# 64-year-old male with new onset seizure, history of untreated HIV, serologies pending

Joseph Ryan, MD, PhD
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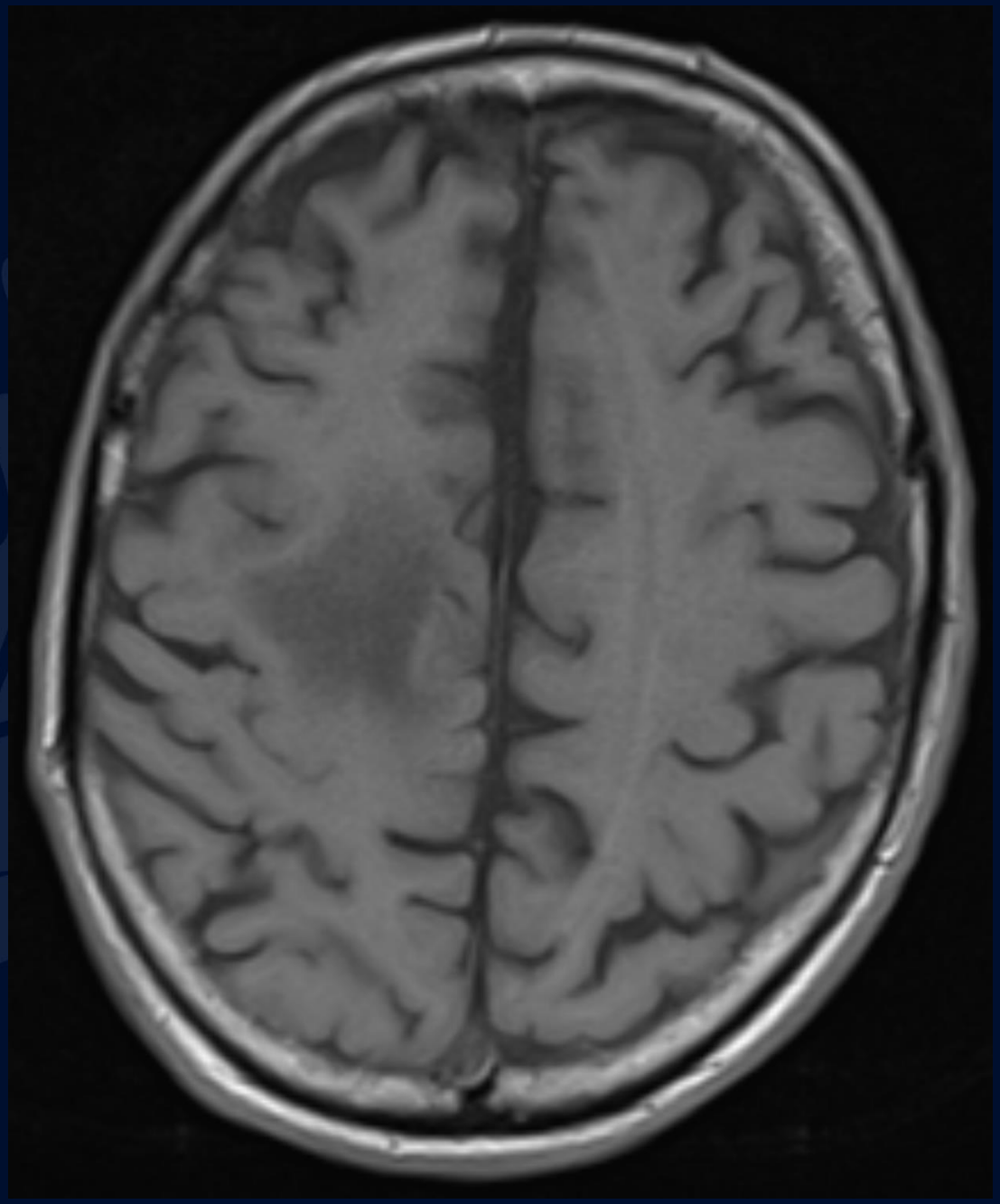
T1



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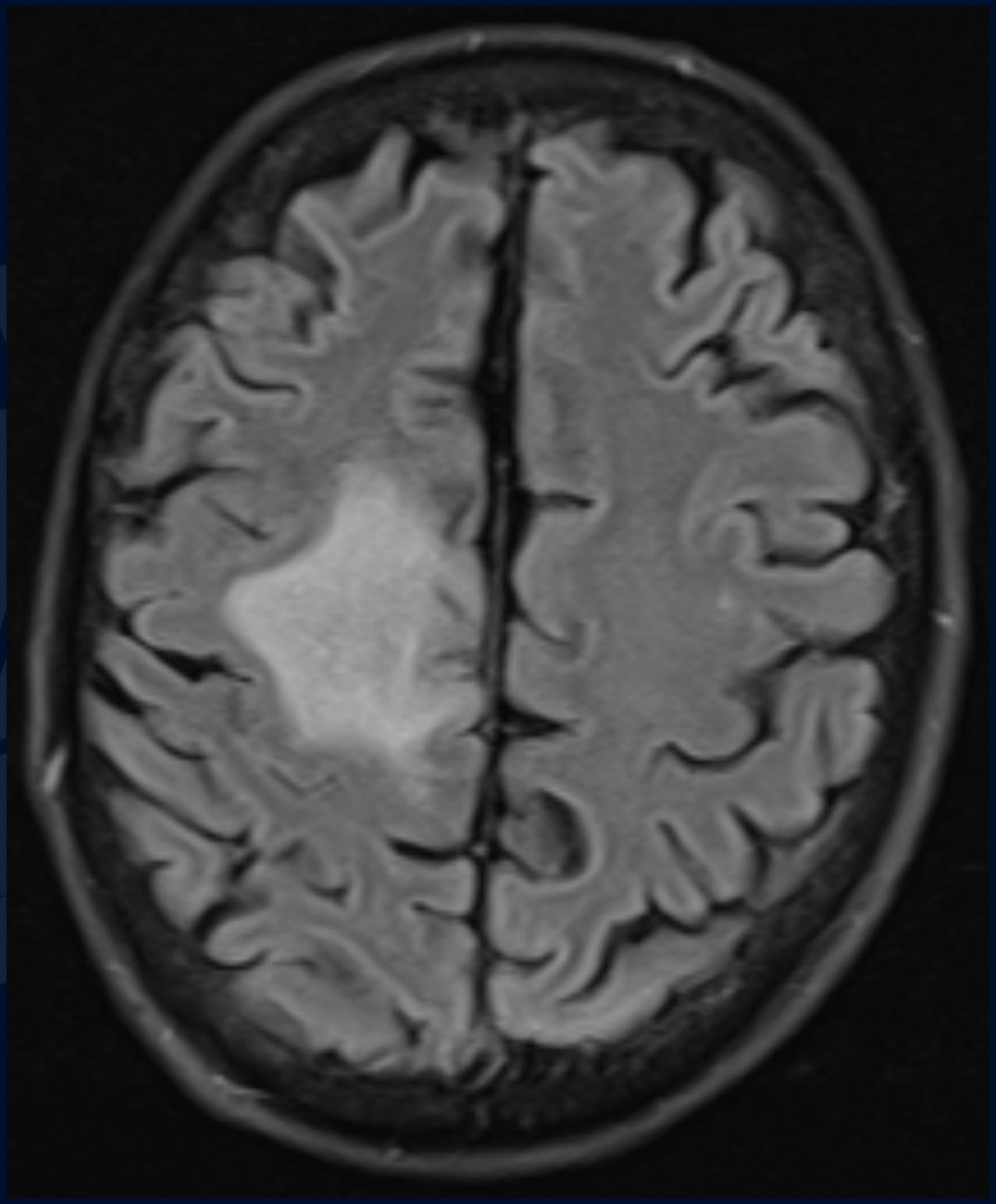
T2 FLAIR



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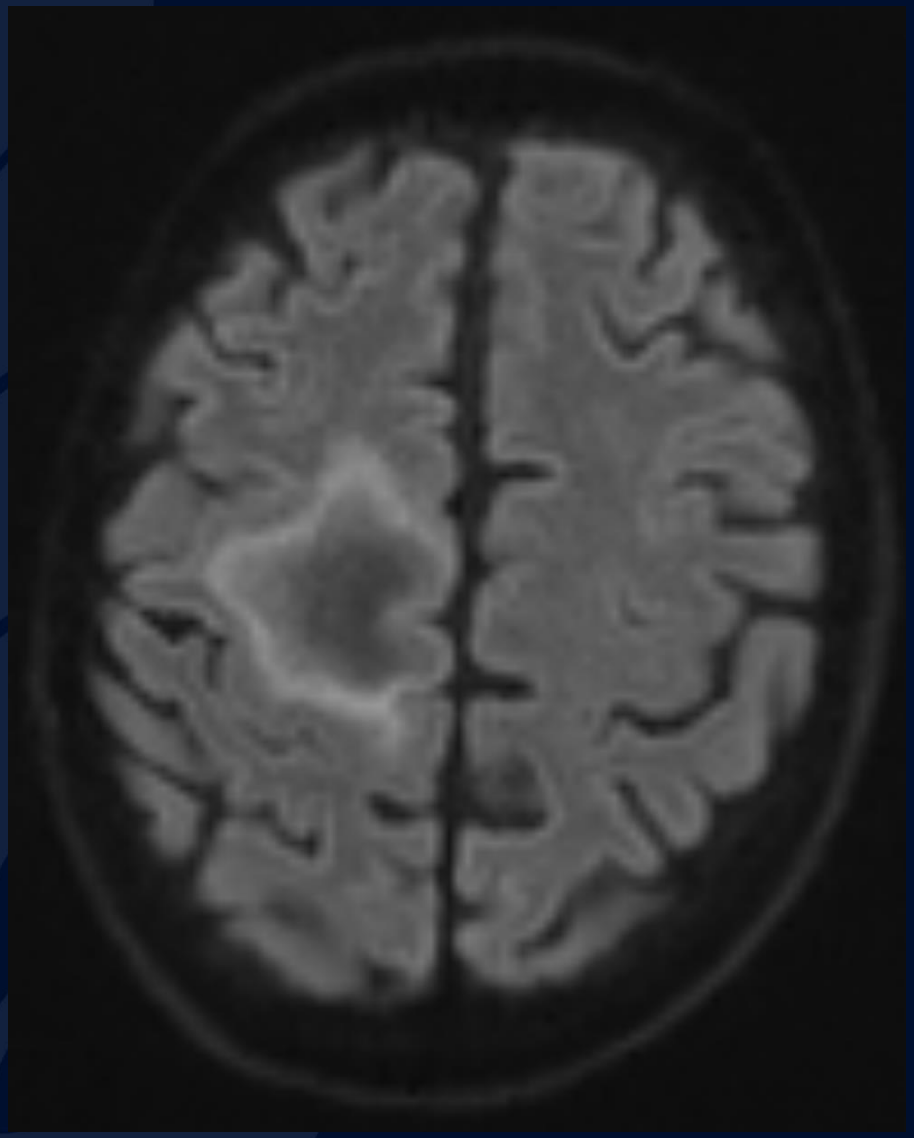

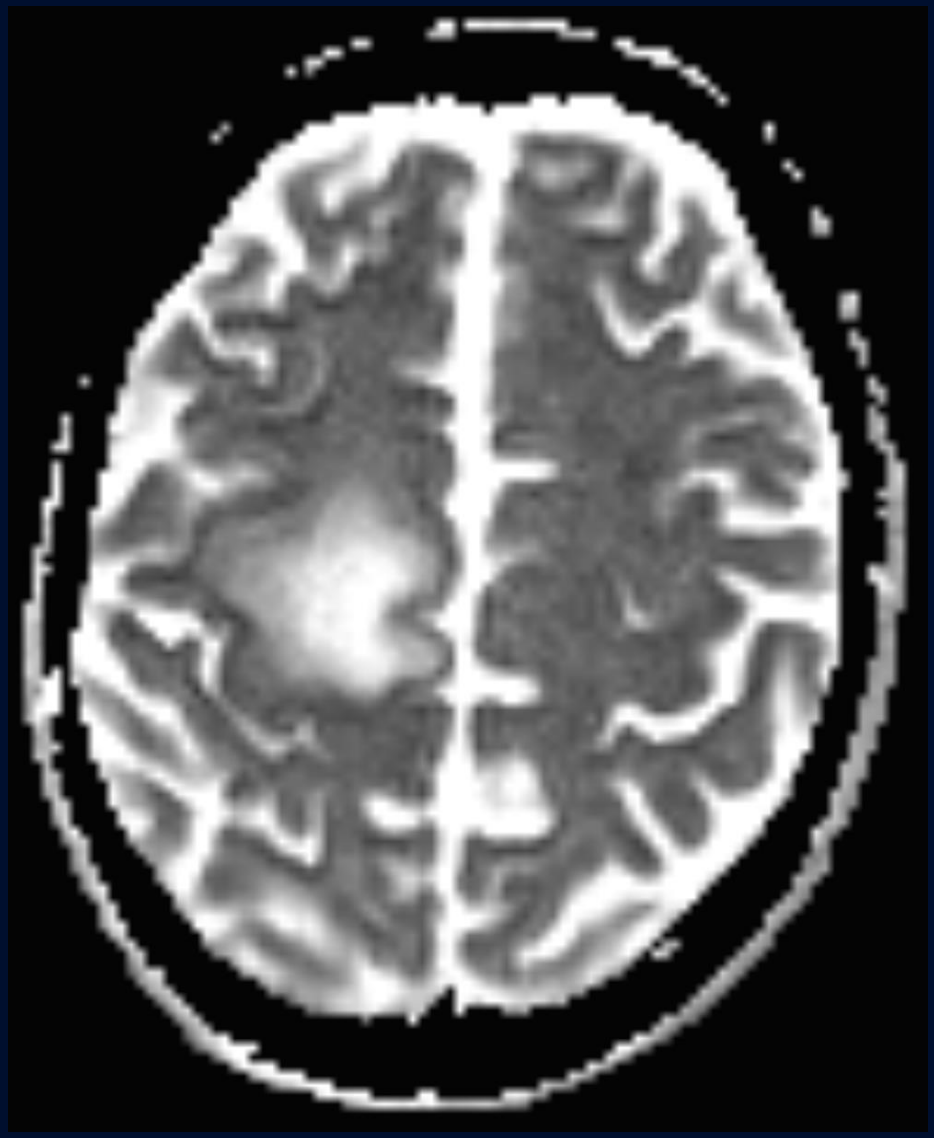

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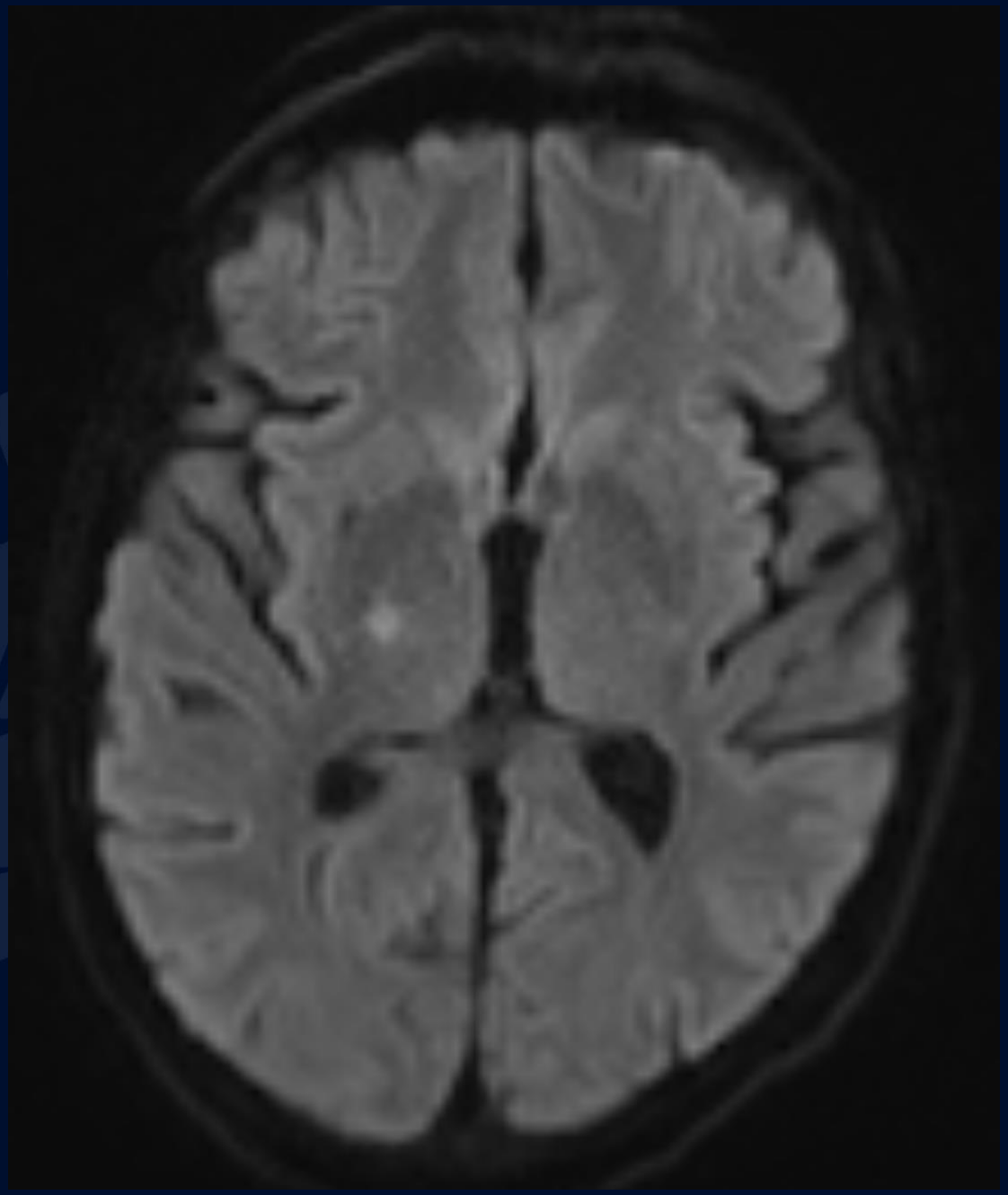

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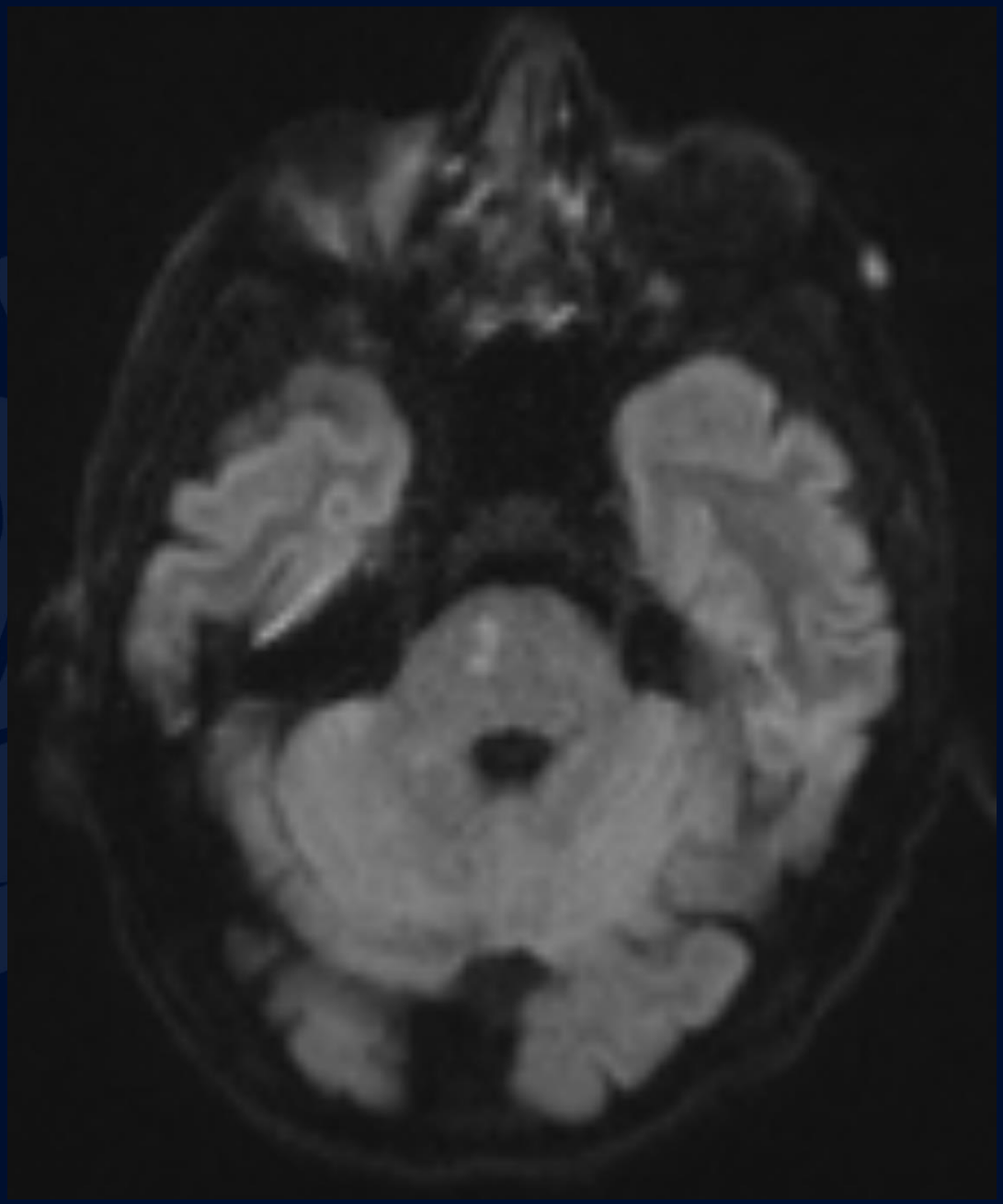

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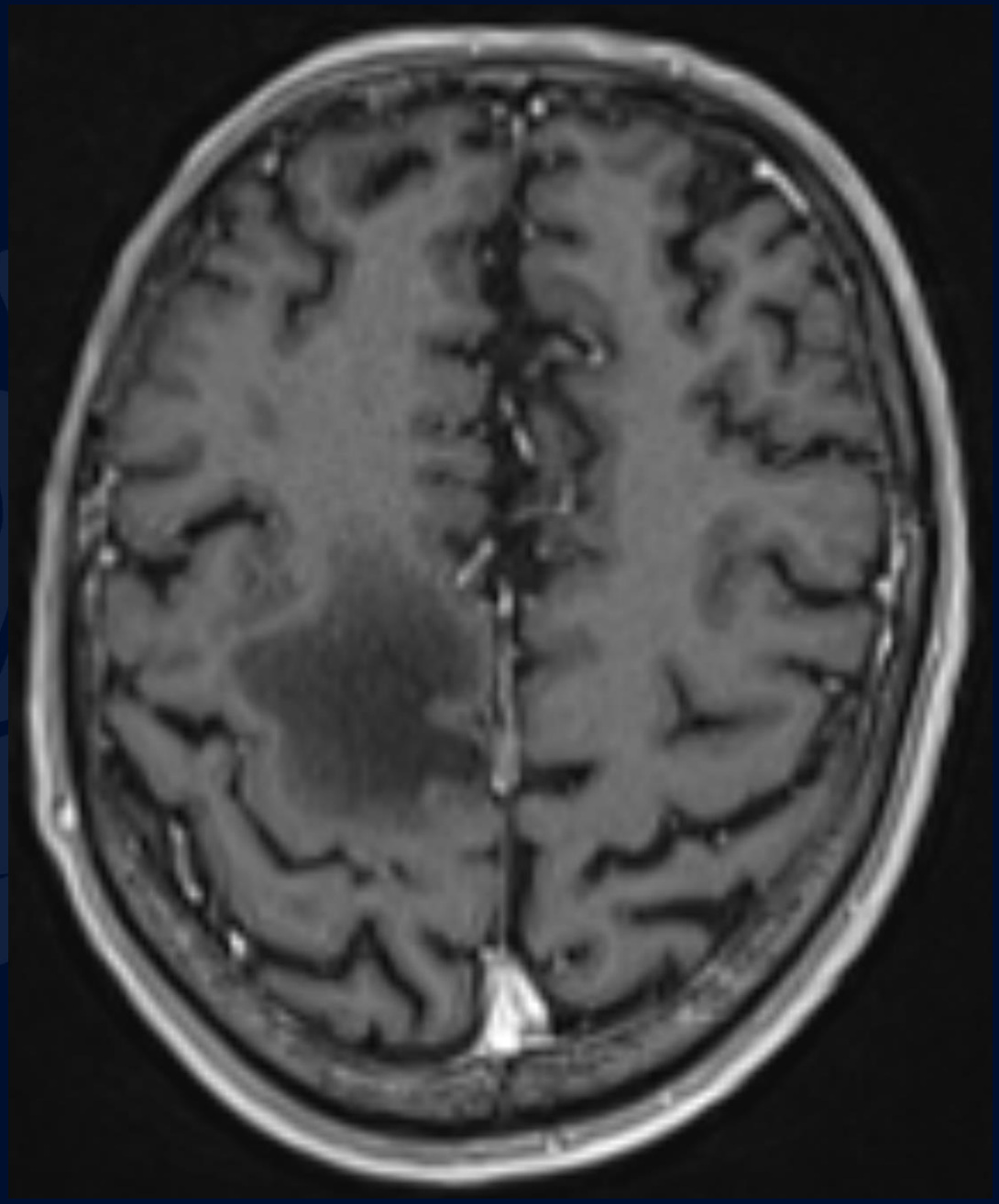
T1 post gadolinium



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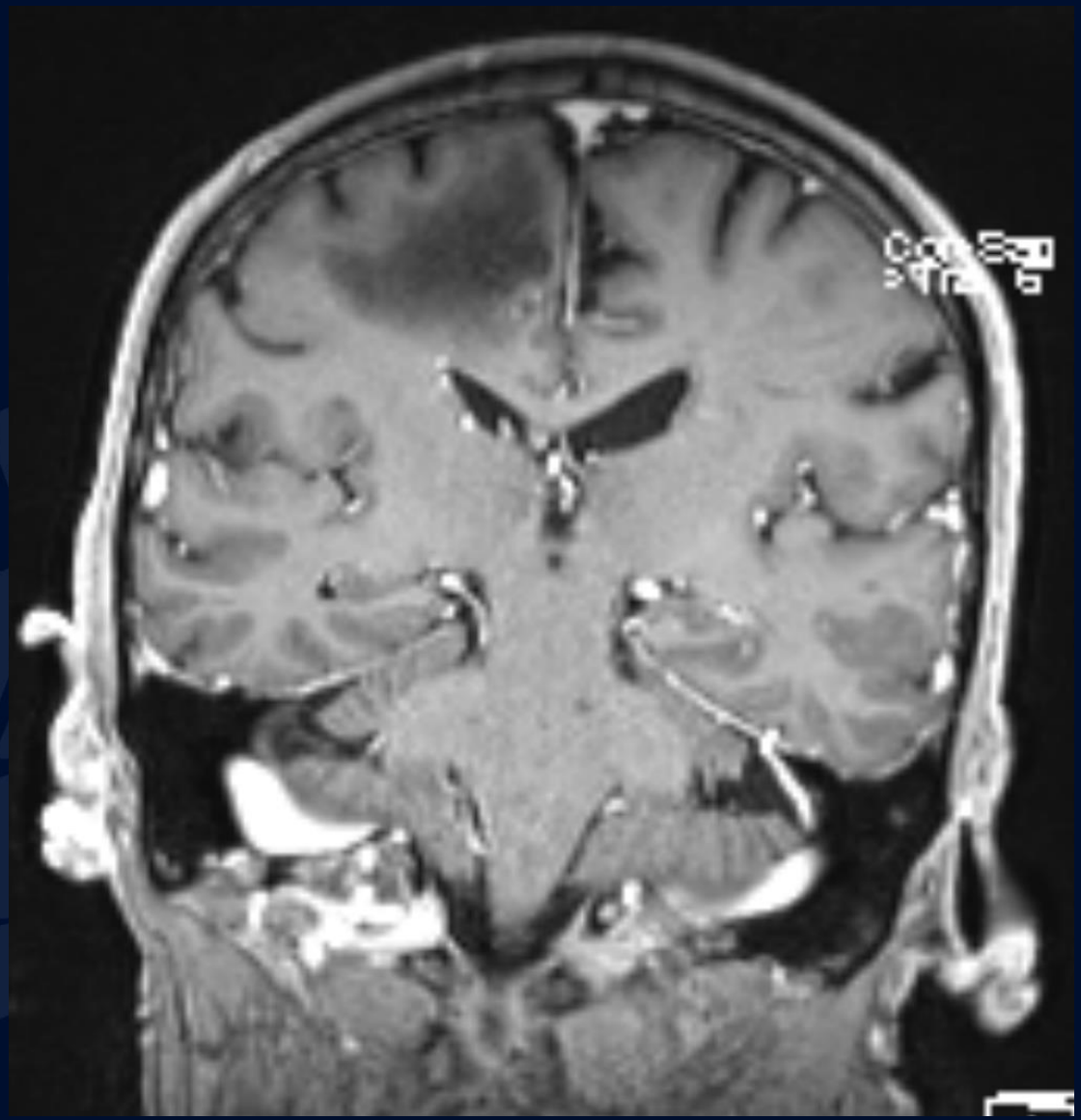
T1 post gadolinium



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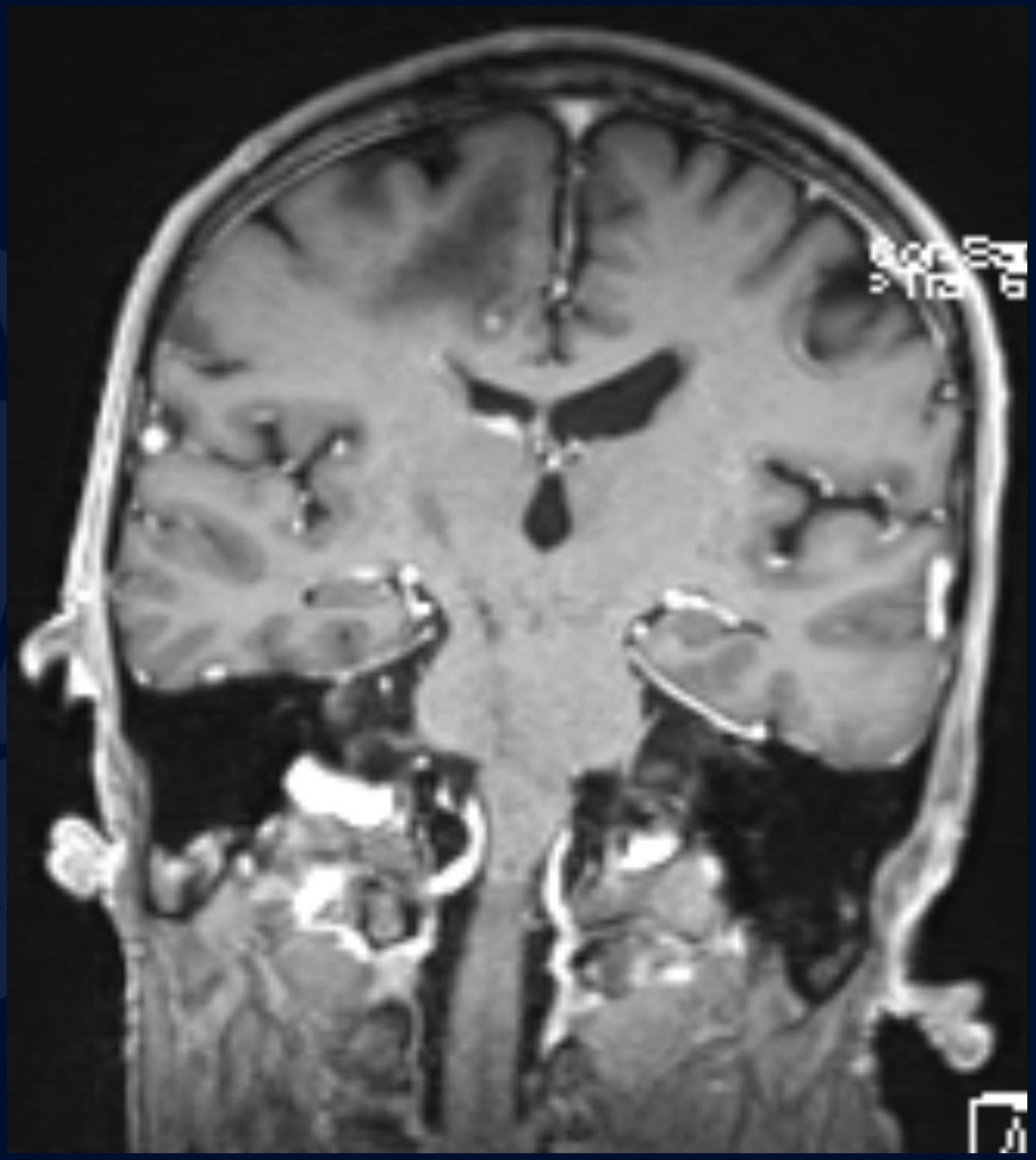
T1 post gadolinium



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# Progressive Multifocal Leukoencephalopathy (PML)

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# Background

- Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease which can occur in patient with compromised immune systems.
- Caused by reactivation of the John Cunningham (JC) virus
- JC virus infects oligodendrocytes
- Classically occurs in AIDS patients with CD4 counts of 50-100 cells/uL
- Non-HIV-related PML can be see in transplant patients, leukemia, other malignancies, inflammatory/autoimmune diseases including SLE and sarcoidosis, isolated CD4 lymphocytopenia, and immunosuppressive monoclonal antibody therapy (natalizumab used in MS, efalizumab, and rituximab)
- Can also occur in patients with recovering immunity, such as in the setting of immune reconstitution inflammatory syndrome (IRIS)

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# Presentation & Diagnosis

- Patients present with neurological symptoms, generally sparing the optic nerve and the spinal cord
- Specific symptoms can include AMS, motor deficits, limb/gait ataxia, visual symptoms, seizure (2/2 subcortical U-fiber and eventually gray matter involvement in more advanced stages)
- Brain lesions are generally confluent, asymmetrically bilateral, mostly involving supratentorial white matter and thalamus. Basal ganglia, brainstem and cerebellum can also be involved.
- Confirmatory diagnosis made at autopsy

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# Imaging Features

- CT imaging shows asymmetric focal areas of low attenuation in periventricular and subcortical white matter (vs. HIV encephalopathy, which is more symmetric)
- MR imaging shows similar pattern/distribution of lesions, with little to no mass effect or enhancement, subcortical U-fiber involvement especially in the parieto-occipital region
  - Subcortical U-fiber lesions often have sharply marginated peripheral border and a hazy, ill-defined inner margin
  - T1-hypointense lesions
    - Generally little or no enhancement on T1-postcontrast
  - T2-hyperintense lesions
    - Multiple punctate (Milky Way sign)
    - Parieto-occipital lesion crossing the splenium (Barbell sign)
    - Cerebellar white matter sparing the dentate nucleus (Shrimp sign)
  - Peripheral patchy diffusion restriction can be seen
- Reduced NAA, lactate; increased choline and lipids on MR spectroscopy
- Increased perfusion at leading edges can be seen on MR perfusion

# Differential diagnosis

- DDX includes:
  - Multiple sclerosis patient with new demyelinating lesions (periventricular or well-defined inner margins favors MS)
  - HIV/AIDS encephalopathy (more diffuse, symmetric white matter, atrophy, spares U-fibers)
  - Posterior reversible encephalopathy syndrome (PRES) – concurrent hypertension
  - Acute disseminated encephalomyelitis (ADEM) – recent infection or vaccine, lesions enhance
  - Cerebral toxoplasmosis (lesions enhance)
  - Primary CNS lymphoma (lesions enhance)

# Prognosis

- Generally poor prognosis with neurological decline, coma, death
- Usually fatal within 1 year, often within 2-6 months, if untreated
- Some patients may benefit from antiretroviral therapy (ART) or high-dose steroids

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