

# AMSER Rad-Path Case of the Month:

67-year-old female with cough, congestion, confusion, and difficulty speaking

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# Patient Presentation

## HPI:

- 67-year-old female presented to her primary care physician for evaluation of cough, congestion, and confusion ongoing for two weeks and worsening over the prior 24 hours
- Patient's family endorses lagging speech and inability to answer questions
- Negative for nausea or vomiting, headache, weakness, vision changes, or sensory deficits

## Physical Exam:

- Notable delay in response to complex questions, suspicious for expressive aphasia
- Patient orientated to person, time, and place. Able to follow commands appropriately. Motor and sensory function intact. Cranial nerves intact.

# Patient Presentation

## PMHx & PSHx:

- The patient has a past medical history of CKD stage III, hyperlipidemia, hypertensive renal disease, hypothyroidism s/p graves s/p radioiodine ablation, immune thrombocytopenia, and psoriasis
- The patient's past surgical history is unremarkable

Abnormal Labs	
Potassium	3.1 (3.7-5.1 mmol/L)
Creatinine	1.66 (0.50-1.10 mg/dl)
BUN	31 (6 - 24 mg/dl)
eGFR	34 ( $\geq 90$ mL/min/1.73m <sup>2</sup> )

What Imaging Should We Order?

# Select the applicable ACR Appropriateness Criteria

**Variant 1:**

**Acute mental status change. Increased risk for intracranial bleeding (ie, anticoagulant use, coagulopathy), hypertensive emergency, or clinical suspicion for intracranial infection, mass, or elevated intracranial pressure. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CT head without IV contrast	Usually Appropriate	☼ ☼ ☼
MRI head without IV contrast	Usually Appropriate	○
MRI head without and with IV contrast	May Be Appropriate	○
CT head without and with IV contrast	May Be Appropriate	☼ ☼ ☼
CT head with IV contrast	Usually Not Appropriate	☼ ☼ ☼

# Head CT Without Contrast (Unlabeled)



# Head CT Without Contrast (Labeled)



Axial CT image of the head showing a 3 cm hypodense region within the left frontal subcortical white matter

# Select the applicable ACR Appropriateness Criteria

**Variant 2:**

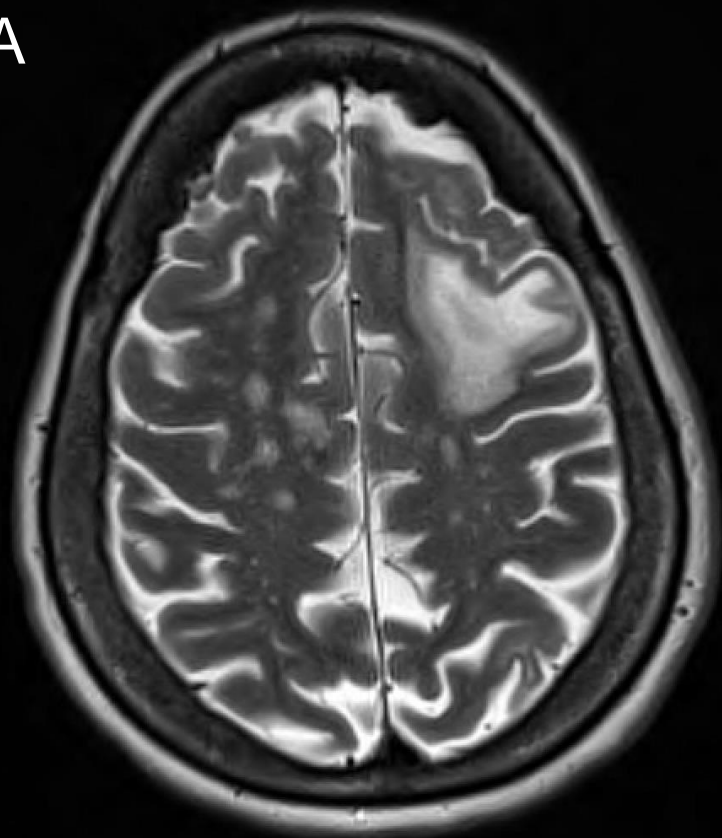
**Acute or progressively worsening mental status change in patient with a known intracranial process (mass, recent hemorrhage, recent infarct, central nervous system infection, etc).  
Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CT head without IV contrast	Usually Appropriate	☼ ☼ ☼
MRI head without and with IV contrast	Usually Appropriate	○
MRI head without IV contrast	Usually Appropriate	○
CT head without and with IV contrast	May Be Appropriate	☼ ☼ ☼
CT head with IV contrast	May Be Appropriate	☼ ☼ ☼

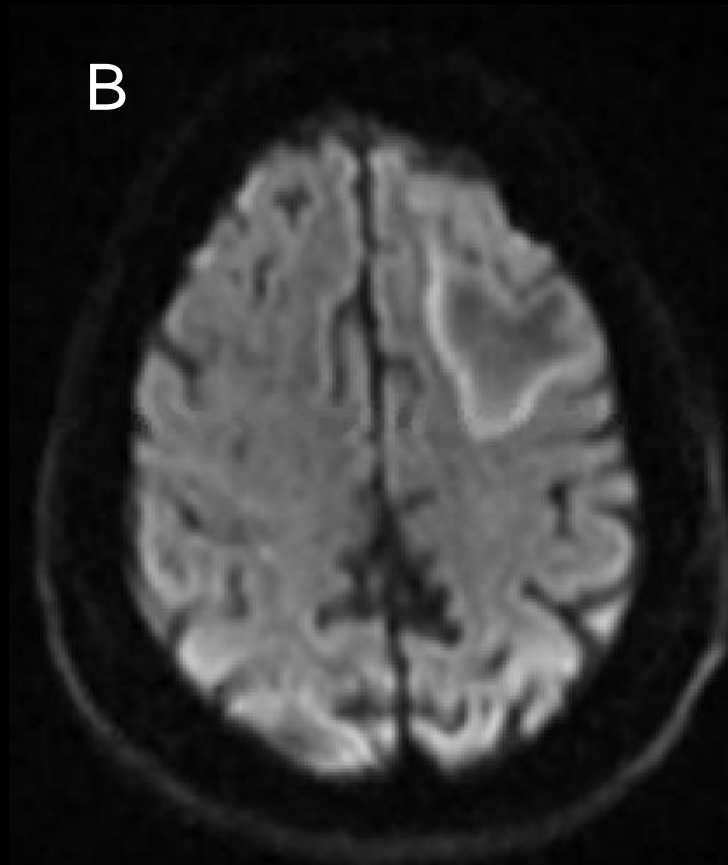


# MRI Brain With and Without Contrast (Unlabeled)

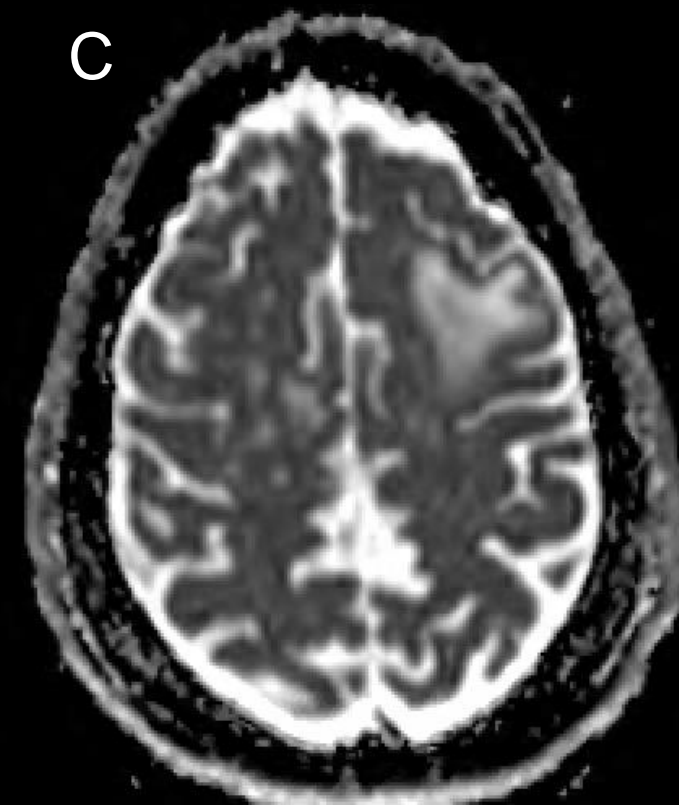
A



B

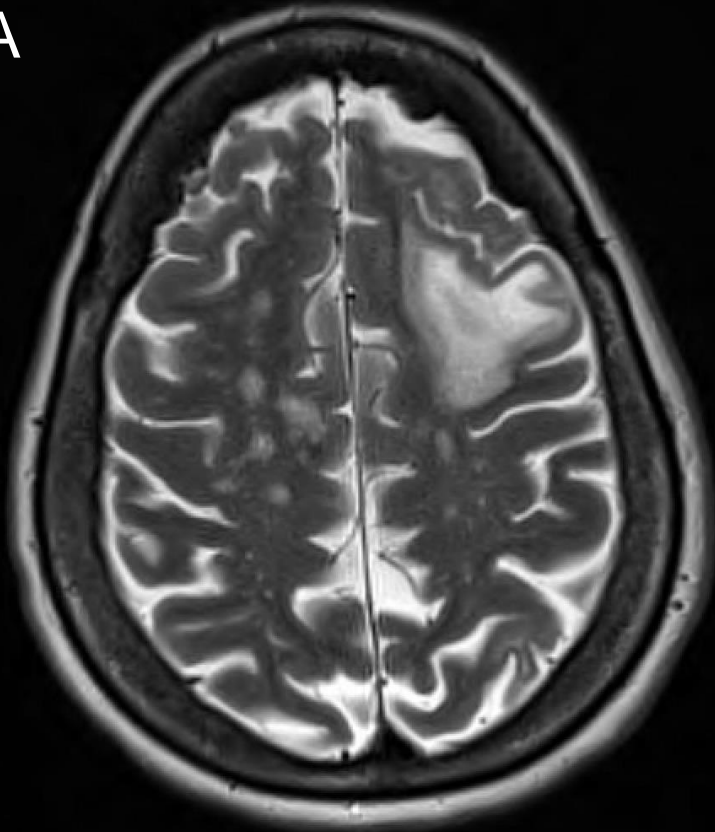


C

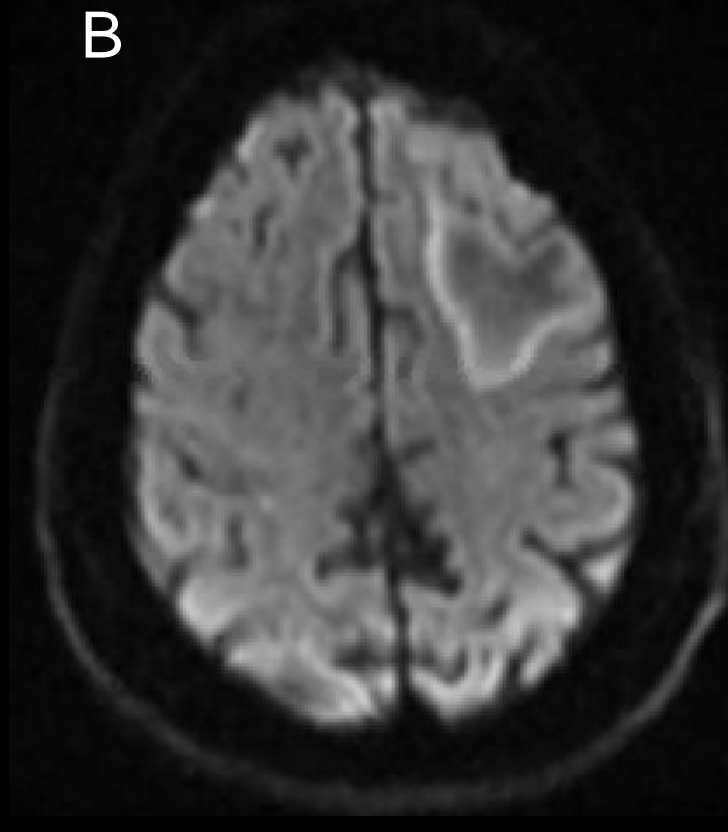


# MRI Brain With and Without Contrast (Labeled)

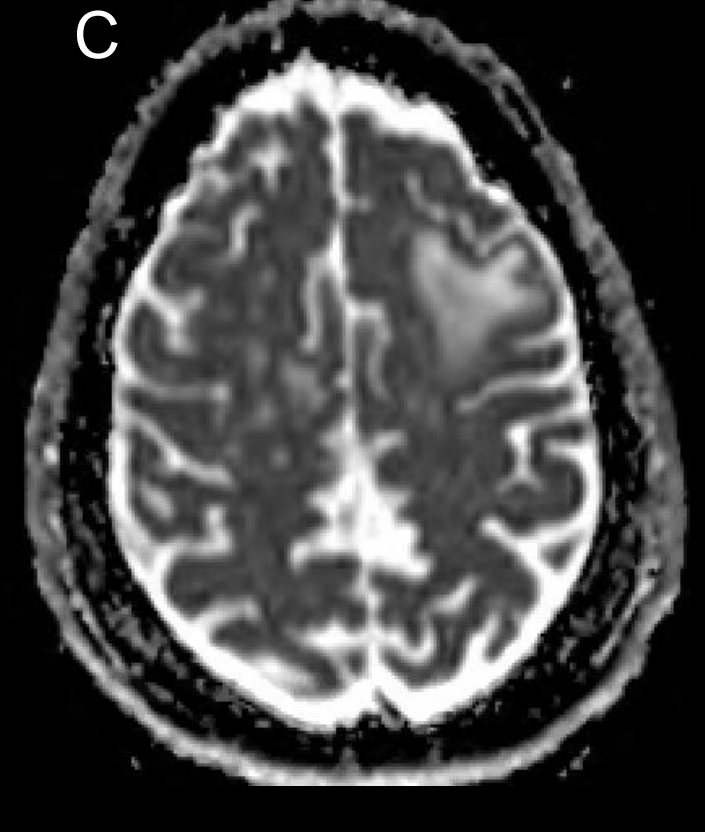
A



B

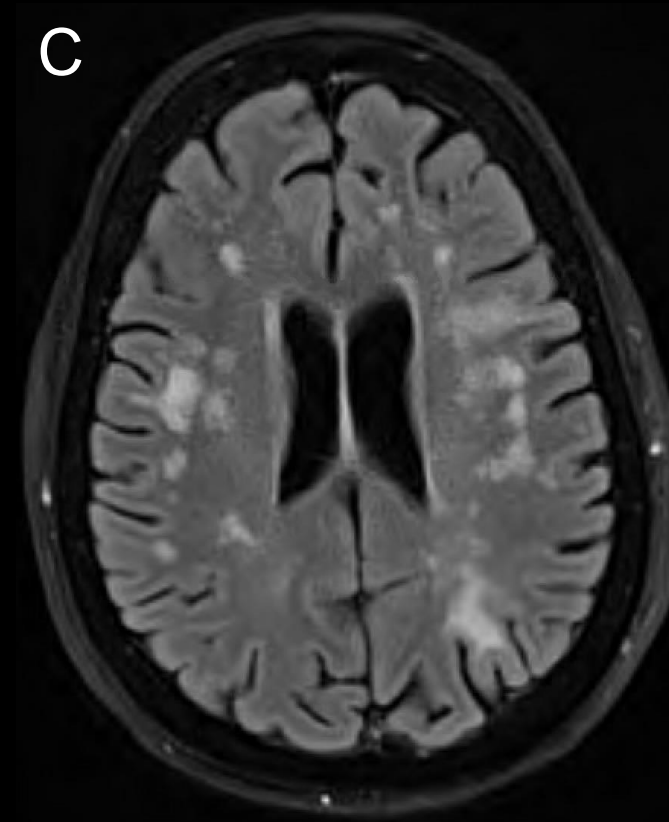
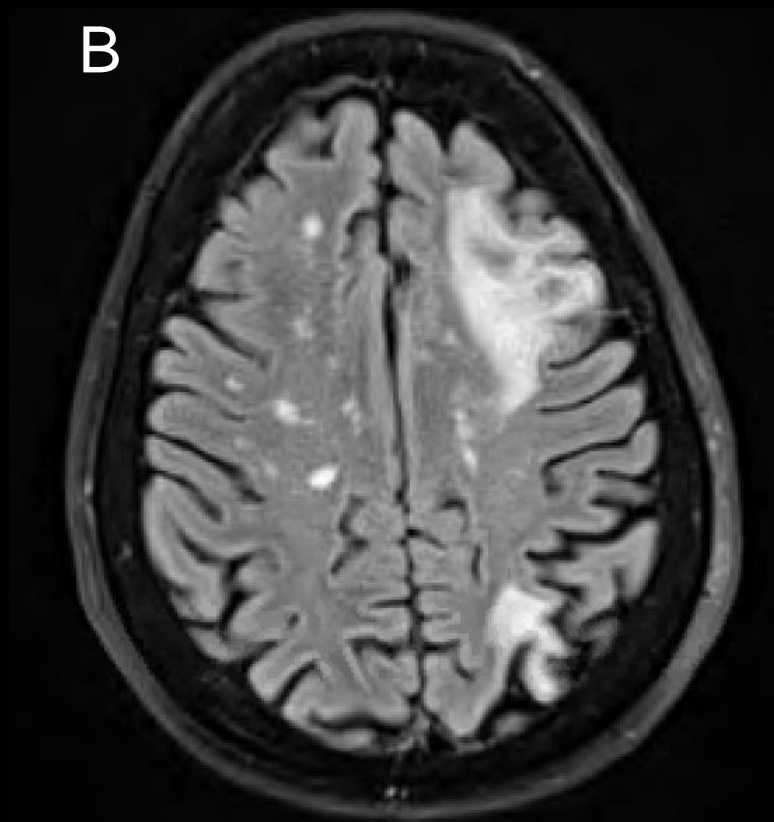
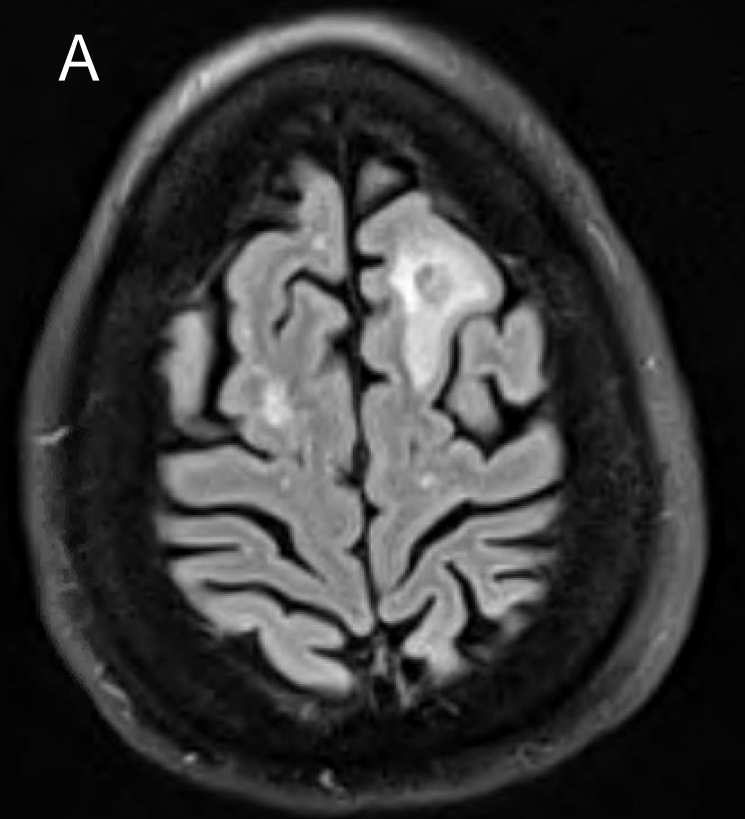


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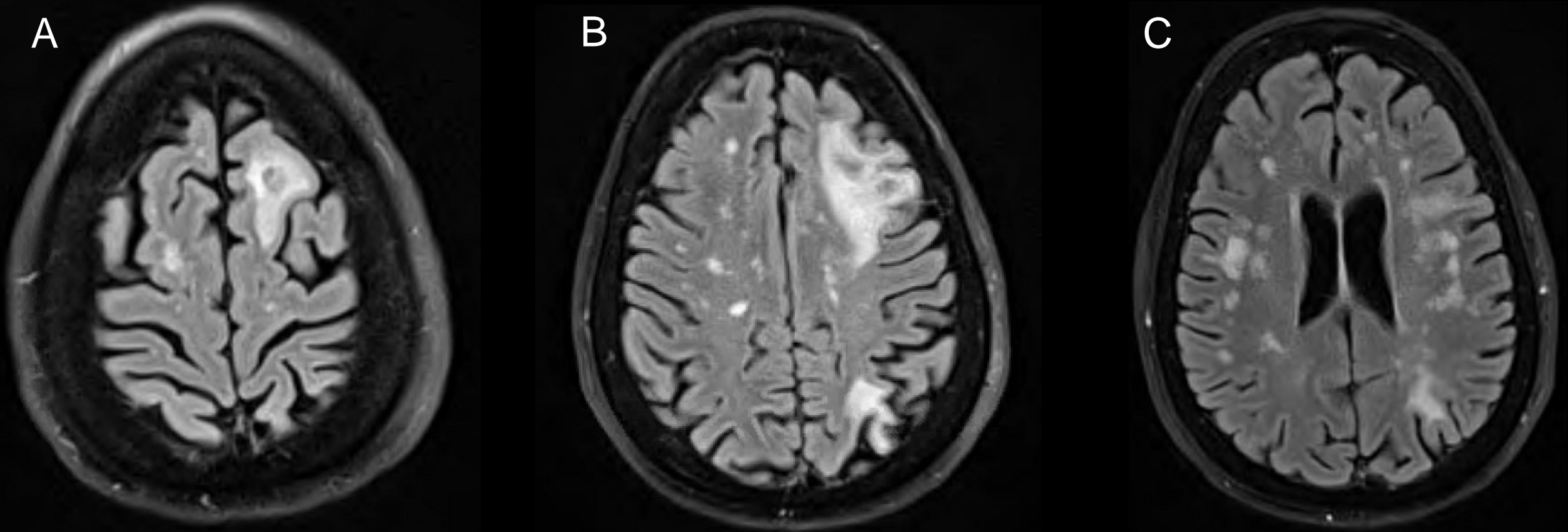


(A) Axial T2-weighted MR image of the brain showing a moderate sized geographic area of intra-axial signal hyperintensity at the left frontal subcortical white matter. (B) Axial diffusion-weighted MR image and (C) Axial ADC map of the brain showing elements of 'leading edge restricted diffusion'

# MRI Brain With and Without Contrast (Unlabeled)



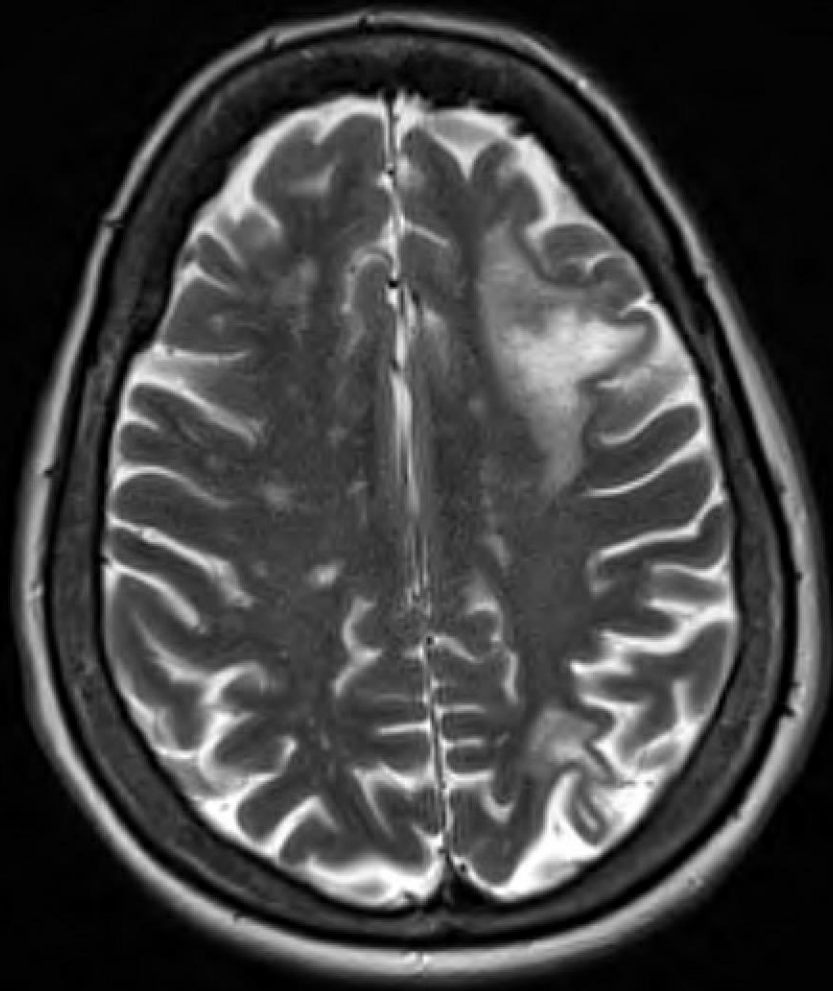
# MRI Brain With and Without Contrast (Labeled)



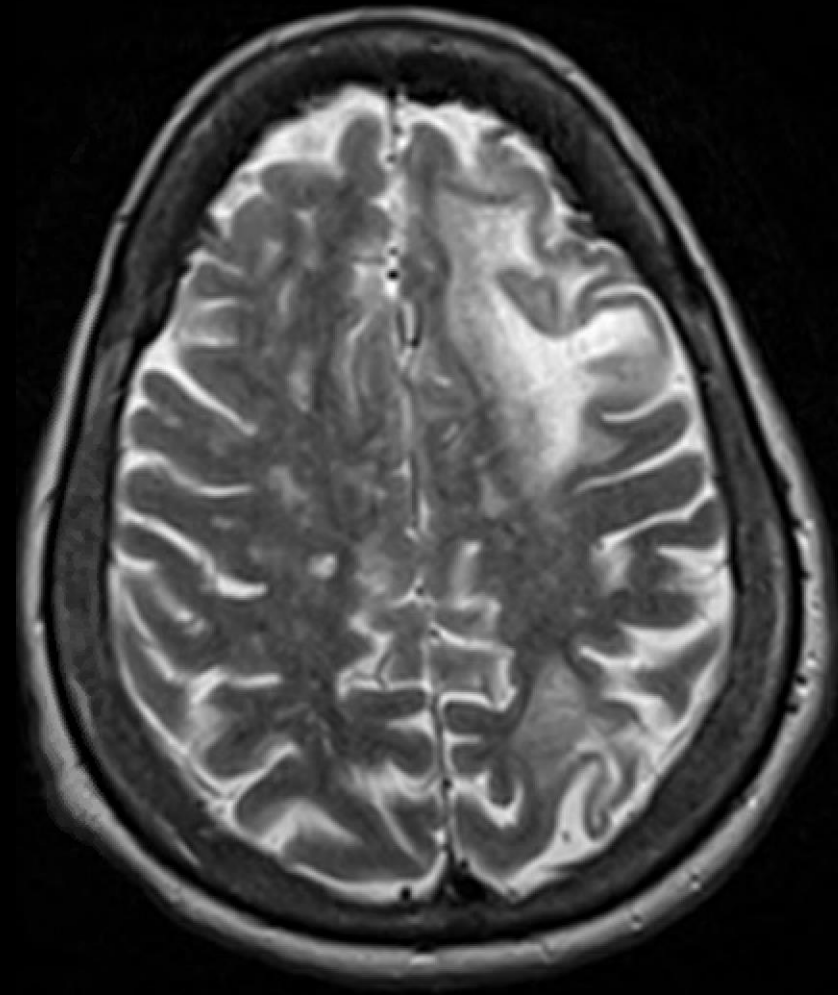
A-C. Axial FLAIR MR images showing multifocal signal abnormalities throughout the cerebral white matter most notably in the left frontal and left occipital regions

# MRI Brain With and Without Contrast (Unlabeled)

January

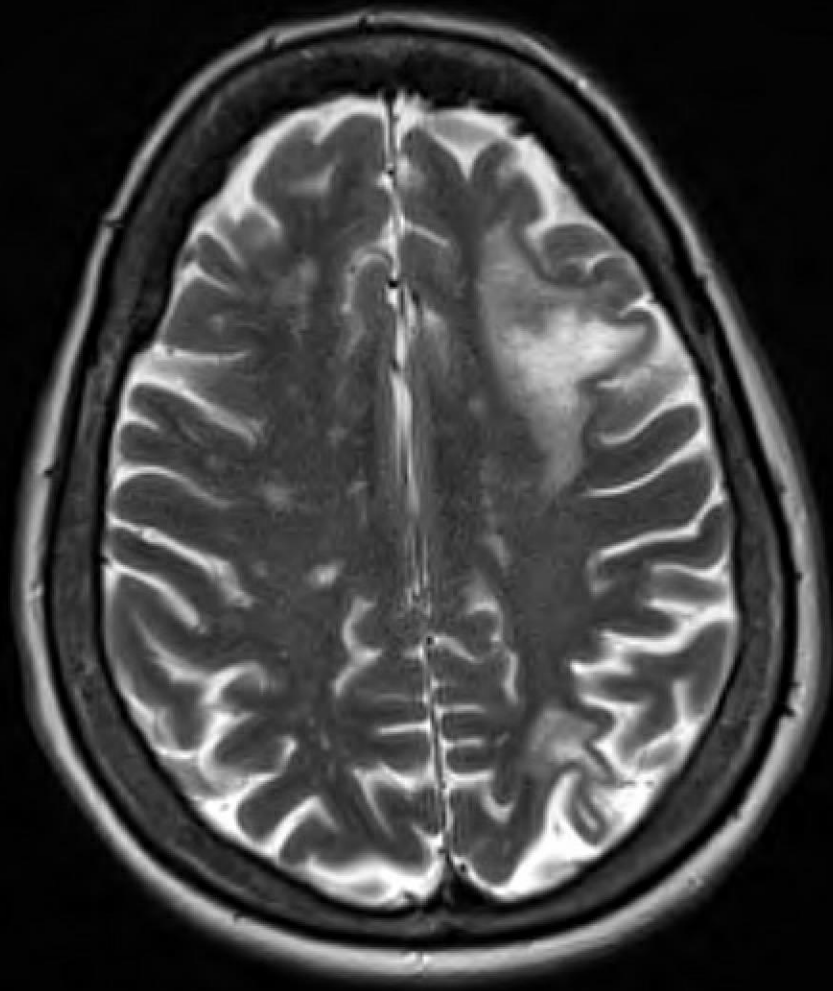


February

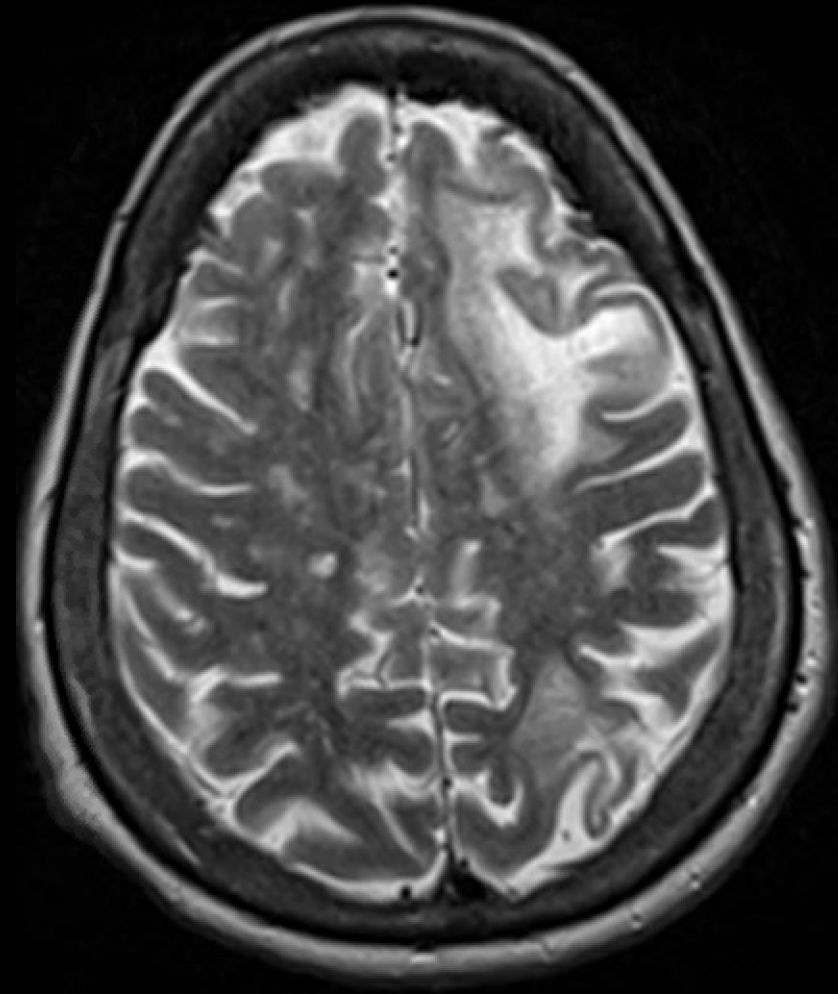


# MRI Brain With and Without Contrast (Labeled)

January



February



Axial T2 weighted MR images one month apart showing progressive disease

# Differential

- Progressive Multifocal Leukoencephalopathy
- Acute Disseminated Encephalomyelitis

# Case Progression

- LP showed clear fluids with no indicators of meningitis or encephalitis, no cells, mild elevated glucose and no proteins.
- JC virus DNA detection test was negative in the CSF

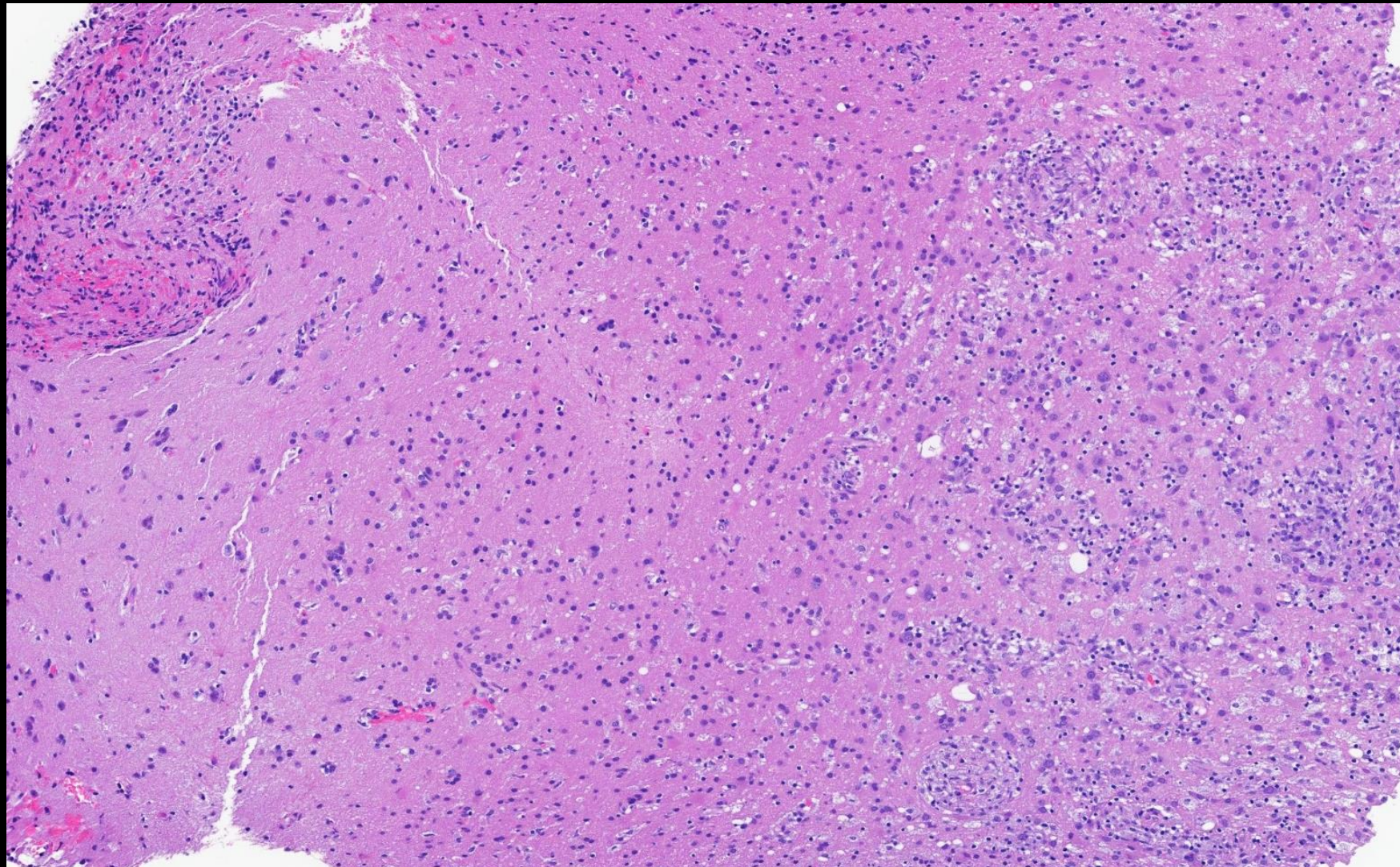
Abnormal Labs During Further Workup	
CD4 T Cell Count	76 (365-1437 cells/mcL)
IgM	27 (37-286 mg/dL)
IgG	743 (767-1590 mg/dL)

- Following a left frontal craniotomy with stereotactic biopsy, JC in situ hybridization studies resulted positive within oligodendrocytes



# Pathology (Labeled)

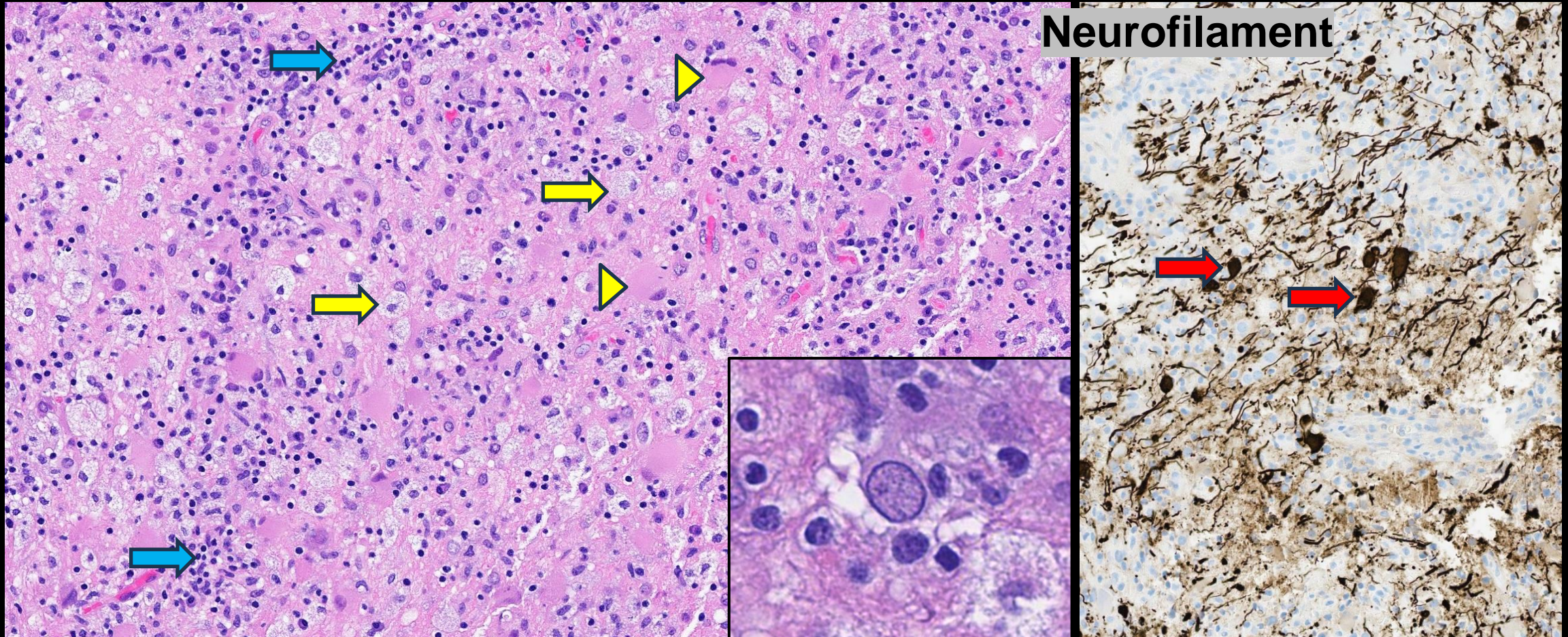
H&E section on low magnification demonstrates a relatively demarcated macrophage-rich inflammatory lesion involving predominantly subcortical white matter.



Left Frontal  
Craniotomy with  
Stereotactic  
Biopsy

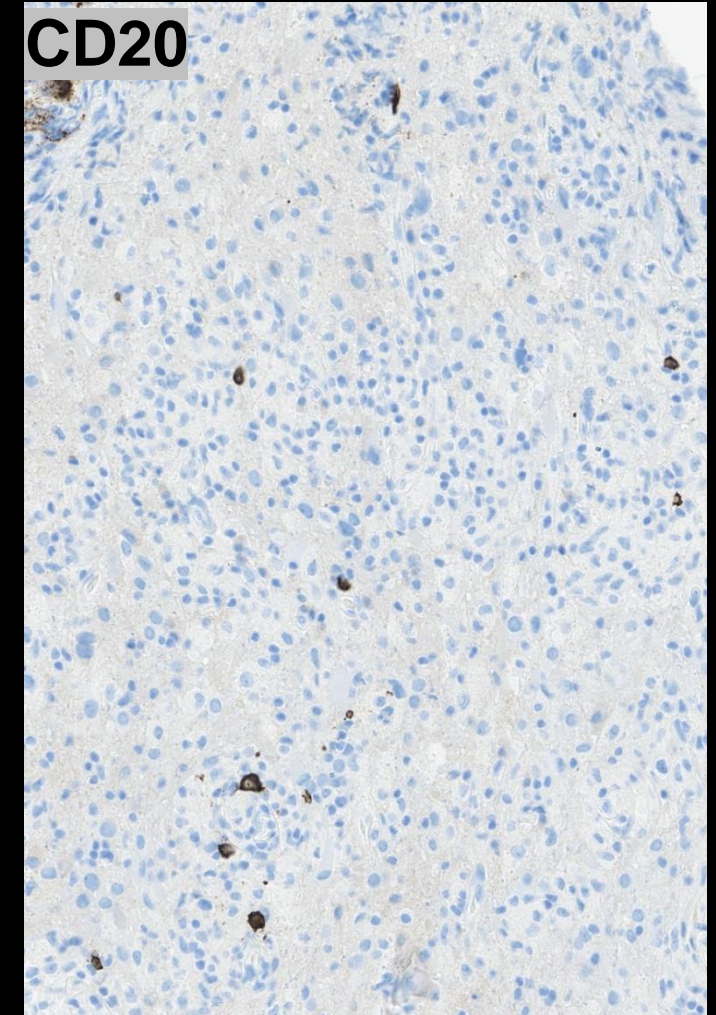
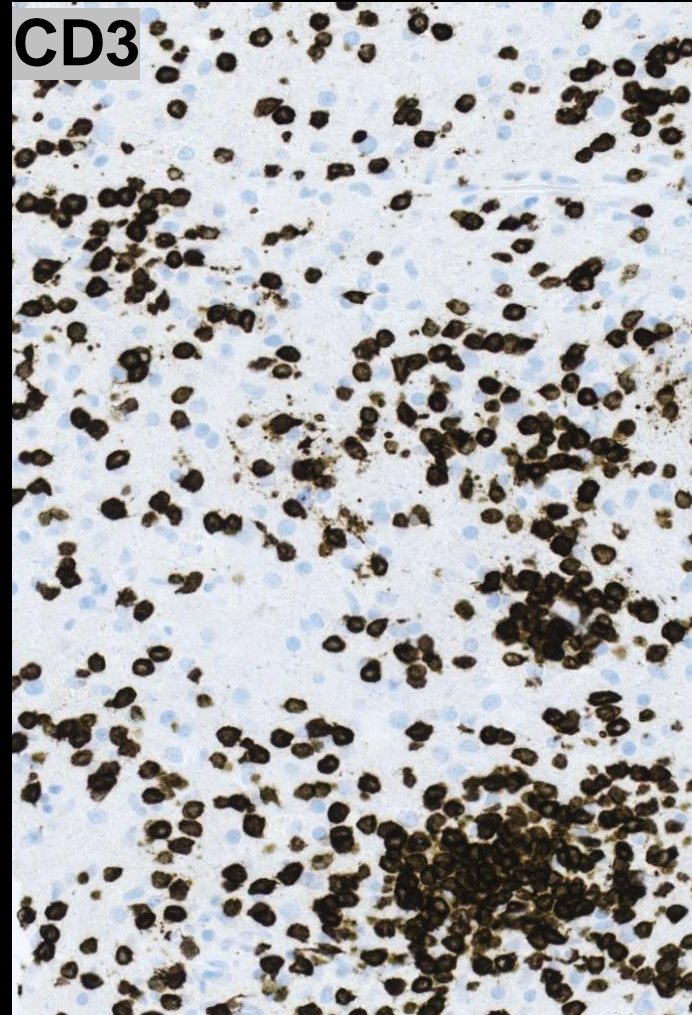
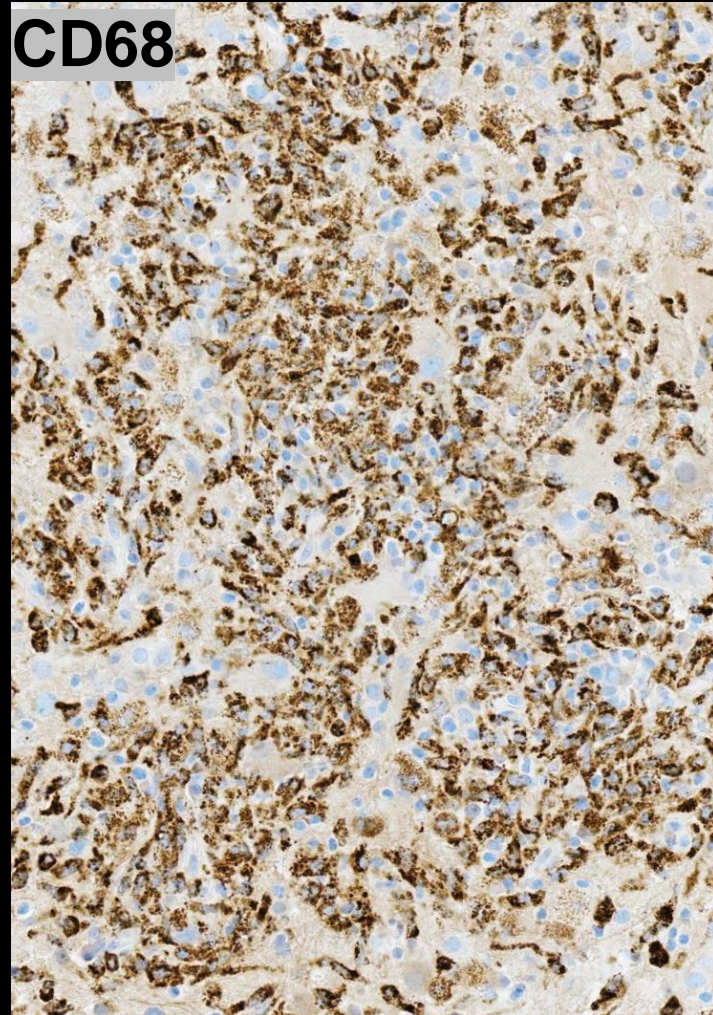
# Pathology (Labeled)

The subcortical white matter shows extensive chronic inflammation with prominent foamy histiocytes (yellow arrows) and small perivascular lymphocytes (blue arrows). Numerous reactive astrocytes with abundant eosinophilic cytoplasm are present in the background (arrowhead). Scattered oligodendrocytes show viral cytopathic changes with enlarged nuclei and margination of the chromatin (inset). Neurofilament immunostain highlights areas with axonal disruption and spheroid formation (red arrows).



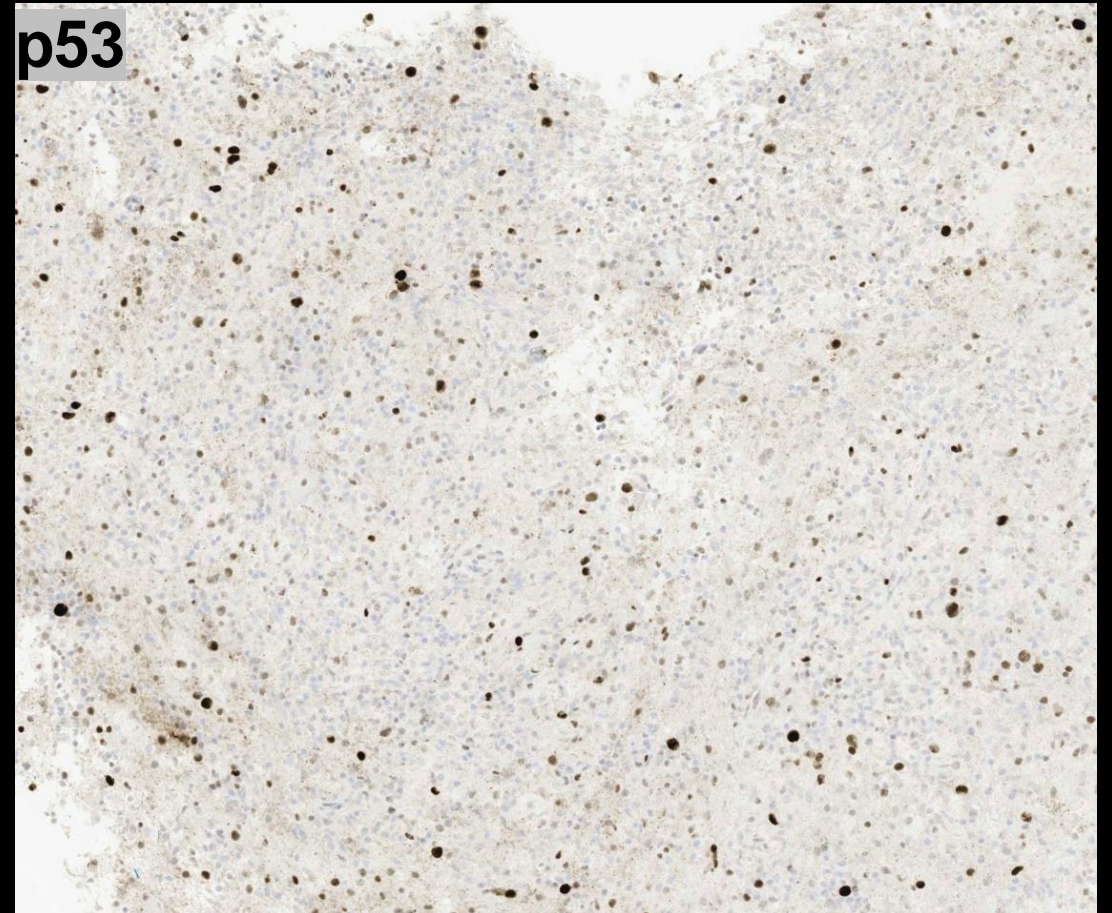
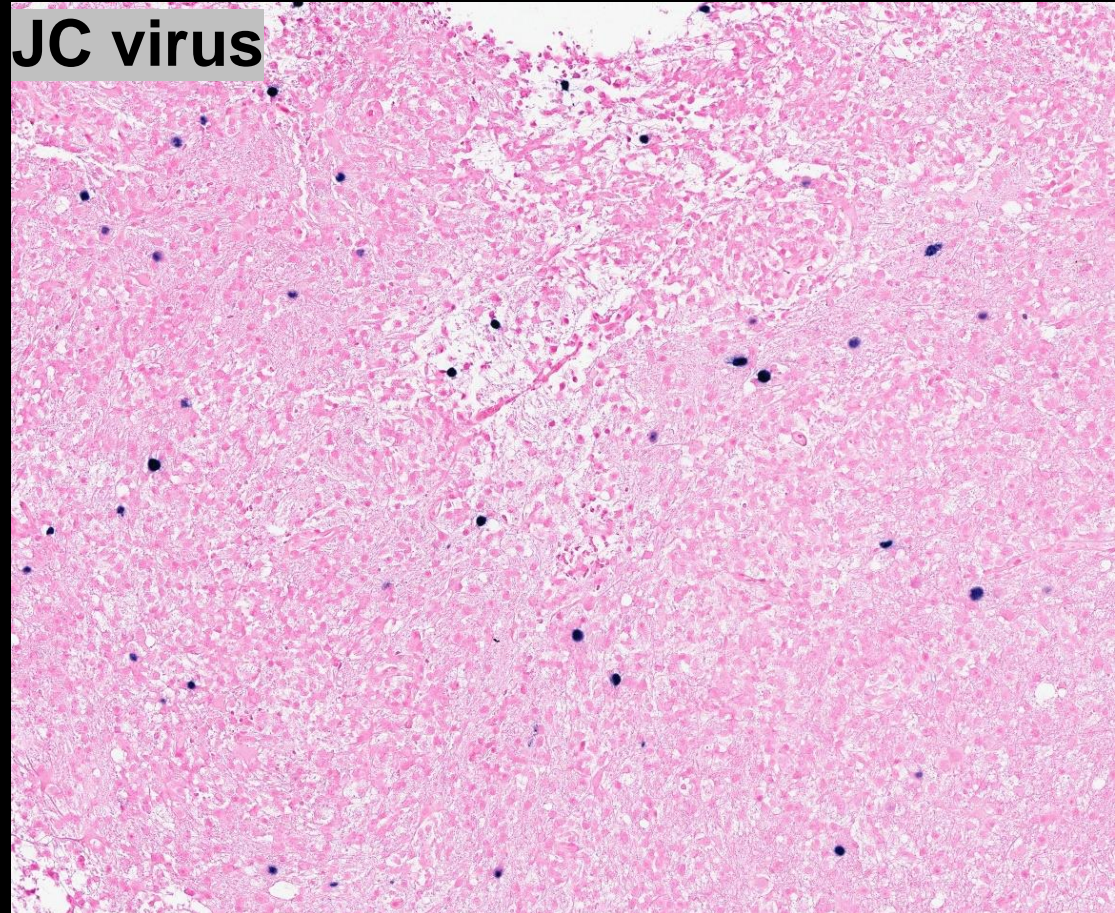
# Pathology (Labeled)

Marked chronic inflammatory infiltrate composed predominantly of CD68-positive histiocytes and small, reactive T-lymphocytes highlighted by CD3 immunostain. Occasional CD20-positive small B-cells are also present.



# Pathology (Labeled)

The lesional cells are positive for JC virus *in-situ* hybridization and exhibit p53 nuclear overexpression, supporting the diagnosis of progressive multifocal leukoencephalopathy.



Final Dx:

Progressive Multifocal Leukoencephalopathy  
(PML)

# PML

## Basics:

- There is a reactivation of JC virus often triggered by immunosuppression, leading to oligodendrocyte infection, and aggressive replication within brain tissue causing demyelination and destruction of oligodendrocytes
- Prognosis is poor - median survival in patients without HIV is 3 months

## Risk Factors:

- Immunosuppression (Lymphoma, Leukemia, Organ Transplant, Autoimmune)
- HIV

## Clinical Features:

- Focal neurologic deficits, isolated encephalopathy, behavioral changes, altered mental status, seizures, and vision changes

# PML

## Diagnostics:

- The diagnosis is usually made based on typical imaging findings
- Confirmatory testing with CSF analysis can be considered, but brain biopsy (although rare) is the gold standard for diagnosis

## Radiographic Features

- MRI brain with and without gadolinium contrast is preferred. Images typically show multifocal, bilateral, asymmetric white matter lesions that are hypointense on T1, hyperintense on T2, and without mass effect (the lack of mass effect helps distinguish from primary CNS lymphoma and toxoplasmosis)
- Frontal, parietal, and occipital lobes are the most commonly involved
- Peripheral restricted diffusion at the leading edge
- CT brain with contrast shows focal hypodense white matter lesions

# Treatment

- Treatment typically consists of supportive care and symptomatic treatment (eg. Seizures)
- In patients with HIV, antiretroviral treatment should be started immediately or optimized to improve immune status
- Monitor for Immune reconstitution inflammatory syndrome (IRIS) which may cause a paradoxical worsening of PML
- In our case, the patient has also benefitted greatly from occupational and speech therapy



# Case Discussion

- This patient initially presented with altered mental status and confusion which later progressed to seizures. Her initial imaging showed classic signs of progressive multifocal leukoencephalopathy. Yet her CSF analysis for JC virus DNA resulted negative twice; however, it should be noted that this is not unheard of in PML, and false negatives can occur in up to 25% of routine PCR tests.
- In addition, there were no obvious causes of immunosuppression. It is presumed that her low CD4 count is a result of an underlying idiopathic T-cell lymphopenia which is an entity known to be associated with PML independent of the use of immunosuppressants or other autoimmune disease.
- Despite a very poor prognosis, this patient is doing well a year out from her initial presentation with improvement of symptoms.

# Case Discussion: Pathology

## Classic Triad

- Demyelination of axons
- Enlarged oligodendrocytes with intranuclear inclusions
- Bizarre astrocytes

# References:

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