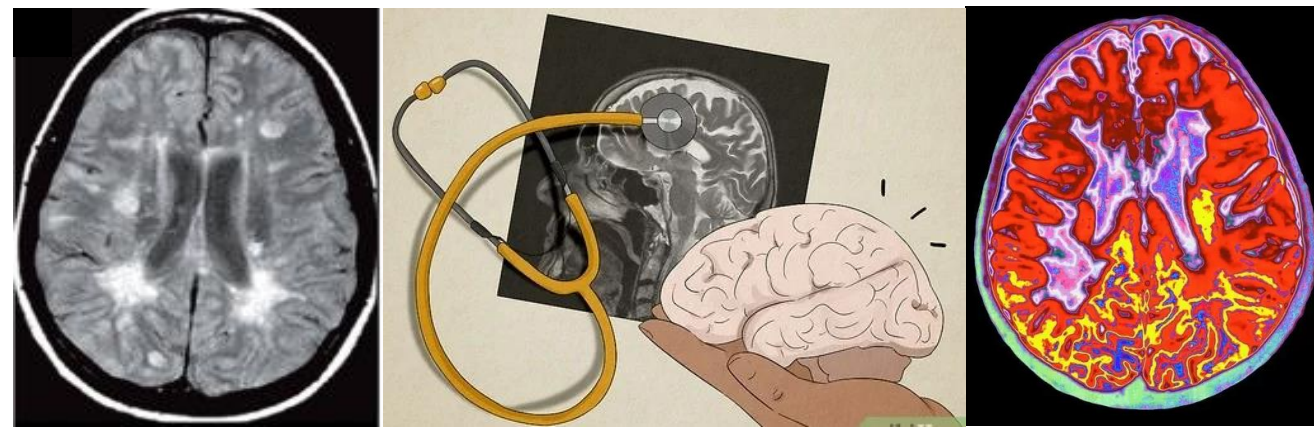




VII CONGRESSO NAZIONALE ANEU

CONTROVERSIE IN NEUROLOGIA
D'EMERGENZA E URGENZA

29 SETTEMBRE
1 OTTOBRE 2022
ROMA



TEACHING NEUROIMAGES: È SCLEROSI MULTIPLA, OPPURE?

Simonetta Gerevini

Direttore UOC ASST Papa Giovanni XXIII - Bergamo -

Outline

- Differential diagnosis of MS : a wide look
- MS and other primary demyelinating diseases: NMO, ADEM
- MS and PML
- Final consideration

The problem of misdiagnosis



What can we do with bright spots?

The problem of misdiagnosis/overreliance



- Around 30% of cases originally referred for MS were finally diagnosed with other diseases.
- One study conducted in four academic MS centers revealed
 - over 50% of patients carried a misdiagnosis for *at least 3 years*
 - 70% had received disease-modifying therapy (DMTs)
 - 31% experienced unnecessary morbidity as a direct result .
- At the end of the 1980s, some diagnostic errors were made because MRI was not available. When MRI became widely used, overestimations of radiological findings started to be reported.
- MRI criteria for MS where not created to differentiate MS from other WM abnormalities

Gaitán MI, Correale J. Multiple Sclerosis Misdiagnosis: A Persistent Problem to Solve. *Front Neurol.* 2019

Solomon AJ, Naismith RT, Cross AH. Misdiagnosis of multiple sclerosis: Impact of the 2017 McDonald criteria on clinical practice. *Neurology.* 2019

Multiple bright objects: are they all MS plaques???

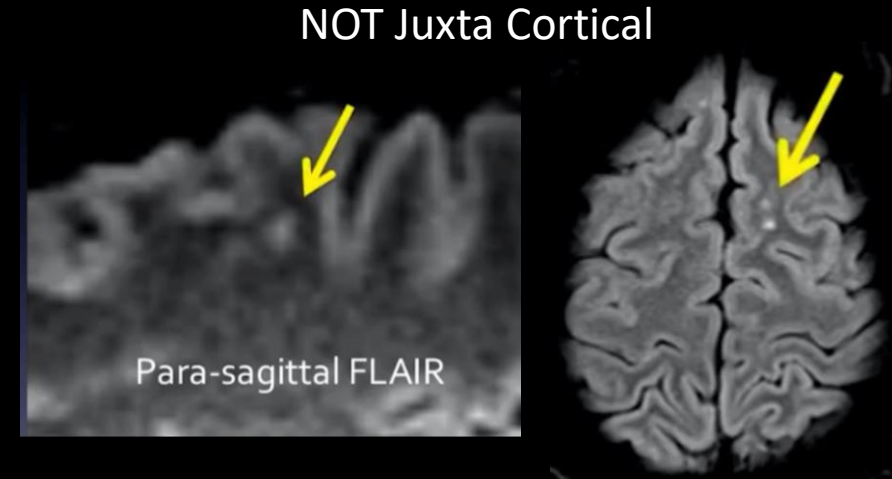
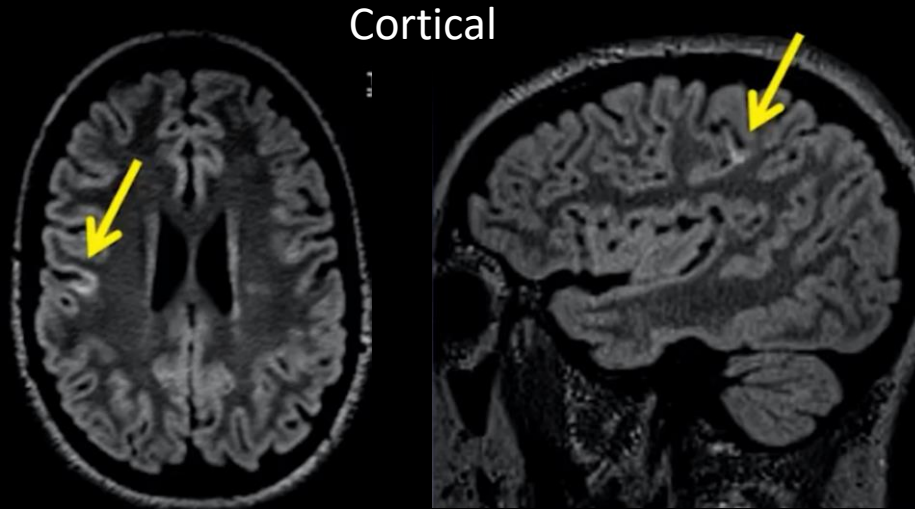


MS lesion definitions...it's not just semantics: **WHITE SPOTS** location

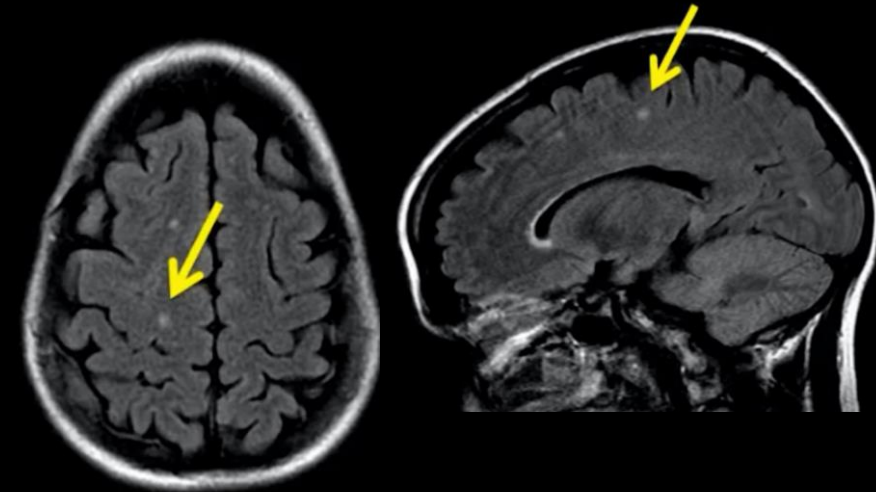
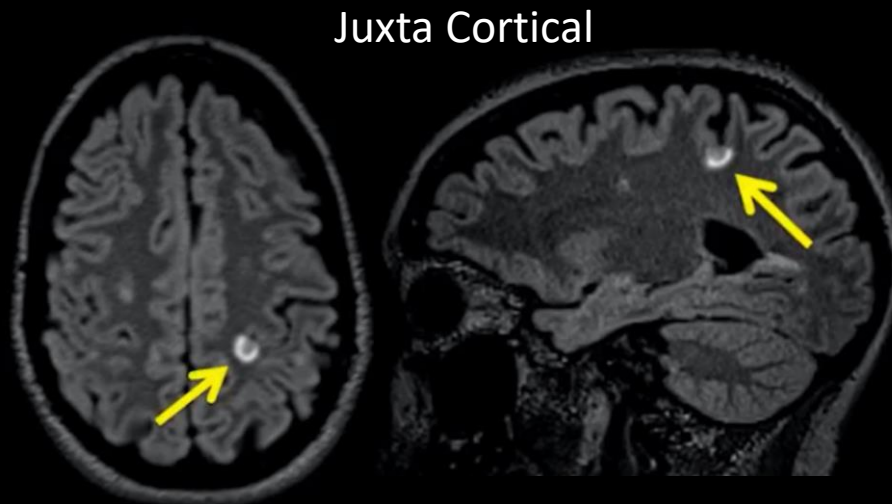
- Cortical
- Juxtacortical WM
- Periventricular WM
- Infratentorial
- Spinal Cord
- Others

- Calloseseptal
- Temporal WM

- Subcortical WM
- DeepWM
- Central Pons



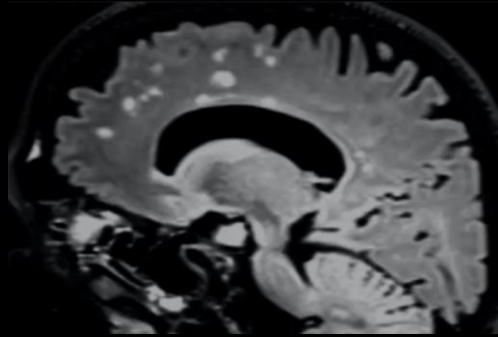
Don't use this term unless you can *directly* see lesion contacting cortex



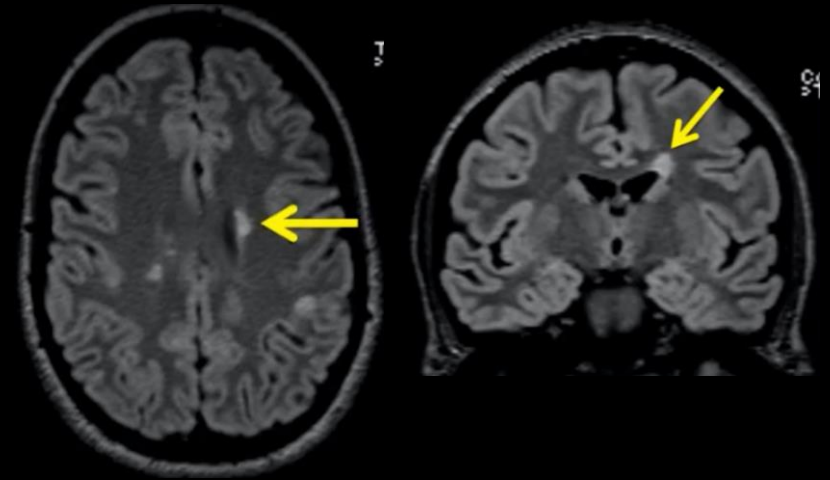
"Subcortical" Lesion

MS lesion definitions...it's not just semantics: **WHITE SPOTS** location

"Deep" WM



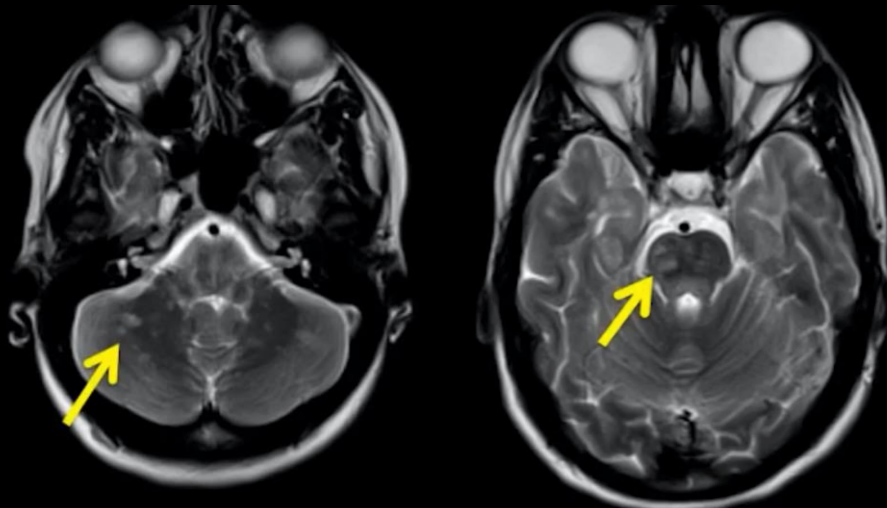
Periventricular WM



- Cortical
- Juxtacortical WM
- Periventricular WM
- Infratentorial
- Spinal Cord
- Others

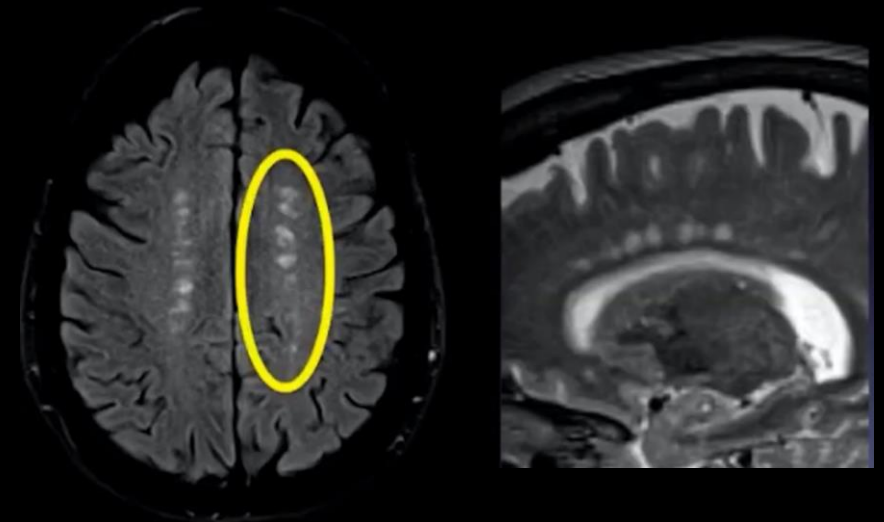
- Calloseseptal
- Temporal WM

Infratentorial

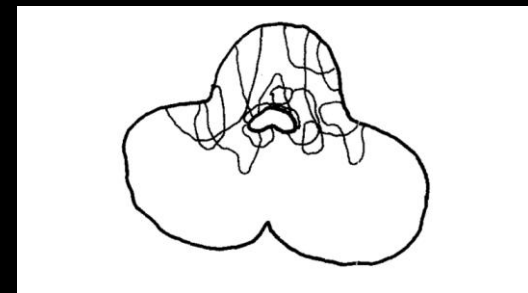
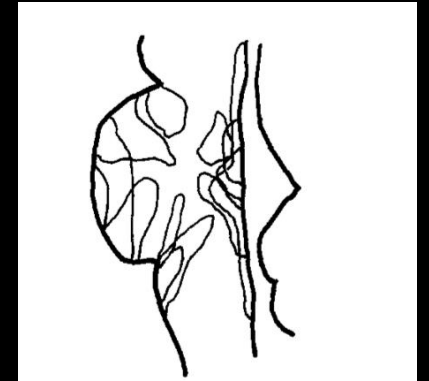
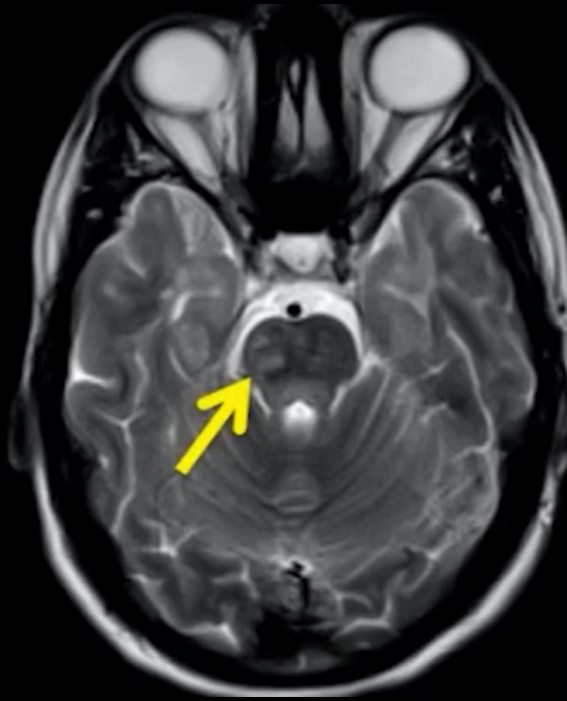
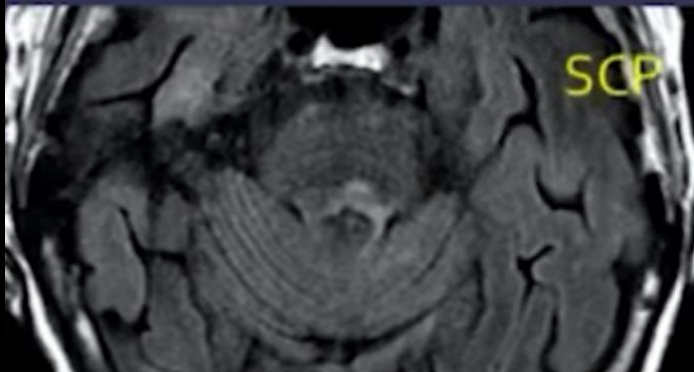
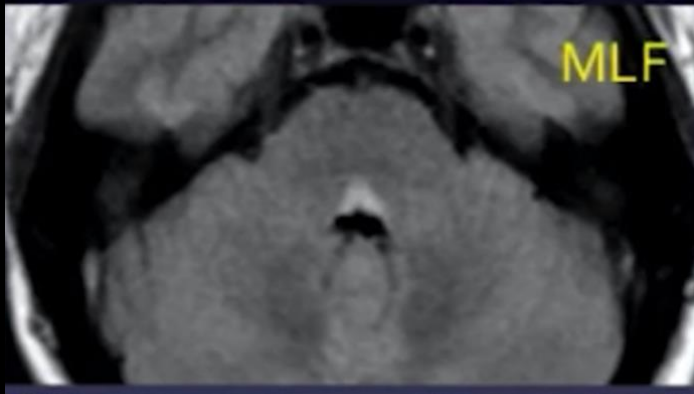
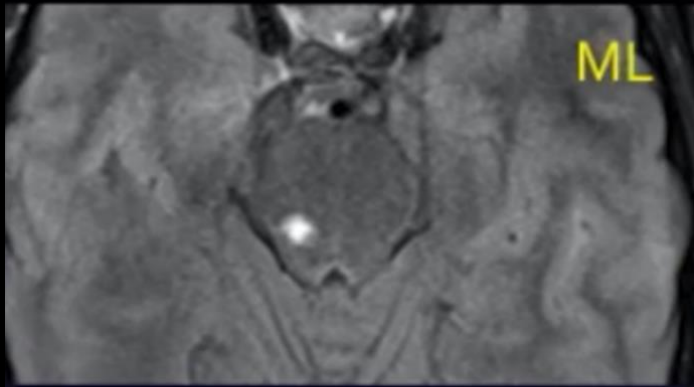


- Subcortical WM
- DeepWM
- Central Pons

NOT Periventricular



Common location for MS brainstem lesions

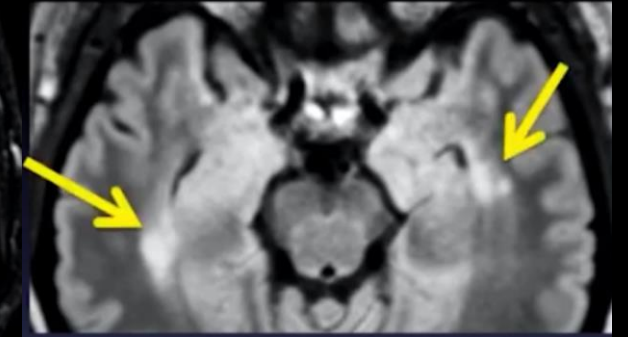
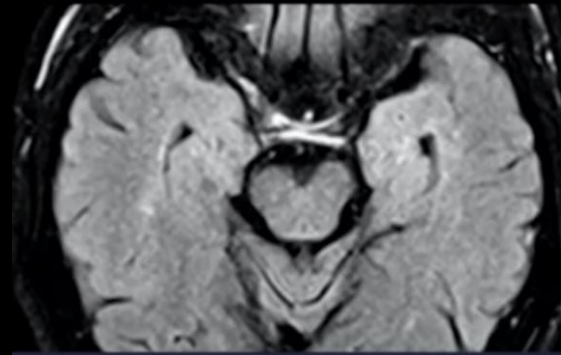
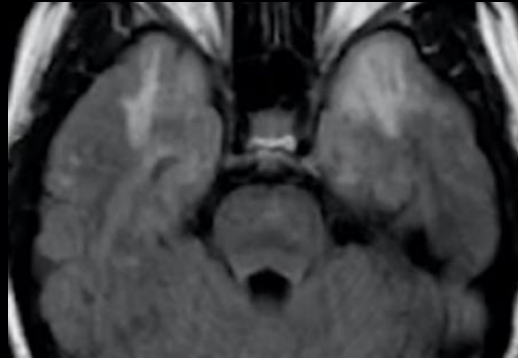


ML Median Lemniscus
MLF Median Longitudinal Fasciculus
SCP Superior Cerebellar Peduncle

MS lesion definitions...it's not just semantics: **WHITE SPOTS** location

DeepWM

- Cortical
- Juxtacortical WM
- Periventricular WM
- Infratentorial
- Spinal Cord
- Others



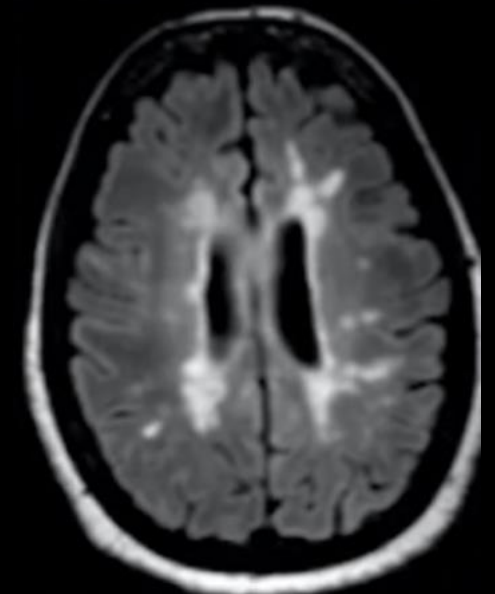
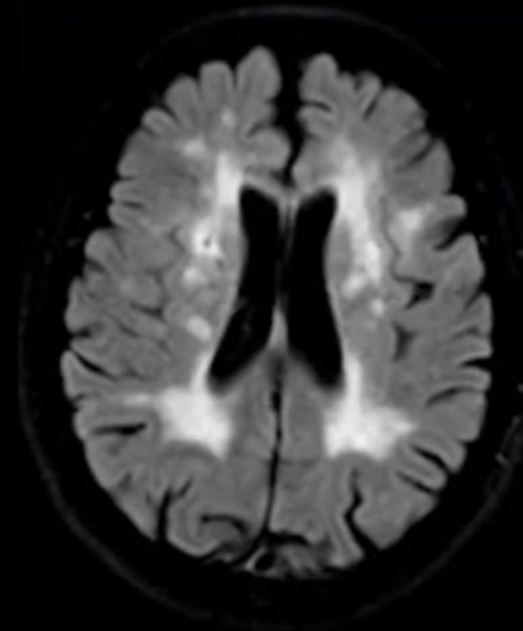
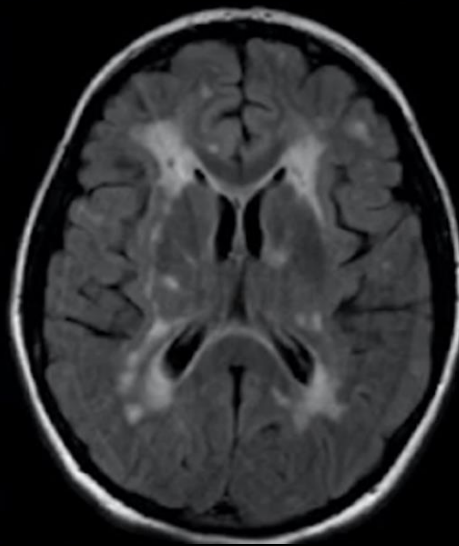
- Calloseseptal
- Temporal WM

CADASIL

MicrovascularWM changes

MS

- Subcortical WM
- DeepWM
- Central Pons



Some Imaging Major RED FLAGS



Cortical infarcts



Embolic disease; thrombotic thrombocytopenic purpura; vasculitis

**Hemorrhages/
microhemorrhages**



Amyloid angiopathy; Moya Moya disease; CADASIL; vasculitis

Meningeal enhancement



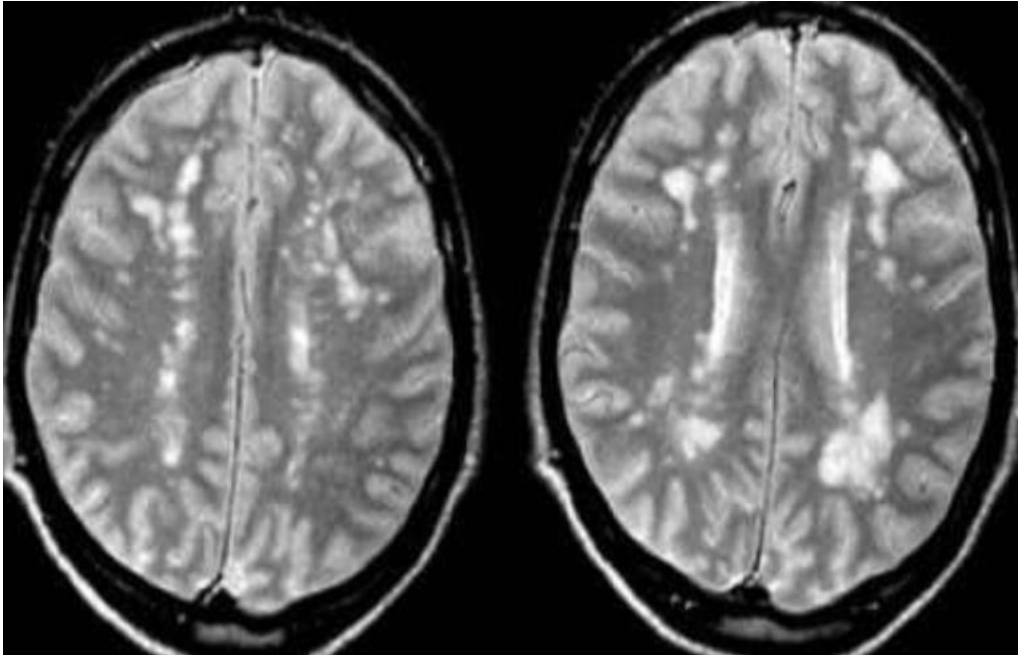
Chronic meningitis; sarcoidosis; lymphomatosis; CNS vasculitis

Calcifications on CT scan



Cysticercosis; toxoplasmosis, mitochondrial disorders

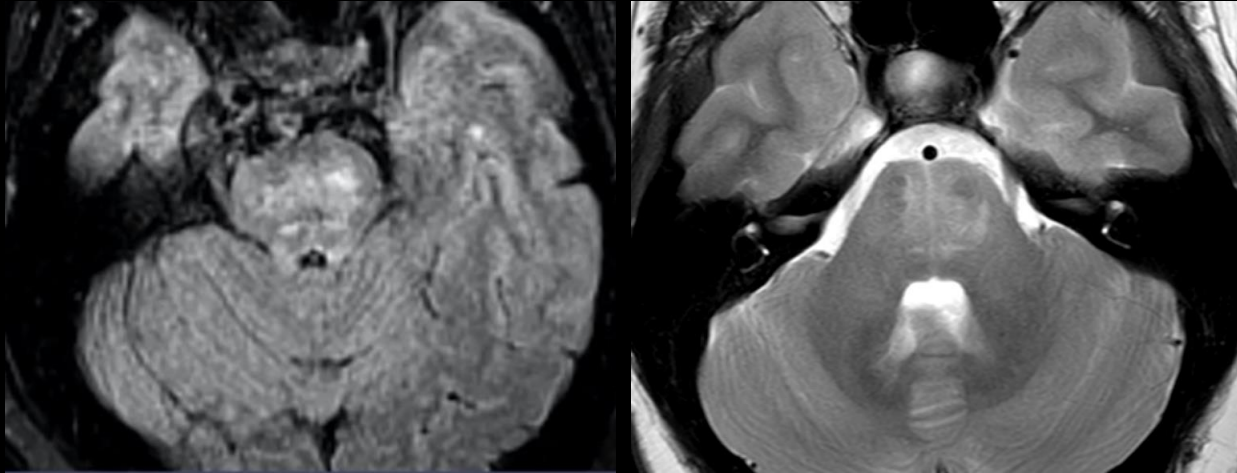
More common differential: Small vessels ischemic disease



	<u>Vascular</u>	<u>MS</u>
Corpus callosum	- uncommon	- common
U-fibers	- uncommon	- common
Cortical lesions	- infarction	- sometimes
Basal nuclei	- typical	- uncommon
Infra tentorial	- uncommon	- typical
Temporal lobe	- uncommon	- early involvement
Periventricular	- uncommon	- typical
Spinal cord	- uncommon	- typical
Gd-enhancement	- no	- yes
Dawson fingers	- no	- typical
Distribution	- asymmetric	- symmetric/diffuse

More common differential: Small vessels ischemic disease

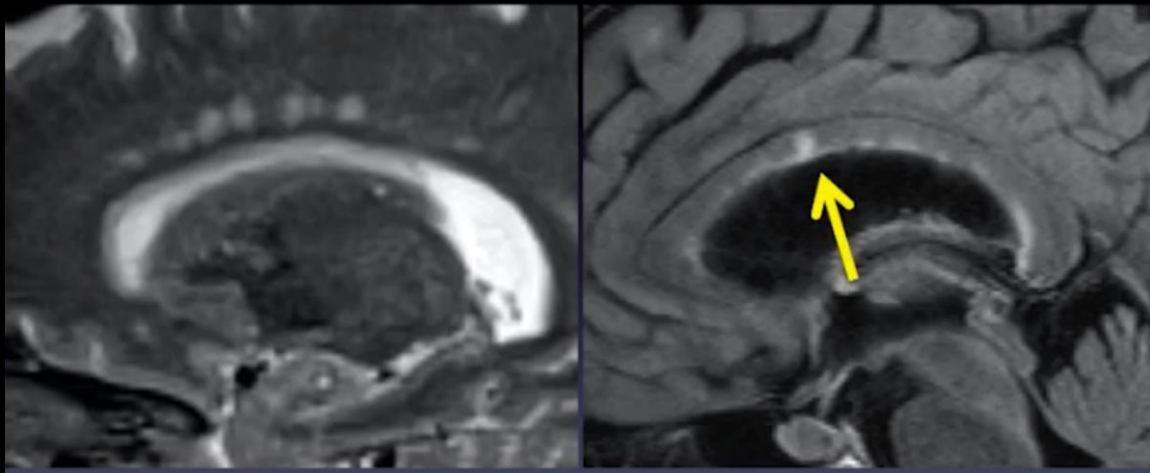
Central pons



Vascular lesions

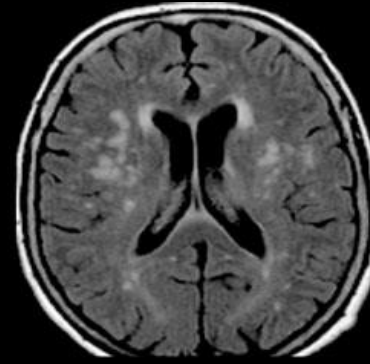
Behçet

Calloso septal lesions

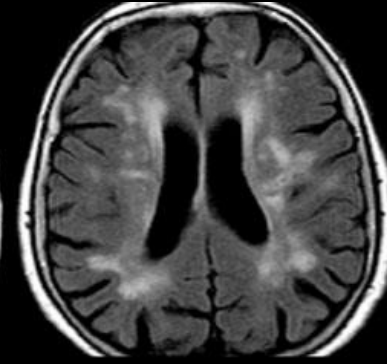


Vascular lesions

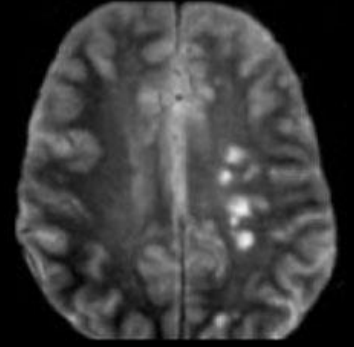
MS plaque



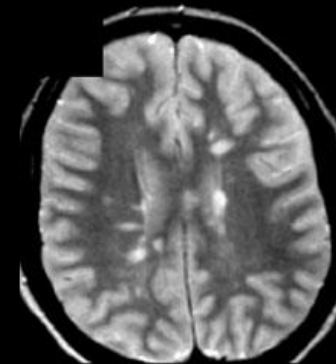
Vascular Mild



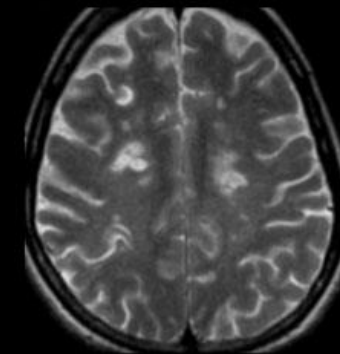
Vascular Severe



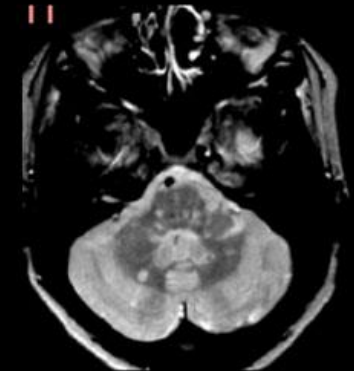
Borderzone infarction



MS Periventricular



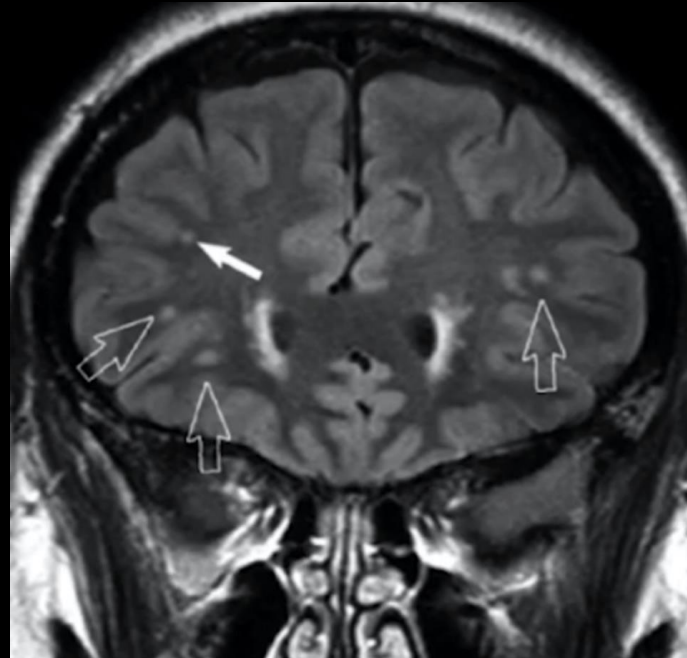
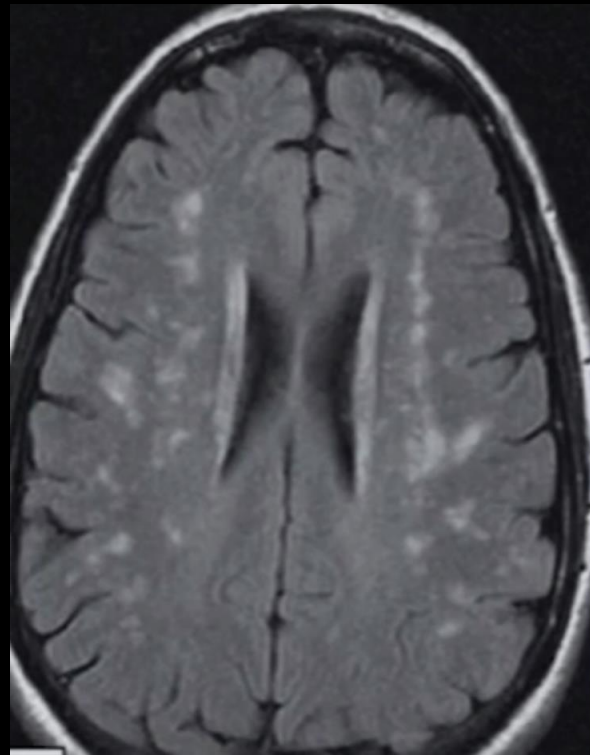
MS Juxtacortical



MS Infratentorial



More common differential: MIGRAINE



Migraine is etiology for MRI WM spots in...
-7.5% US population(")

- **Too subcortical**
- **Too symmetric**



Applebee. The clinical overlap of MS & migraines. Headache 2012,52,52:111-116)

Liu et al. Prevalence of brain MRI meeting Barkhof & McDonald criteria for dissemination in space among headache patients. MSJ 2019,19(8)11101-5

WMLs differential diagnosis

Hypoxic/ischemic

- Atherosclerosis
- Hyperhomocysteinaemia
- Amyloid angiopathy
- Diabetic microangiopathy,
- Hypertension
- Migraine

Inflammation

- MS
- Vasculitis: SLE, M. Behcet, Sjögren,
- Sarcoid,
- Inflammatory bowel disease
- (Crohn, colitis ulcerosa, coeliakie)

Infectious

- HIV, syphilis, Lyme (borreliose),
- PML: progressive multifocal leukoencephalopathy
- postinfectious: ADEM

Toxic/metabolic

- CO-intoxication, B12 deficiency
- Central pontine myelinolysis

Traumatic

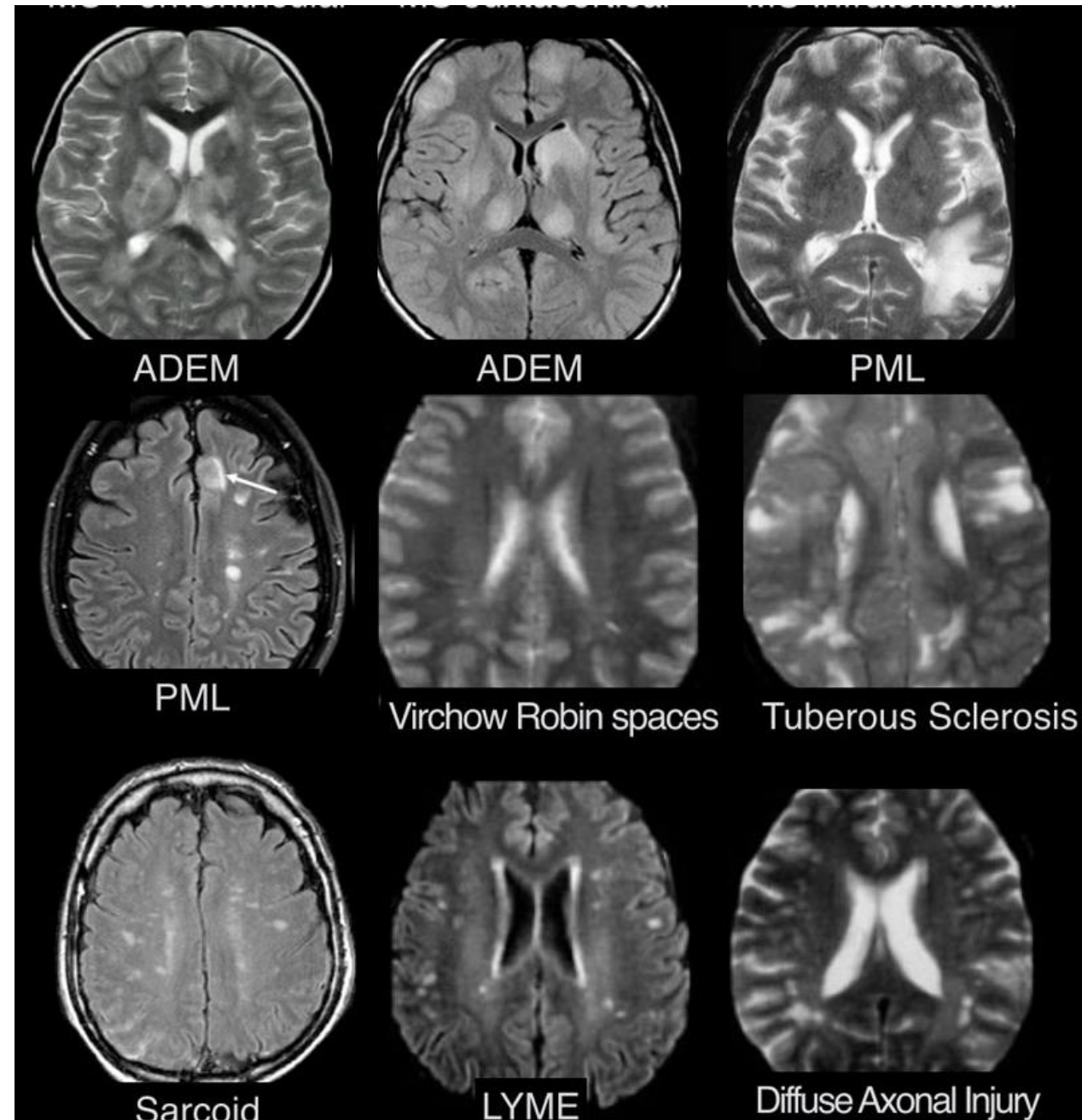
- Radiotherapy
- Postcontusion

Hereditary

- Metabolic (symmetrical, dd: toxic)

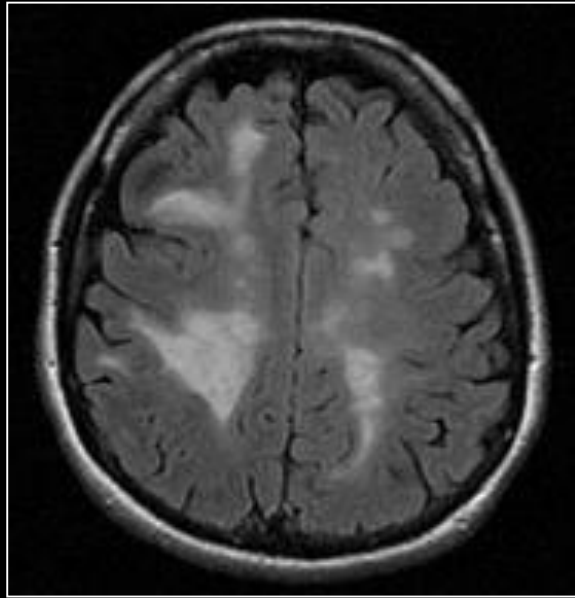
Normal

- VR-spaces - Fazekas I

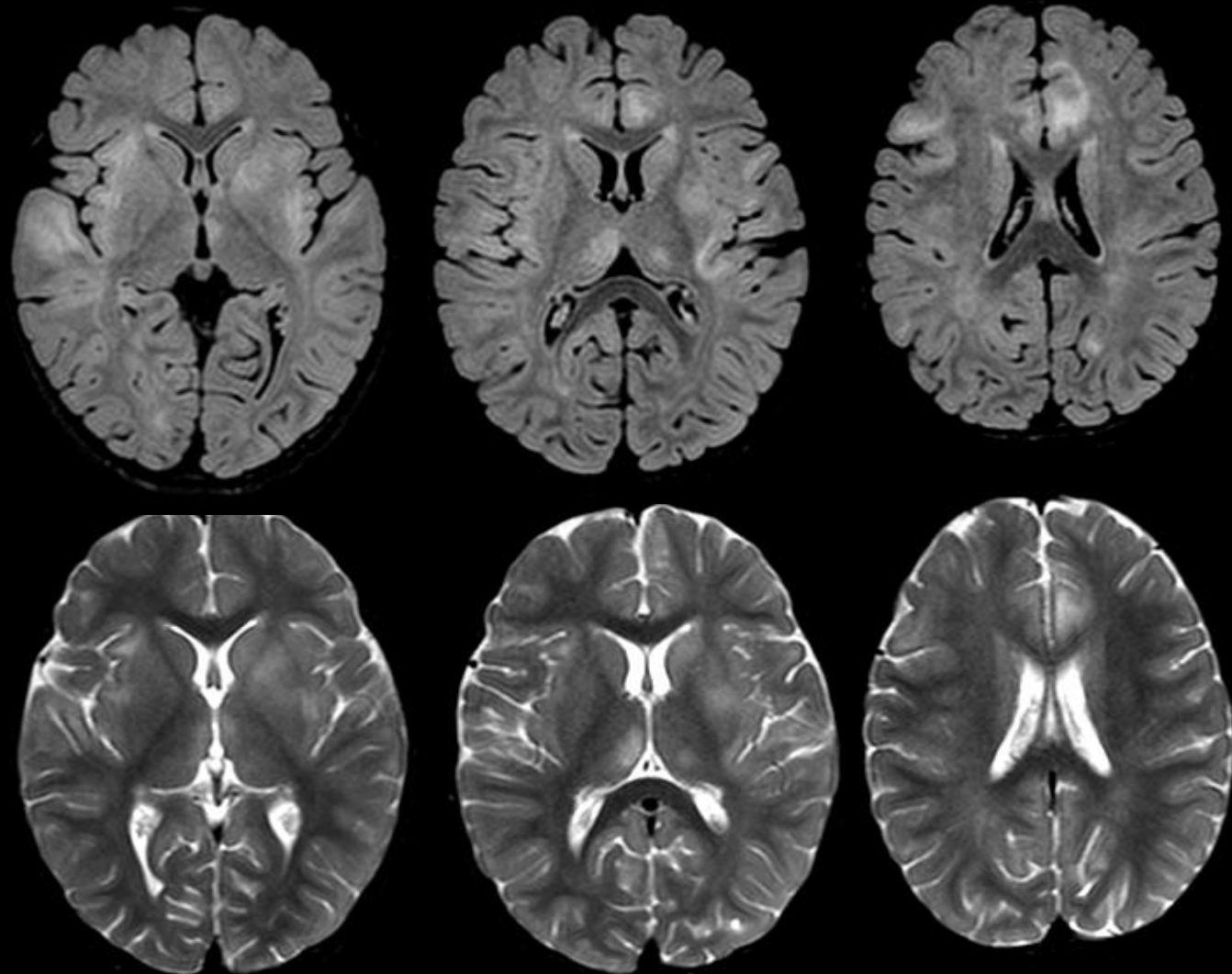


Lesion morphology

Fluffy aspect of WM lesions



MS

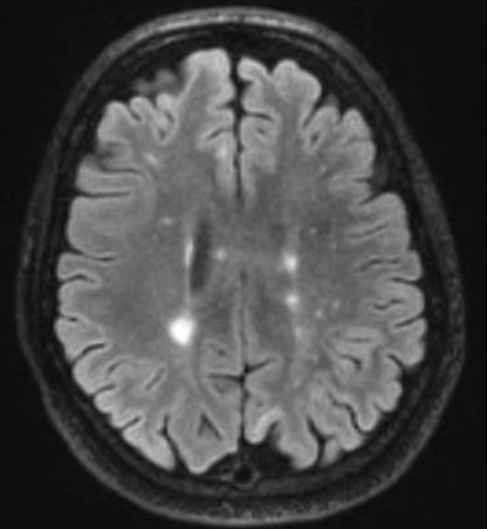
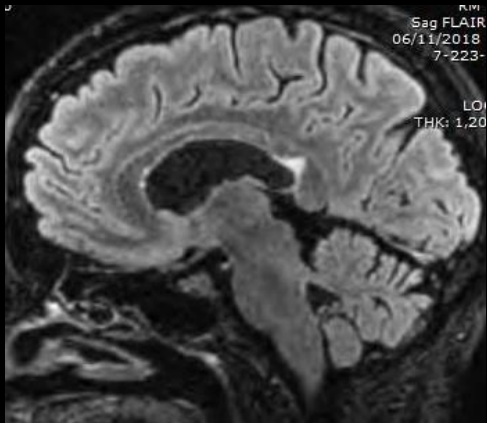


ADEM

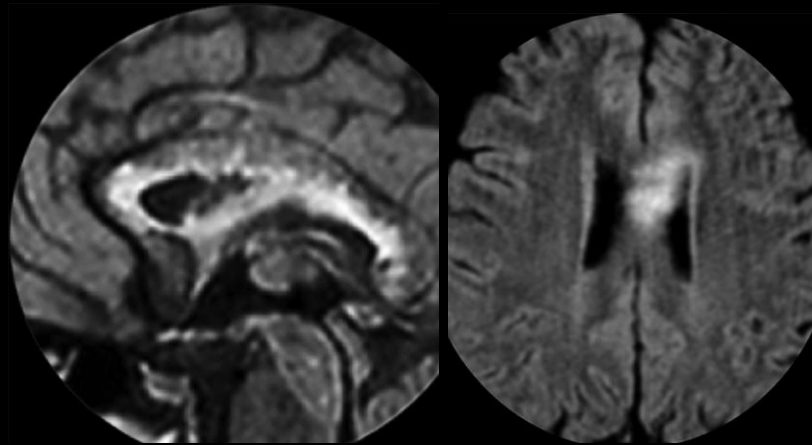
Lesion location

Peri-ependymal under corpus callosum in NMSOD

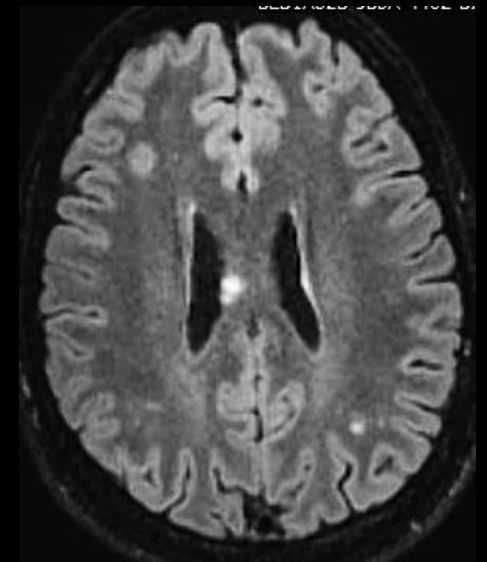
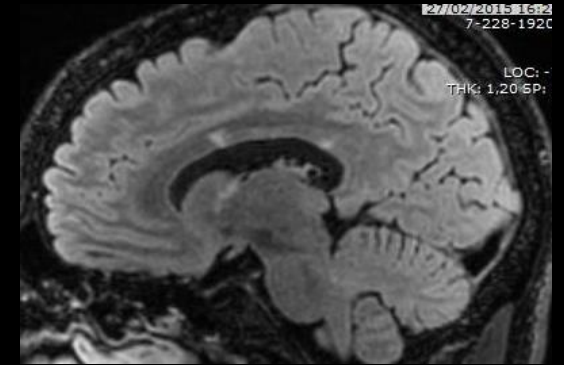
MS



NMOSD



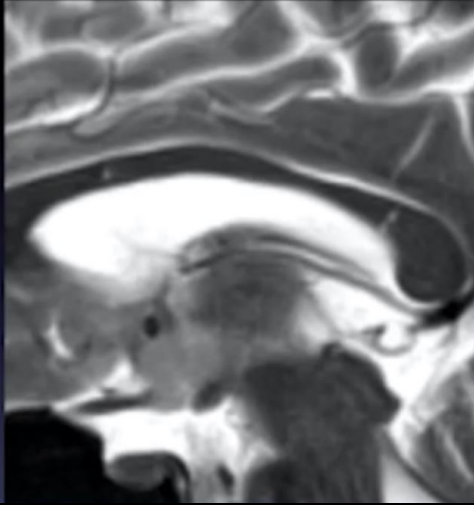
SUSAC



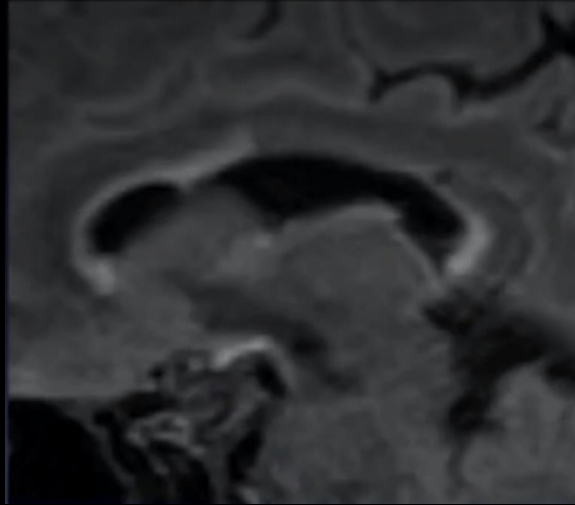
Marble pattern of the corpus callosum with the arch bridge appearance on axial images

Dutra et al Radiographics 2018

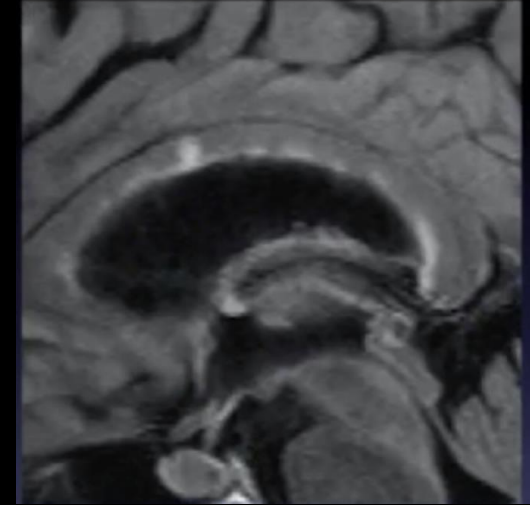
Calloso septal involvement



Susac:
Focal, central callosal

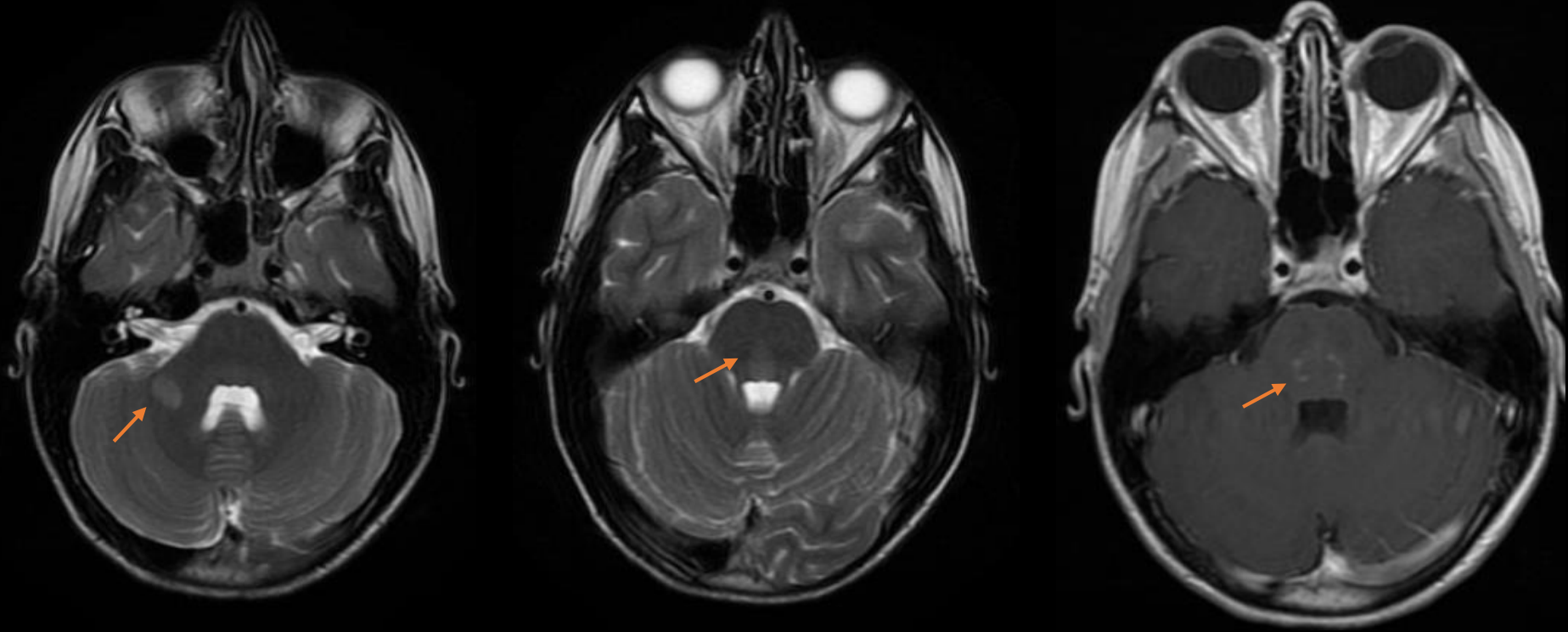


NMO:
Wide, long & thin ependymal



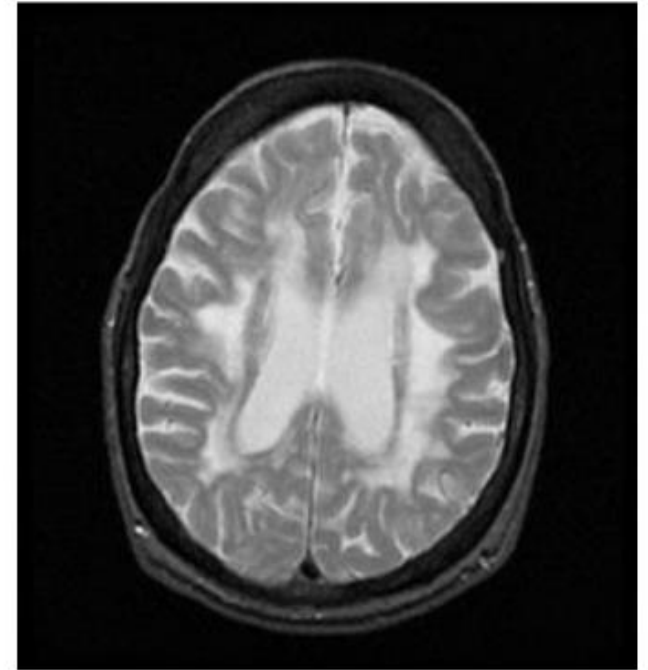
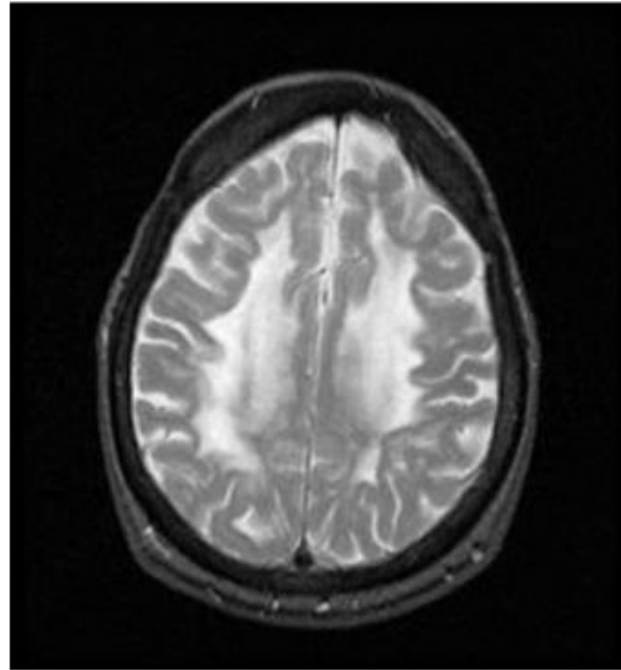
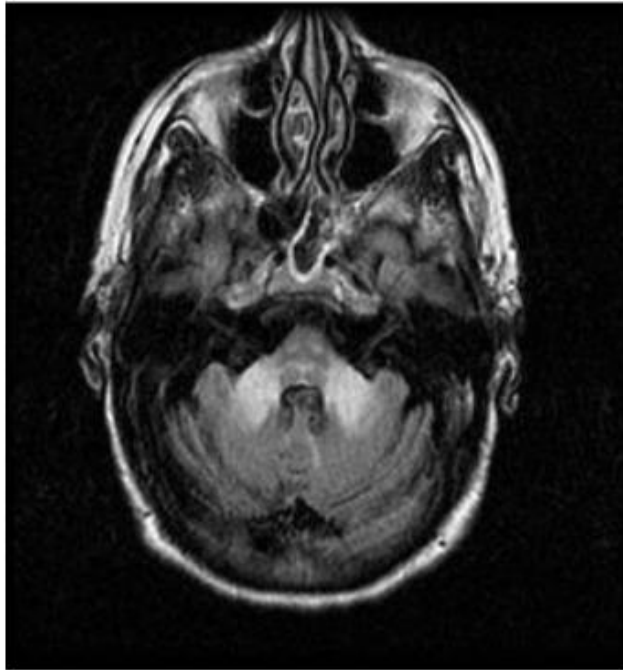
MS:
Focal, calloso septal

Atypical brainstem lesions



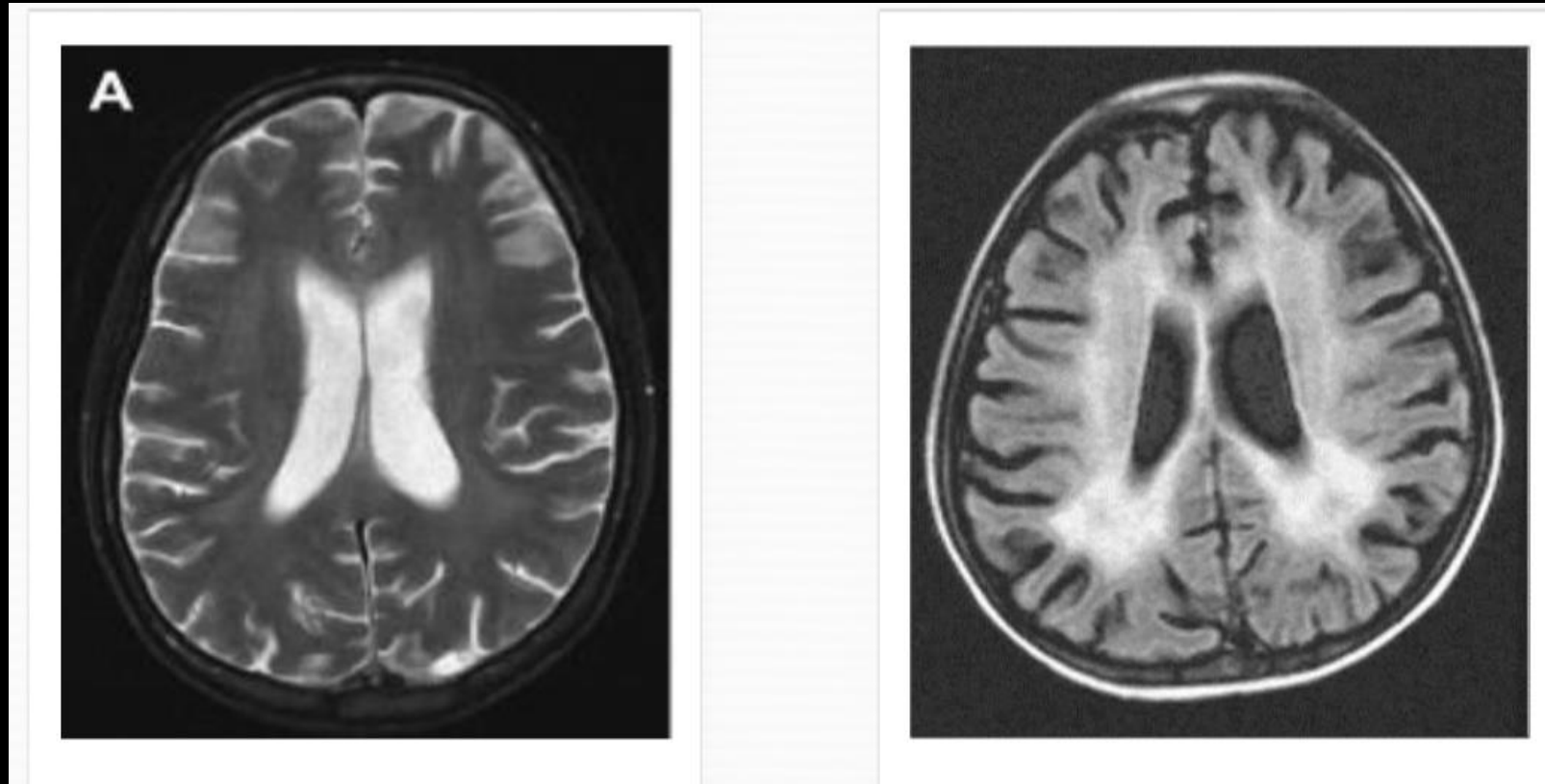
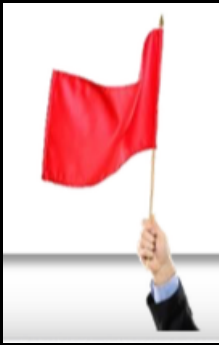
Neuro-Behçet

Diffuse/Symmetric white matter involvement



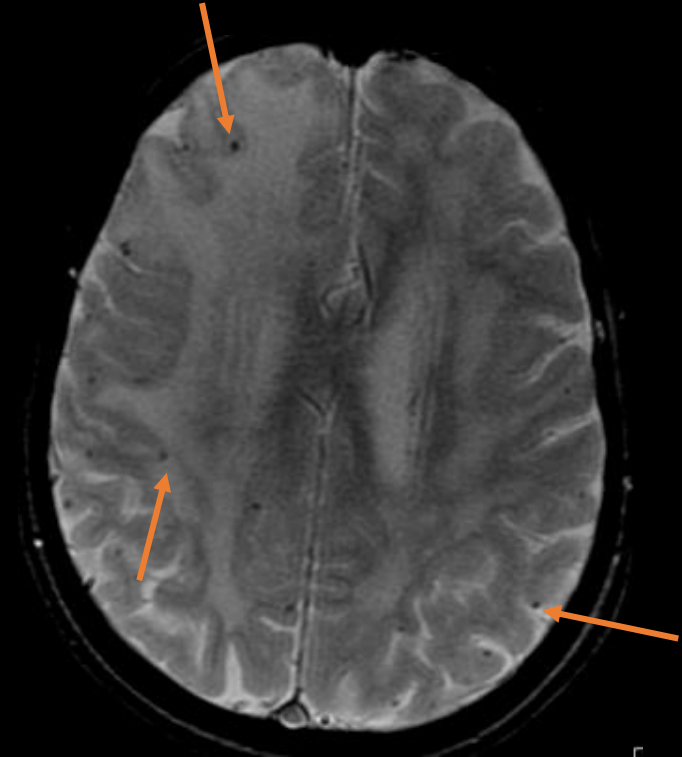
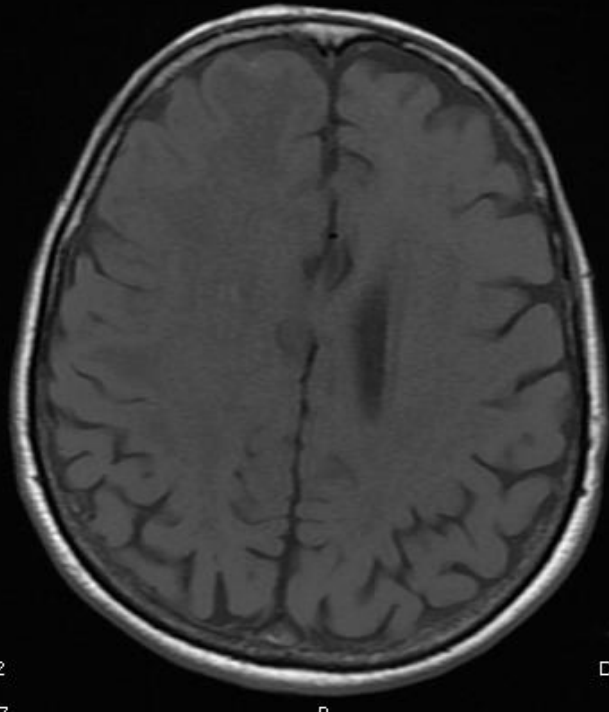
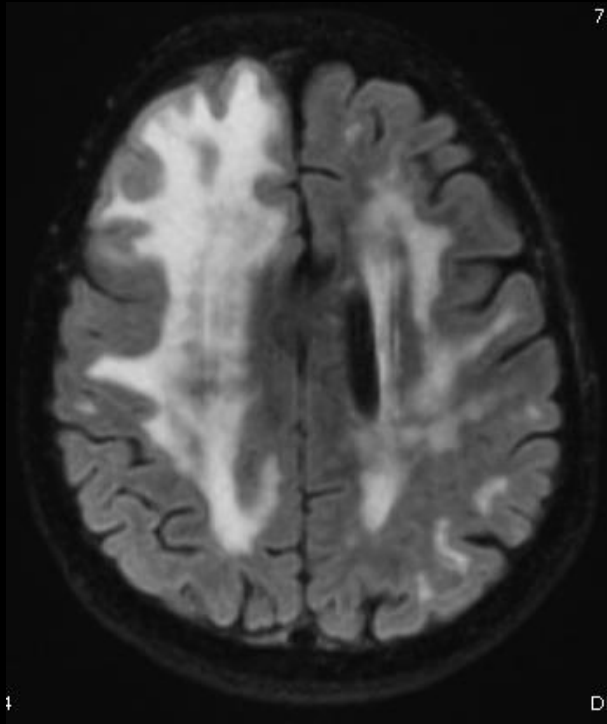
Adult onset AD Leukodystrophy

Diffuse/Symmetric white matter involvement



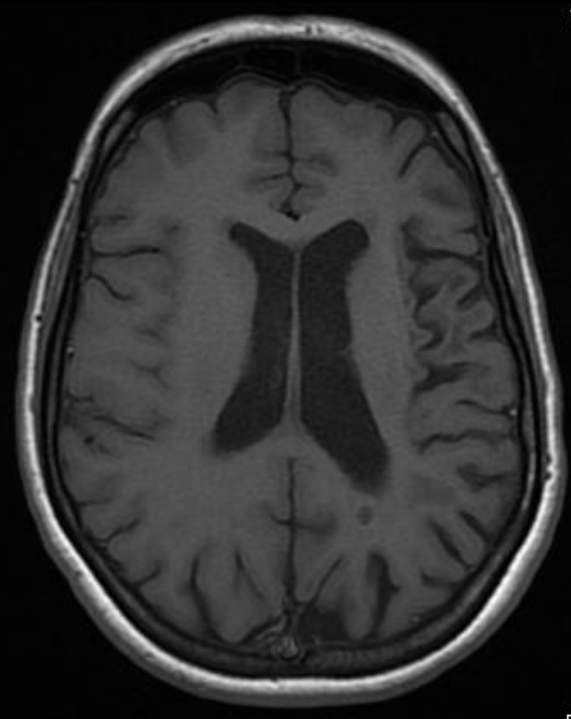
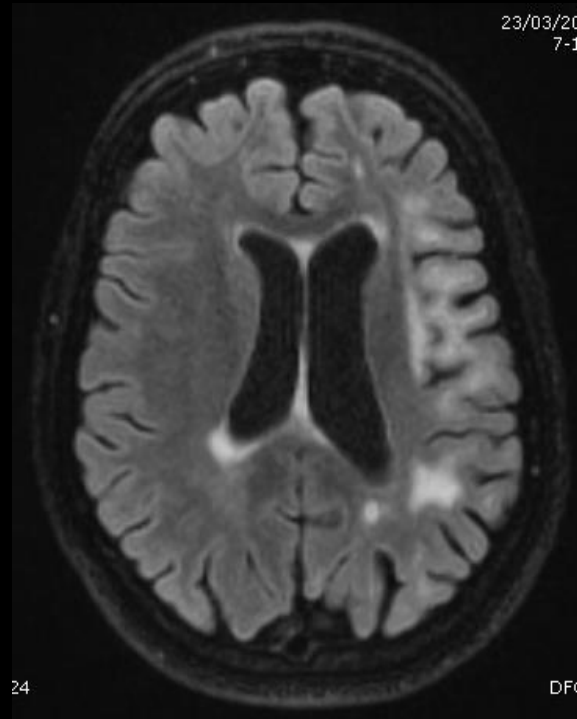
HIV related Encephalopathy

Microhemorrhage



Amyloid angiopathy

Poorly defined lesion border/ U fiber involvement



Progressive Multifocal Leukoencephalopathy

Differential diagnosis of PML in MS patients treated with natalizumab

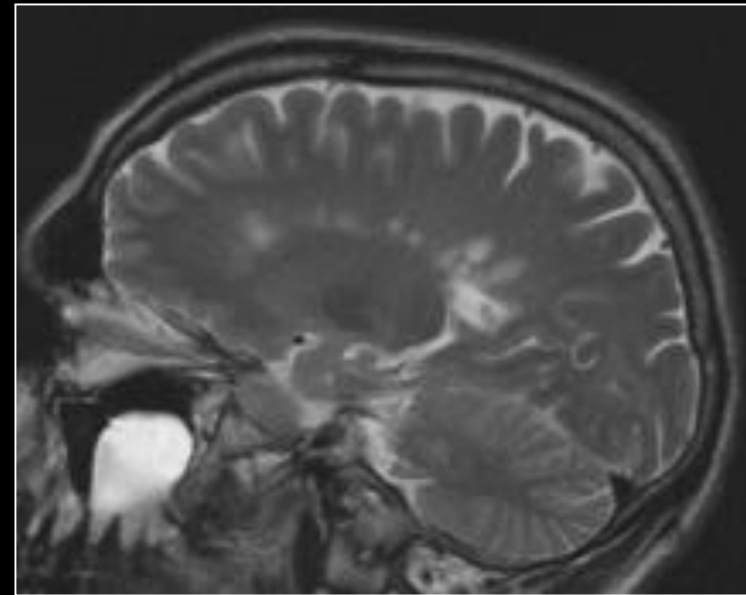
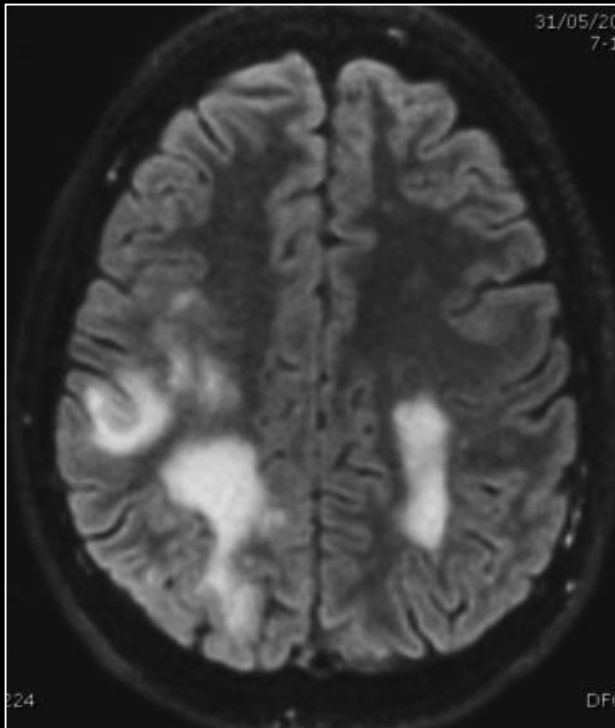
(location)

Natalizumab-associated PML

MS

Subcortical WM involving the U-fibers

Periventricular



Differential diagnosis of PML in MS patients treated with natalizumab

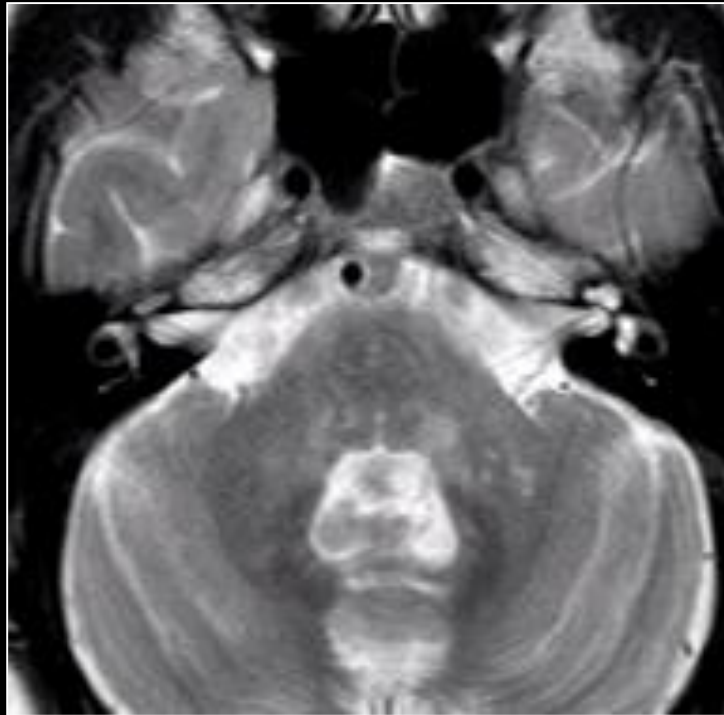
(location)

Natalizumab-associated PML

MS

Cerebellum

Cerebellum



Differential diagnosis of PML in MS patients treated with natalizumab

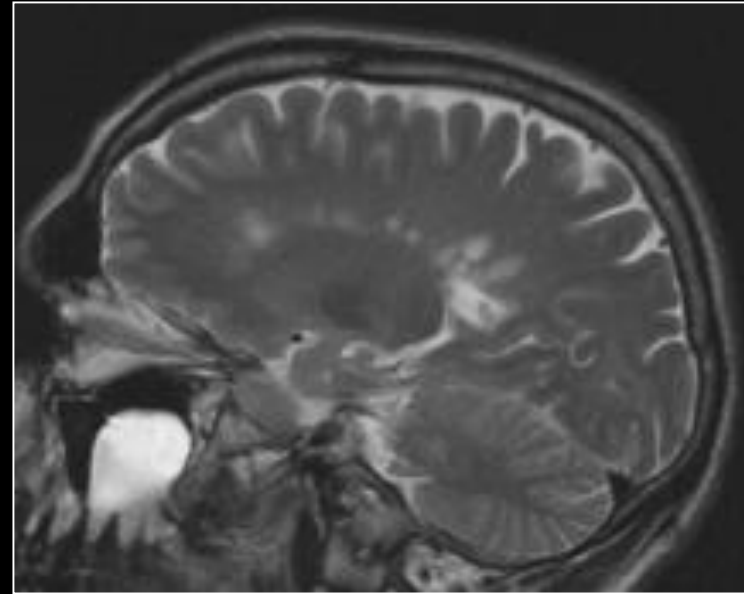
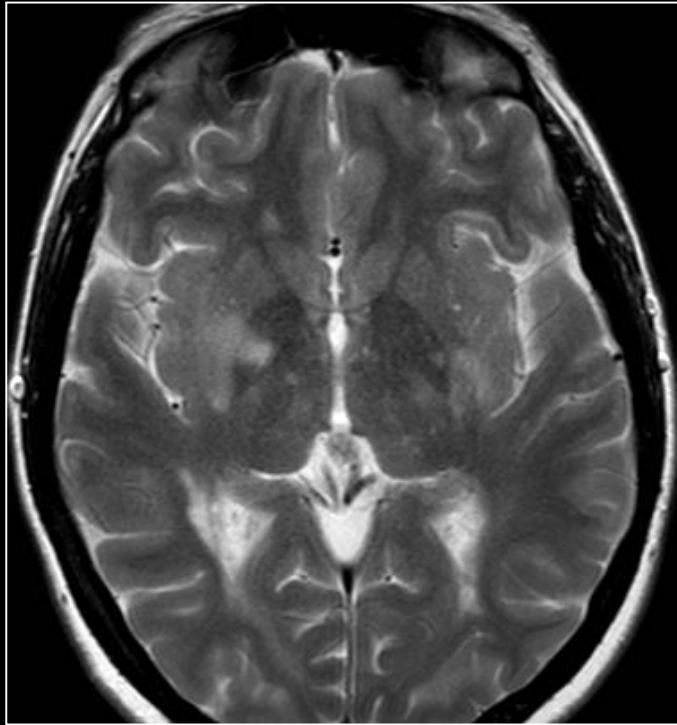
(location)

Natalizumab-associated PML

MS

Basal Ganglia

Periventricular



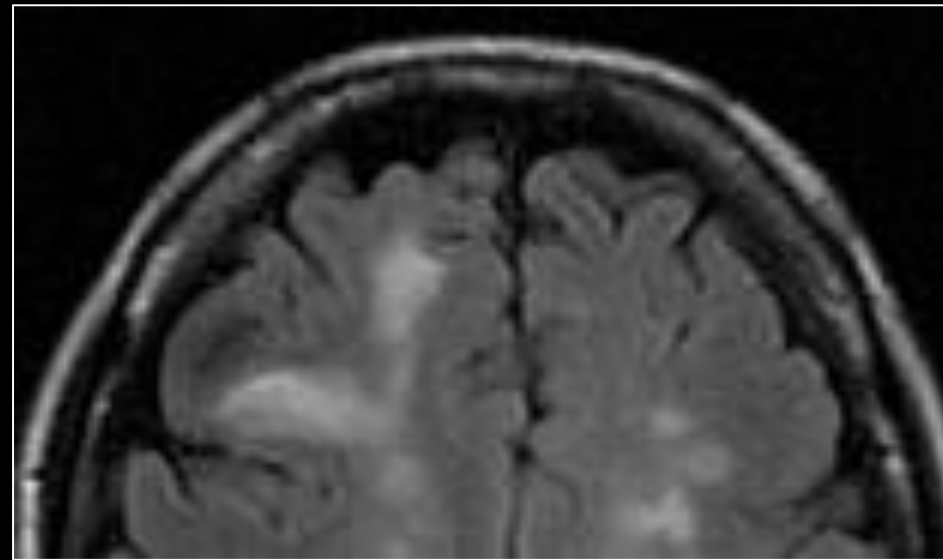
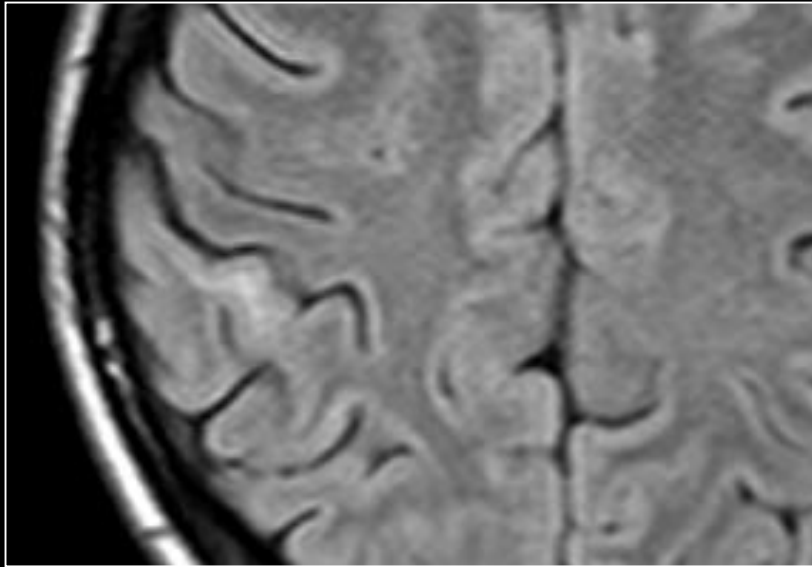
Differential diagnosis of PML in MS patients treated with natalizumab

Natalizumab-associated PML

MS

Infiltration of the adjacent GM

Juxtacortical



Differential diagnosis of PML in MS patients treated with natalizumab

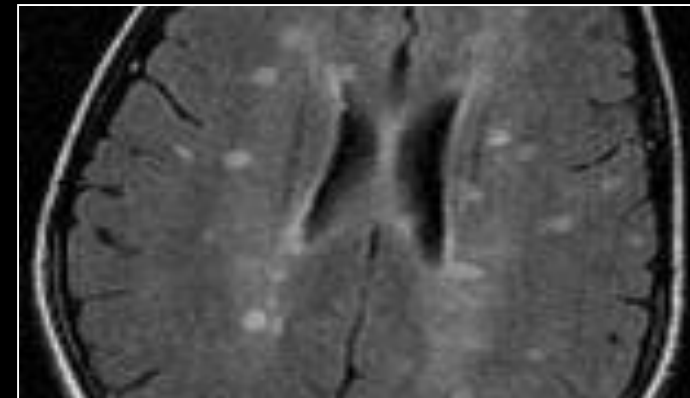
Natalizumab-associated PML

Fills the gyrus (heart of the gyrus)



MS

Perivascular distribution



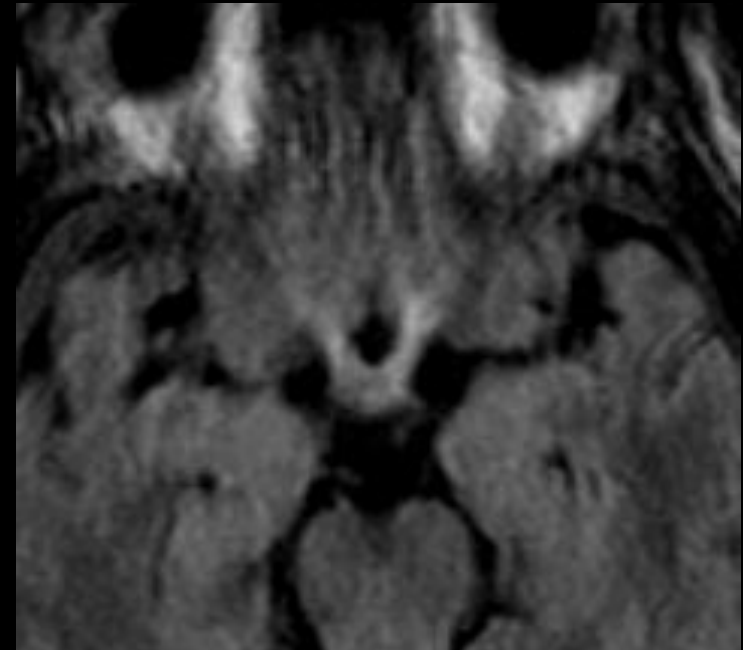
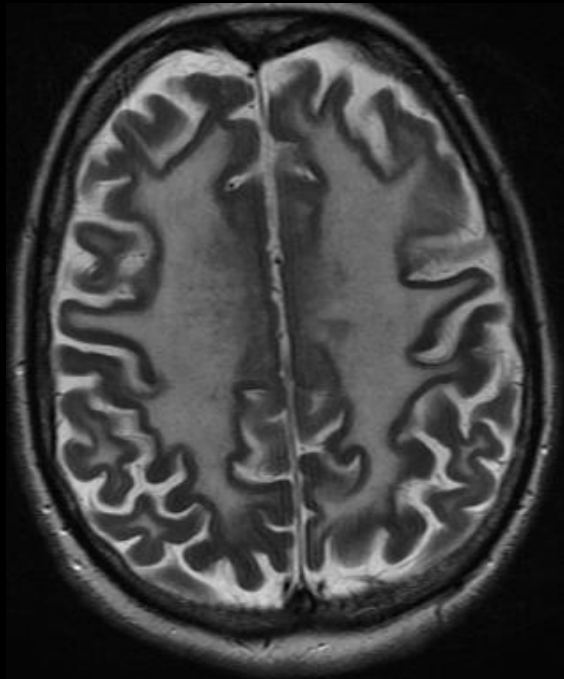
Differential diagnosis of PML in MS patients treated with natalizumab

Natalizumab-associated PML

MS

NOT Spinal cord and Optic nerves

Spinal cord and Optic nerves



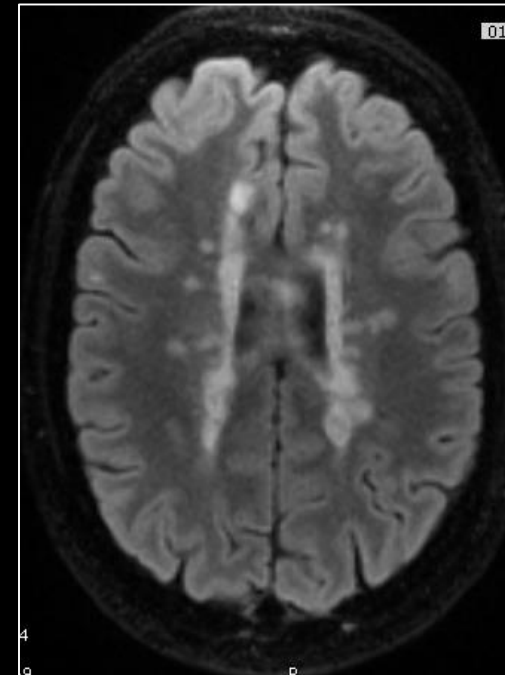
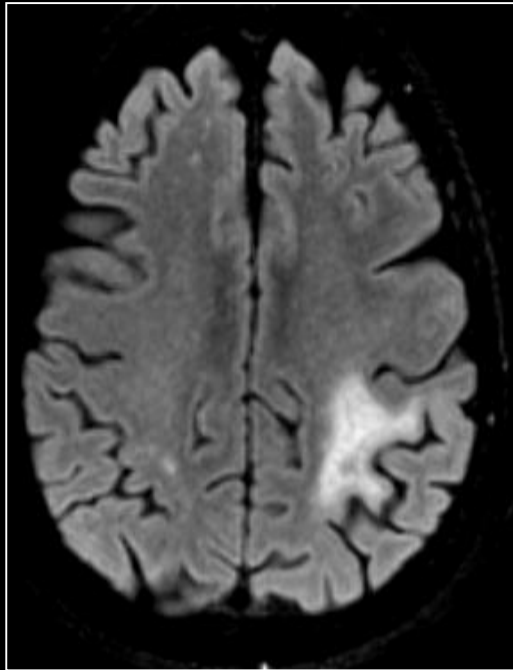
Differential diagnosis of PML in MS patients treated with natalizumab

Natalizumab-associated PML

MS

Large >3 cm

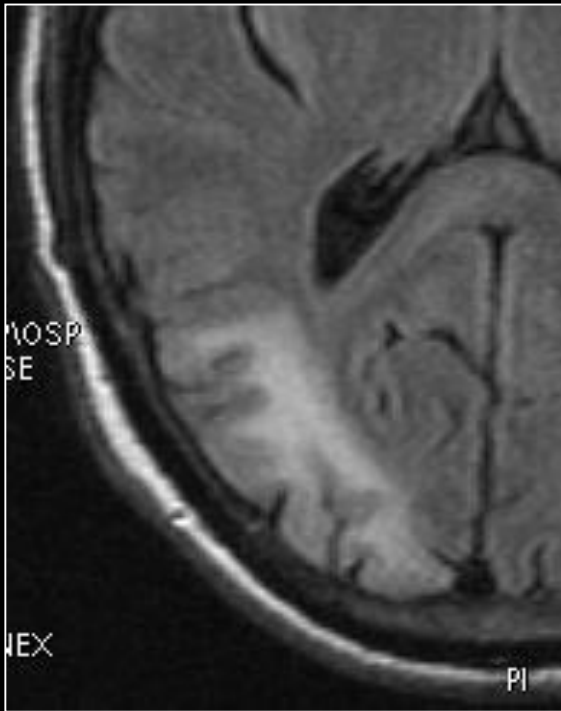
Small <3 cm



Differential diagnosis of PML in MS patients treated with natalizumab

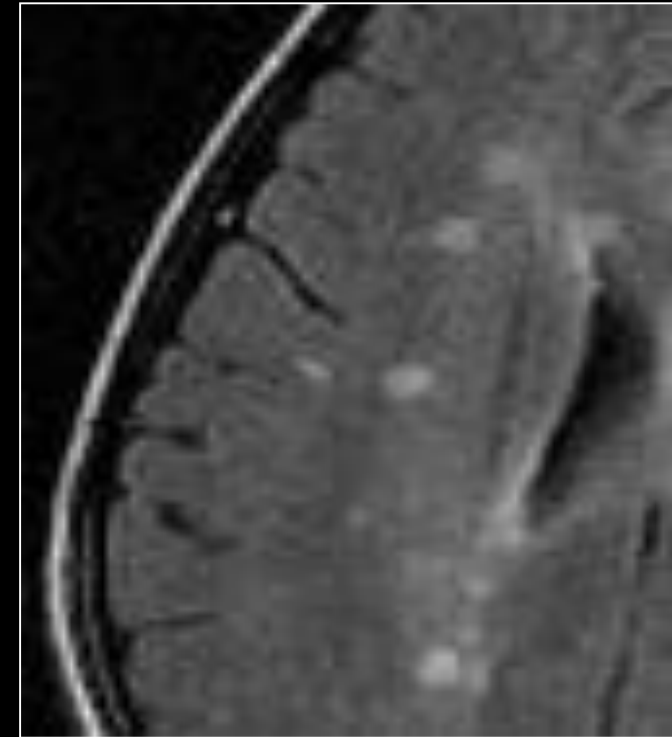
Natalizumab-associated PML

Confluent irregular



MS

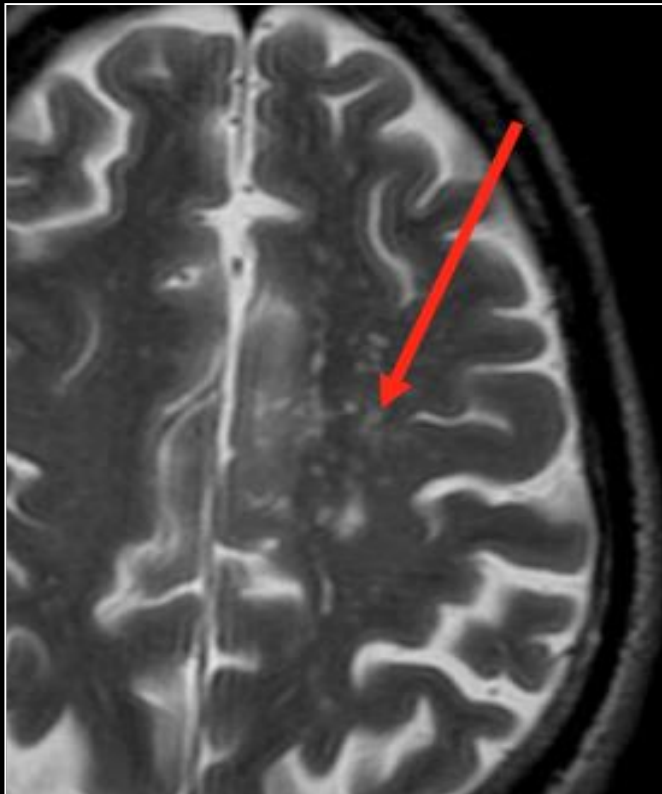
Round or ovoid shape



Differential diagnosis of PML in MS patients treated with natalizumab

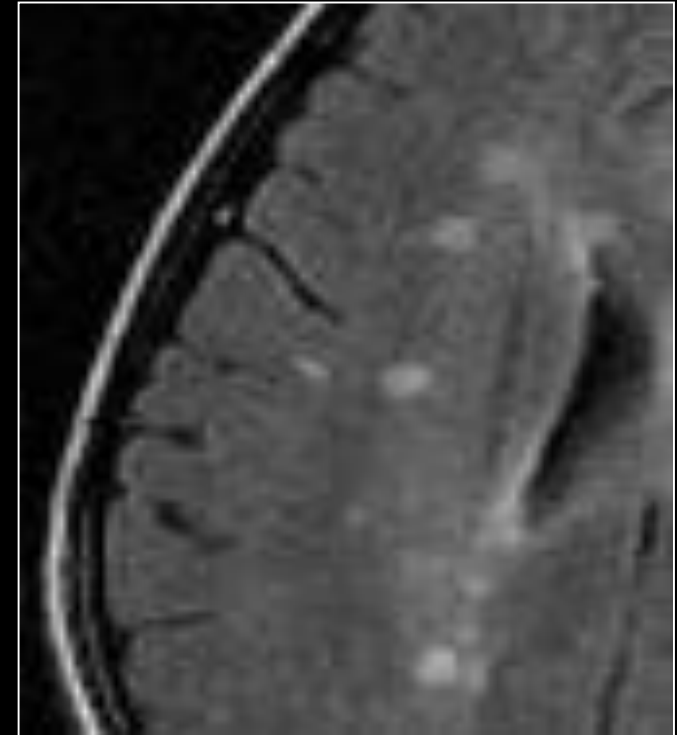
Natalizumab-associated PML

Microcysts (“milky way appearance”)



MS

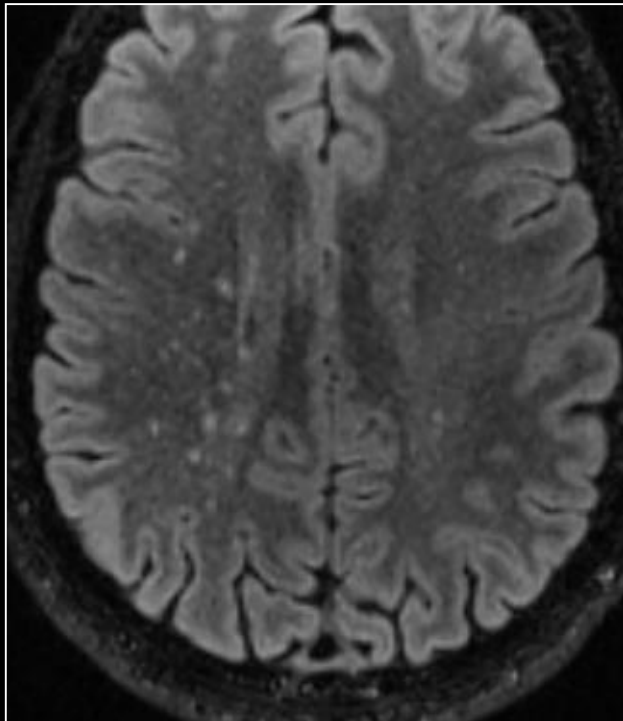
Round or ovoid shape



Differential diagnosis of PML in MS patients treated with natalizumab

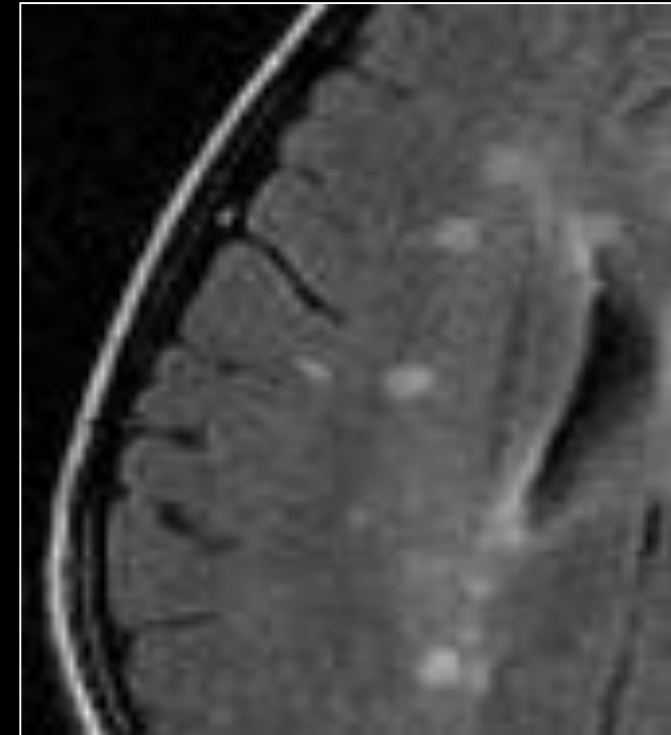
Natalizumab-associated PML

Multiple small focal lesions in the vicinity



MS

Round or ovoid shape



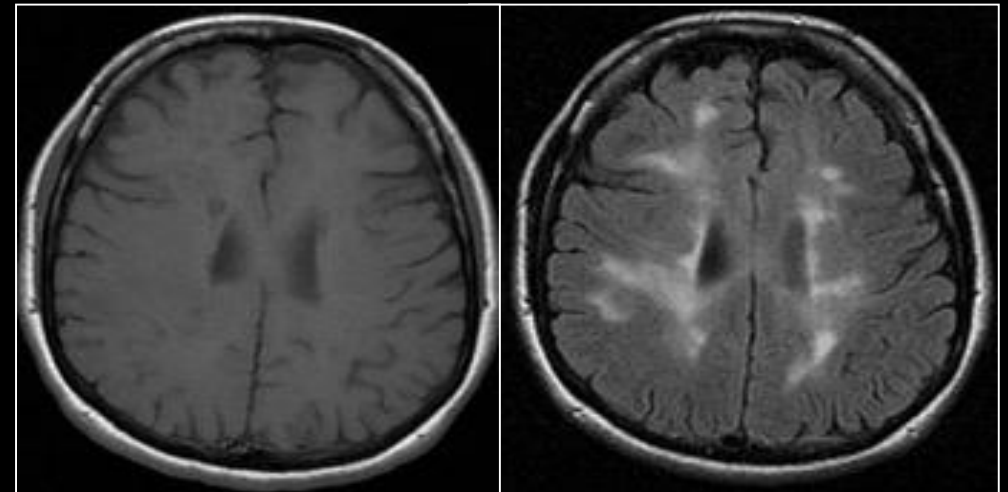
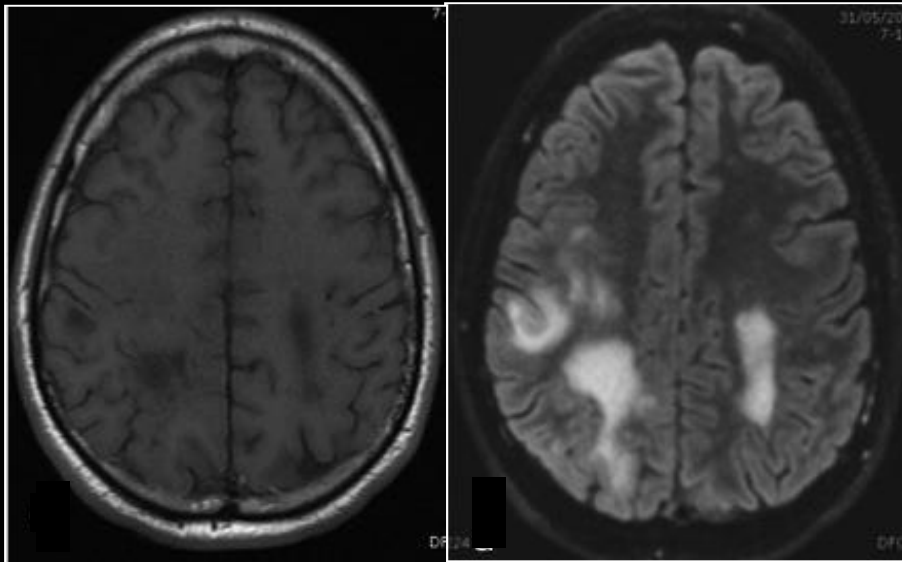
Differential diagnosis of PML in MS patients treated with natalizumab (Shape-Appearance)

Natalizumab-associated PML

MS

T1 hypointensity for demyelination

T1 isointensity for demyelination and black holes



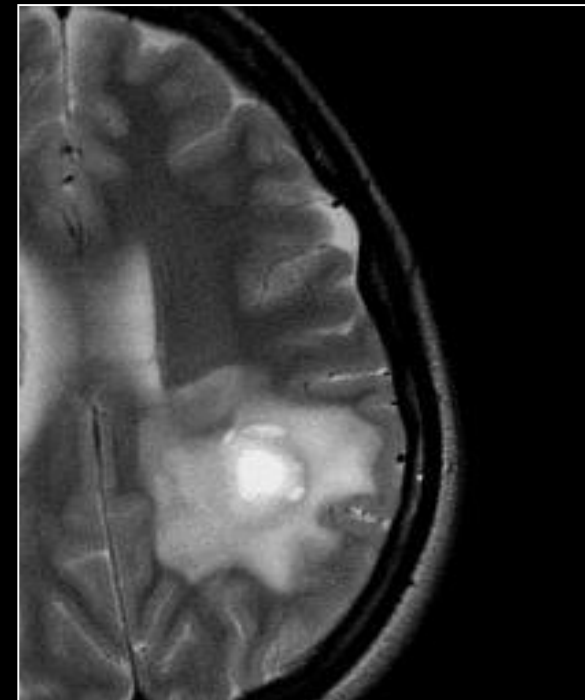
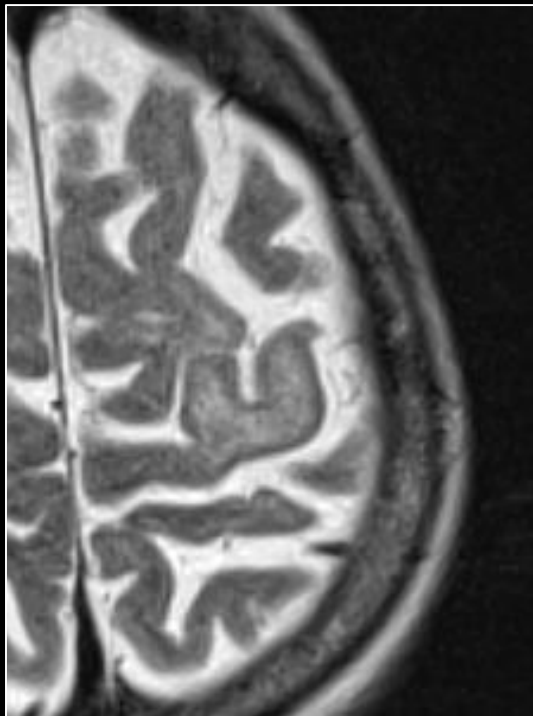
Differential diagnosis of PML in MS patients treated with natalizumab (Shape-Appearance)

Natalizumab-associated PML

MS

No mass effect

Mass effect



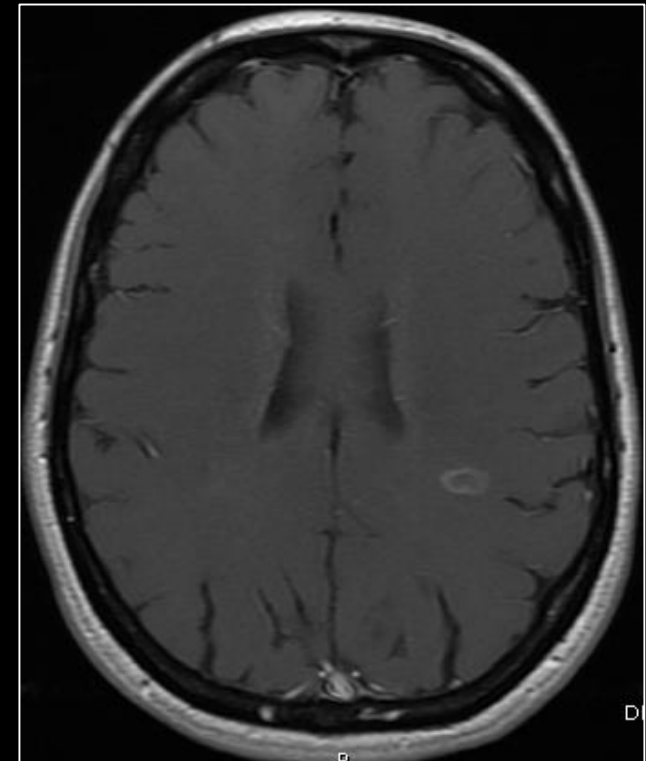
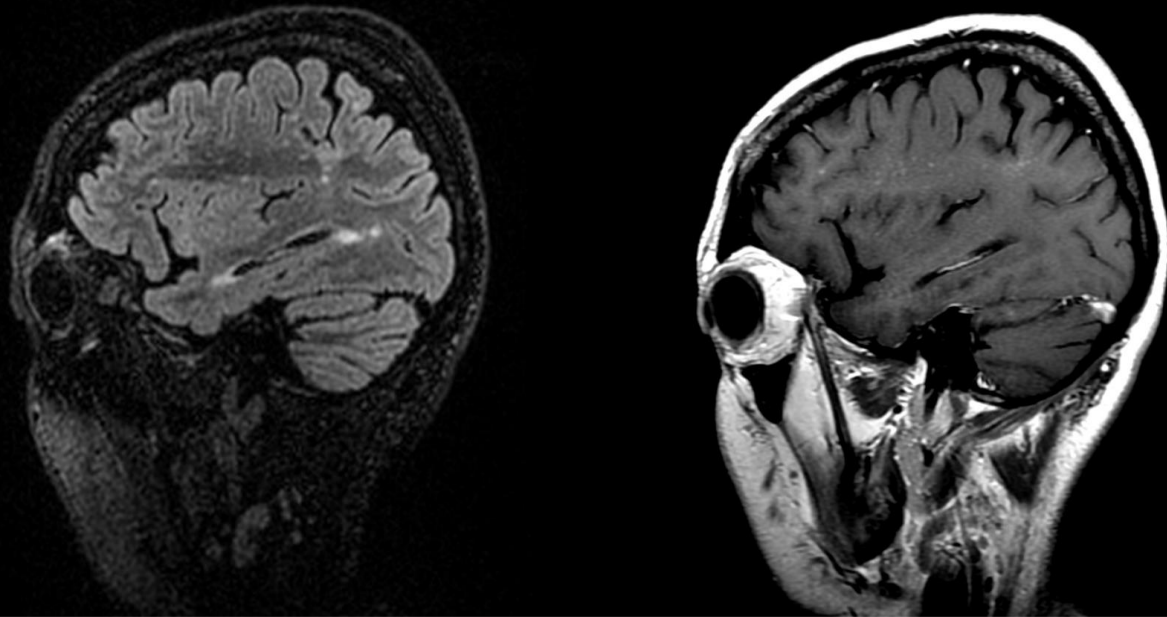
Differential diagnosis of PML in MS patients treated with natalizumab (contrast enhancement)

Natalizumab-associated PML

MS

Punctate- Perivascular

Ring like



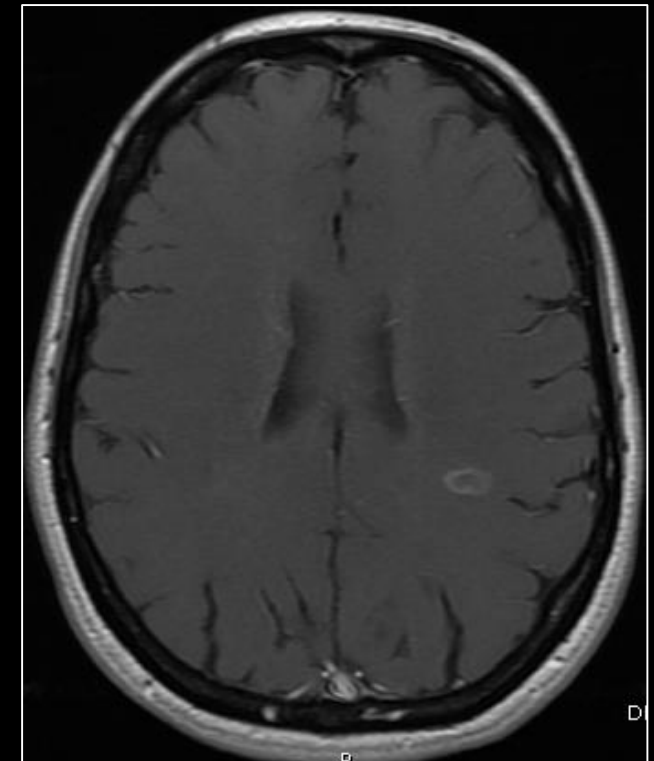
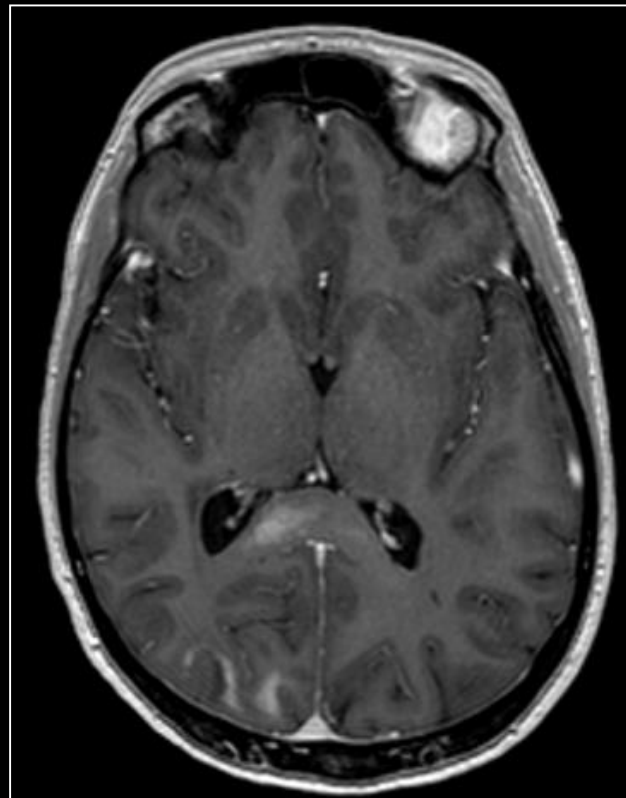
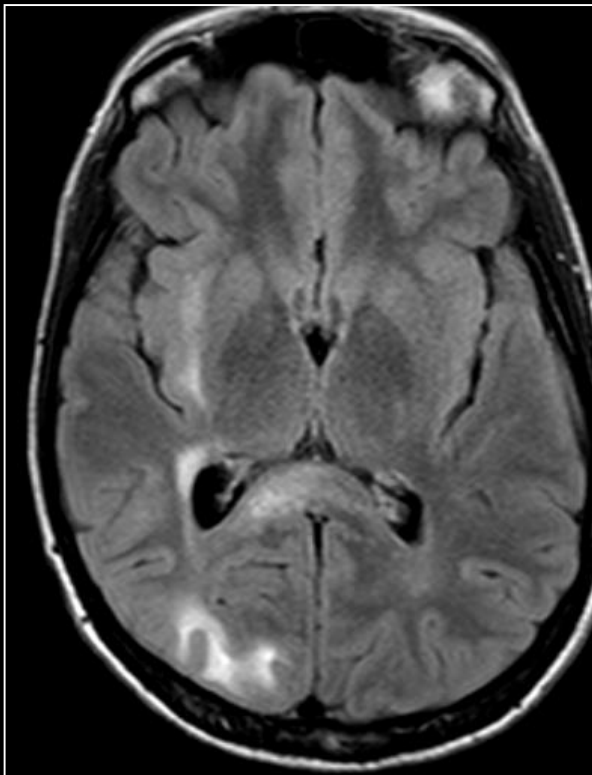
Differential diagnosis of PML in MS patients treated with natalizumab (contrast enhancement)

Natalizumab-associated PML

MS

Marginal

Ring like



MRI: role in diagnosis of MS

1. Dissemination in time
2. Dissemination in space
3. No better explanation



MRI and the diagnosis of multiple sclerosis: expanding the concept of "no better explanation"

Arnaud Charil, Tarek A Yousry, Marco Rovaris, David H Miller, Stefano Steffano, Franz Fazekas, David H Miller, Xavier Montalban, Jack H Simon, Chris Polman, Massimo Filippi

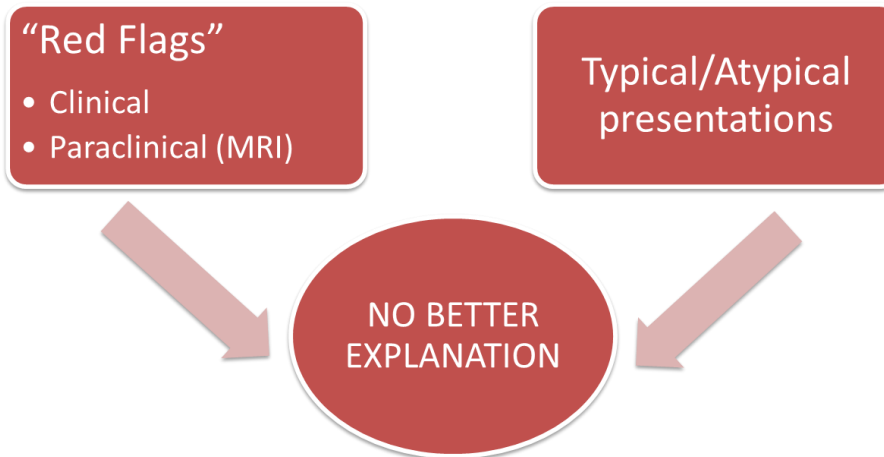
REVIEW

Multiple Sclerosis 2008; 14: 1157–1174

Differential diagnosis of suspected multiple sclerosis: a consensus approach

DH Miller¹, BG Weinshenker², M Filippi³, BL Banwell⁴, JA Co
M Hutchinson⁸, RT Johnson⁹, L Kappos¹⁰, J Kira¹¹, FD Lublin⁷
H Panitch¹⁵, JR Richert¹⁶, SC Reingold^{16,17} and CH Polman¹⁸

Diagnosis of MS Ensure that there is no better explanation



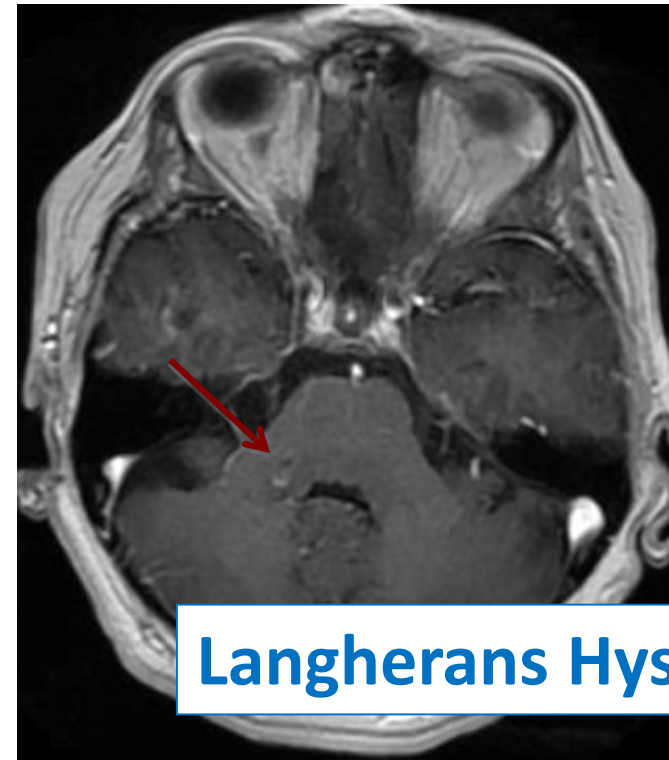
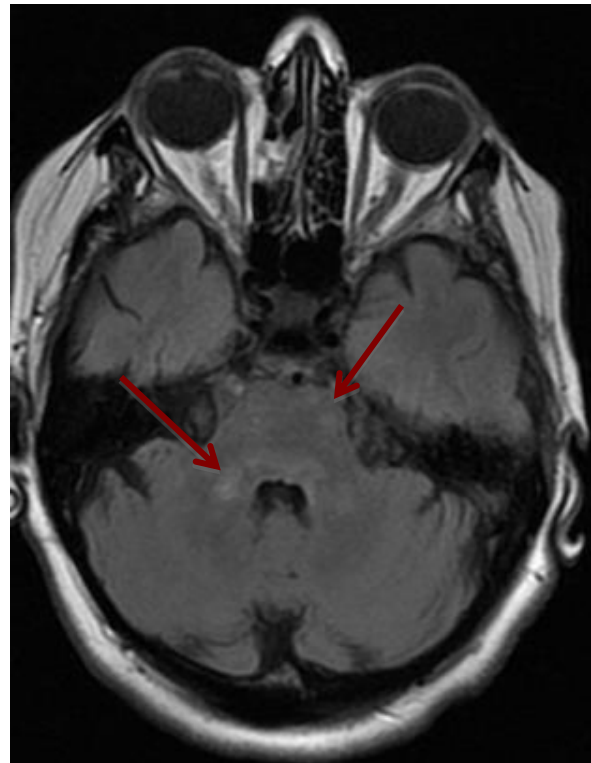
Misdiagnosis: some cases

- Female, 50 years old
- Presenting symptoms with cerebellar syndrome
- Responsive to corticosteroid treatment
- Negative immunoblot

History of diabetes insipidus

Evidence of ulcerated palatal lesions

DIS +, DIT +



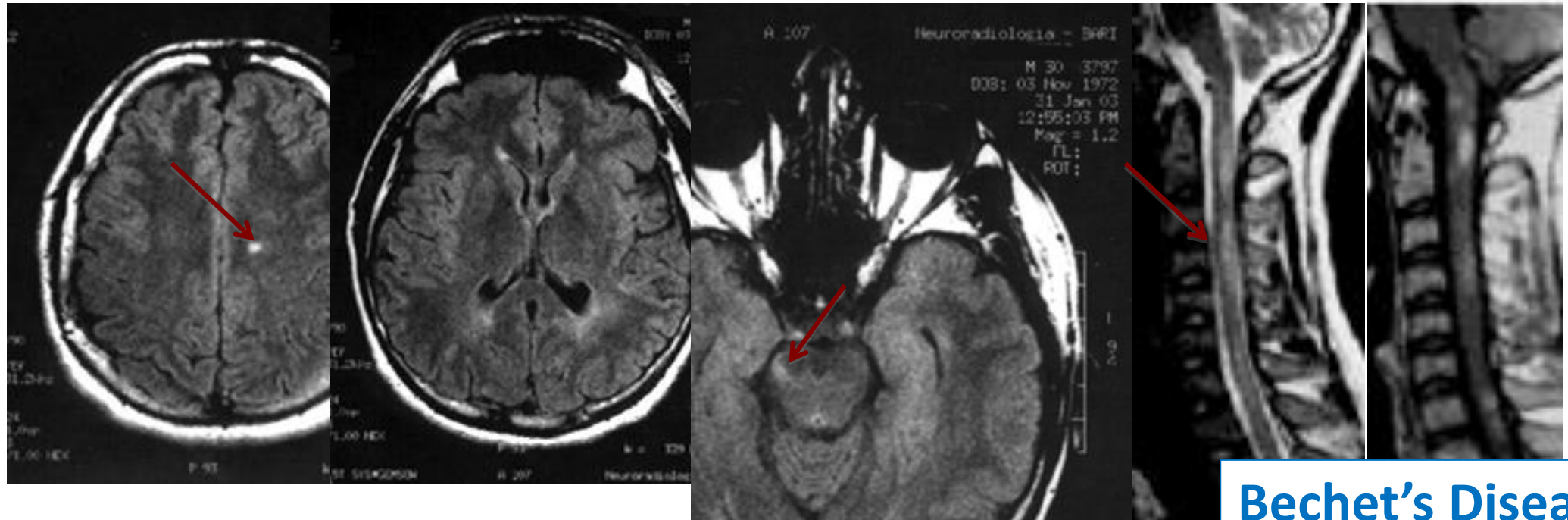
Langherans Hystiocitosis

Misdiagnosis: some cases

- Male, 39 years old
- Recurrent arthritis
- Two episodes of scotoma in the last 3 years
- Sudden paraparesis
- Immunoblot positive

Mucosal ulcers

HLA B51+
Pathergy test +



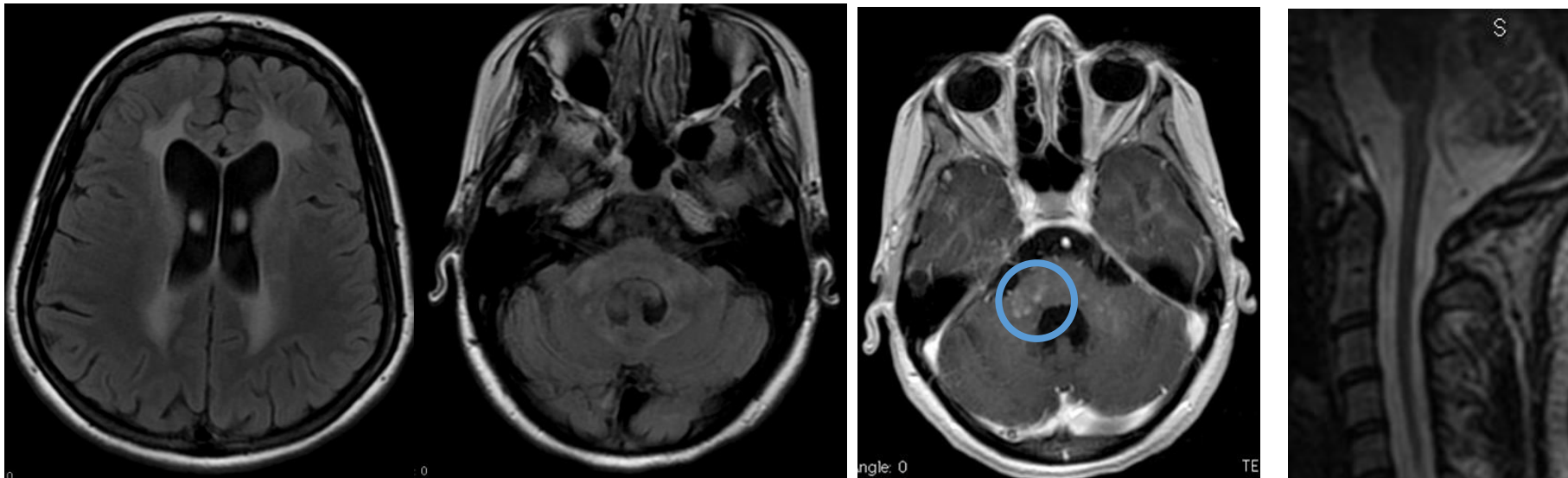
DIS +, DIT +

Bechet's Disease

Misdiagnosis: some cases

- Female, 22 years old
- Scoliosis of high severity
- Since childhood difficulties during running
- Ataxia spastic paraparesis
- Negative immunoblot

*Heterozygous mutations of
GFAP gene exon I
(missense substitution
c1246C>T R416W)*

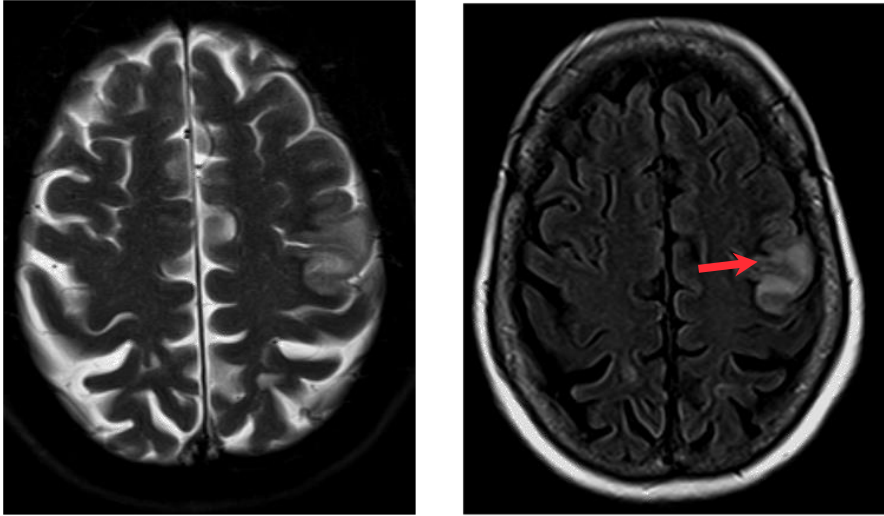


DIS +, DIT +

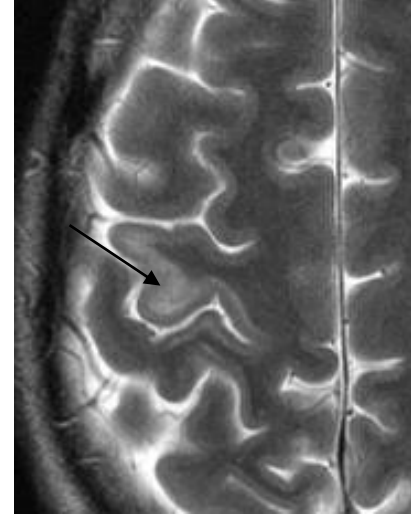
Malattia di Alexander

Patologia della sostanza bianca vs patologia della corteccia

Case 1

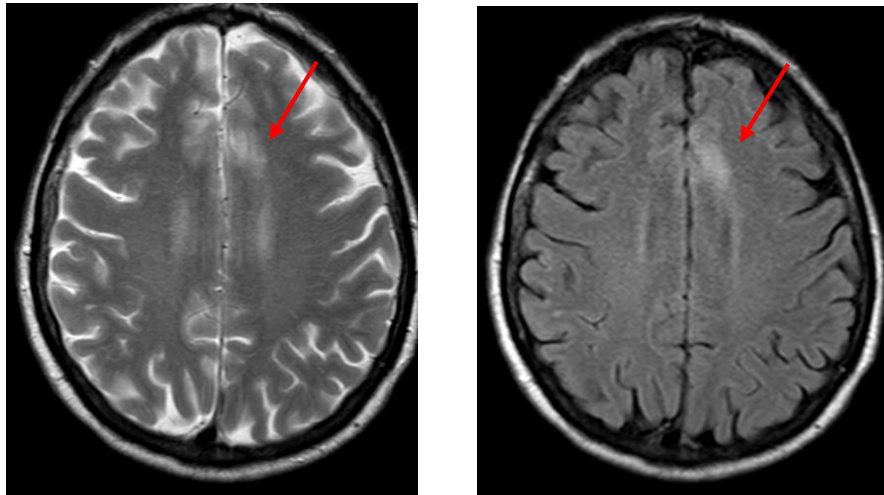


Case 2

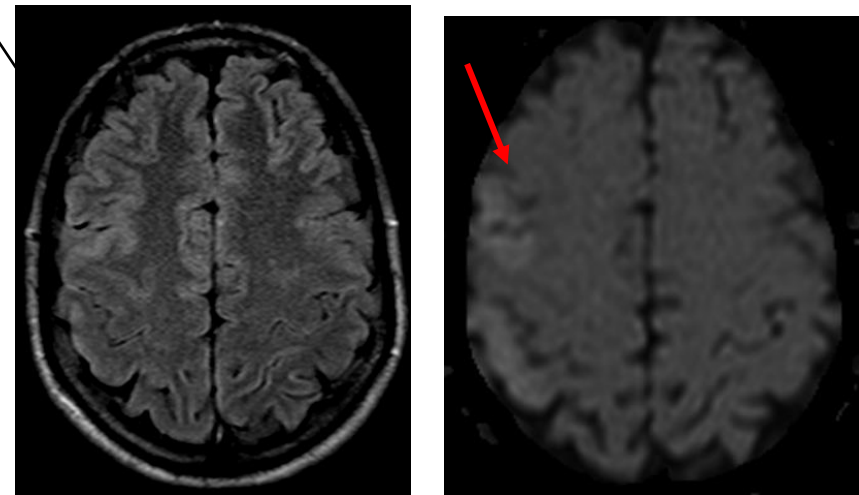


- 1) MS
- 2) PML
- 3) Vascular
- 4) Post epileptic

Case 3

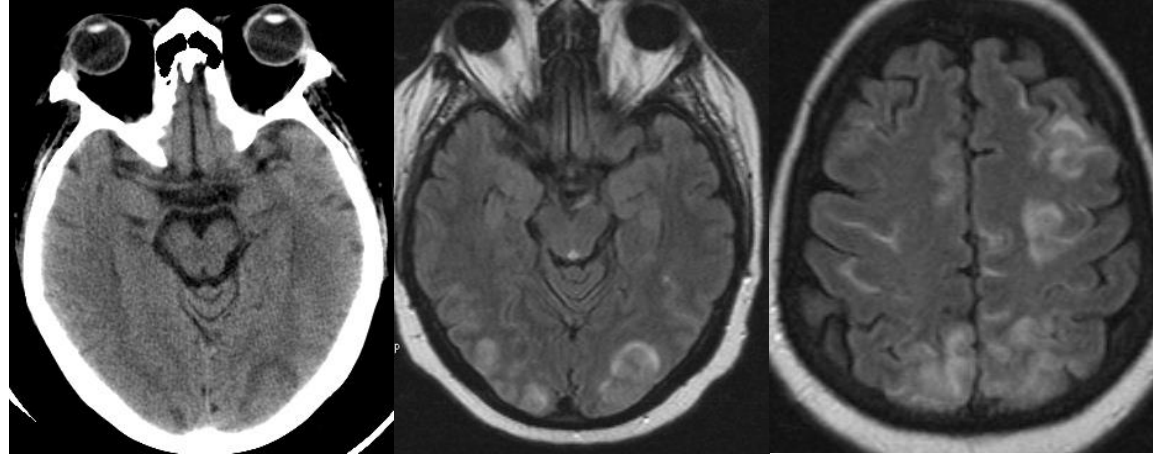


Case 4

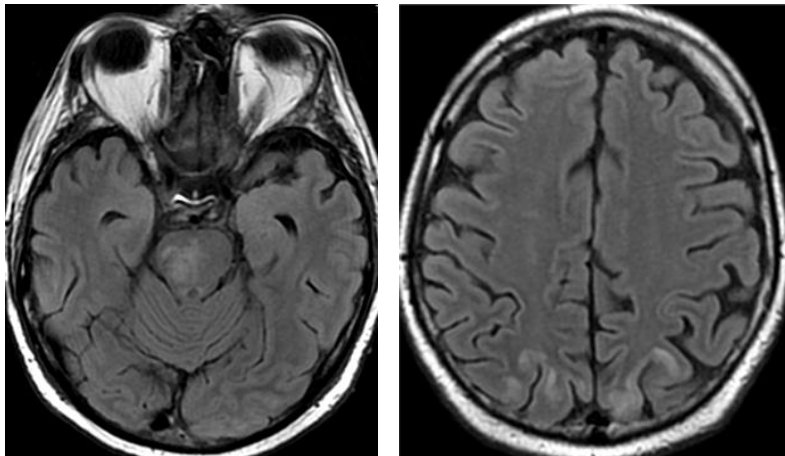


Patologia della sostanza bianca vs patologia della corteccia

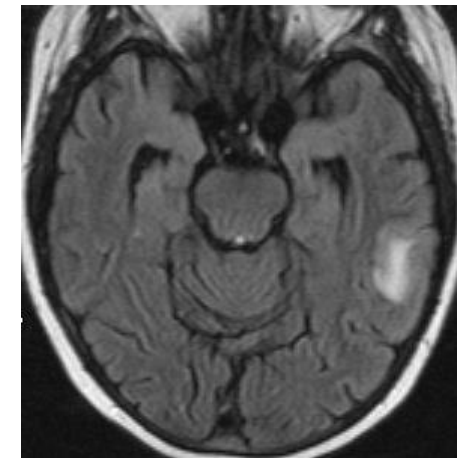
Toxic disorders



Ciclosporine



Ciclophosfamide



Tacrolimus

CONCLUSIONI: è UNA SM???

- SEDE, NUMERO, MORFOLOGIA DELLE LESIONI, SIMMETRIA DI DISTRIBUZIONE

- SEGNALE TUE, TOWIE' ANCORA TUTTO DA VEDERE.

- PRESA DI CONTRASTO

- EVOLUZIONE NEL TEMPO

- CLINICA DEL PAZIENTE!!!!



Ringraziamenti e collaborazioni

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Dott.ssa Valeria Barcella

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Dott.ssa Cristina Scarpazza

