Vall d'Hebron Hospital

Institut Català de la Salut

Generalitat de Catalunya
Departament de Salut

IDI
INSTITUT DE DIAGNÒSTIC PER LA IMATGE

**ECTRIMS 2017**

Paris. October 25, 2017

NAIMS/MAGNIMS ACTRIMS/ECTRIMS Teaching Course

Imaging the non-MS lesion in MS

# "Atypical imaging presentations of MS and other idiopathic demyelinating diseases"

Magnims
Magnetic Resonance Imaging in Multiple Sclerosis

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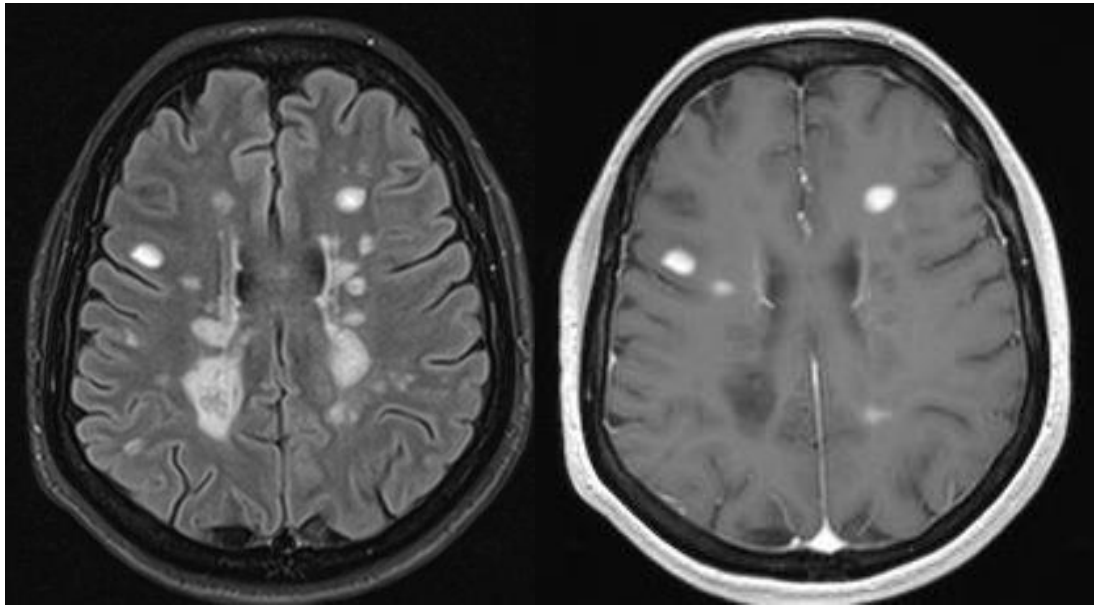
# MR imaging in MS and other IDDs

T2-weighted (FLAIR)



Post-contrast T1-weighted

- Highly sensitive for detecting lesions (white matter)
- Provide quantitative assessment of disease activity and severity
- Characterize disease course over time
- Monitor and predict treatment response
- Most important paraclinical tool for diagnosing and monitoring MS and other IDDs

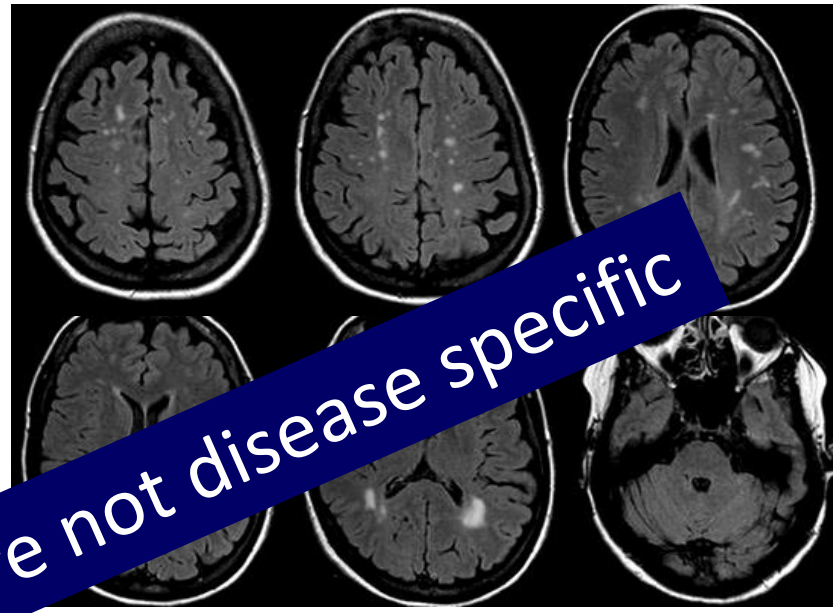
# Multifocal WM signal abnormalities: “white spots”

**Incidental finding**
- aging (80-100%)
- normal young adult population (5-10%)
- migraine (x4)
- Virchow-Robin spaces

**Hipoxic-ischemic vasculopathies**
- Lipohyalinotic small-vessel disease
- Cerebral amyloid angiopathy
- Genetic vascular disorders: CADASIL

**Primary demyelinating diseases**
- multiple sclerosis and va
- ADEM
- neuromyel

**Vasculitis**
- prim
- systemic: *lupus, Behçet, APLAS*



Brain MRI changes are not disease specific

**Miscellaneous**
- neurosarcoidosis
- Lyme disease
- PML
- metabolic: Leber, xantomatosis, adult forms of leukodystrophy
- effects of radiation therapy or drugs
- lymphoma
- metastasic disease

Sánchez Aliaga E, Barkhof F. Handb Clin Neurol 2014;122:291-316; Charil et al. Lancet Neurol 2006;5:841-52

# Multifocal WM signal abnormalities: “white spots”

•Evaluation of focal white matter hyperintensities (WMH) on MRI is always challenging (particularly in young patients)

•Their cause may vary from infectious, inflammatory, neoplastic, or demyelinating findings to nonspecific findings related to aging and other systemic conditions

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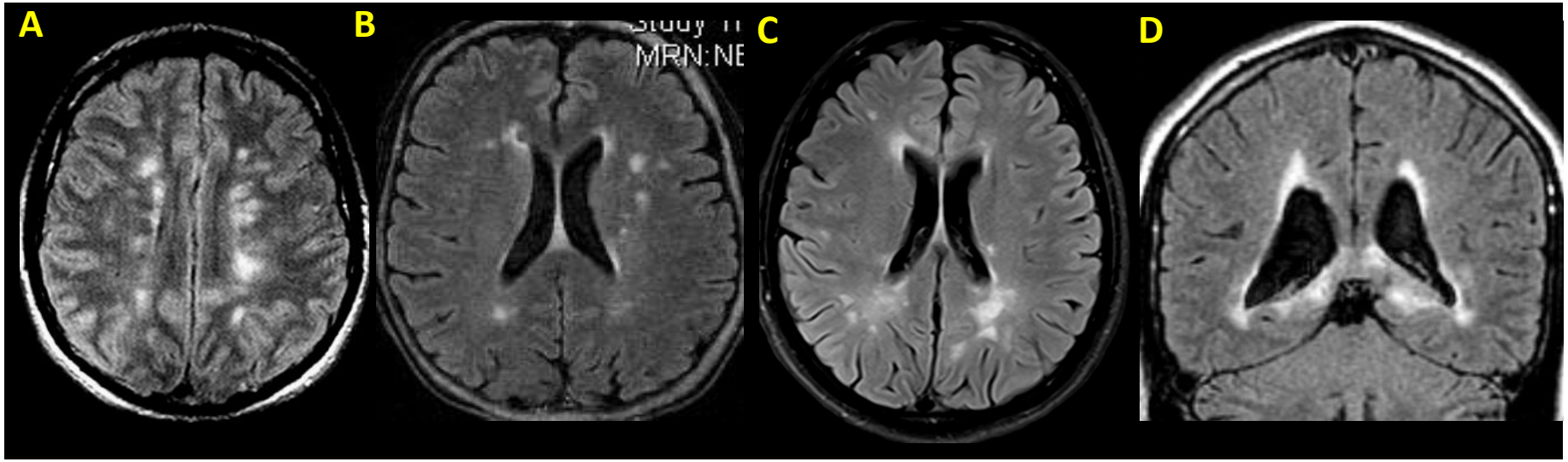
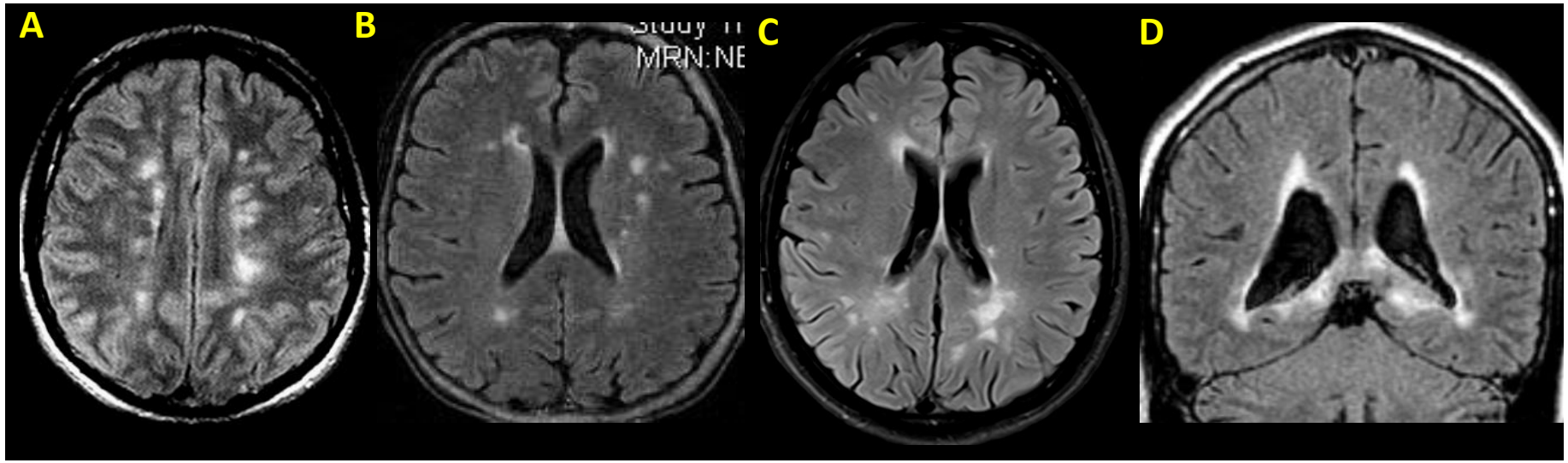


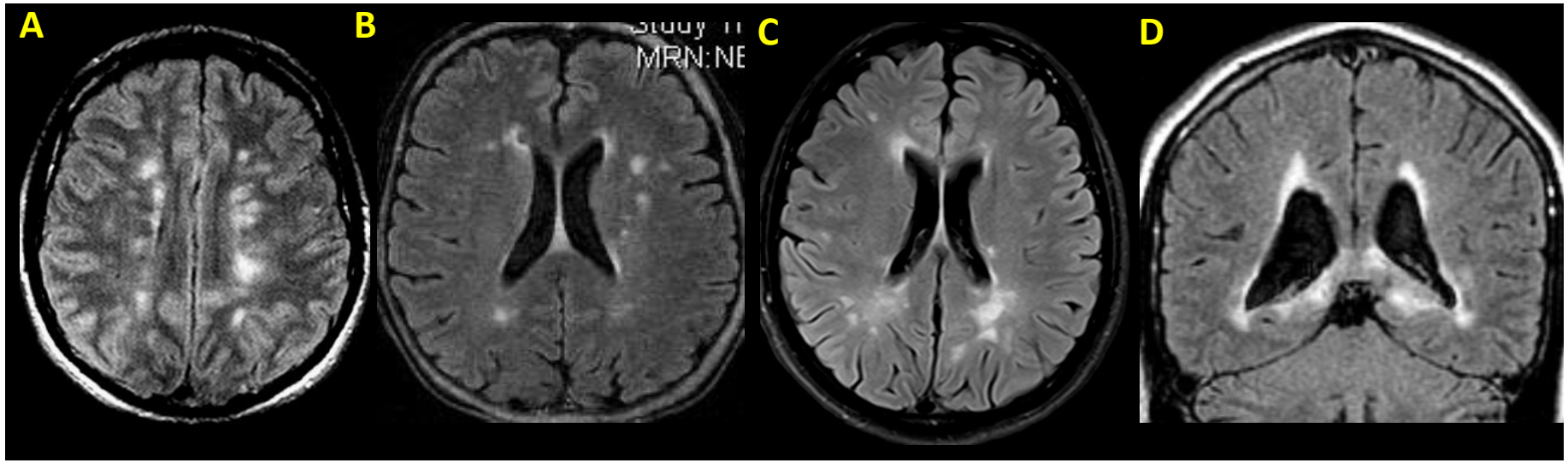
# MCQ1




Indicate which of these four patients has Multiple Sclerosis:

1. A
2. B
3. C
4. D

# MCQ1

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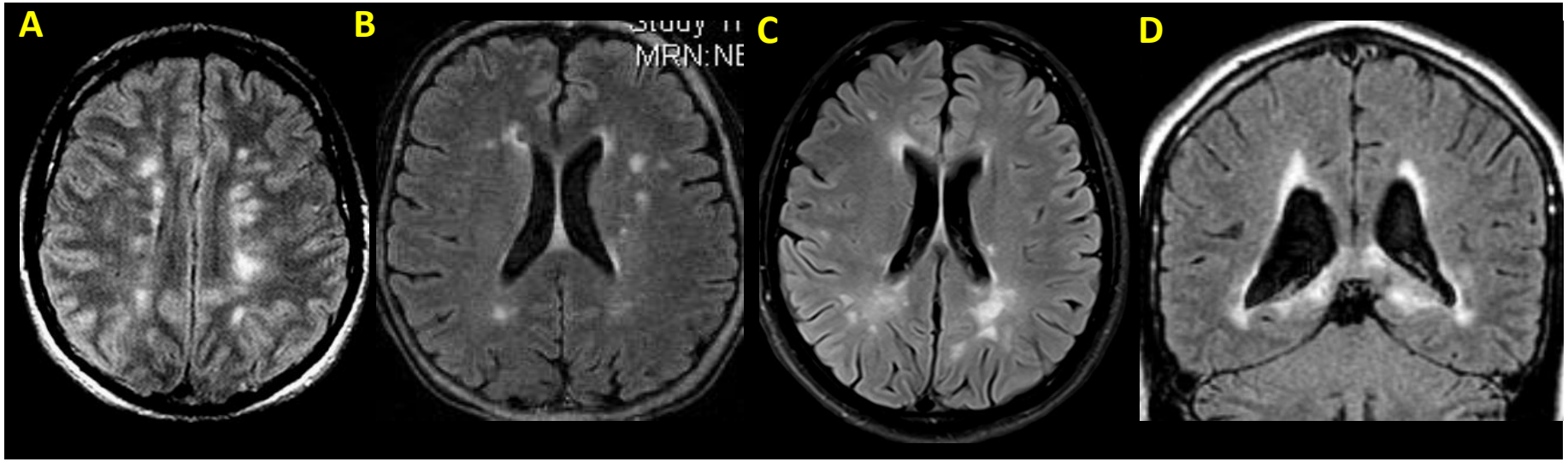



Fat embolism | Lyme disease | Multiple sclerosis | Neurosarcoidosis

# Diagnostic strategy in subjects with incidental multifocal brain T2 lesions of unknown origin

## Comprehensive checklist for evaluation of WM spots

### Systematic reading

- **Lesion distribution / involvement**
  - ✓subcortical/periventricular
  - ✓U-fibers
  - ✓cortical grey matter
  - ✓deep grey matter
  - ✓corpus callosum
  - ✓brainstem
  - ✓spinal cord
- **Enhancement pattern**
- **Lesion shape**
- **Central vein sign**
- **Intralesional susceptibility signal**

→

**Brief and precise diagnostic impression that must consider:**

- ✓Demographics
- ✓Family history
- ✓Vascular risk factors
- ✓Clinical information and question
- ✓Lab findings

# McDonald 2010 criteria

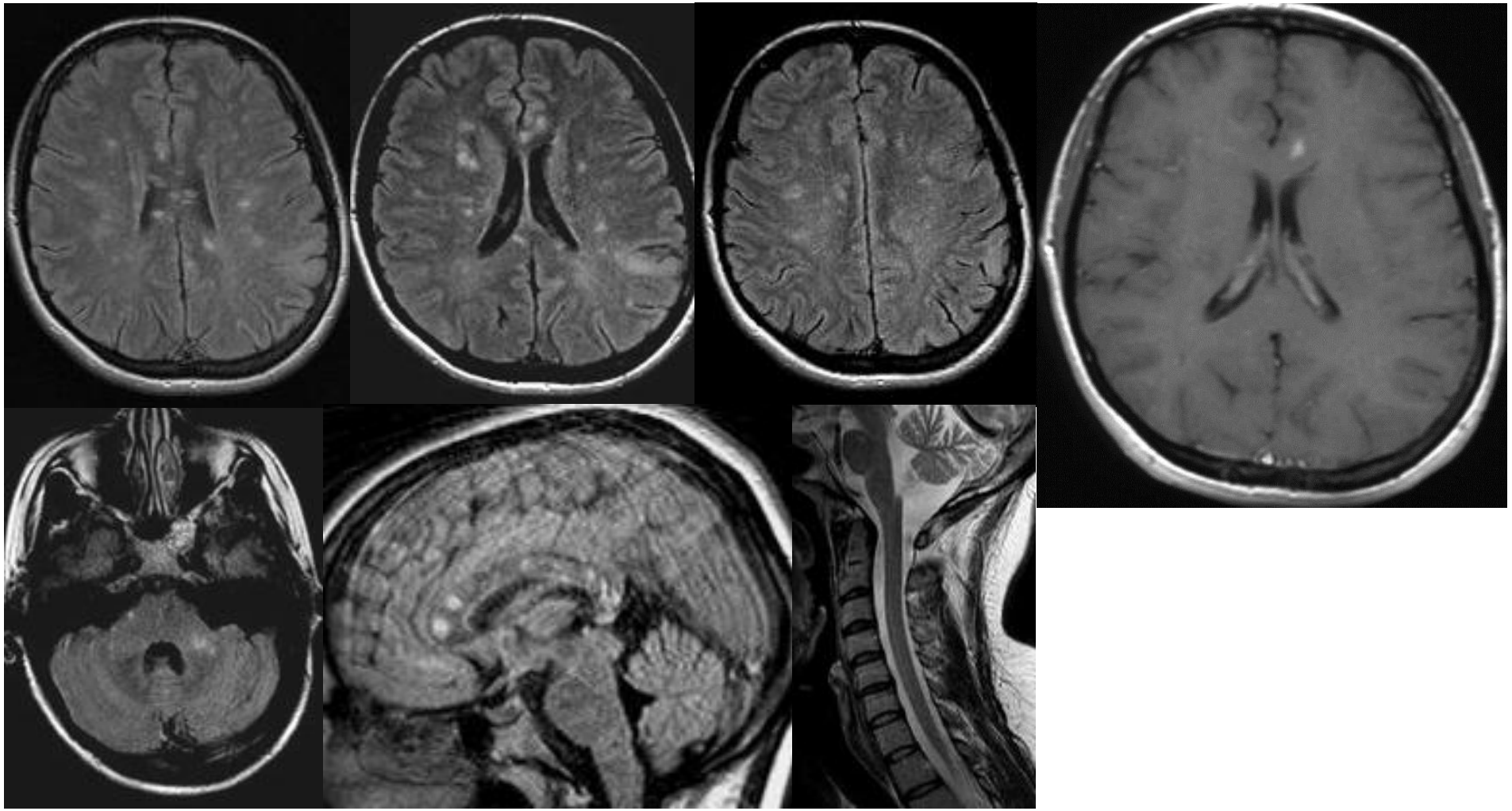
## The McDonald 2010 Criteria

| Clinical Attacks[a] | Clinical Evidence of Lesions | Additional Requirements for MS Diagnosis |
|---|---|---|
| ≥2 | Objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack | None |
| ≥2 | Objective clinical evidence of 1 lesion | **Dissemination in space**, defined as:<br>• **≥1 $T_2$ asymptomatic lesion in ≥2 MS-typical CNS regions**; ***or***<br>• Await further clinical attack implicating a different CNS site |
| 1 | Objective clinical evidence of ≥2 lesions | **Dissemination in time**, defined as:<br>• **Simultaneous asymptomatic Gd-enhancing and non-enhancing lesions at any time; *or***<br>• **New $T_2$ and/or Gd-enhancing lesion(s) on follow-up MRI, irrespective of its timing; *or***<br>• Await a second clinical attack |
| 1 | Objective clinical evidence of 1 lesion (clinically isolated syndrome) | **Dissemination in space *AND* time (as defined above)**<br>• Requirements can be met by a ***single MRI scan*** |

[a]An attack (relapse; exacerbation) is defined as patient-reported or objectively observed events typical of an acute inflammatory demyelinating event in the CNS, current or historical, with duration of at least 24 hours, in the absence of fever or infection.

Polman CH et al. *Ann Neurol* 2011;69:292-302.

# 33 year-old woman with a three week clinical picture of behavioural disturbance, visual loss, bradipsychia, sommnolence, headache, and memory loss



# MCQ2

Does this patient fullfil the MRI diagnostic criteria for MS?

1. Only dissemination in time
2. Only dissemination in space
3. Both disemination in space and time
4. The MRI criteria cannot be applied

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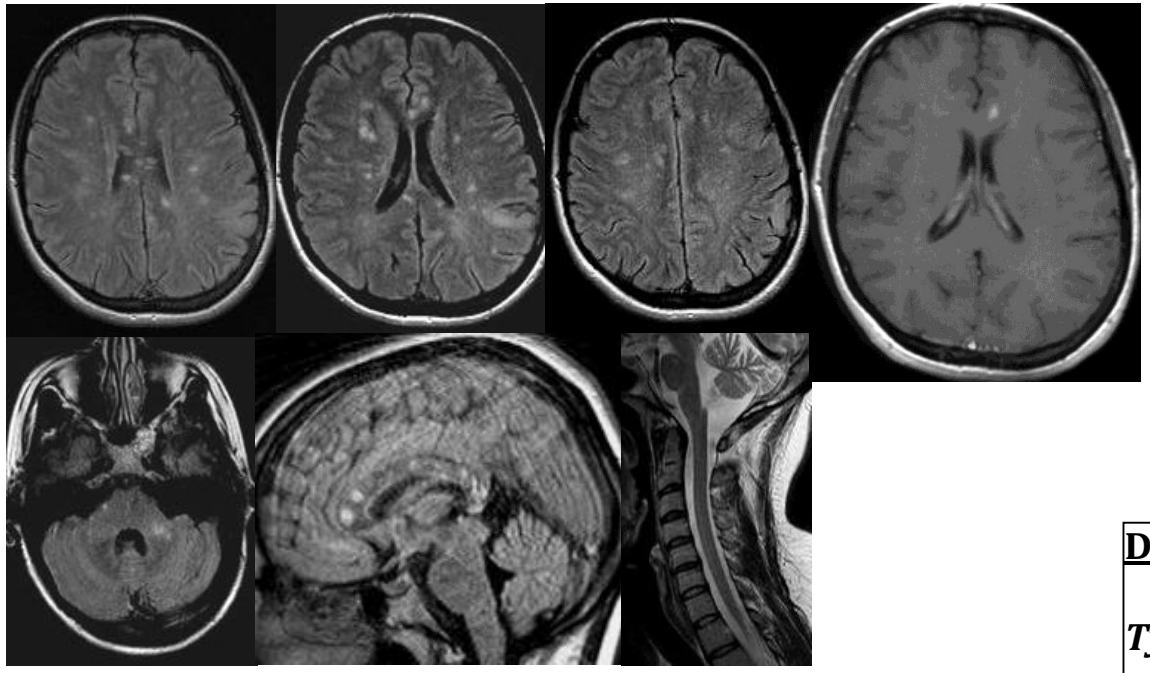
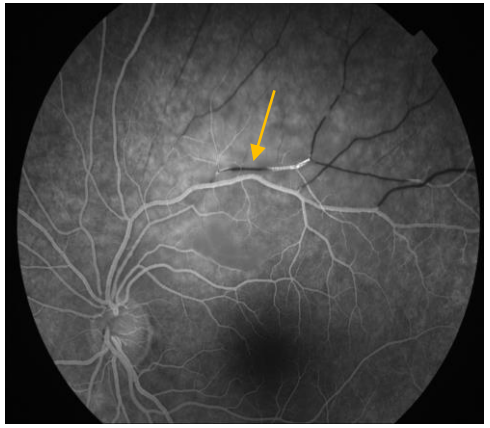




Are the findings suggestive of MS: **NO**

## Susac syndrome

**Diagnostic criteria**

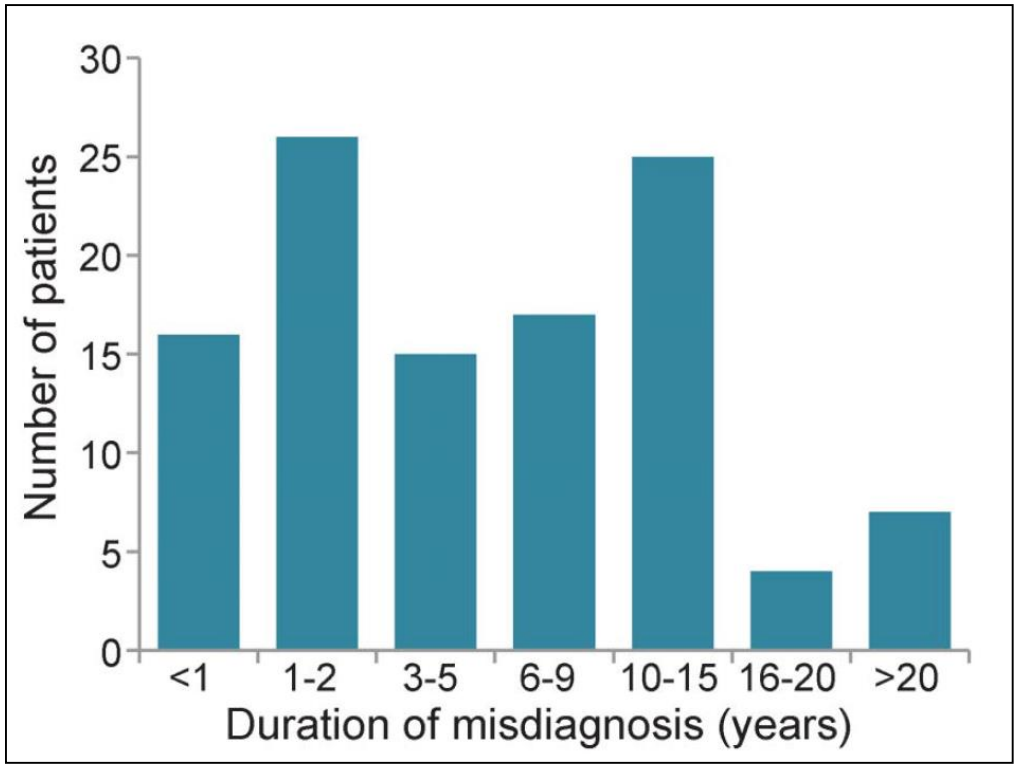
***Type of CIS:*** multifocal

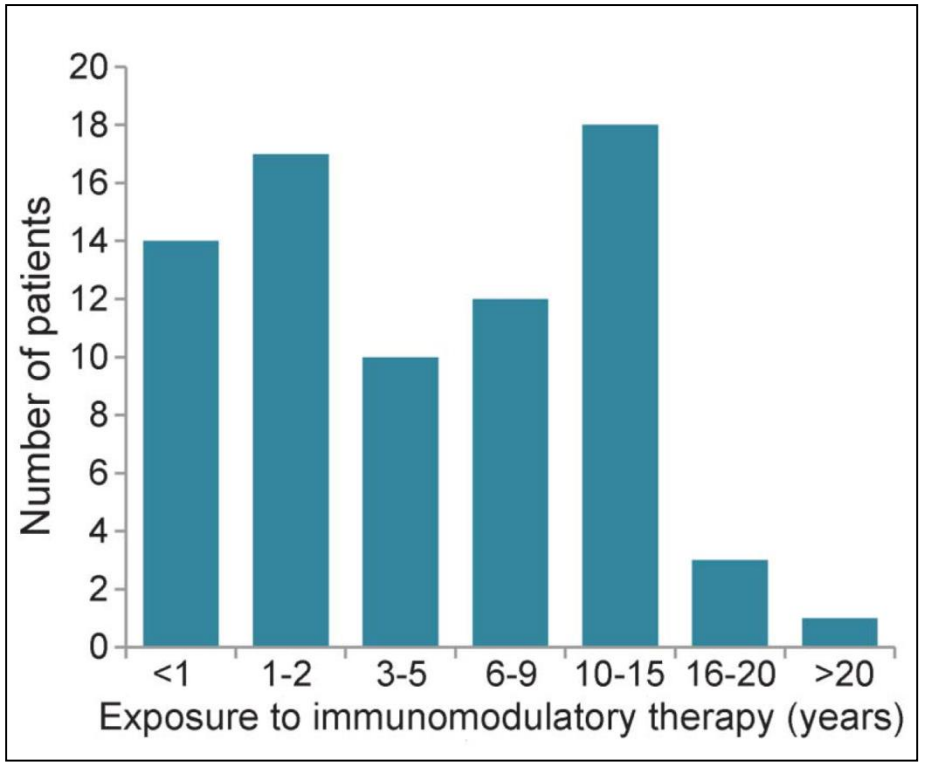
| | |
|---|---|
| ***Dissemination in space*** | **Y** |
| Juxtacortical | y |
| Periventricular | y |
| Brainstem/cerebellum | y |
| Spinal cord | n |
| ***Dissemination in time*** | **Y** |
| Enhancing/non enhancing | y |
| New T2 | NA |

# Misdiagnosis of Multiple Sclerosis

- Neurologists at 4 academic MS centers submitted data on patients determined to have been misdiagnosed with MS.
- 110 misdiagnosed patients:
  - ✓51 (46%) “definite” misdiagnoses
  - ✓59 (54%) “probable ” misdiagnoses

**70% received ≥ 1 DMD**




Solomon et al. Neurology 2016

# MCQ3

Which is in your opinion the main contributor to MS misdiagnosis?

1. Overreliance on the presence of MRI abnormalities meeting DIS to confirm a diagnosis of MS in a patient with “nonspecific or atypical neurologic symptoms”
2. Erroneous determination of juxtacortical or periventricular lesion location to fulfill DIS
3. Erroneous determination of DIT because of variability of MRI slice orientation (i.e., MRIs performed on different scanners leading to the appearance of new lesions)
4. Lack of enough expertise in evaluating MRI scans

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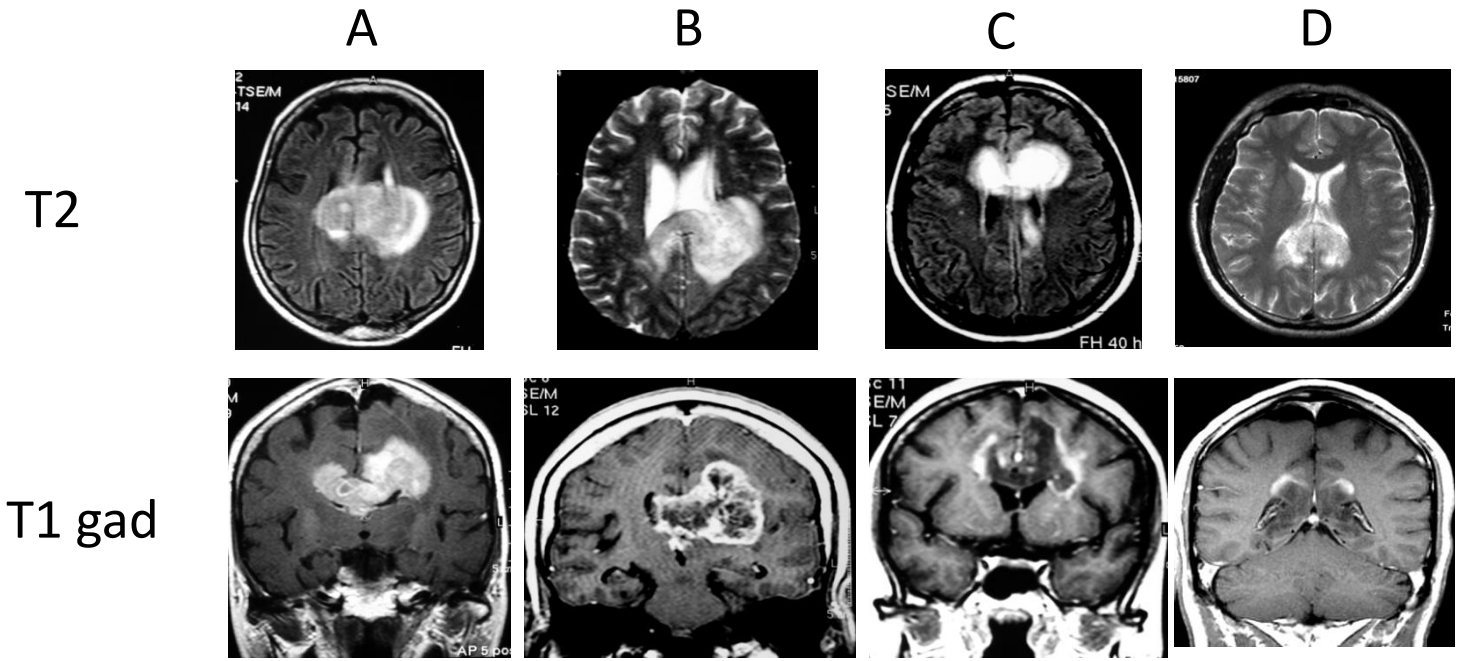
# Misdiagnosis of Multiple Sclerosis

| Contributors to MS misdiagnosis | Yes<br>n (%) | No<br>n (%) | Unknown<br>n (%) |
|---|---|---|---|
| Inappropriate application to MS diagnostic criteria of neurologic symptoms atypical for a demyelinating attack | | | |
| Inappropriate application to diagnostic criteria of a historical episode of neurologic dysfunction without corroborating objective evidence of a lesion (on neurologic examination, evoked potentials, or imaging) | | | |
| Overreliance on the presence of MRI abnormalities meeting DIS to confirm a diagnosis of MS in a patient with "nonspecific neurologic symptoms" | | | |
| Erroneous determination of juxtacortical or periventricular lesion location to fulfill DIS | | | |
| Neuromyelitis optica spectrum disorder | 7 (6) | | |

Solomon et al. Neurology 2016

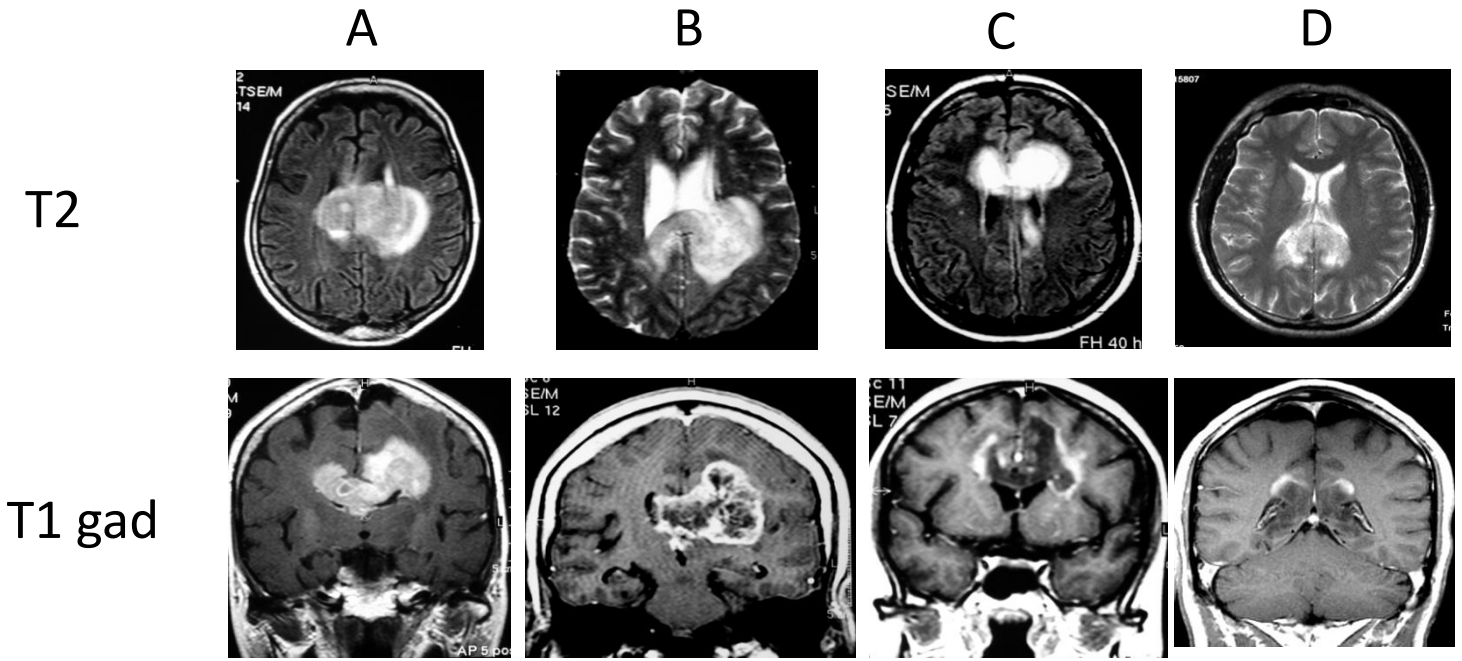
# Differential diagnosis of tumefactive lesions MCQ4




Which of these lesions require a biopsy?

1. A, B and C
2. A and B
3. C and D
4. All lesions

# Differential diagnosis of tumefactive lesions MCQ4

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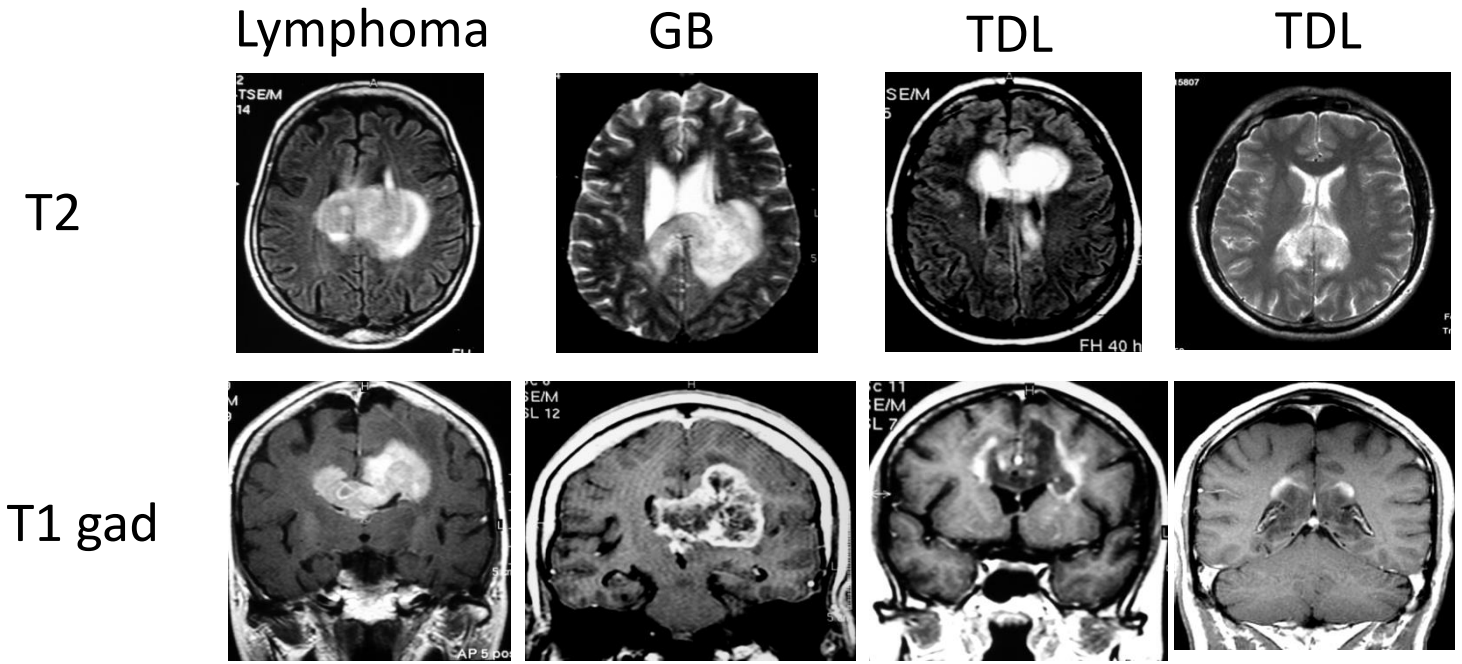


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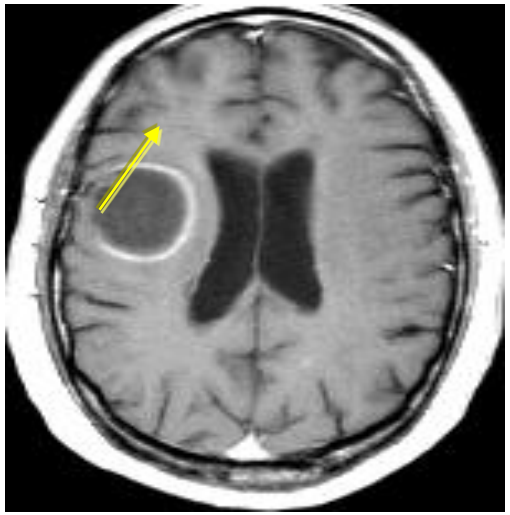
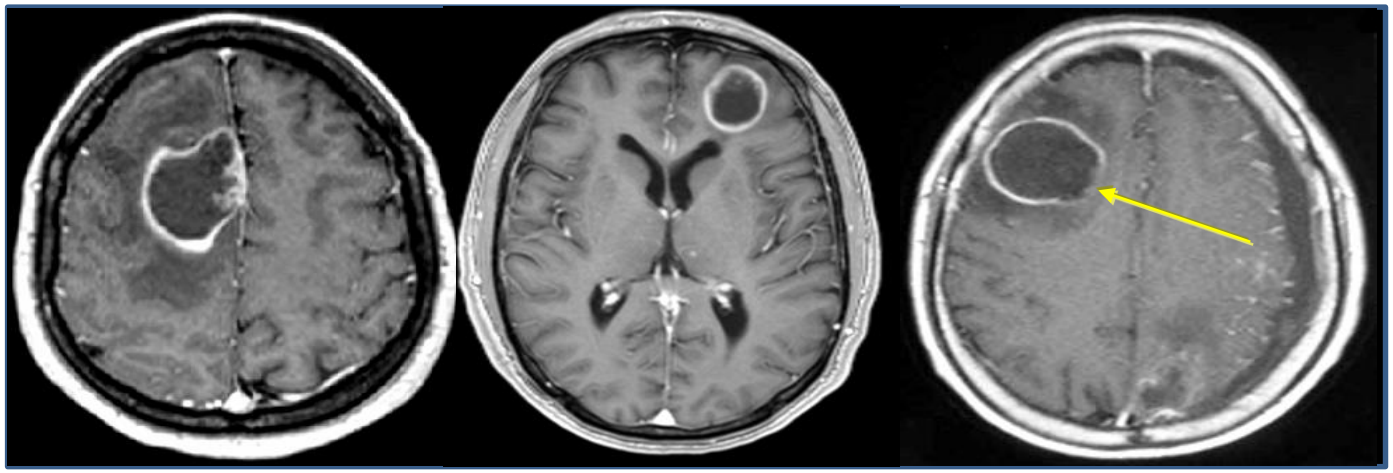
# Open-ring - enhancement

## Incomplete (open) ring enhancement in active MS

open border facing the cortical /deep gray matter

**MS**





**Glioblastoma** **Metastasis** **Abscess**

Masdeu et al. Neurology 2000

# Patterns of contrast uptake

## Open-ring - enhancement

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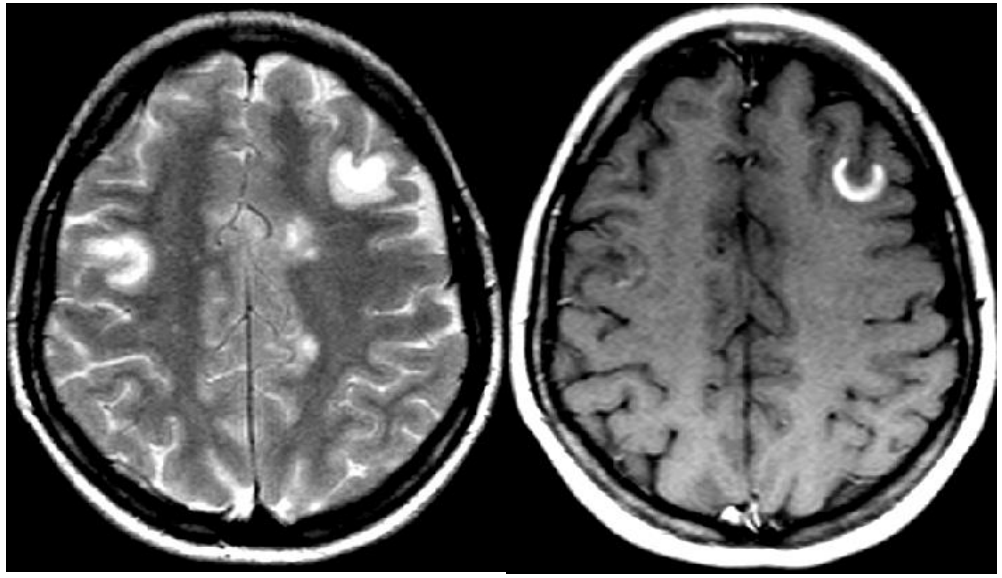
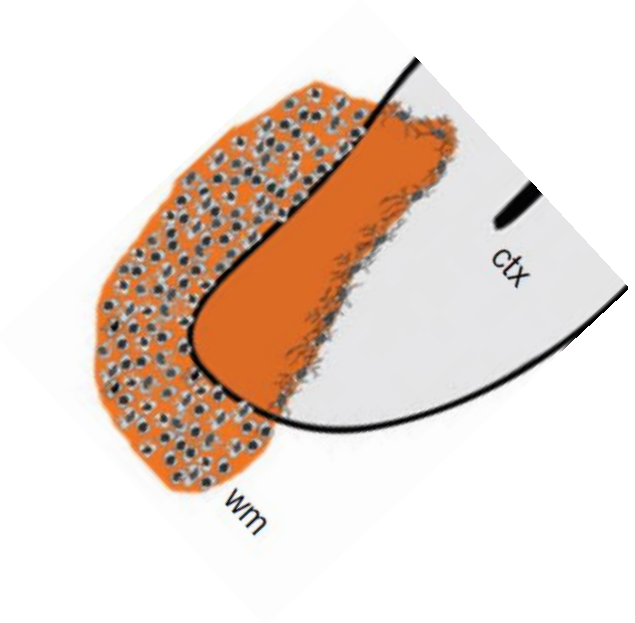


## Cortical lesions in MS

Less BBB disruption (no protein leakage)
Much less macrophage infiltration
Minimal or absent contrast uptake




Masdeu et al. Neurology 2000; Horssen et al. J Neuropathol Exp Neurol 2007; Trapp and Nave. Ann Rev Neurosci 2008

# MCQ5

Is the presence of open ring enhancement a specific MRI feature for inflammatory demyelinating lesions?

1. Yes, 100%
2. Highly specific
3. Has low specificity
4. Only seen in pseudotumoral IDLs

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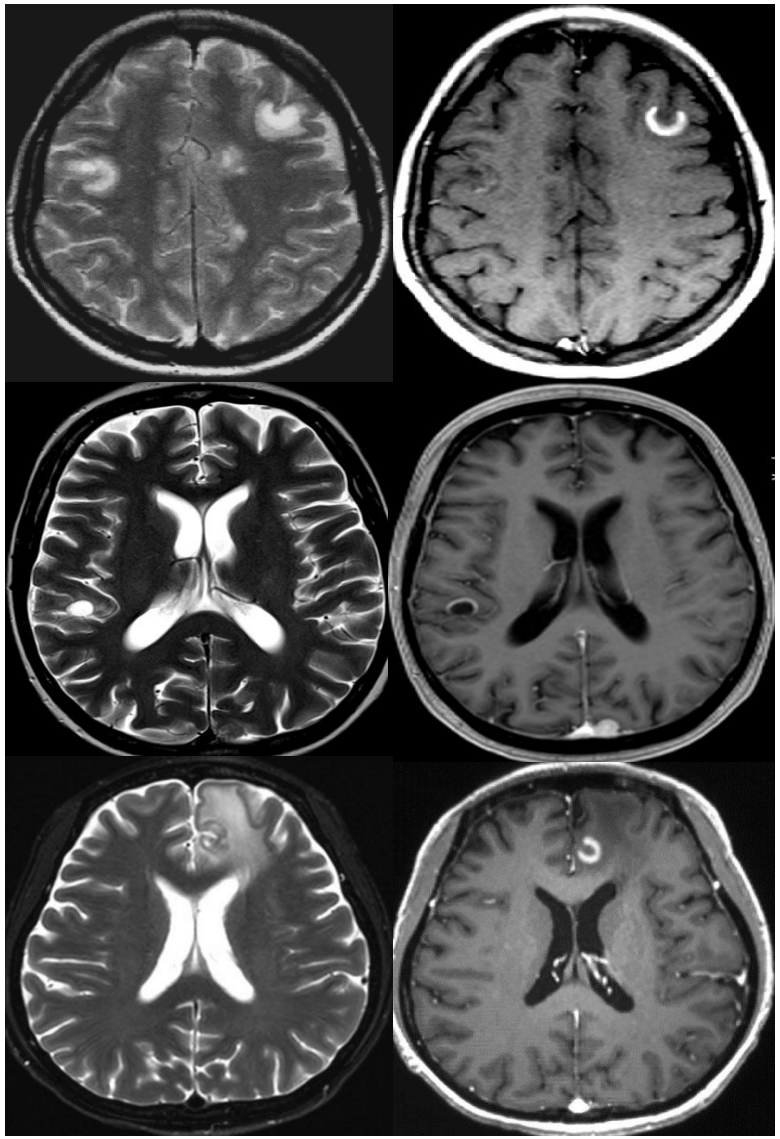
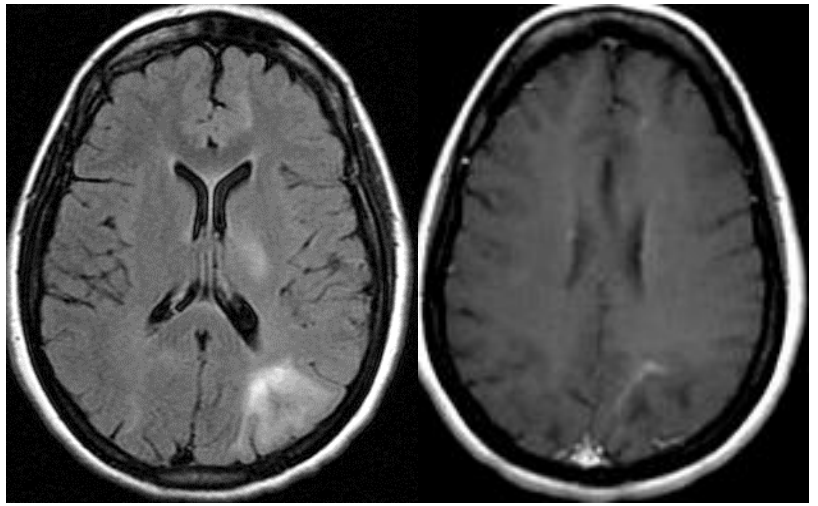
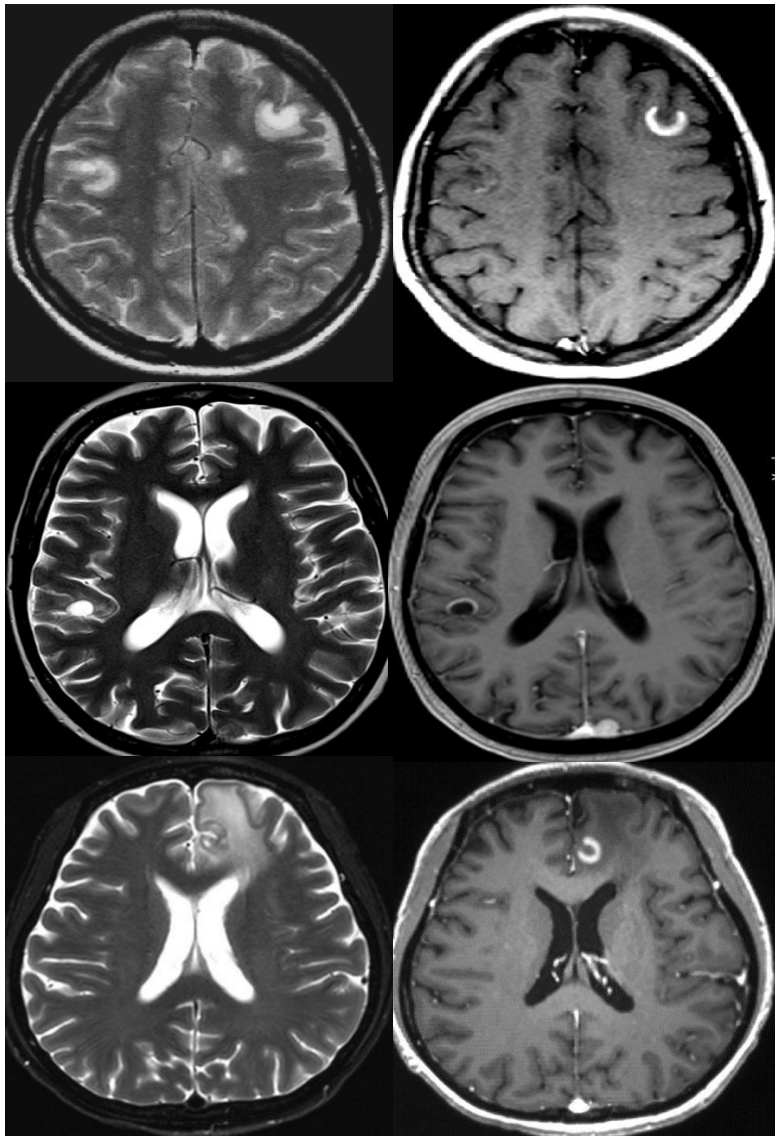
# Open-ring enhancement





# Open-ring enhancement

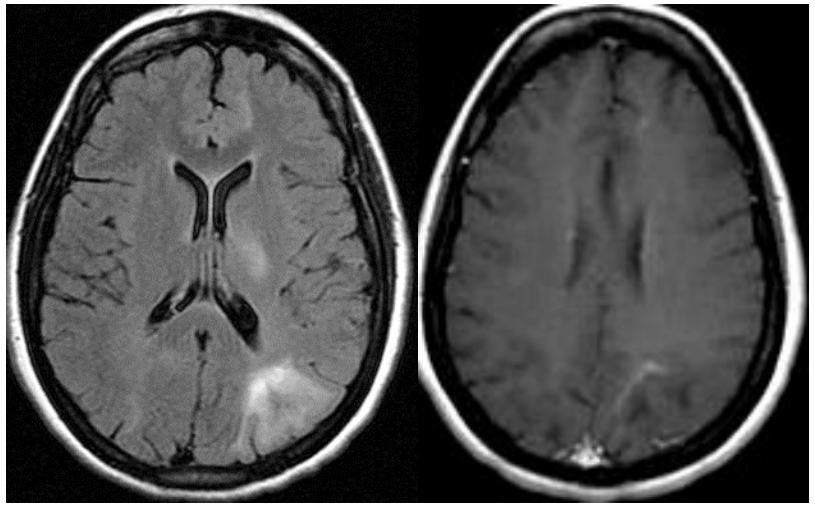


Multiple sclerosis

Metastasis

Lymphoma

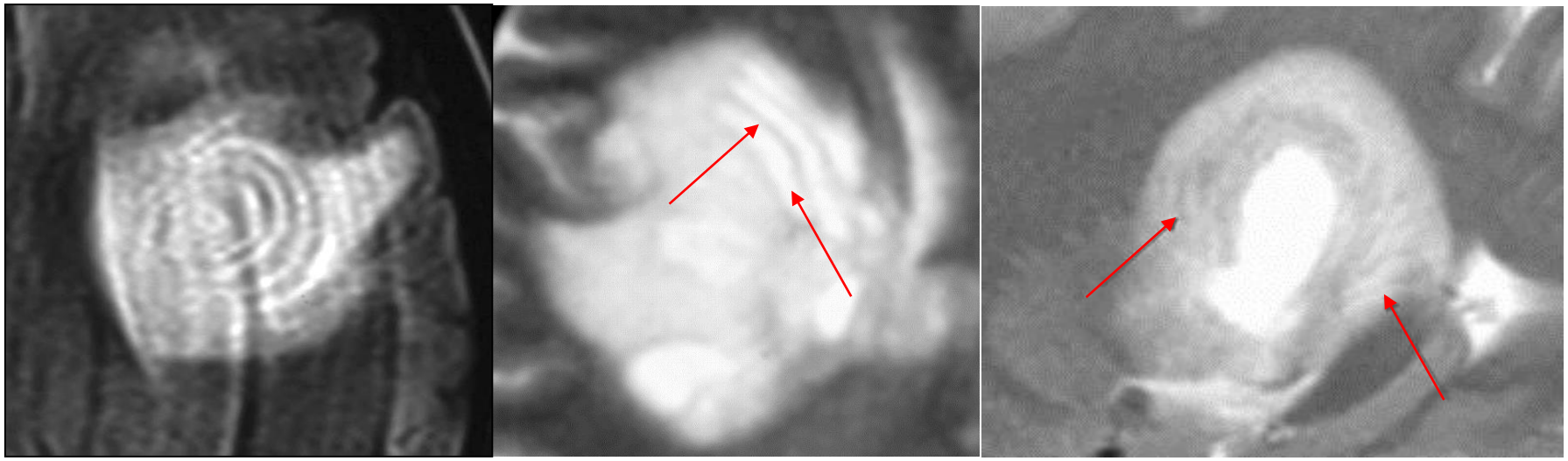
Courtesy M. Castillo.
Chapell Hill



PML-Natalizumab

Zhang et al. Korean J Radiol 2010

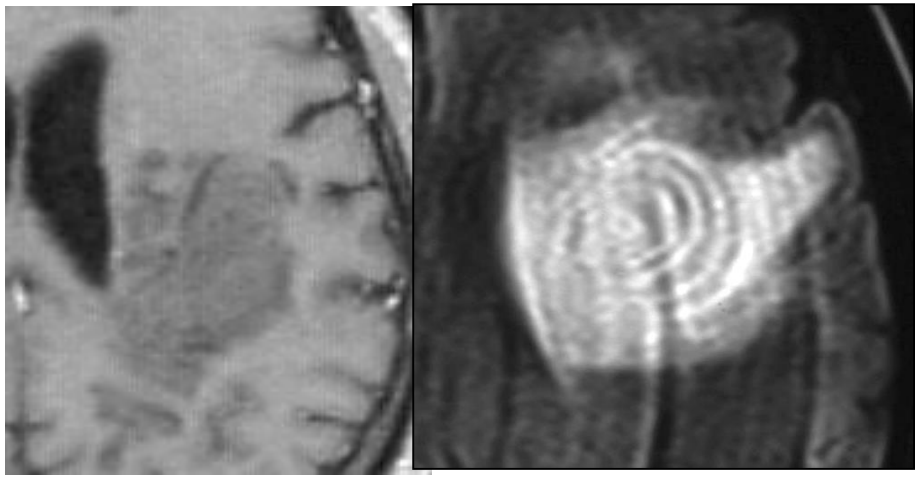
# MR imaging features



- Multiple concentric layers (onion skin lesions), as a mosaic, or as a “floral” configuration
- T2 hiperintense bands (DM) and thinner isointense bands (preserved myelin)
- The center of the lesion usually shows no layering because of massive demyelination

# Key MRI features for the diagnosis of pseudotumoral IDLs

Baló-like pattern



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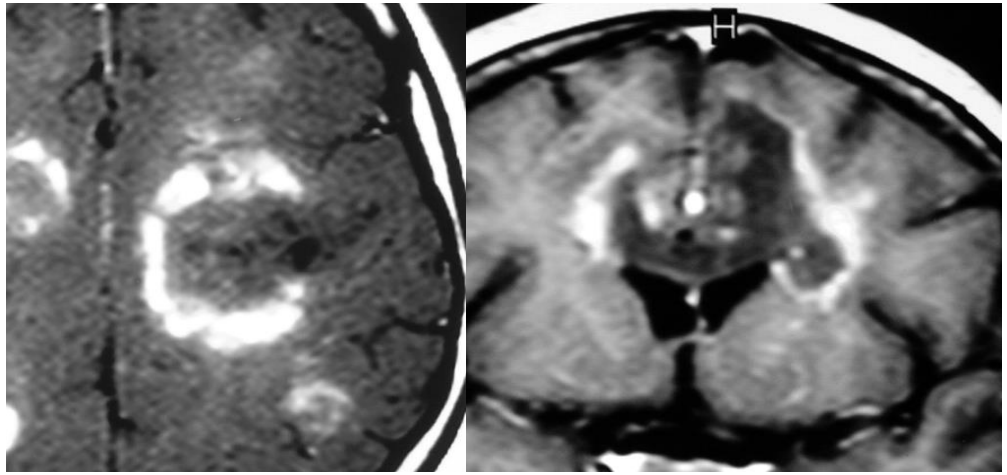


More than 50% of pseudotumoral ID lesions

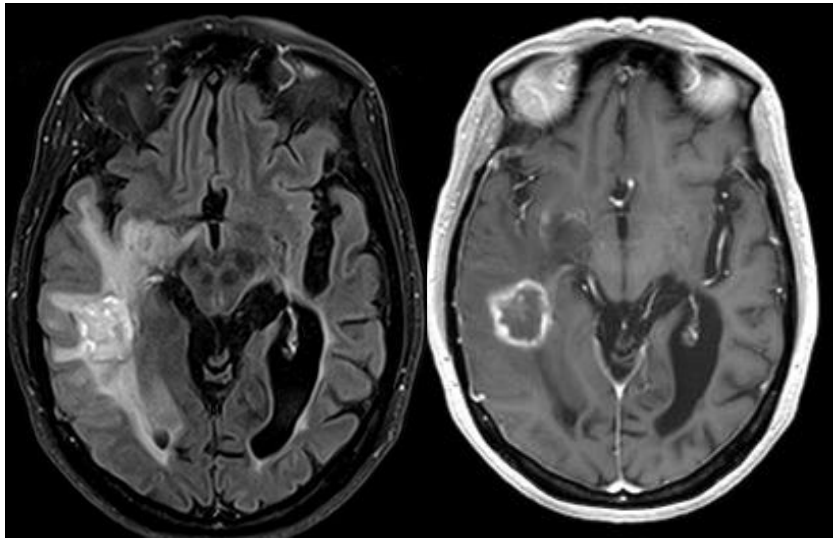
**Open-ring enhancement**

**Baló-like pattern**

# MRI in tumefactive lesions

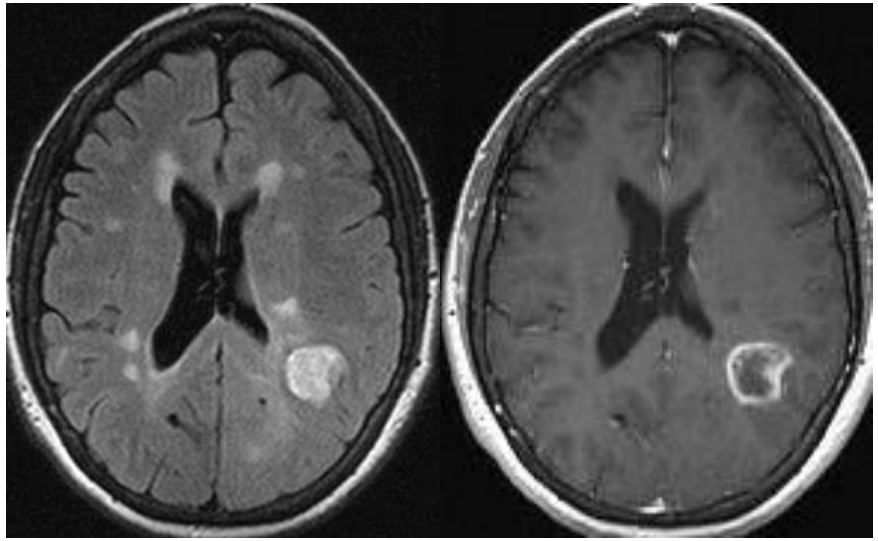
## Pseudotumoral inflammatory-demyelinating lesion?
## RRMS patients

Patient 1



47 year old woman
RRMS
30 years disease duration
EDSS 5
DMT
Left side hemiparesis

Patient 2

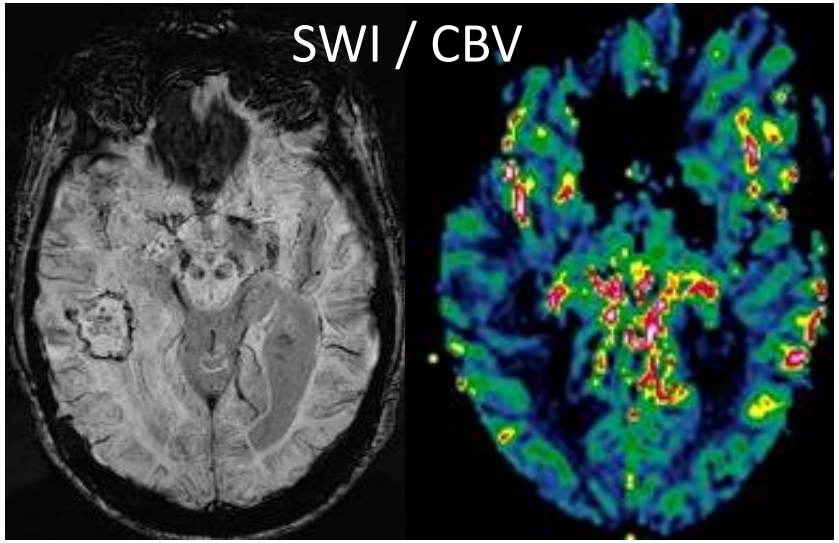


55 year old woman
RRMS
15 years disease duration
EDSS 4
DMT
Seizures

# MRI in tumefactive lesions

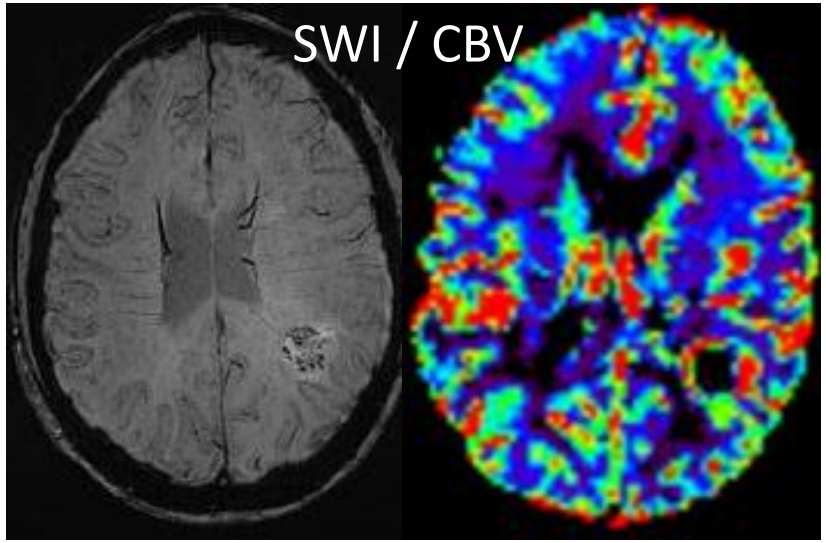
## Pseudotumoral inflammatory-demyelinating lesion?
## RRMS patients

Patient 1

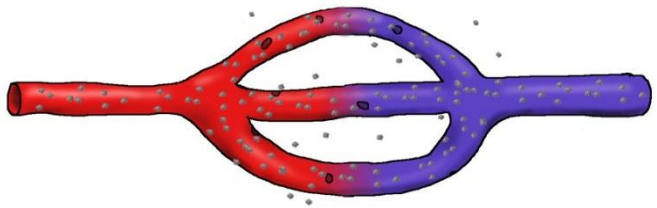


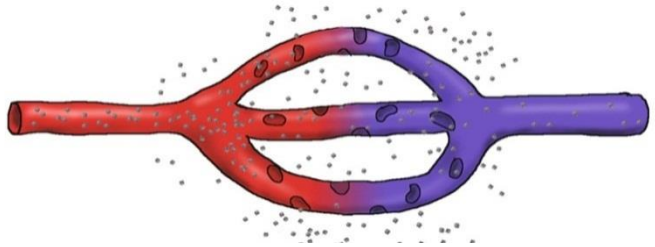

**Low angiogenesis**

Patient 2




**High angiogenesis**

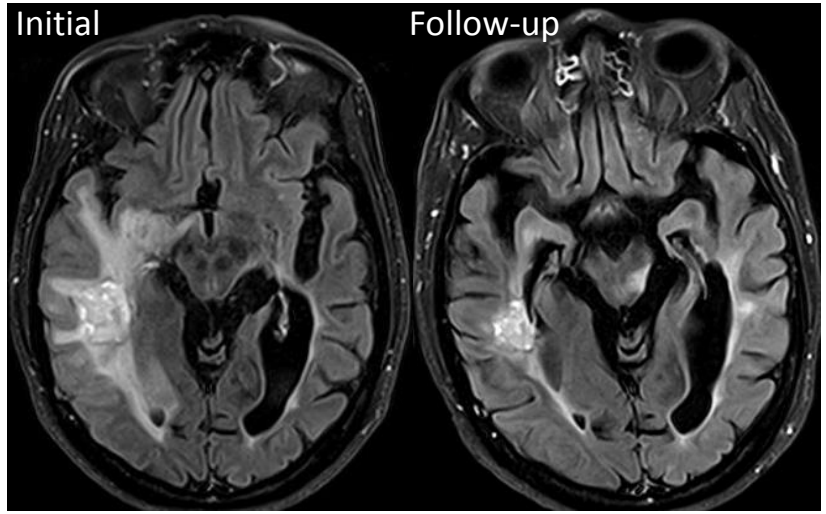




# Patterns of contrast uptake in tumefactive lesions

## Pseudotumoral inflammatory-demyelinating lesion?
## RRMS patients

Patient 1: Pseudotumoral MS lesion

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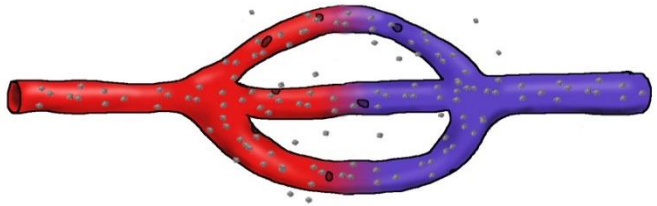
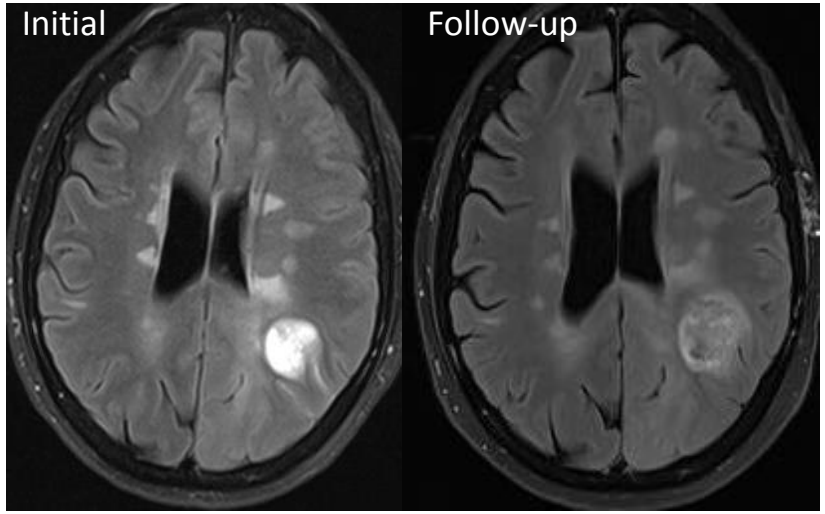
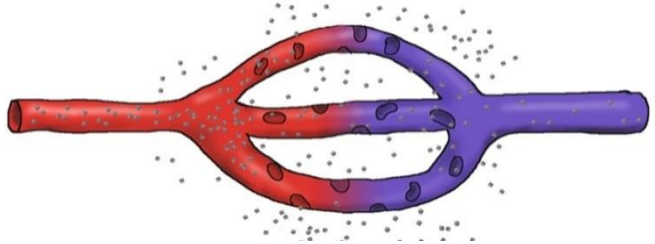


Patient 2: Glioblastoma



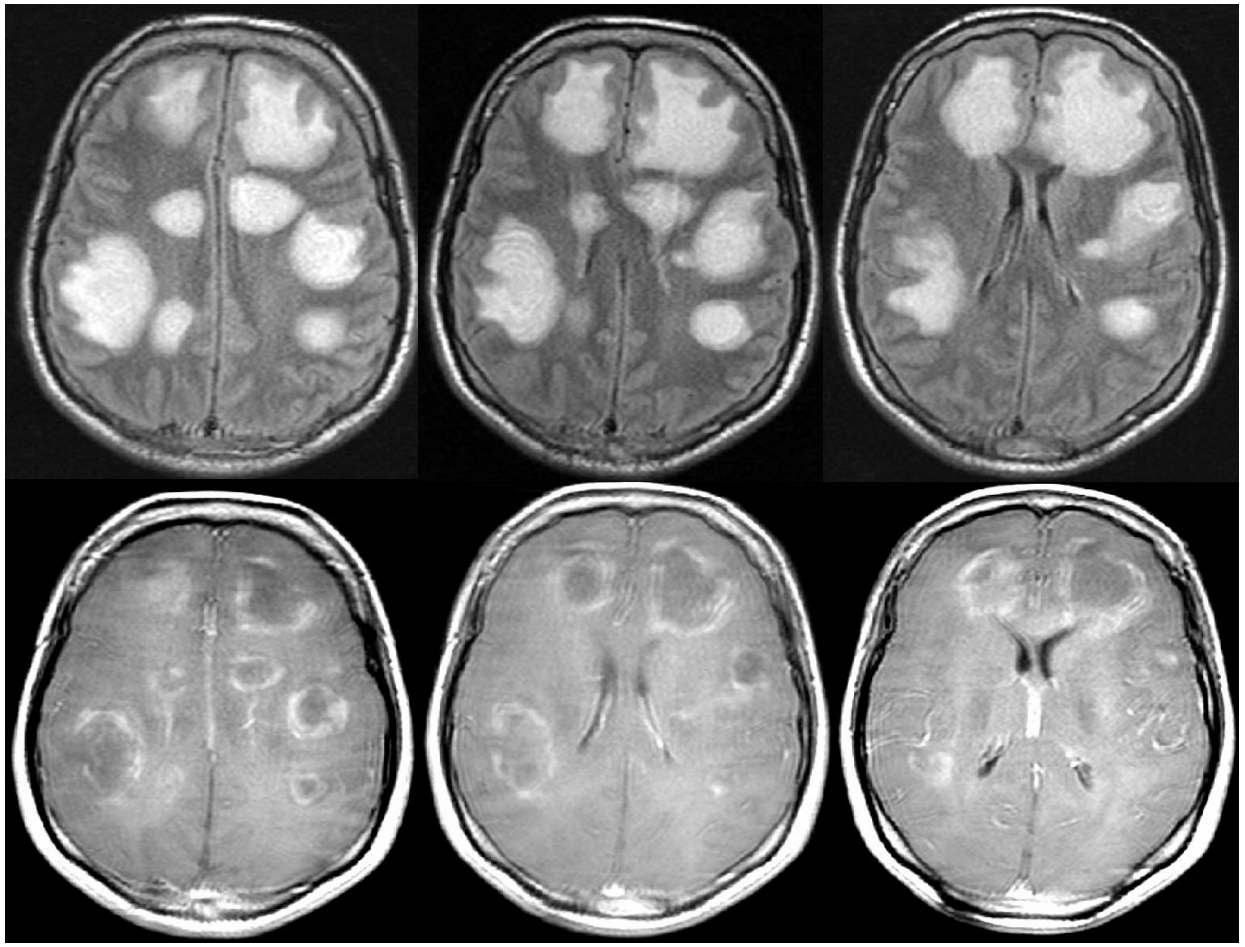

**High angiogenesis**

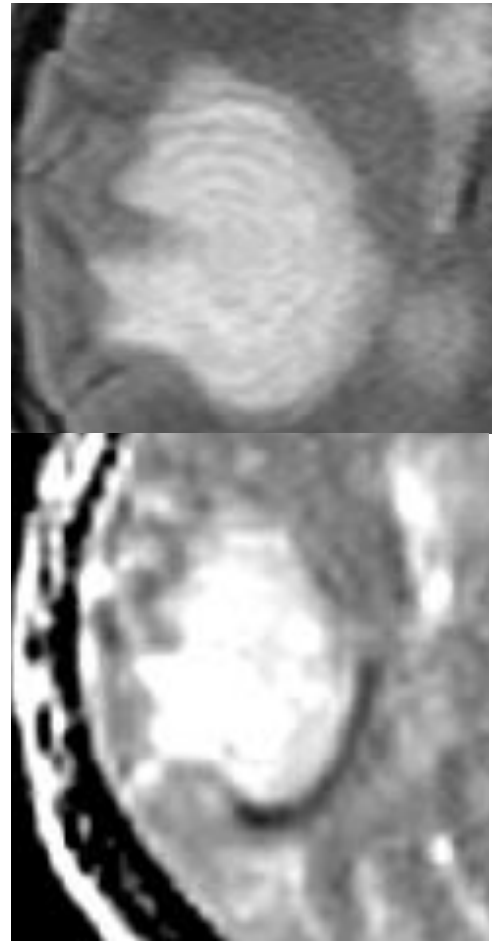


# Clinical case

A 39-year-old man,

- ✓ History of drug abuse (cocaine, cannabis and intravenous heroin)
- ✓ 3-weeks progressive course of dysarthria, fatigue, spatial disorientation, cognitive and behavioral dysfunction.
- ✓ HIV serology was negative.





# MCQ6

Diagnosis?

1. Balo concentric sclerosis
2. Metastasis
3. Multifocal glioma
4. Toxic leukoencephalopathy

# MCQ6

Diagnosis?

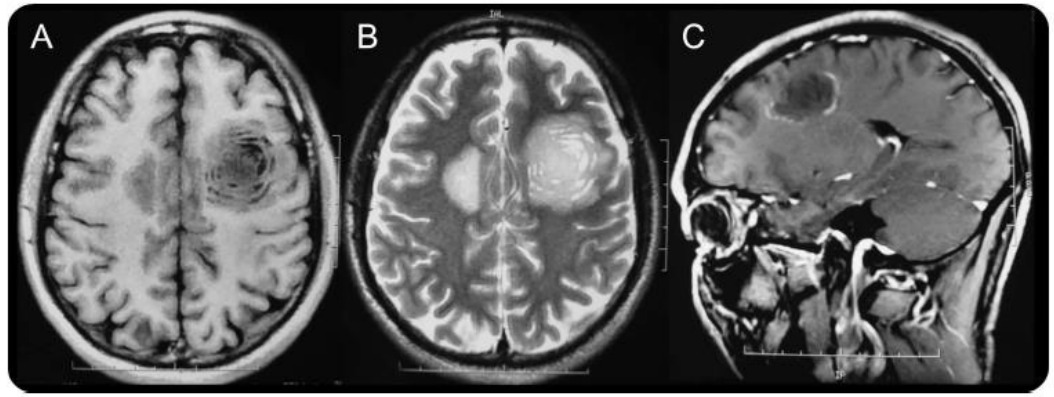
1. Balo concentric sclerosis
2. Metastasis
3. Multifocal glioma
4. **Toxic leukoencephalopathy**

# Clinical case

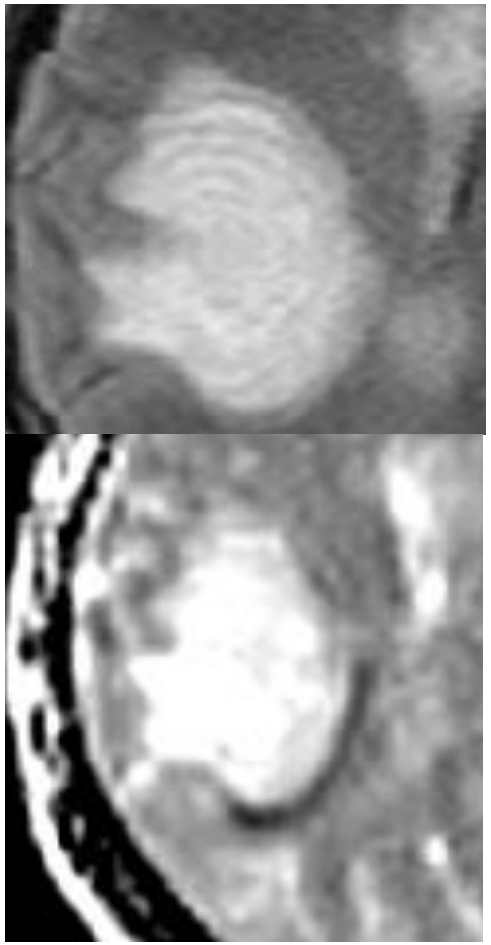
NEUROIMAGES

## Levamisole-induced leukoencephalopathy mimicking Baló disease

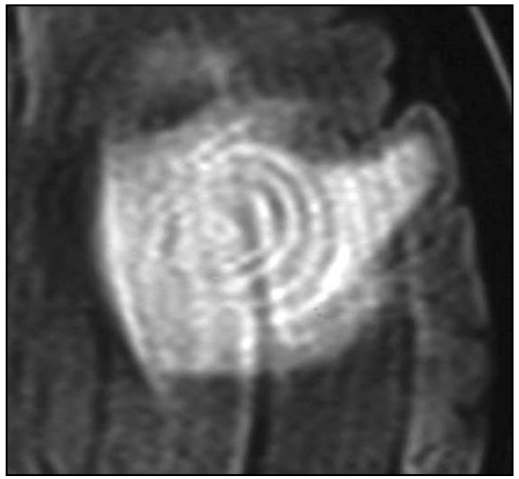
Figure Brain MRI in a patient with levamisole-induced leukoencephalopathy



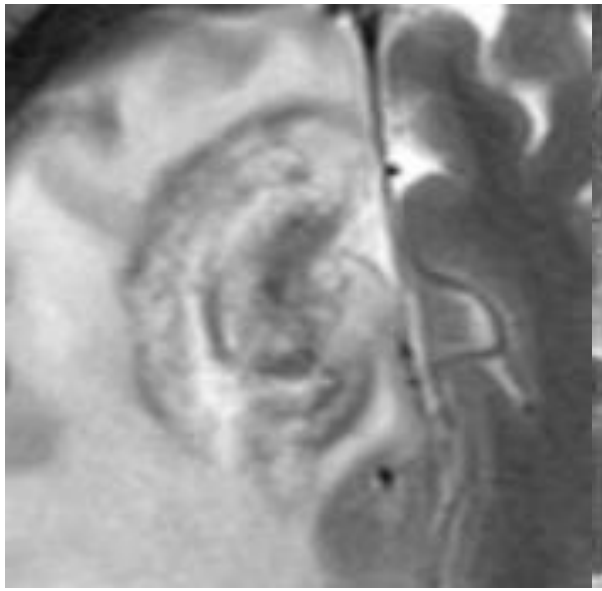

Long et al. Neurology 2015



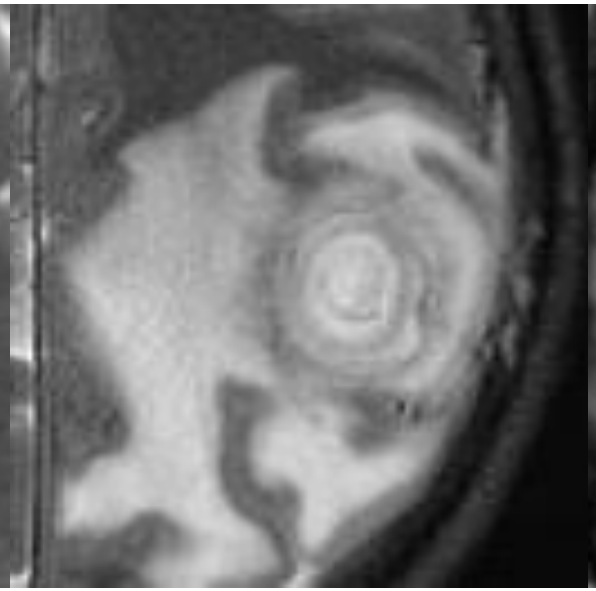
# Concentric layer sign (Balo-like pattern)



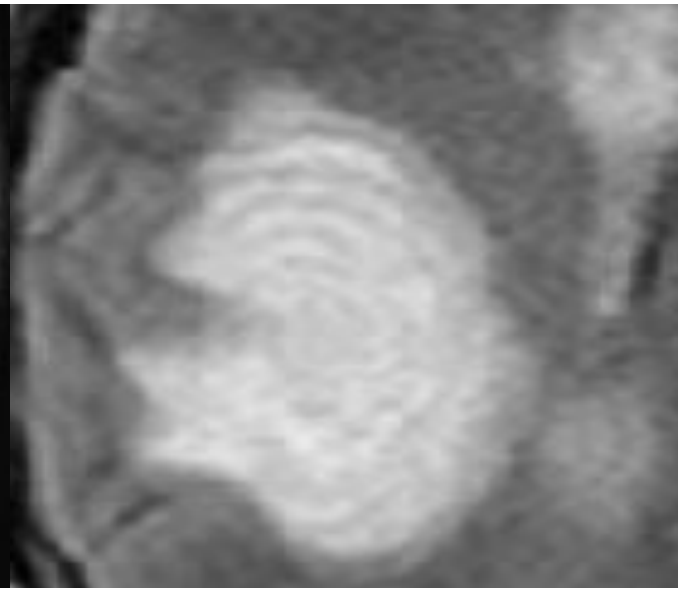
Balo concentric sclerosis



**Toxoplasmosis**



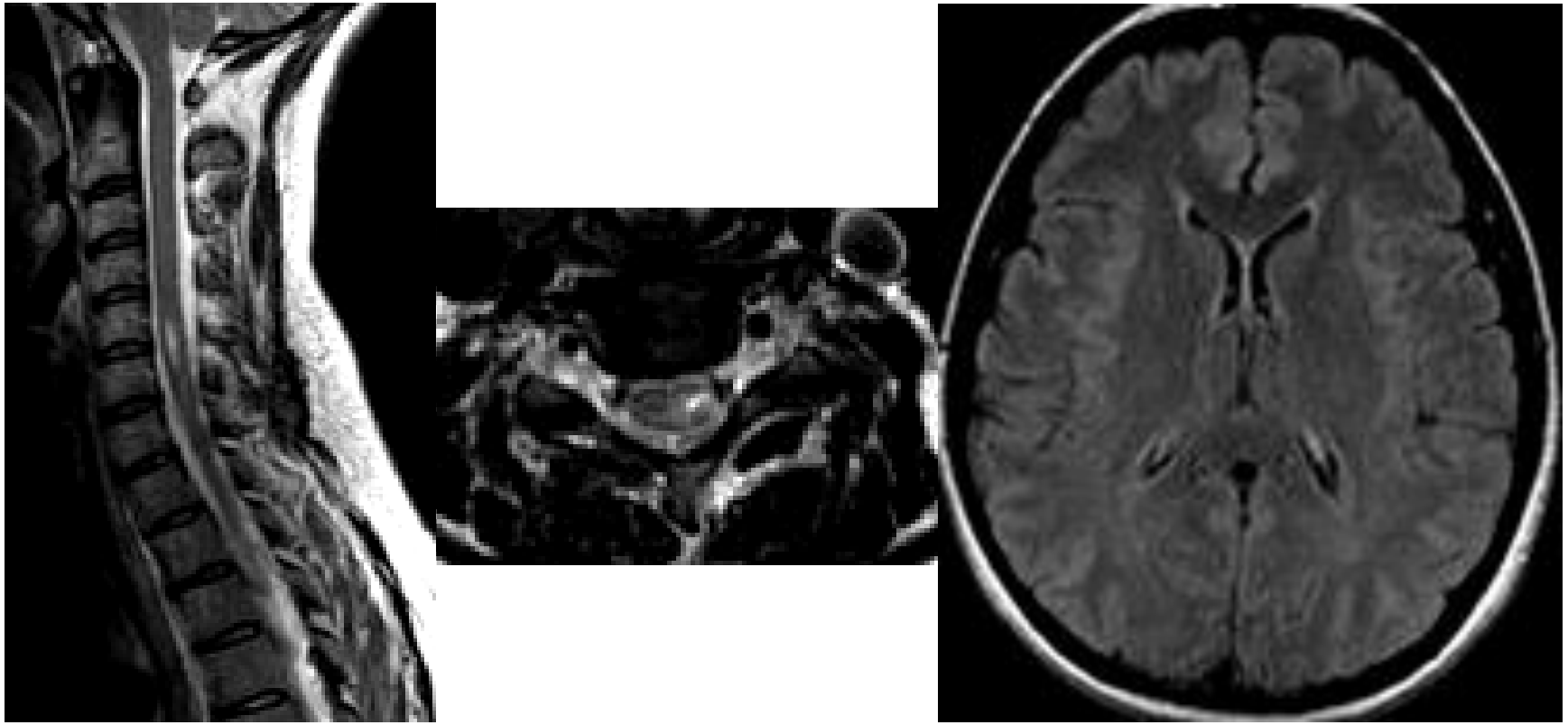
**Pyogenic brain abscesses**



**Levamisole-associated multifocal inflammatory leukoencephalopathy (cocaine user)**

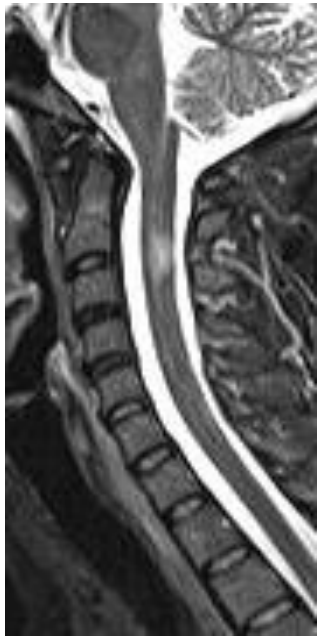
# Clinical case

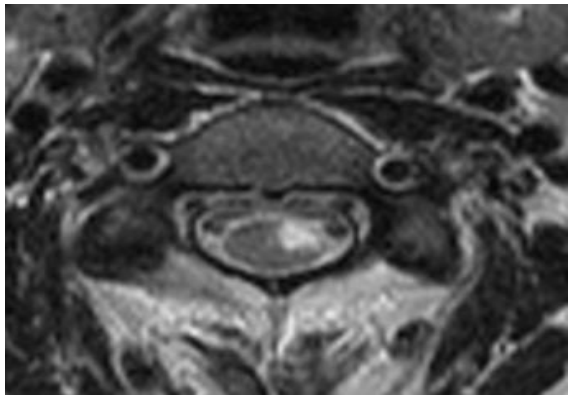
43 year old woman
Acute partial TM



# Typical MR imaging findings: spinal cord

- ✓ No cord swelling (unless active)
- ✓ Unequivocal hyperintense T2 or Gd-enhancing; focal lesions
- ✓ ≥3mm in size; <2 vertebral segments long
- ✓ Peripheral location, cigar shaped
- ✓ Occupying only part of cord cross-section (less than 50%)

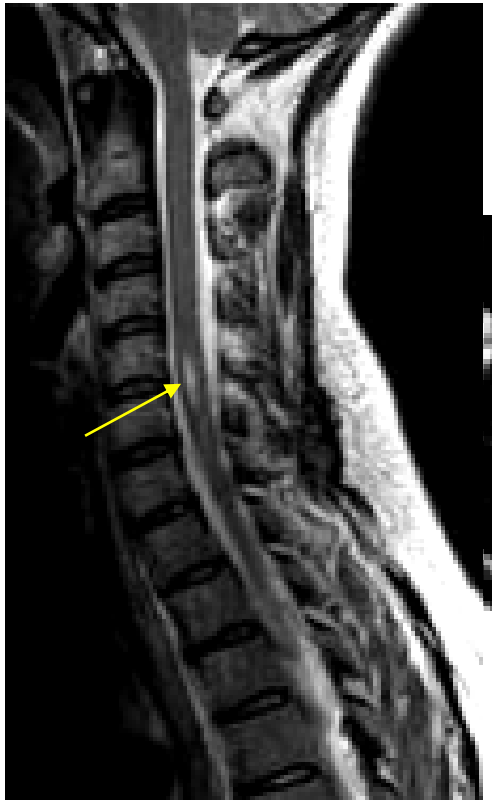




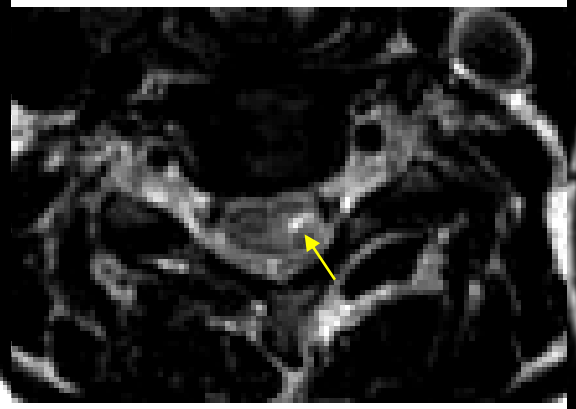
Bot et al. Neurology. 2004; 62:226-33; Weier et al. Mult Scler 2012;18:1560-9; Gass et al. Lancet Neurol 2015;14:443-54

# Clinical case

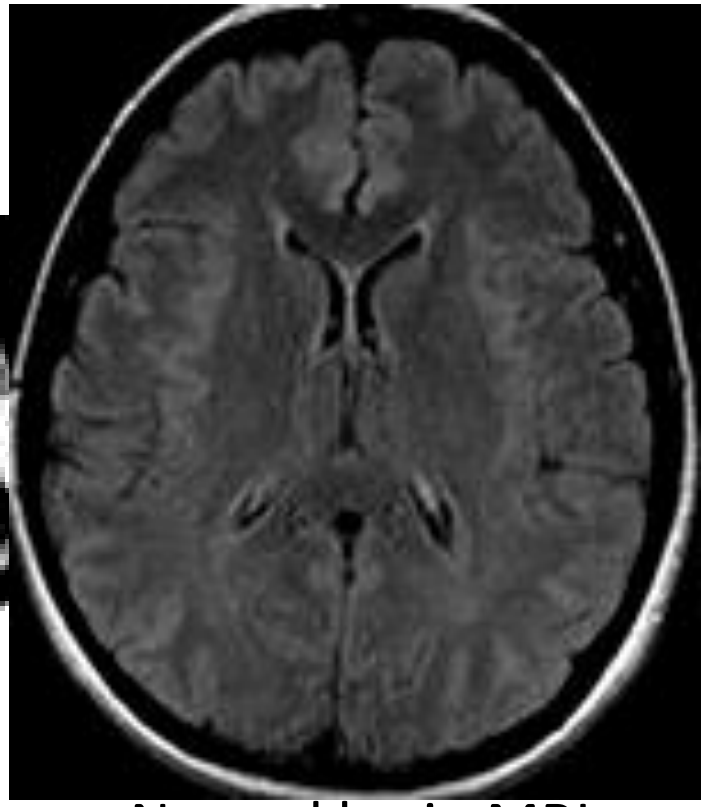
43 year old woman
Acute partial TM



Short segment



Bright lesion



Normal brain MRI

# MCQ7

Diagnosis?

1. Multiple sclerosis
2. NMOSD
3. Spinal cord infarct
4. Idiopathic transverse myelitis

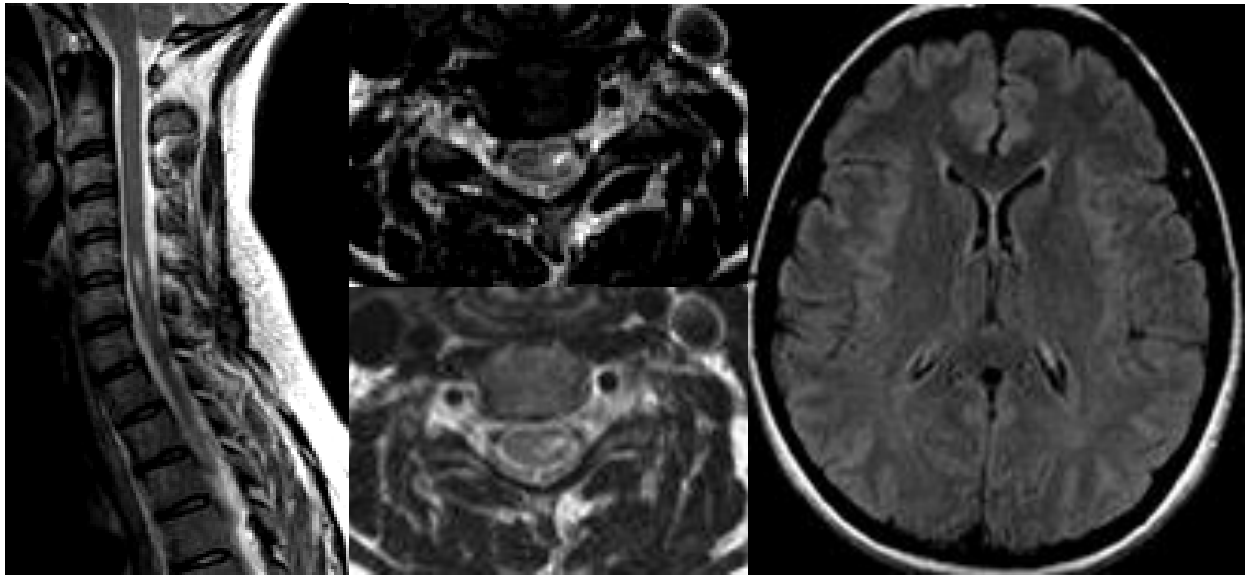
# MCQ7

Diagnosis?

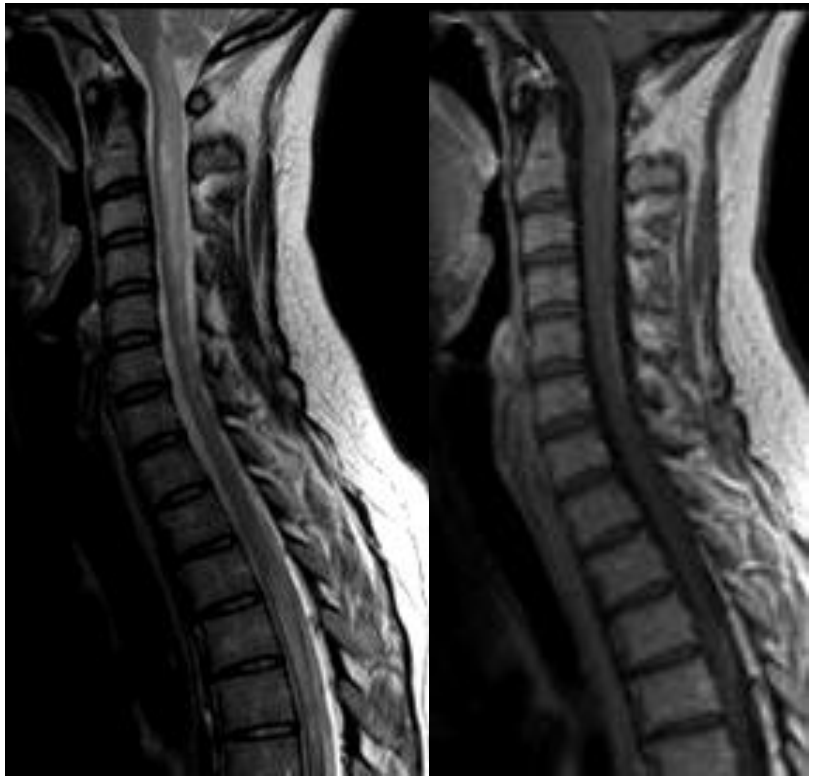
1. Multiple sclerosis
2. **NMOSD**
3. Spinal cord infarct
4. Idiopathic transverse myelitis

# Clinical case

43 year old woman
Acute partial TM

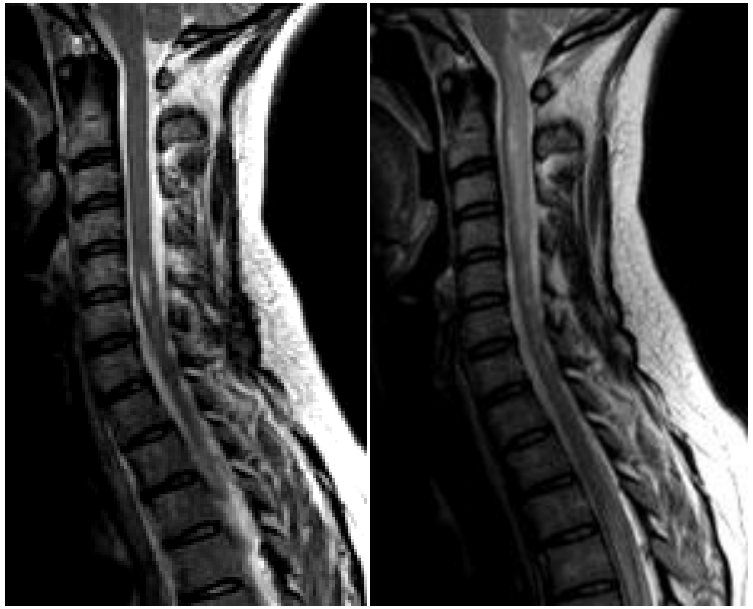


3 months later



AQP4 Ab +

# Short Myelitis Lesions in Aquaporin-4-IgG Positive NMOSD



- 25 patients (Mayo Clinic): 14% of initial myelitis episodes (NMOSD)
- Subsequent LETM in 92%
- Characteristics (compared to short myelitis lesions in Aquaporin-4-IgG negative):
  - coexisting autoimmunity
  - central cord lesions on MRI
  - T1 hipointensity
  - brain MRI inconsistent with MS
  - OB in CSF lacking

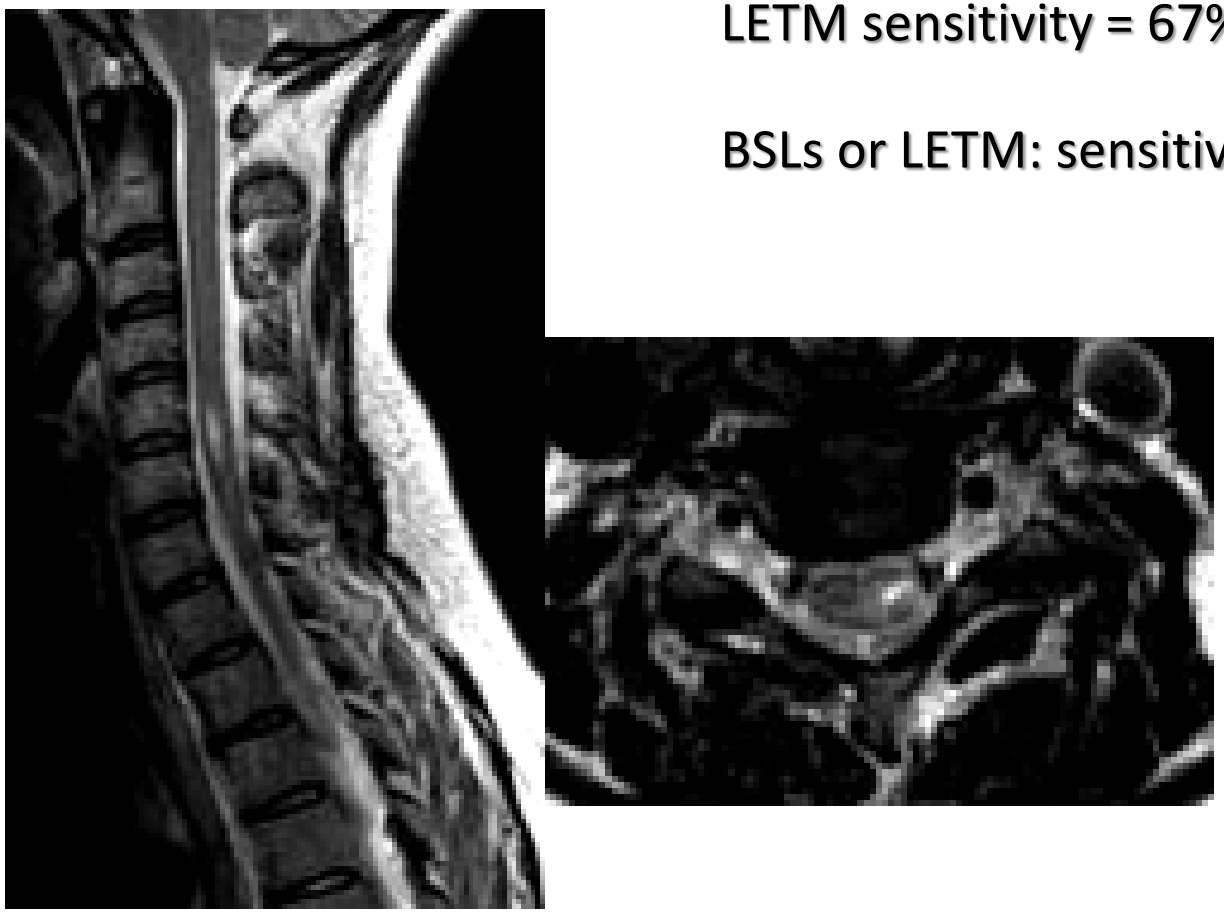
Flanagan et al. JAMA Neurol 2015

# Bright spotty lesions (BSLs) in NMO

- Very hyperintense spotty lesions on axial T2WI
- More hyperintense than that of surrounding cerebrospinal fluid

BSLs  sensitivity = 54%; specificity = 97%
LETM sensitivity = 67%; specificity=97%

BSLs or LETM: sensitivity 88%



Yonezu T et al. Mult Scler  2013

# Summary

- Wide variety of causes may present with multifocal WM lesions
- MRI is the preferred imaging technique for diagnostic workup
- Radiological interpretation with demographic, clinical history, and lab findings
- Standardized brain (spinal cord) MRI protocol
- Comprehensive checklist for evaluation of WM spots is crucial

Sánchez Aliaga E, Barkhof F. Handb Clin Neurol 2014;122:291-316; Charil et al. Lancet Neurol 2006;5:841-52; Rovira et al. Nat Rev Neurol 2015;11:471-82