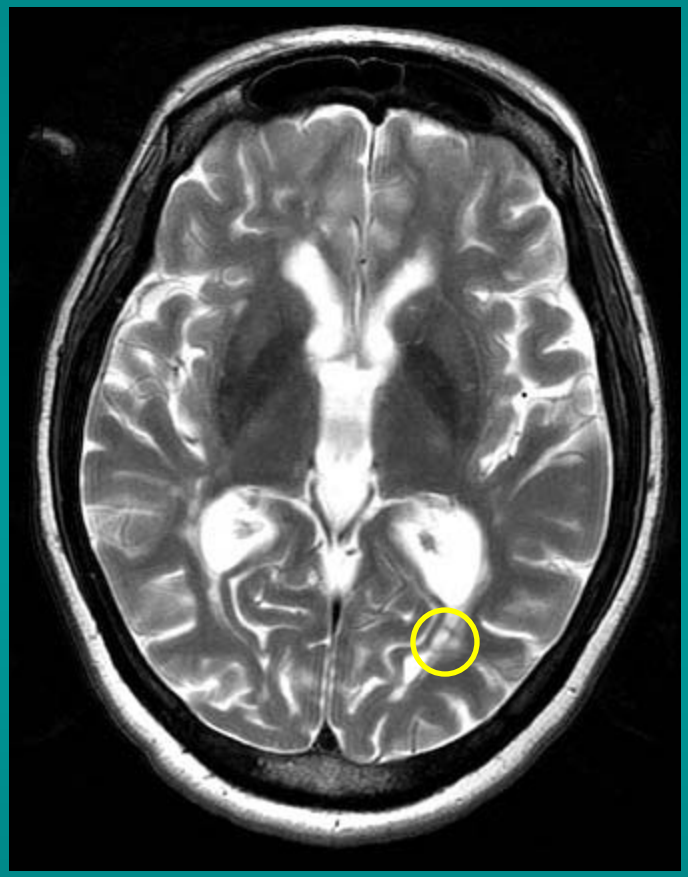
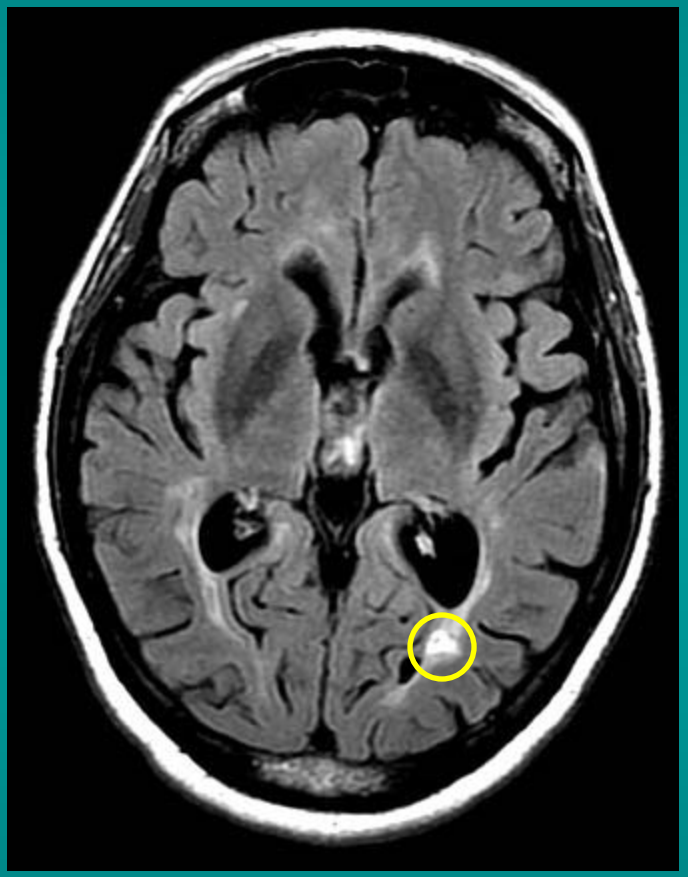
Fluid-Attenuated Inversion Recovery (FLAIR) Sequence in our Patient WM



T2 Weighted Image
Patient WM
Axial View



FLAIR Sequence
Patient WM
Axial View

Images Courtesy of Dr. Peri, BIDMC

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Short TI Inversion Recovery (STIR) Suppresses Fat for Spinal Cord Imaging

- STIR sequence allows for better contrast with fat in spinal cord
- Especially useful because spinal cord lesions are more specific for MS diagnosis
- Standard sequence used for spinal cord imaging in MS

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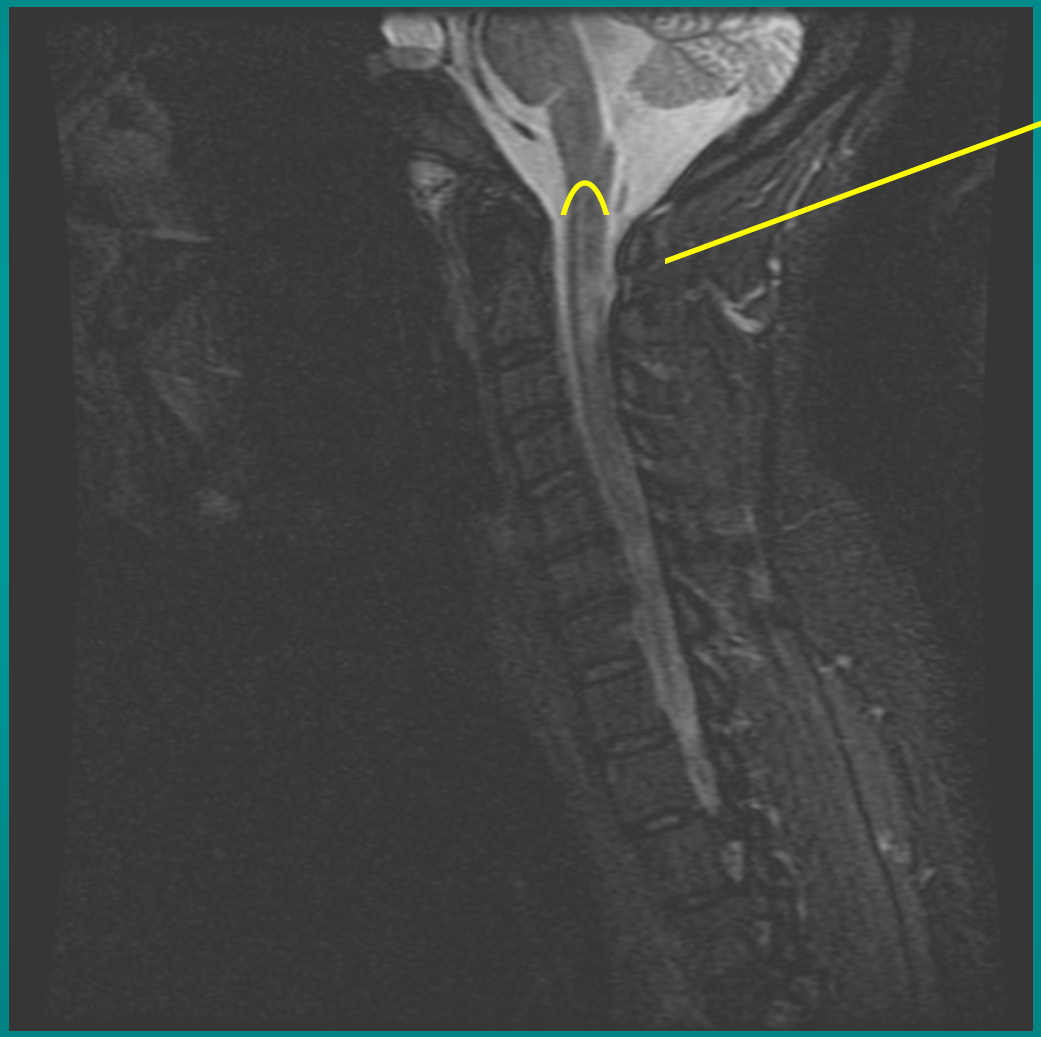
Short TI Inversion Recovery (STIR) Sequence in Spinal Cord of our Patient WM



STIR Sequence
Patient WM –Sagittal View

Image Courtesy of Dr. Peri, BIDMC

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Typical Characteristics of MS Lesions

- Our patient's MRI scans demonstrate several typical characteristics of MS plaques

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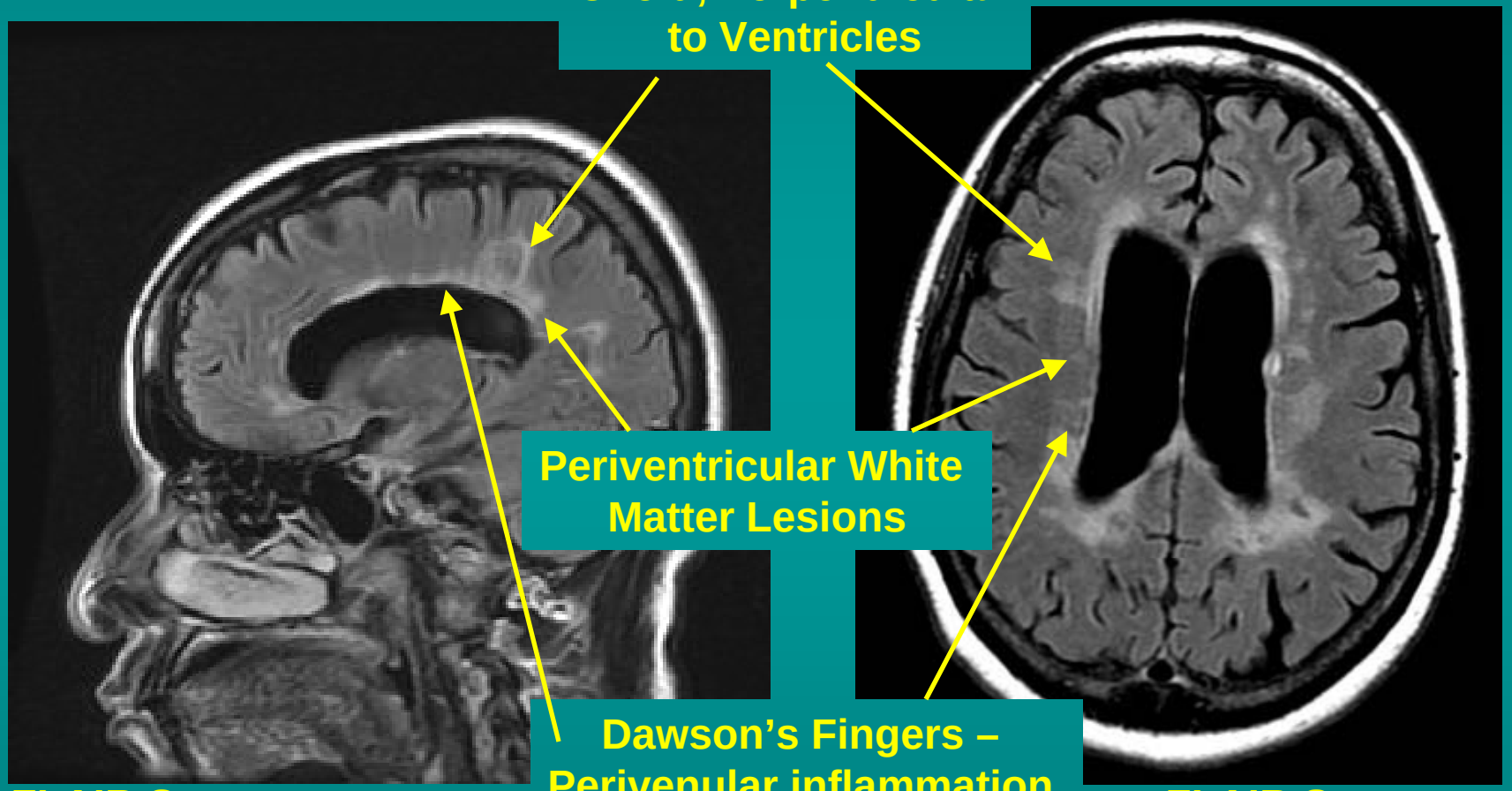
Our Patient WM



FLAIR Sequence
Patient WM
Sagittal View

FLAIR Sequence
Patient WM
Axial View

Images Courtesy of Dr. Peri, BIDMC

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Typical Characteristics of MS Lesions

- A companion patient's scans demonstrate another typical feature of MS lesions

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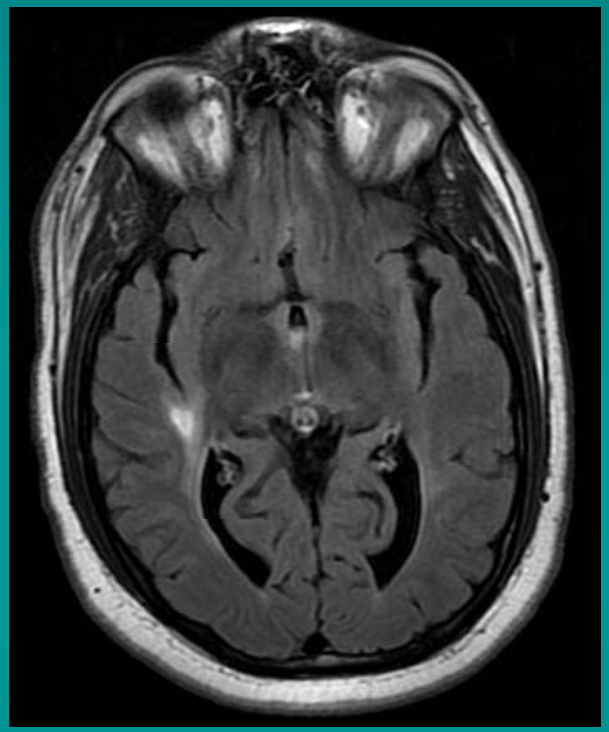
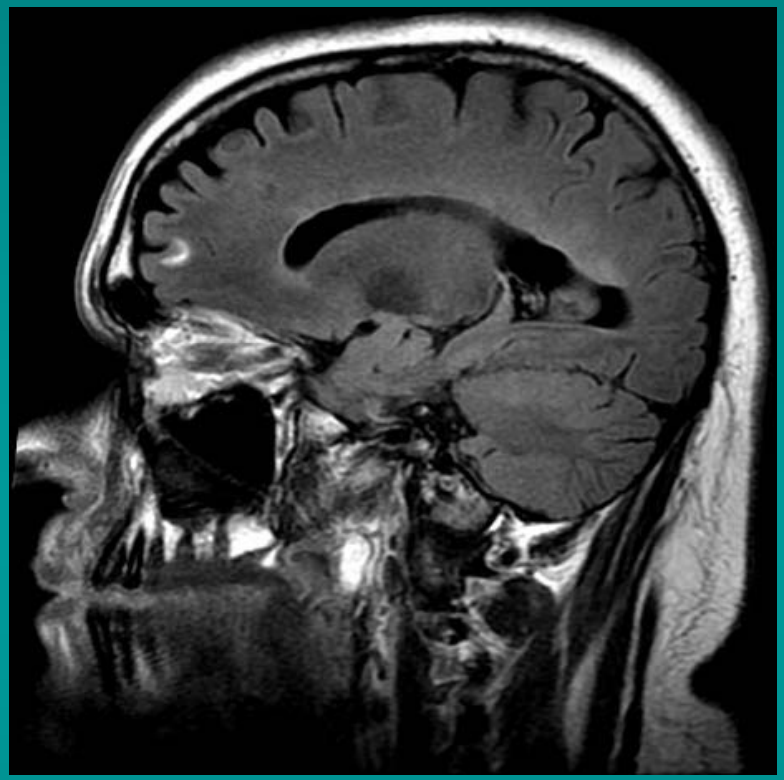
Companion MS Patient #1



**FLAIR Sequence
Companion Patient #1
Axial View**



**FLAIR Sequence
Companion Patient #1
Sagittal View**

Characteristic "horseshoe"-shaped lesion w/ advancing edge

Images Courtesy of Dr. Peri, BIDMC

Acute Lesions on MRI

- May disrupt the Blood-brain Barrier, leading to gadolinium enhancement
- May last for days to weeks
- Start as homogeneously enhancing and progress to ringlike enhancements
- Contrast-enhanced T1WI – in vivo measure of inflammatory activity
- Detects disease 5-10 times more frequently than clinical evaluation of relapses

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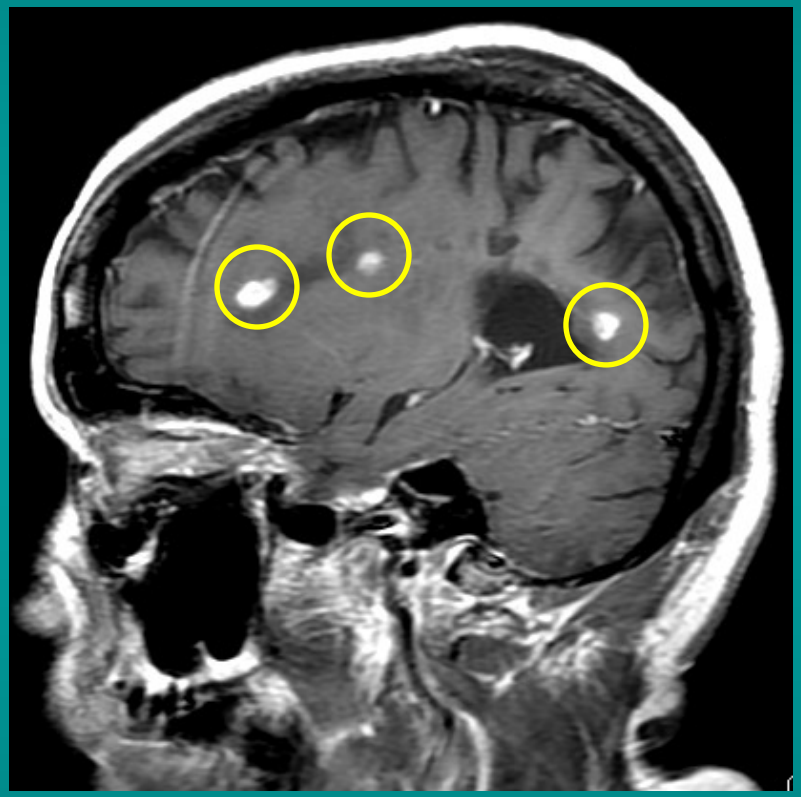
Acute Lesions in our Patient WM



T1WI – post gadolinium
Patient WM
Sagittal View

Image Courtesy of Dr. Peri, BIDMC

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Optic Neuritis in MS Patients

- As in our patient, optic neuritis is a frequent presenting symptom in MS
- Optic neuritis is nicely demonstrated in the following images of two more companion MS patients

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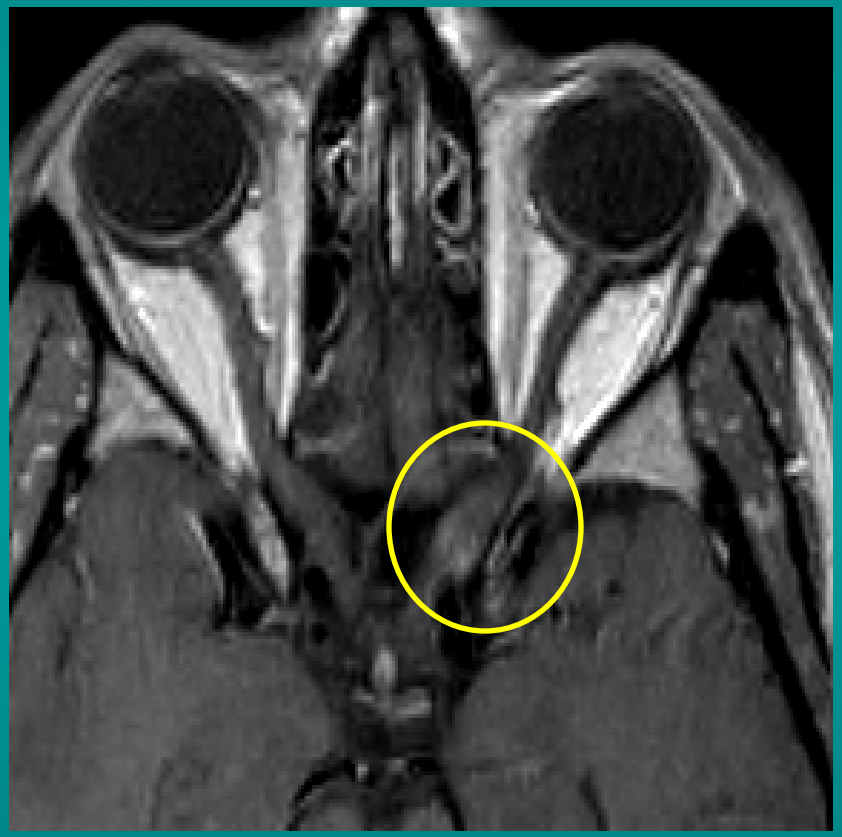
Optic Neuritis – Companion MS Patient #2
Frequently Presenting First MS Episode



T1WI – post gadolinium
Companion Patient #2
Axial View

Image Courtesy of Dr. Ganguli, BIDMC

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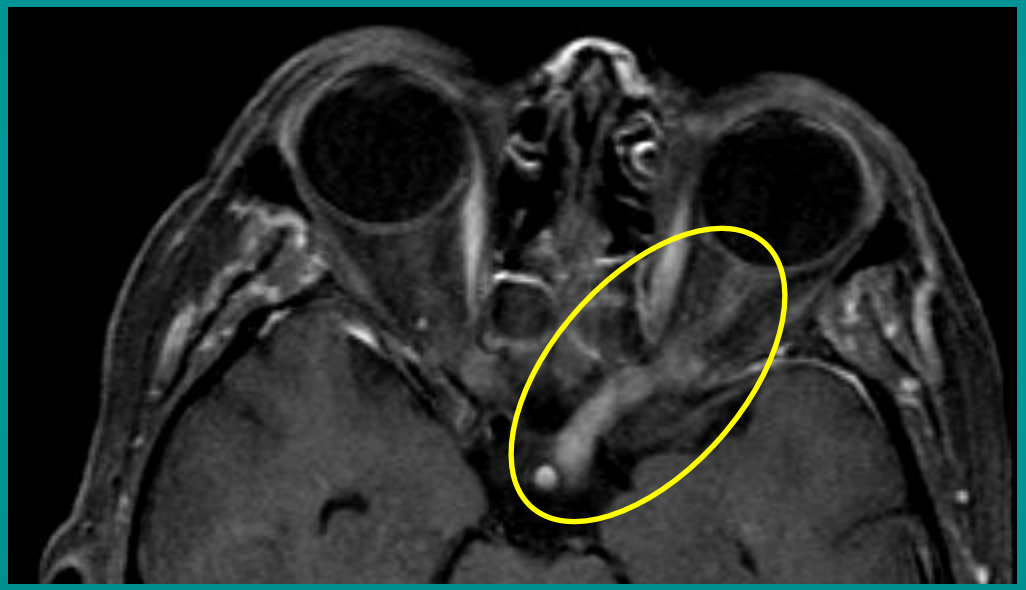
Optic Neuritis – Companion MS Patient #3 Frequently Presenting First MS Episode



T1WI – post gadolinium
Companion Patient #3
Axial View

Image Courtesy of Dr. Ganguli, BIDMC

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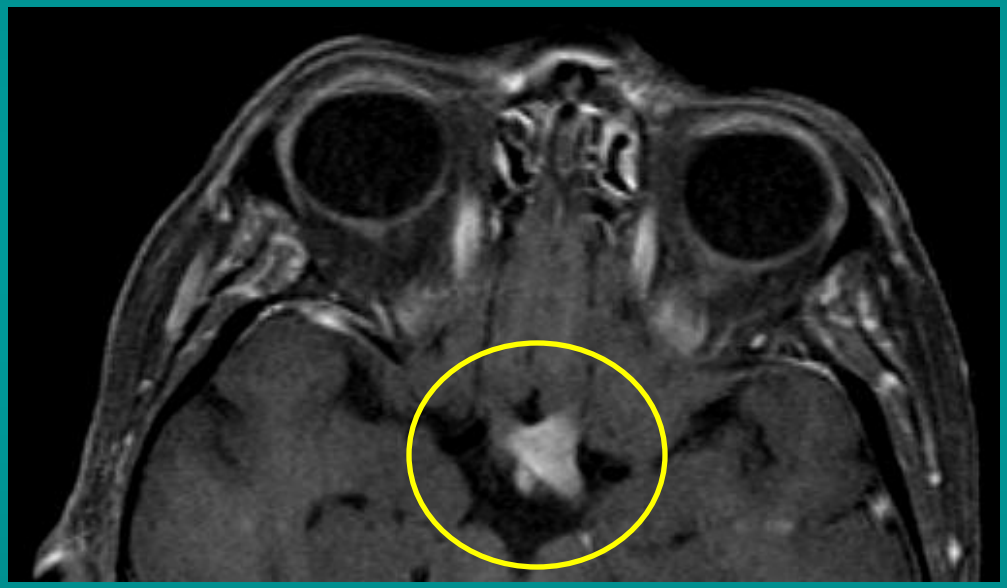
Optic Neuritis – Companion MS Patient #3 Frequently Presenting First MS Episode



T1WI – post gadolinium
Companion Patient #3
Axial View

Image Courtesy of Dr. Ganguli, BIDMC

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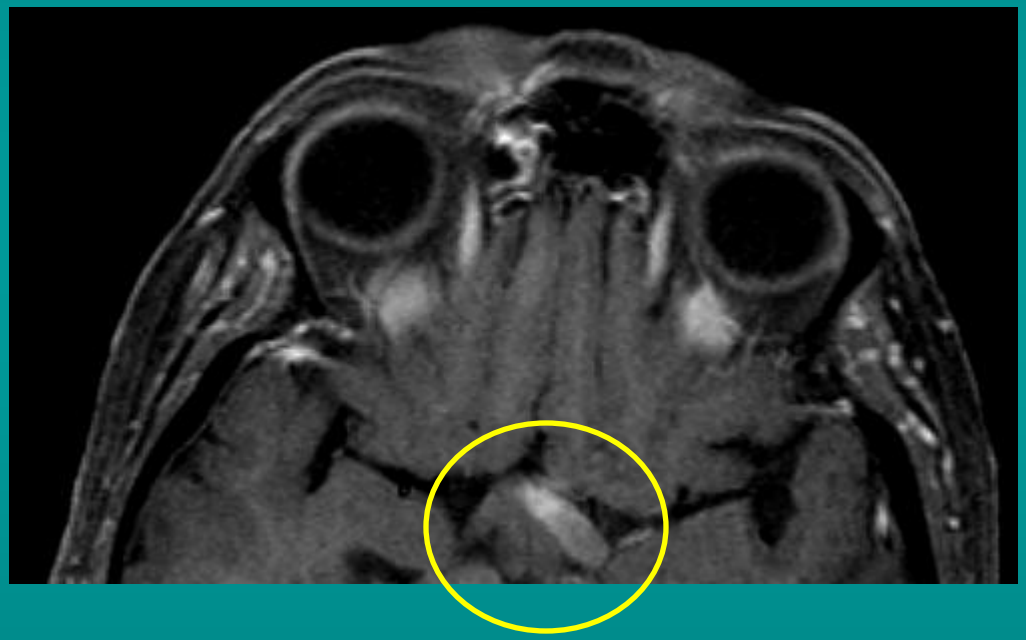
Optic Neuritis – Companion MS Patient #3 Frequently Presenting First MS Episode



T1WI – post gadolinium
Companion Patient #3
Axial View

Image Courtesy of Dr. Ganguli, BIDMC

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Cortical Atrophy in MS Patients

- In the later stages of MS, cortical atrophy can often be seen due to accumulation of damage from multiple prior events
- Cortical atrophy is seen in our patient, as compared with comparable scan from a much younger companion MS patient

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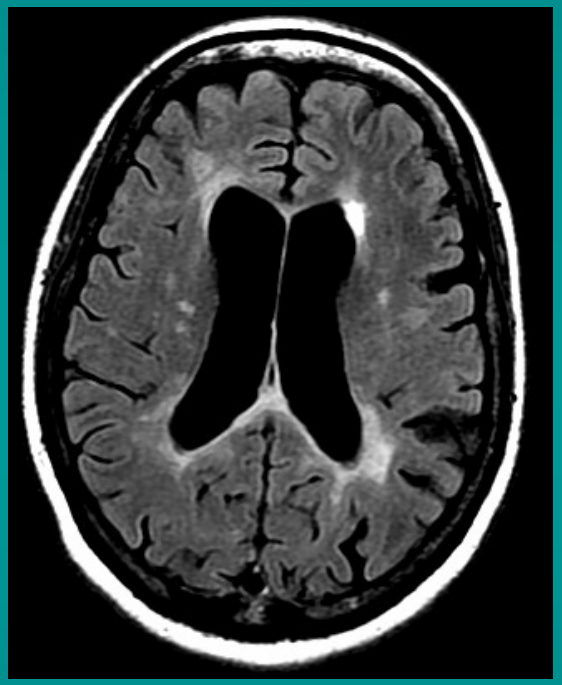
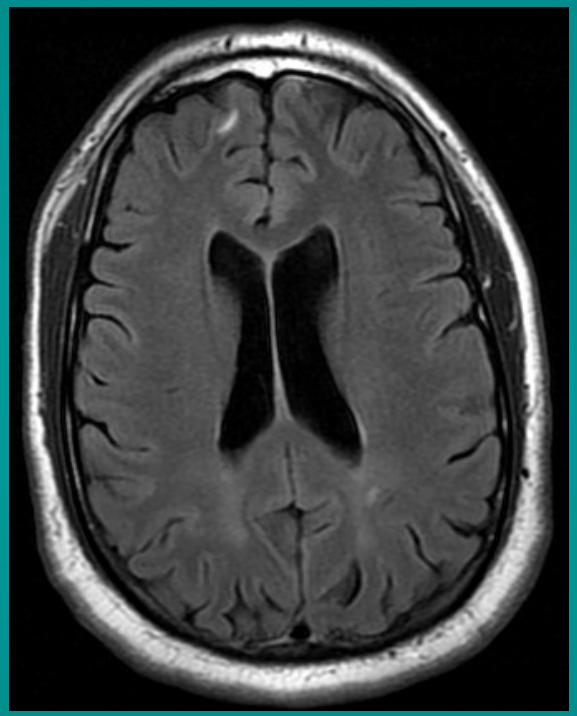
Cortical Atrophy – Our patient WM compared with Companion Patient #1



Cortical Atrophy
(large ventricles, decreased cortical volume)
FLAIR Sequence
Patient WM
Axial View
49 yoF – 22 yrs after 1st episode



Normal Cortex/Ventricles
FLAIR Sequence
Companion Patient #1
Axial View
34 yoM – 5 yrs after 1st episode

Images Courtesy of Dr. Peri, BIDMC

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Progression of Disease on MRI

- Patient WM's gadolinium-enhancing lesions were not present on prior scan in 2004
- MRI thus allows for objective assessment of disease progression
- In this case, MRI findings led to altered treatment plan for Patient WM – Tysabri was added to her current regimen

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Sensitivity and Specificity of MRI for MS

- Two-year follow-up of 200 patients evaluated for suspected MS
- 30% had developed clinically definite MS
  - Of these,
    - 84% had initial MRIs strongly suggestive of MS
    - 95% had at least one MS-like lesion on initial MRI
    - 69% had initial CSF oligoclonal bands
    - 69% had abnormal visual evoked potentials initially
    - 39% had abnormal CT on initial evaluation

Lee et al. *Neurology* 1991

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Sensitivity and Specificity of MRI for MS

- Five-year follow-up of 89 patients evaluated for suspected MS
- 57 patients initially had abnormal MRI
  - 65% of these developed clinically definite MS
- 32 patients initially had normal MRI
  - 3% of these developed clinically definite MS

Morrissey et al. *Neurology* 1993

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Differential Diagnosis of White Matter Lesions on MRI

- Important to remember that clinical symptoms/signs are necessary part of diagnosis
- Diagnosis should never be made on single MRI or single attack alone
- Multiple disease states can present with similar findings to MS plaques on MRI

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Differential Diagnosis of White Matter Lesions on MRI

- Infectious - AIDS encephalitis, Progressive multifocal leukoencephalopathy, Lyme Disease, Syphilis, Brain abscess
- Inflammatory - Acute disseminated encephalomyelitis, Acute hemorrhagic encephalomyelitis, Vasculitides, Systemic Lupus Erythematosus, Subacute sclerosing panencephalitis
- Neoplasm – primary or metastatic
- Vascular – Ischemia, Infarction, Migraines
- Iatrogenic – Radiation therapy
- Trauma
- Normal Aging

Future Trends of MRI in MS

- Conventional MRI – increase detectability of gray matter lesions
- Magnetization Transfer Imaging – Measure injury in normal-appearing white matter (NAWM)
- Diffusion Tensor Imaging – Measure injury in NAWM
- Perfusion imaging – Explore ischemic mechanism in certain lesions
- Proton-MR Spectroscopy – New insights into biochemical pathology in MS

Summary

- MS is a chronic, progressive autoimmune demyelinating disease
- Multiple Attacks (“Dissemination in Time”)
- Multiple Lesions (“Dissemination in Space”)

Summary

- Characteristic MRI lesions
  - Periventricular white matter
  - T1 hypointense
  - T2 hyperintense
  - FLAIR provides better contrast with CSF
  - Ovoid lesions perpendicular to ventricles
  - Acute lesions enhance with Gadolinium
- MRI extremely sensitive and specific for MS when combined with clinical picture
- MRI useful in diagnosis, monitoring of disease progression, and monitoring of therapeutic response

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