

Opportunistic CNS Infections

(What is that brain lesion on MRI in your patient with HIV and a CD4 count less than 50?)

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Disclaimer

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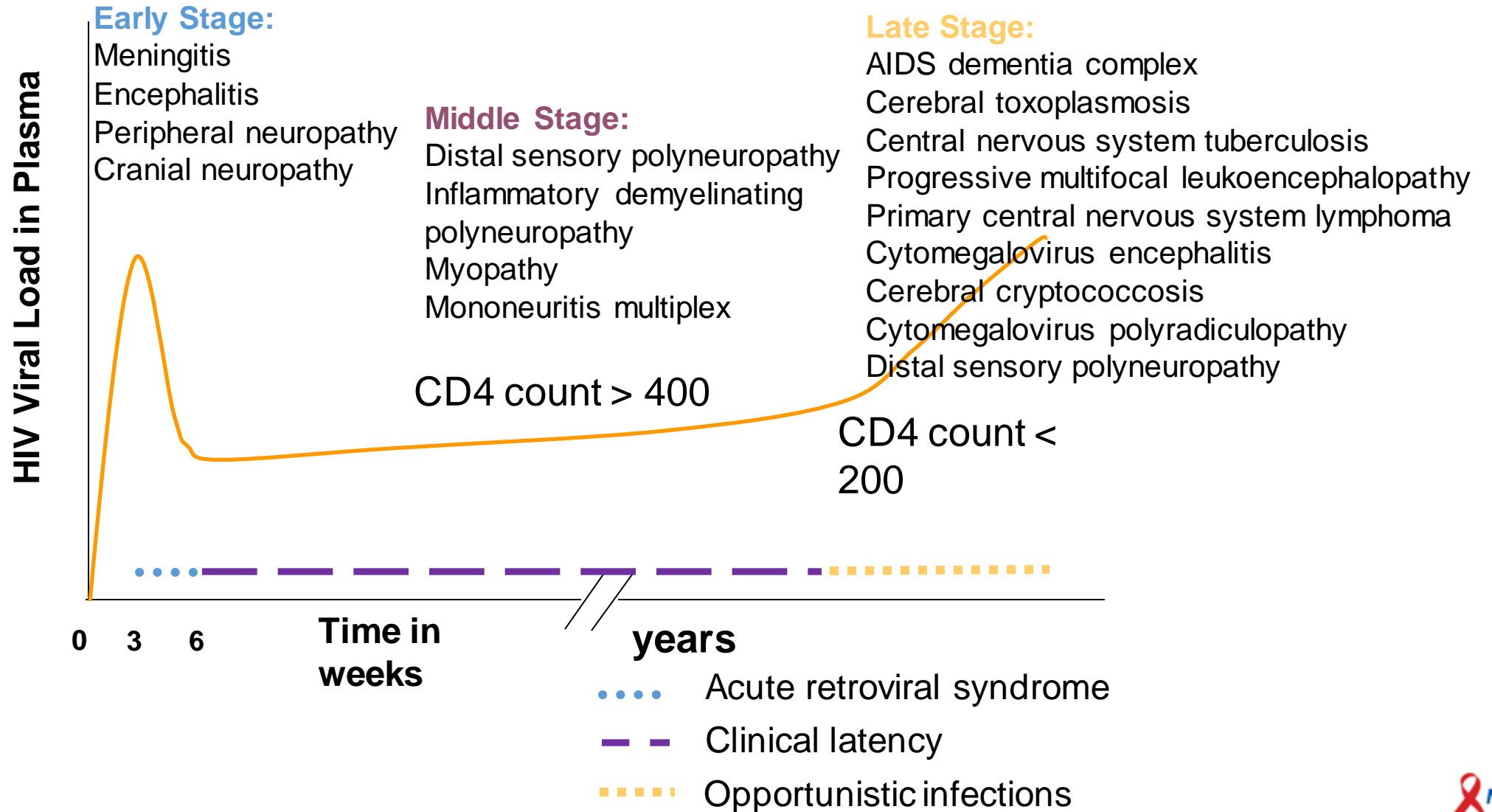
Mr. P: the headache

36 year old man living with HIV from Mexico with a headache and left arm weakness.

Key history questions in Patients with HIV

- Absolute CD4 count, HIV VL.
- On or off antiretroviral therapy (ART)?
- Which stage of HIV infection?
- On any prophylactic therapy?
- Any recent opportunistic infections/conditions?
- Travel and exposure history

Time Course of Events in HIV-1 Infection

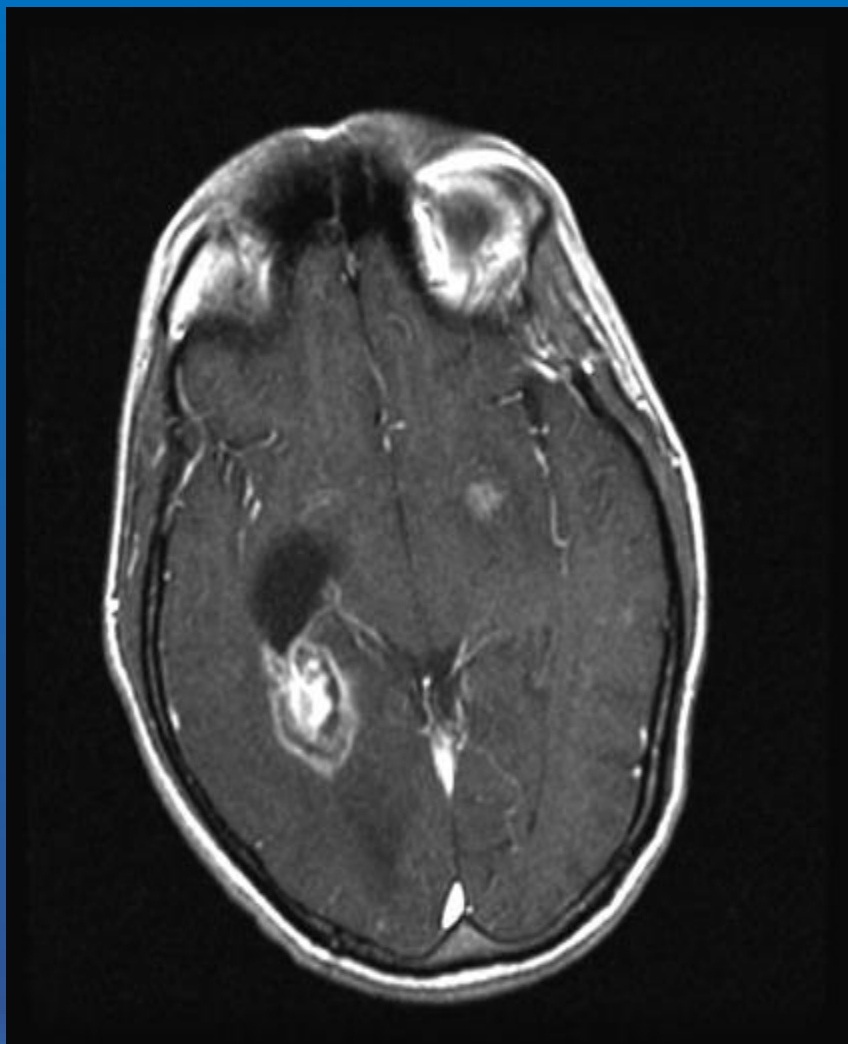


Back to Mr. P and the headache

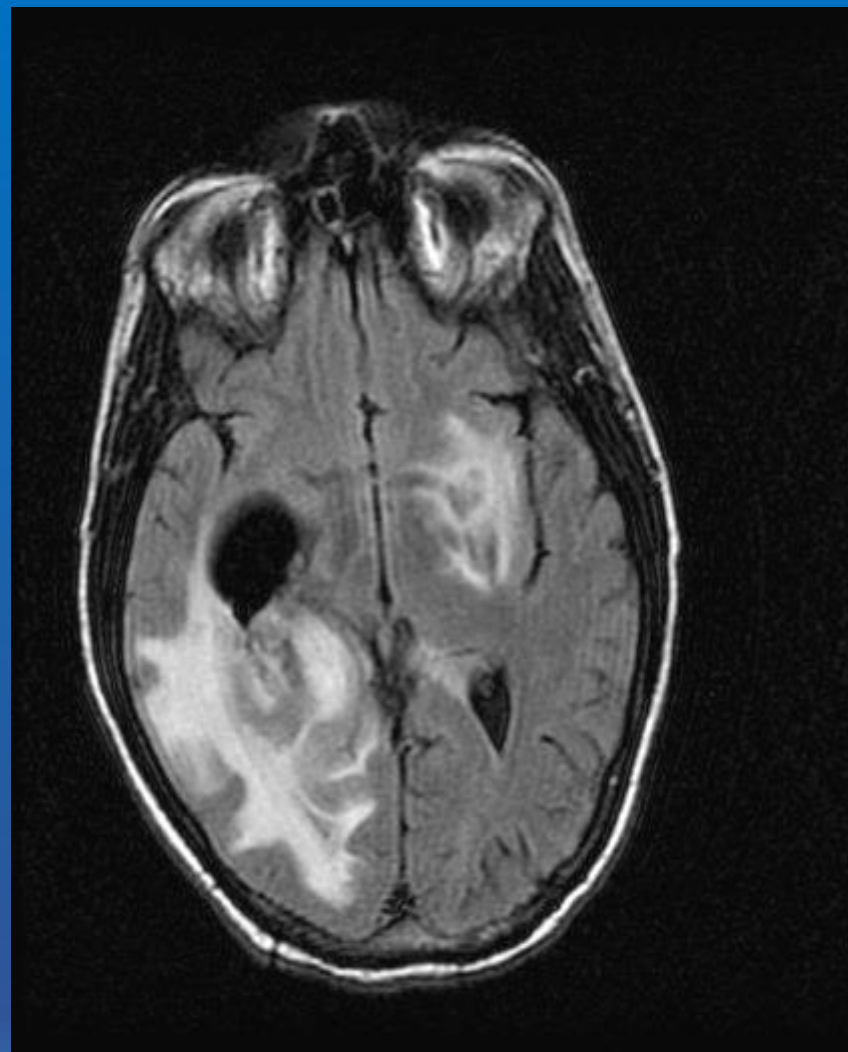
36 yo man living with HIV from Mexico with a headache and left arm weakness.

- CD4 count 30, VL unknown
- Off of ART for two years
- HIV diagnosed in 1991
- Not on any prophylactic medications
- Recently presented with CMV esophagitis
- Wants re-establish care and start antiretroviral therapy

Mr. P - MRI Scan



T1 MRI with gadolinium



FLAIR MRI

Focal CNS lesions in immunocompromised patients

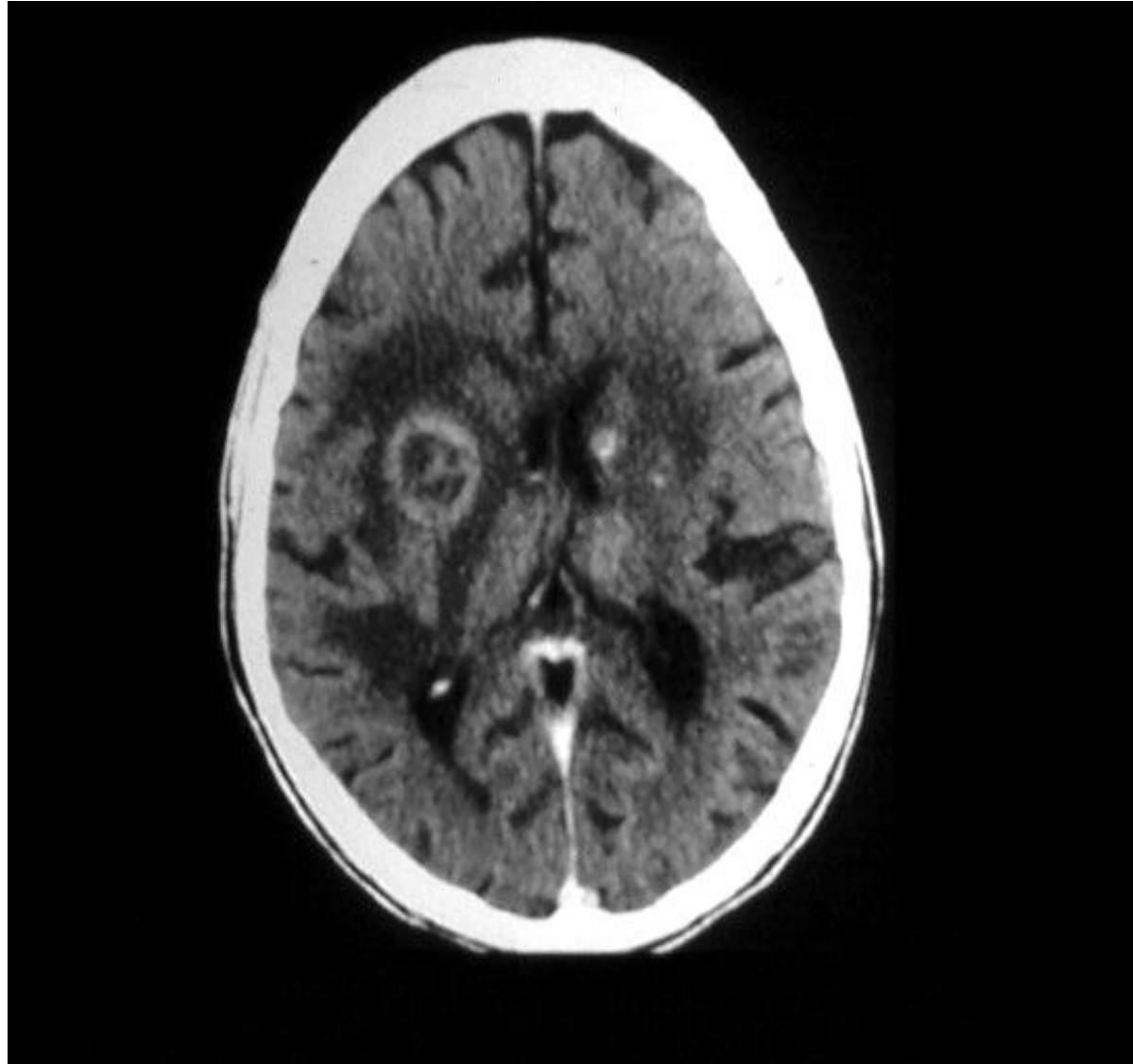
What etiologies should one consider in a patient like this?

- CNS Toxoplasmosis, CNS lymphoma
- Less common: bacterial abscesses (*Staph*, *Strep*, *nocardia*, *listeria*, *bartonella*), candidal abscess, tuberculoma (extremely common in Asian subcontinent and Africa), cryptococcus or other fungal infections
- Non-HIV related diagnoses

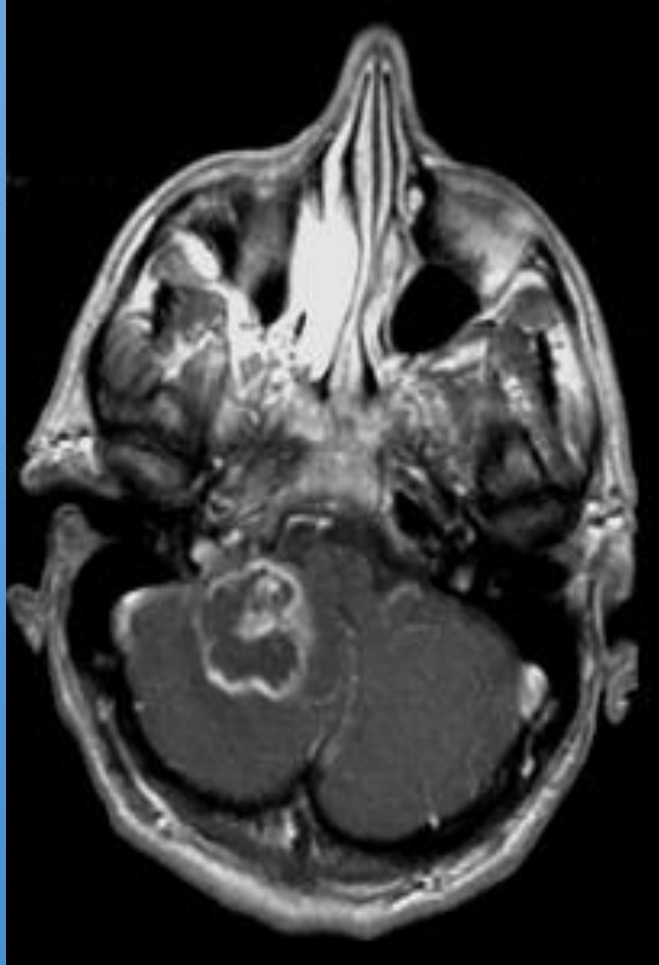
Toxoplasmosis



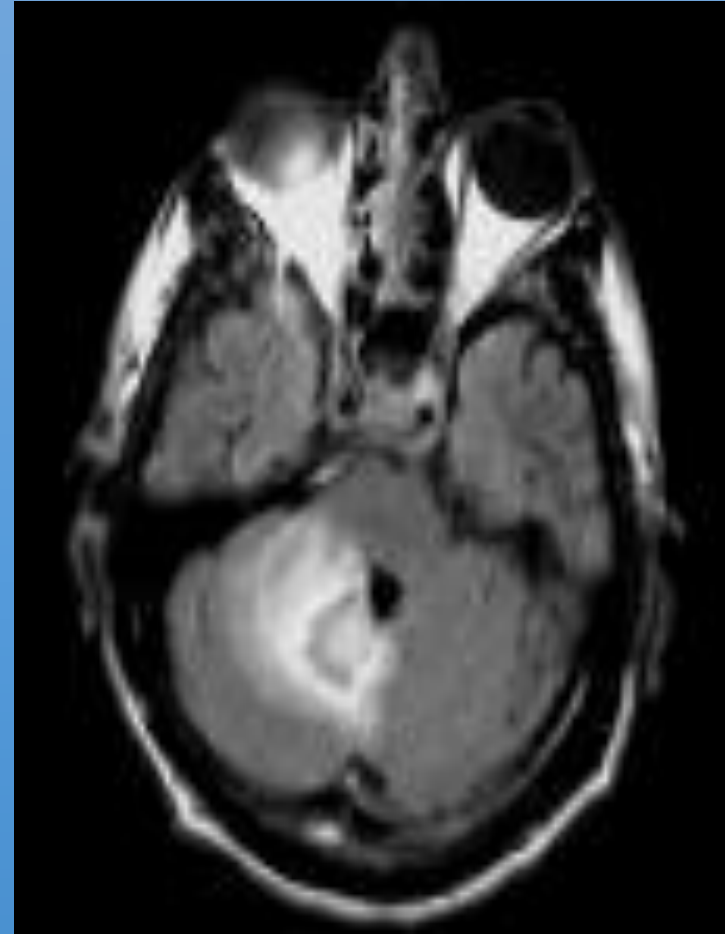
CT in Toxoplasmosis



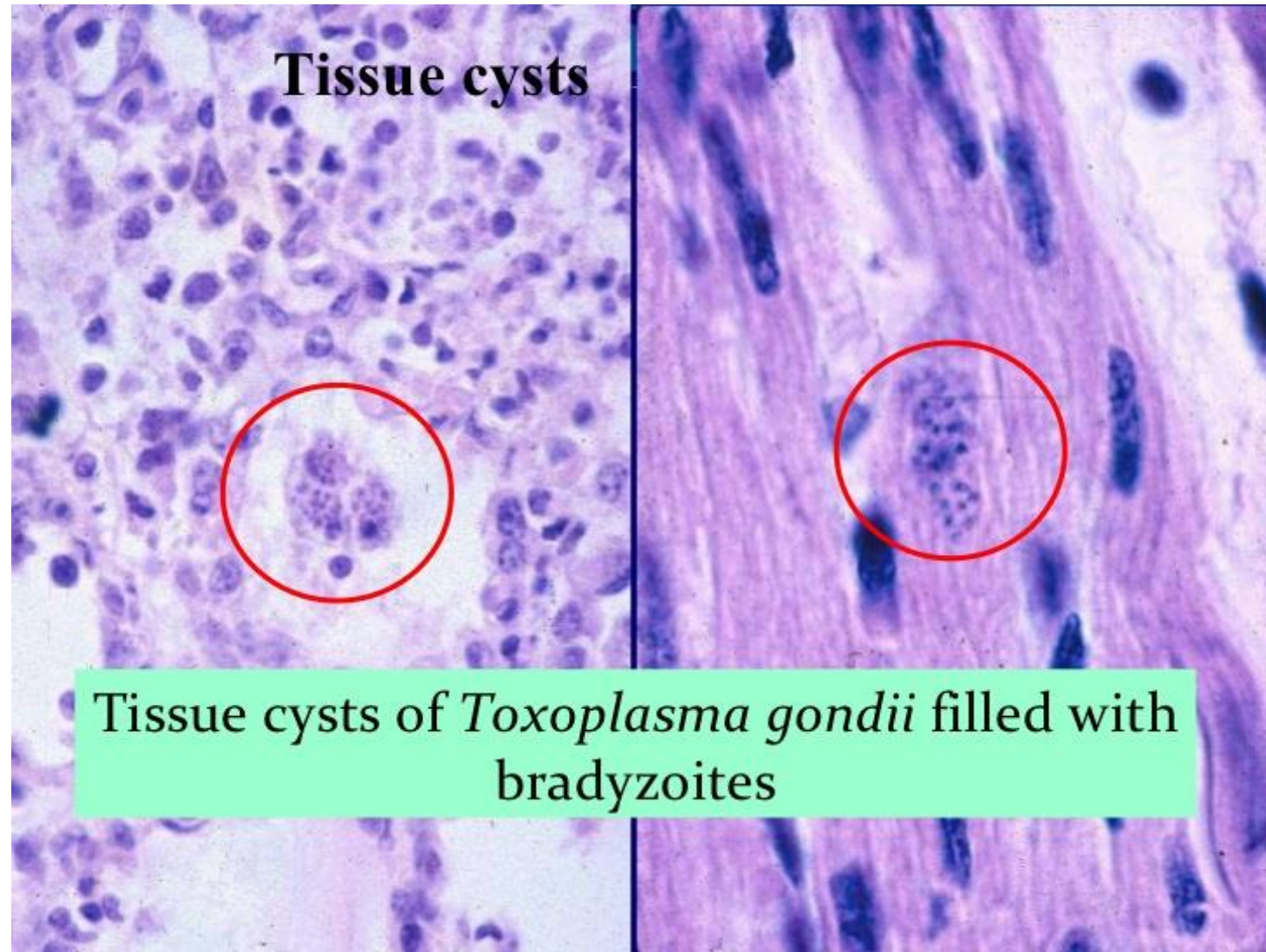
MRI in Toxoplasmosis



T1 with gadolinium



FLAIR sequence



CNS Toxoplasmosis

- AIDS pts with CD4 <100
- Most common cause of CNS lesion
- Sx: +/- fever, headache, focal neurologic findings on exam, seizures (15-40%)
- Dx: Serology (negative serology should prompt consideration for an alternative diagnosis)
- Tx: pyrimethamine (with folinic acid) + sulfadiazine or clindamycin for 6 weeks
- Empiric treatment should be started in newly diagnosed HIV with high clinical suspicion

Primary CNS lymphoma

- Different from systemic lymphoma
- High grade lymphoma, isolated to the CNS, and associated with EBV
- Typically occurs in HIV+ patients, CD4 count < 50
- Sx are the same as toxo: focal symptoms, low grade fever, headache, +/- seizures, malaise
- Subacute onset (weeks)

Clinical features of primary CNS lymphoma

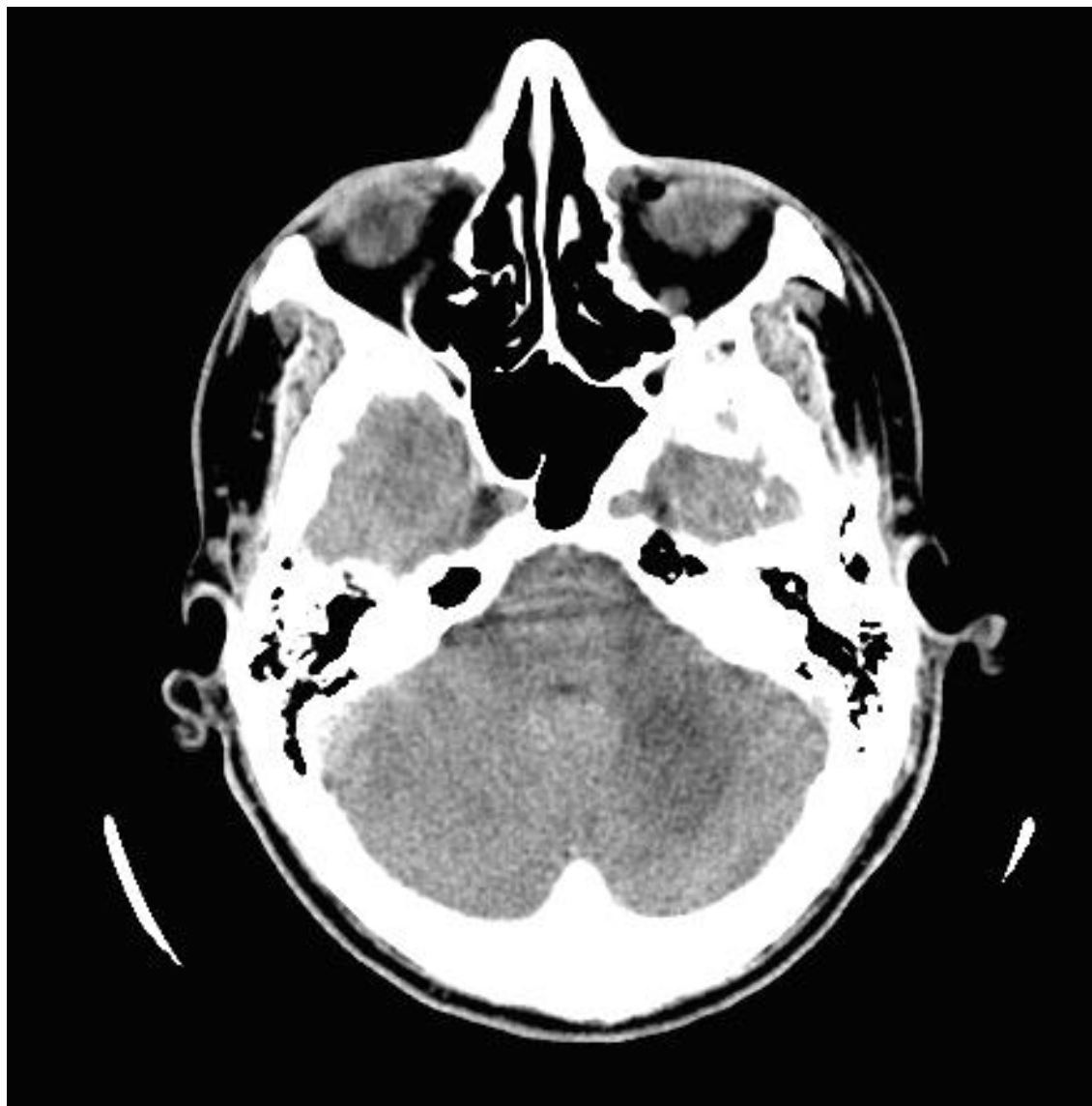
- Typical CSF profile Normal to elevated WBC, no RBC, nl glucose and elevated protein (>100 cells/mm³)
- CSF EBV PCR 80-98% sensitive, 79-98% specific; use of quantitative test ($>10K$ copies) may increase specificity
- Cytology insensitive ($<15\%$) but specific
- Limited treatment options (median survival 2-4 months)
 - Improved survival in Primary CNS Lymphoma with ART; high dose IV methotrexate + ART is the treatment of choice (median survival 1.5 years)
 - Whole brain XRT is an option but has high morbidity

Mr. M and gait difficulty

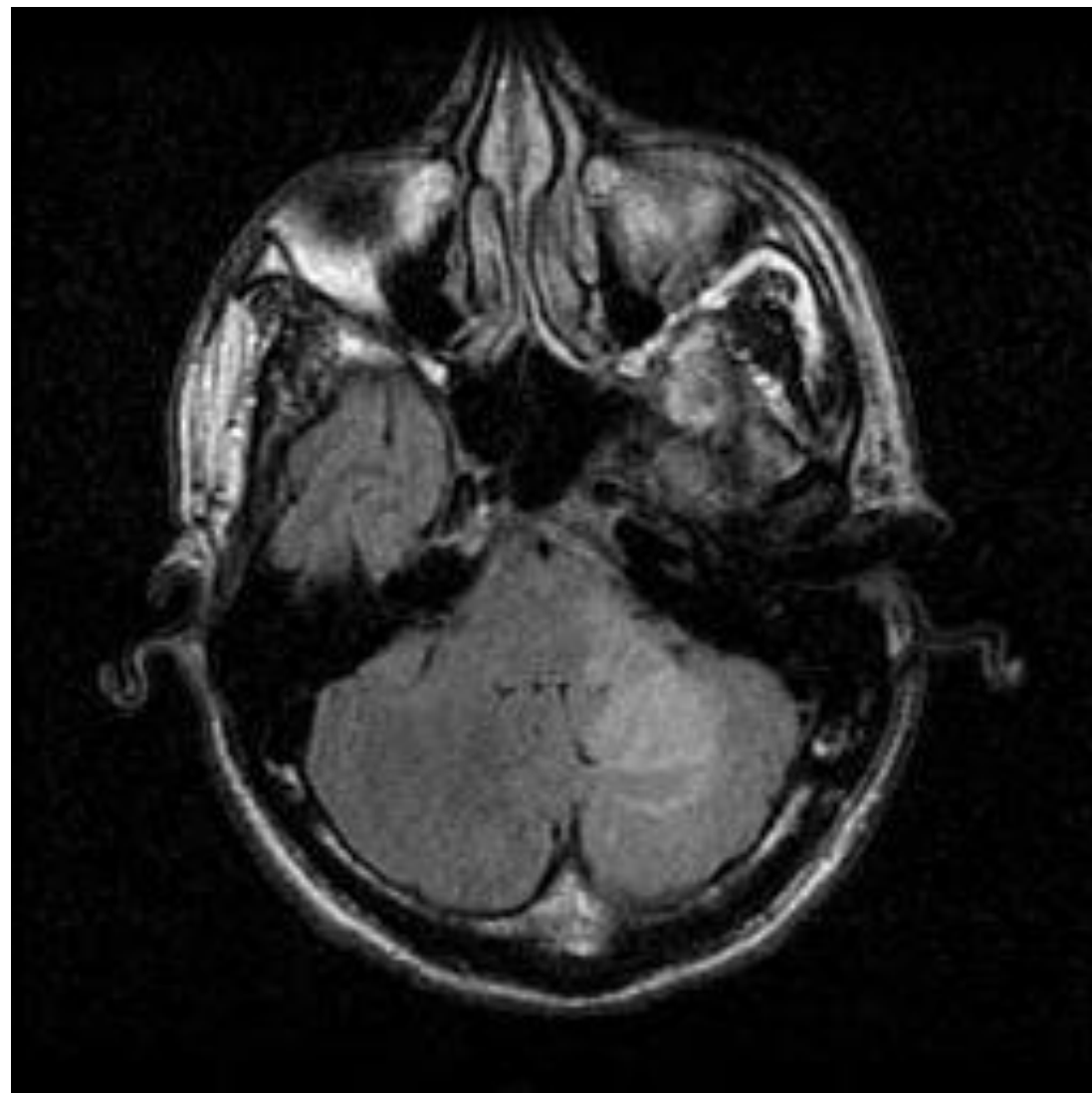
36 yo man with a ten-year history of HIV

- On antiretroviral therapy from 1/99 – 6/01
- Presented in 1/02 with difficulty with his balance which had progressed over prior 4 weeks
- Exam showed nystagmus, and appendicular & gait ataxia

Mr. M - CT without Contrast



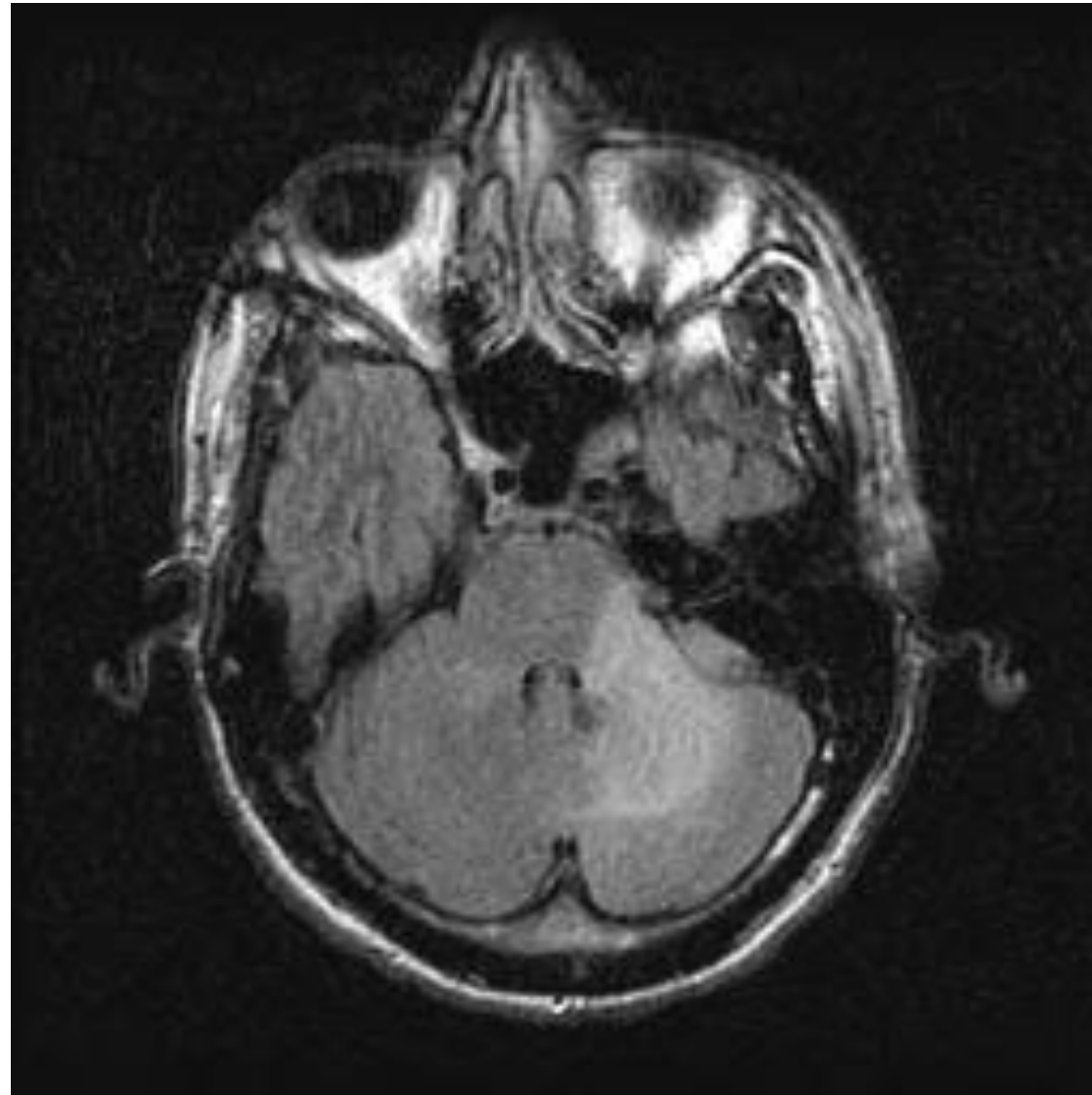
Mr. M - Initial FLAIR MRI



Mr. M and gait difficulty

- CD4 count 241, HIV VL > 500K
- Neuroimaging showed predominantly white matter abnormalities with little mass effect, no enhancement with contrast
- Normal CSF cell counts, glucose, protein, VDRL NR, CSF JC virus PCR negative
- Exam deteriorated over two weeks: weakness of his left face, severe dysarthria, dysphagia, diplopia, and inability to walk

Repeat FLAIR MRI after two weeks



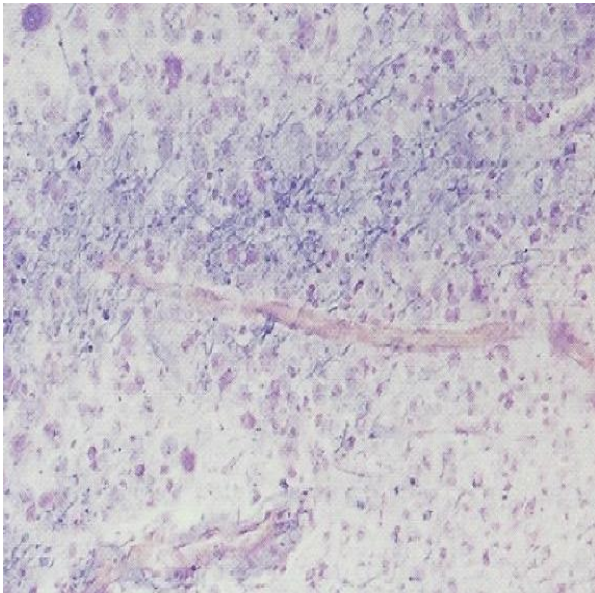
MR. M: GAIT DIFFICULTY
DIFFERENTIAL?

Mr. M and gait difficulty

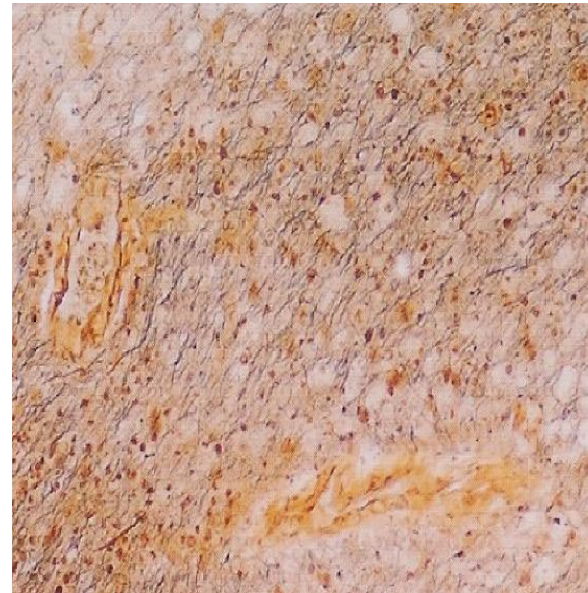
- CSF JC virus PCR positive from second LP 5 days later
- Patient re-initiated ART
- Continued to worsen for 2 months, then began to improve
- 18 months after presentation, he had persistent dysarthria, limb incoordination, and gait ataxia, but able to do most ADLs
- F/u CD4 count was 800, VL <50

Progressive Multifocal Leukoencephalopathy (PML)

JC virus infection of oligodendrocytes, leading to demyelination in the brain



Myelin stain



Silver stain demonstrates intact axons

Clinical features of PML

- In setting of HIV, typically occurs at CD4 count < 200
- Incidence: up to 5% of AIDS patients in US
- 86% of healthy adults in US have serum IgG for JCV; latent JCV infection in kidney
- Sx: focal deficit, no fever, no headache
- Subacute onset over weeks - months

Clinical features of PML

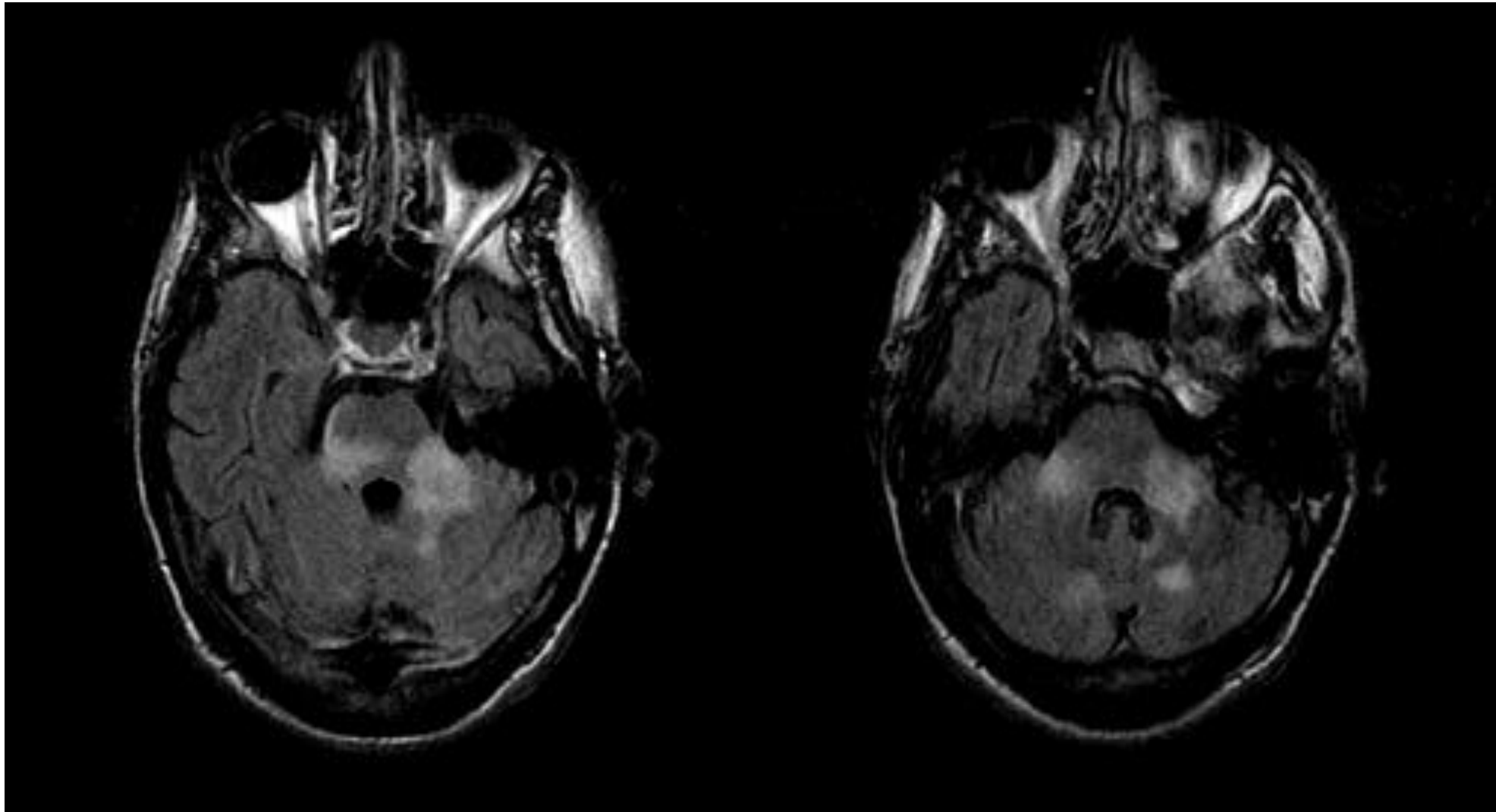
CSF:

- Typical CSF profile *normal*, no WBC, no RBC, nl glucose and protein
- CSF JC virus PCR 72-92% sensitive, 92-100% specific in pre-HAART era
- *In HIV patients*, JC virus PCR found to be 58% sensitive

CT without Contrast in PML



FLAIR MRI in PML



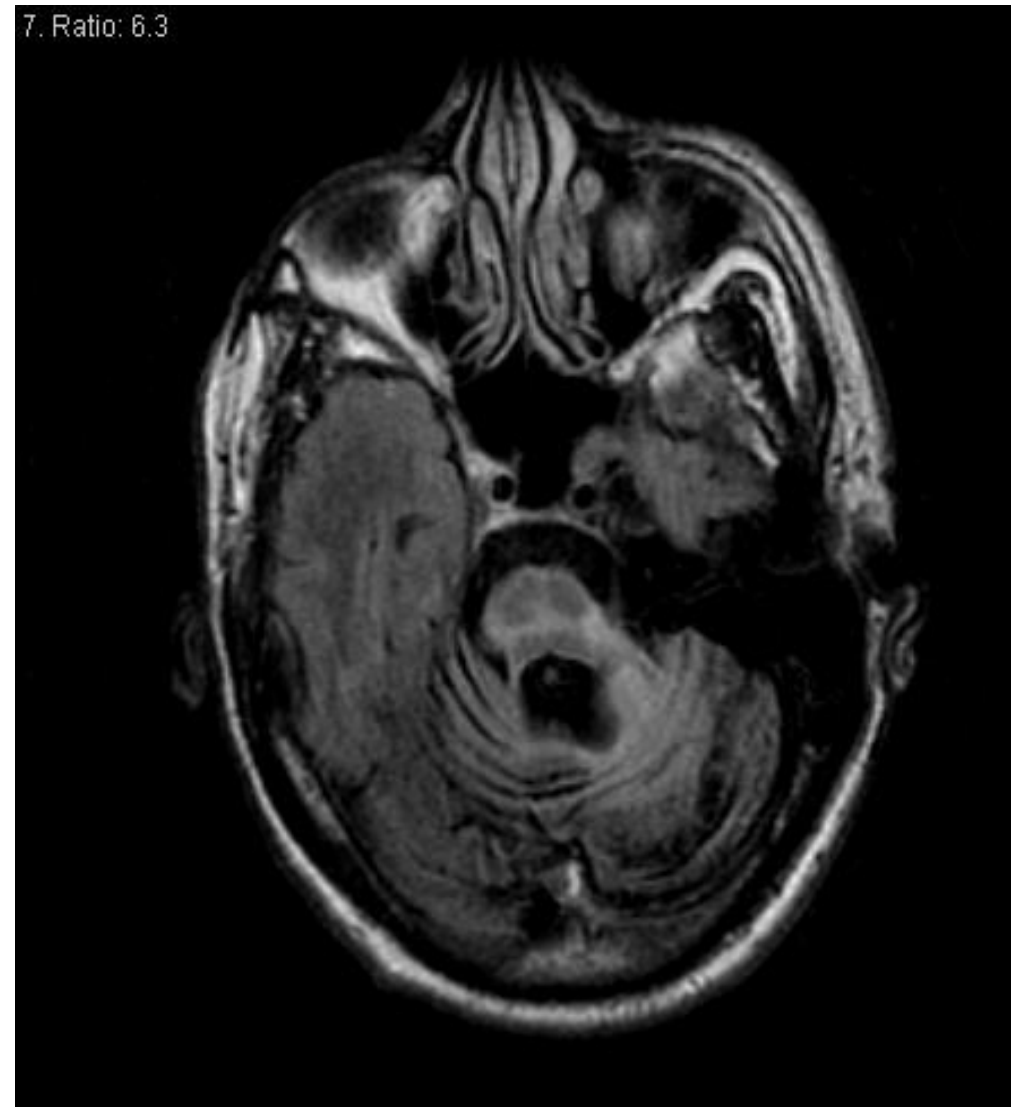
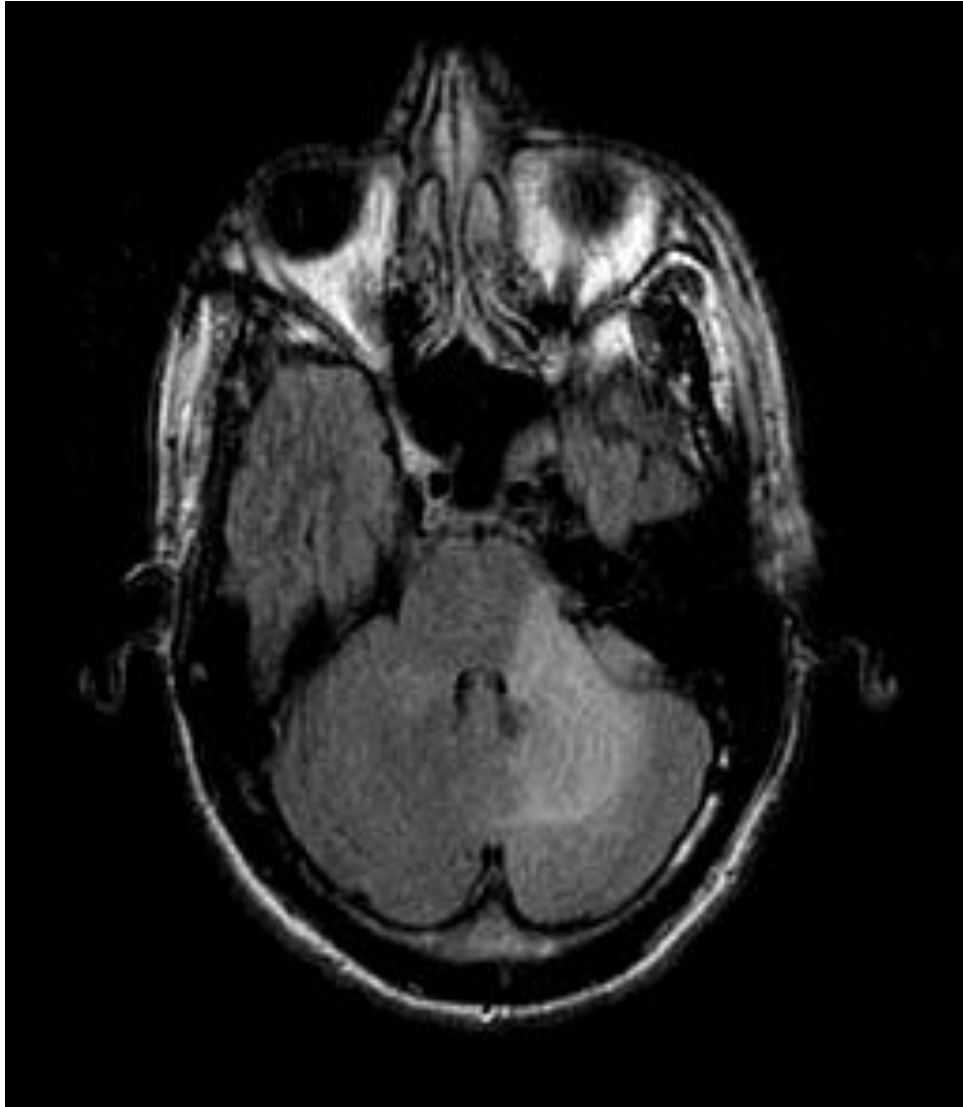
Neuroimaging:

- Imaging demonstrates abnormalities in white matter (extending to subcortical U fibers)
- Lesions are hypodense on CT, bright on T2/FLAIR, dark on T1
- Classically no edema or mass effect on neuroimaging
- *Rare* enhancement w/ standard contrast (7-10% lesions)
- Most cases are multifocal, although not always

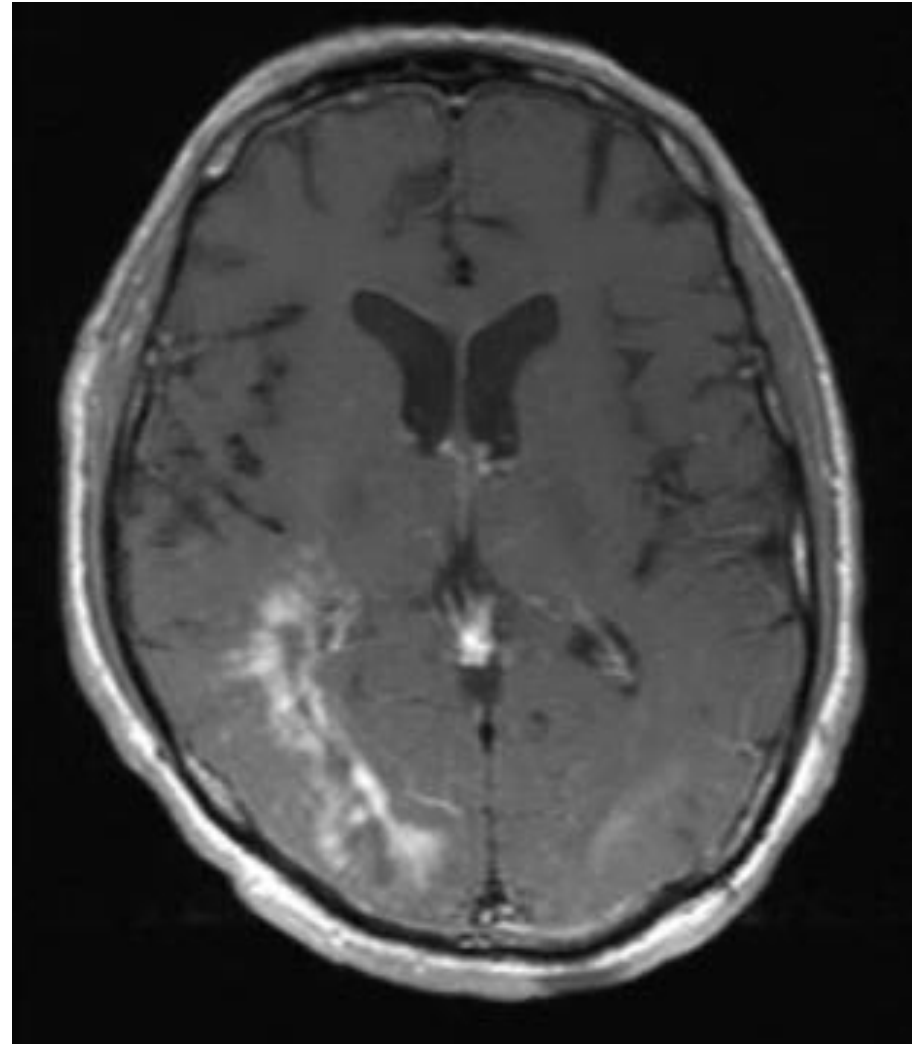
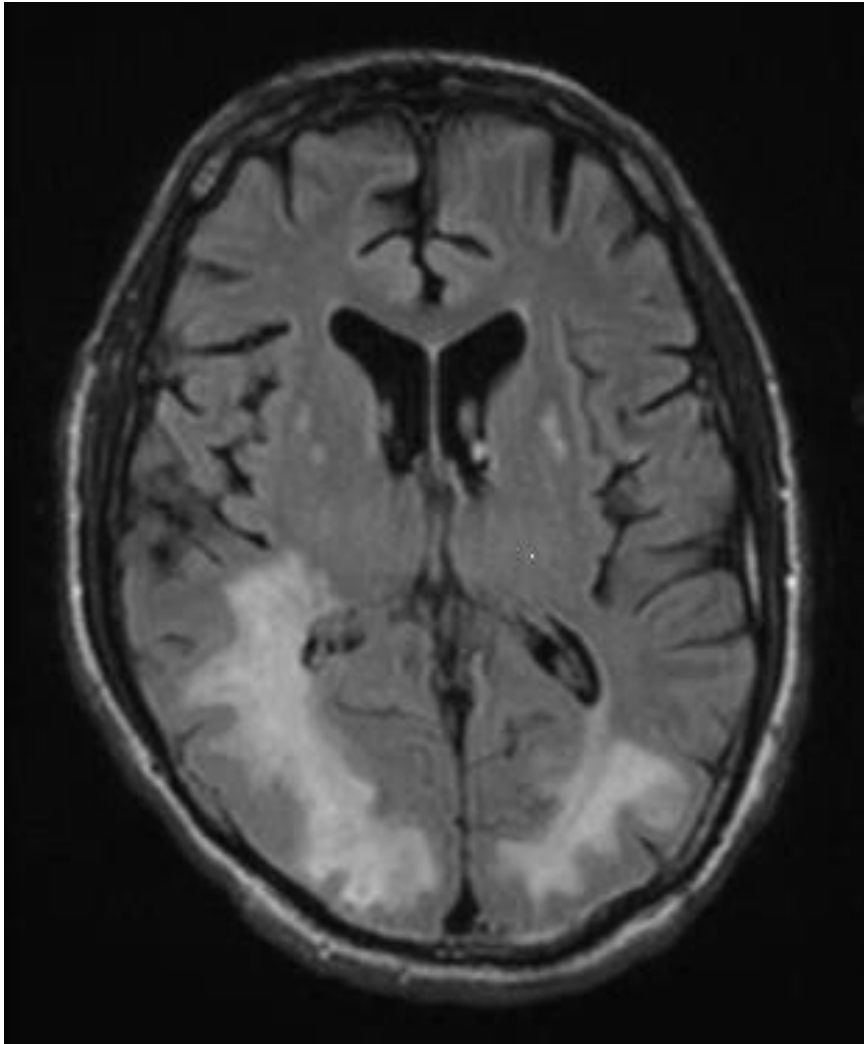
Clinical features of PML

- 50% survival rate 3-6 months after dx, 10% at 1 year
- With restoration of immune competence while on ART survival increases from months to years, 50% at 1 year
- *Cidofovir, cytarabine, topotecan* ineffective for rx
- Systemic response to ART leads to halt in progression of deficits, and mild improvement – *but usually after a 4-8 week period of continued progressive decline*
- Neuroimaging indicates atrophy or ‘burned out’ lesions
- Rare cases of immune reconstitution inflammatory syndrome with initiation of ART

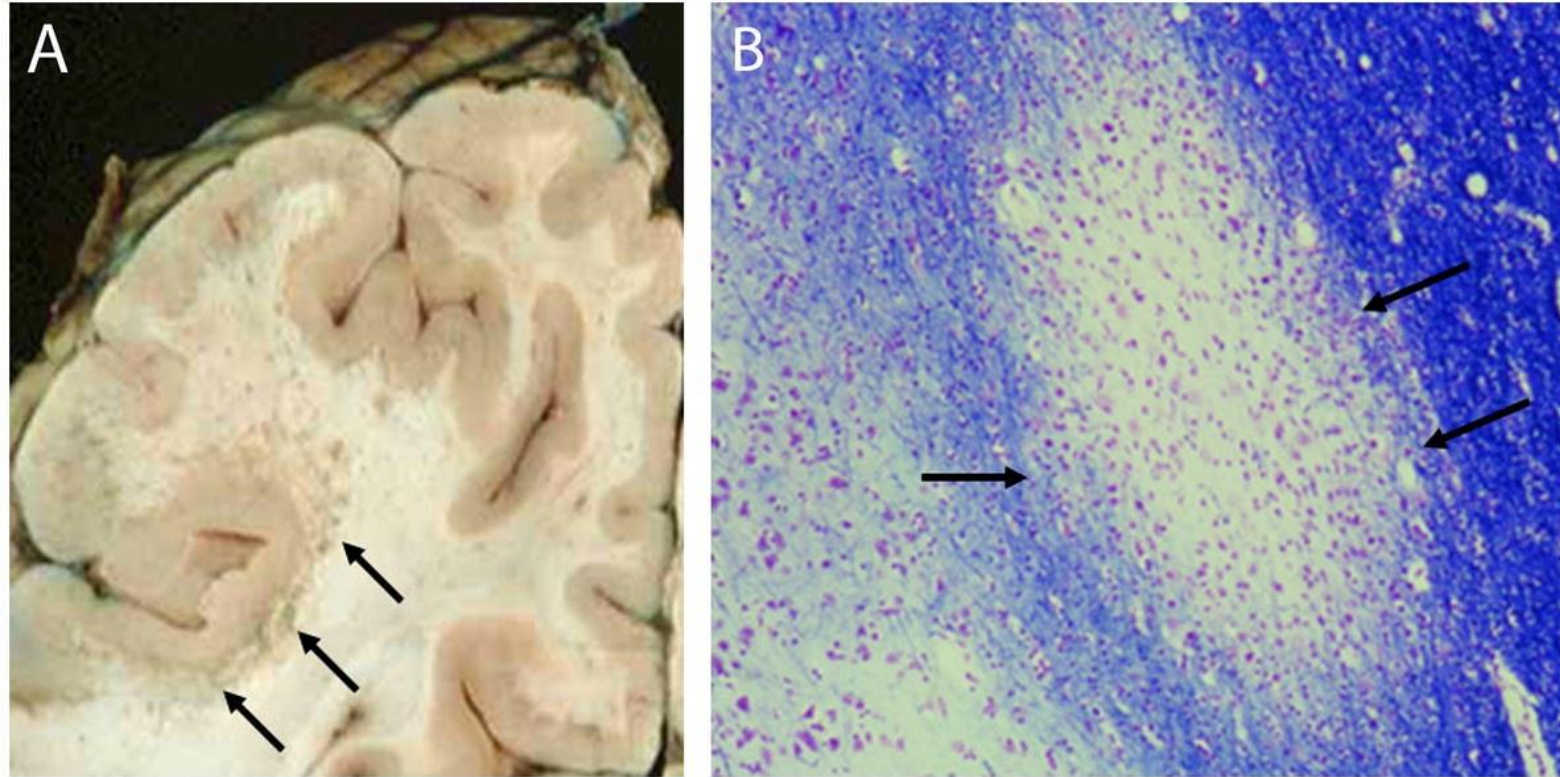
Atrophy from PML on FLAIR MRI



Immune Reconstitution Inflammatory Syndrome in PML



PML



A, This is a coronal section of fixed PML brain. The subcortical white matter is undermined by multifocal punctate coalescent demyelinating lesions (black arrows). B, Luxol fast blue stain shows a microscopic demyelinated lesion (between opposing black arrows) in the white matter immediately subcortical

DEPARTMENT OF NEUROLOGY EVALUATIONS



SCAN ME!
THANK YOU!



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