AMSER Case of the Month September 2025

65 year old woman with shortness of breath and palpitations

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Patient Presentation

HPI: 65-year-old female presents to the emergency department with acute onset of shortness of breath and palpitations.

Medical History: atrial fibrillation, hypertension, and end-stage renal disease status post-kidney transplant

Past Surgical History: renal transplant (2024)

Family History: No known history

Social History: 60 pack-year history (quit 20+ years ago) and no current alcohol use

Physical exam: Initial examination revealed tachycardia and tachypnea with normal vesicular breath sounds and respiratory effort. Skin, abdominal and neurological examinations were unremarkable

Pertinent Labs

- D-Dimer: positive
- CMP/CBC: sodium of 125
- BNP: 297
- EKG: sinus tachycardia with a left anterior fascicular block and right bundle branch block.

What Imaging Should We Order?

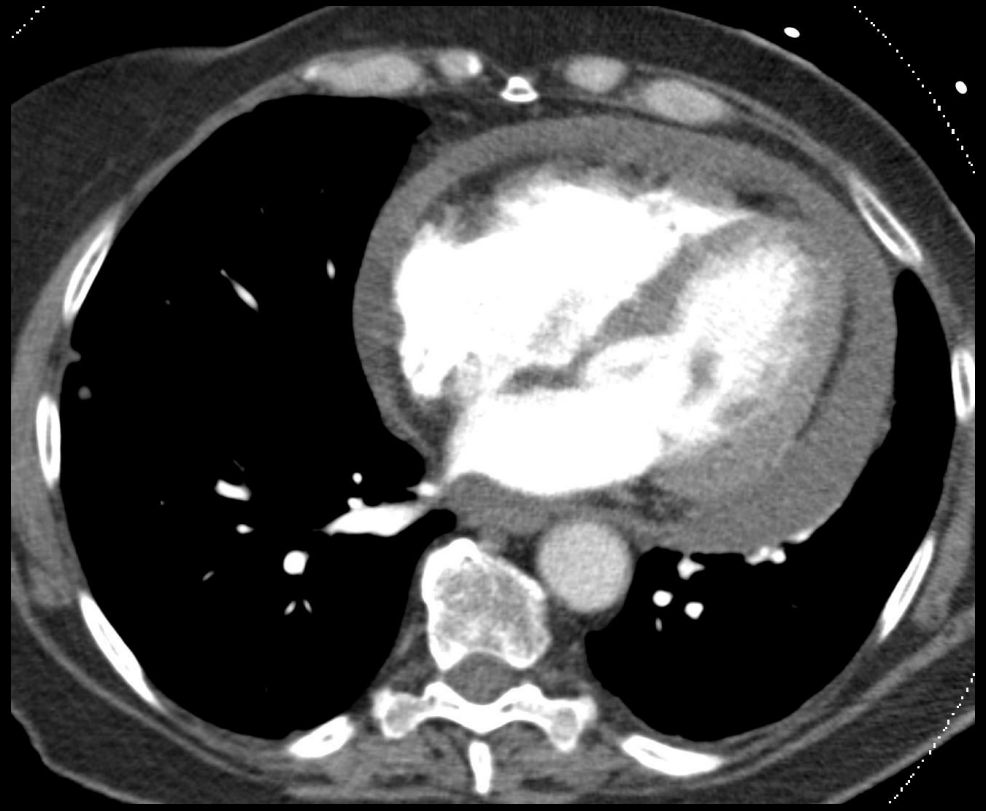
Select the applicable ACR Appropriateness Criteria

Variant 2: **Suspected pulmonary embolism. Low or intermediate pretest probability with a positive D-dimer. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CTA pulmonary arteries with IV contrast	Usually Appropriate	☢☢☢
V/Q scan lung	Usually Appropriate	☢☢☢
MRA pulmonary arteries without and with IV contrast	May Be Appropriate	O
CTA triple rule out	May Be Appropriate (Disagreement)	☢☢☢
US duplex Doppler lower extremity	Usually Not Appropriate	O
US echocardiography transesophageal	Usually Not Appropriate	O
US echocardiography transthoracic resting	Usually Not Appropriate	O
Arteriography pulmonary with right heart catheterization	Usually Not Appropriate	☢☢☢☢
MRA pulmonary arteries without IV contrast	Usually Not Appropriate	O
CT chest with IV contrast	Usually Not Appropriate	☢☢☢
CT chest without and with IV contrast	Usually Not Appropriate	☢☢☢
CT chest without IV contrast	Usually Not Appropriate	☢☢☢
CTA chest with IV contrast with CTV lower extremities	Usually Not Appropriate	☢☢☢

This imaging modality was ordered by the EM physician

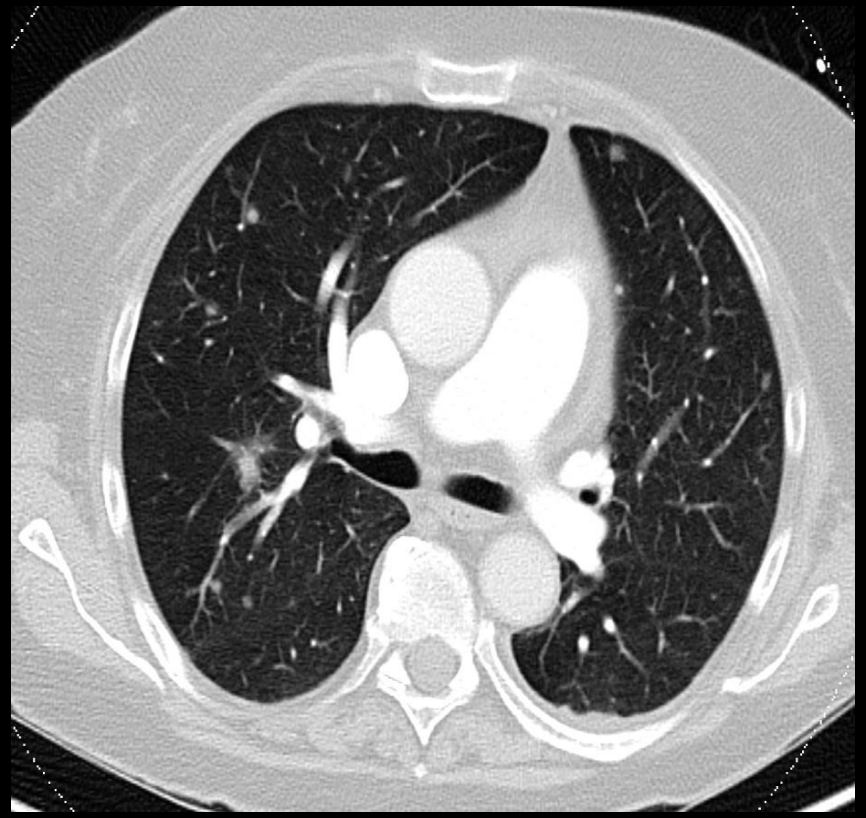
Findings (unlabeled)



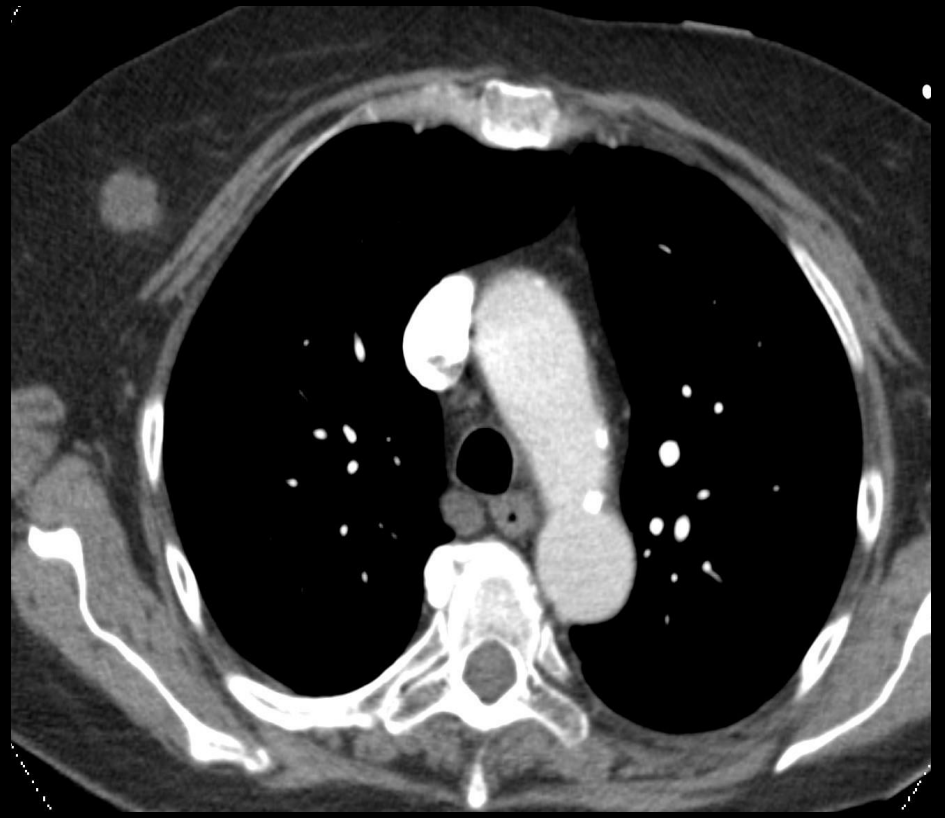
Axial CTA Chest

Axial CTA Chest

Findings (unlabeled)



Axial CTA Chest



Axial CTA Chest

Axial CTA Chest

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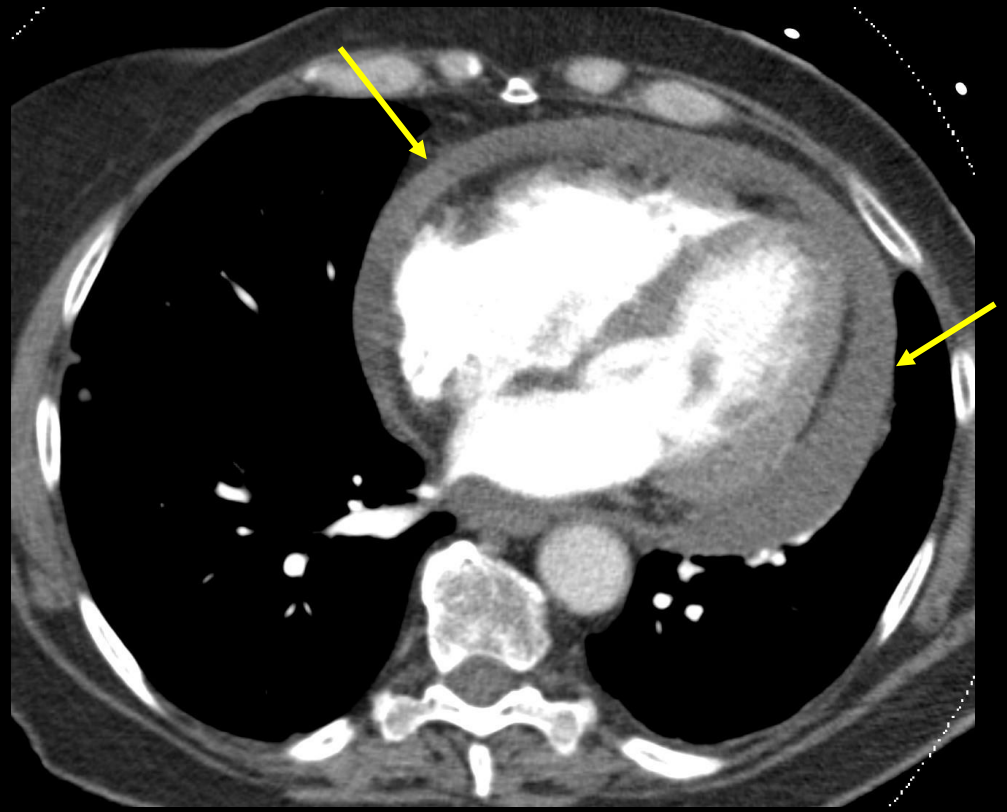
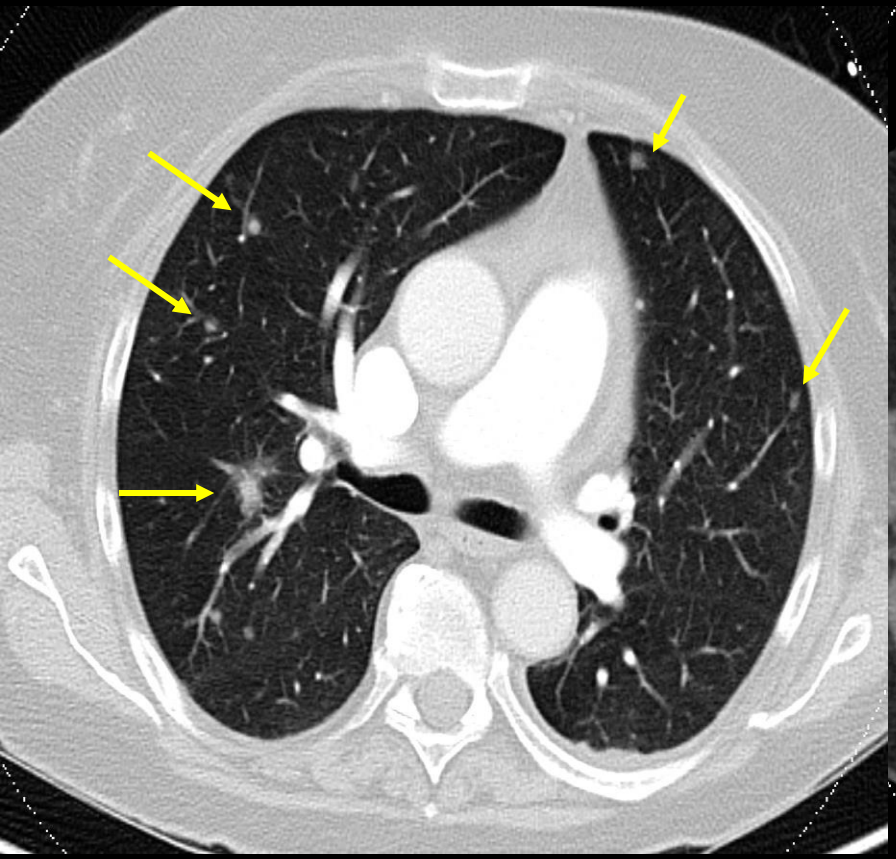
Findings (labeled)



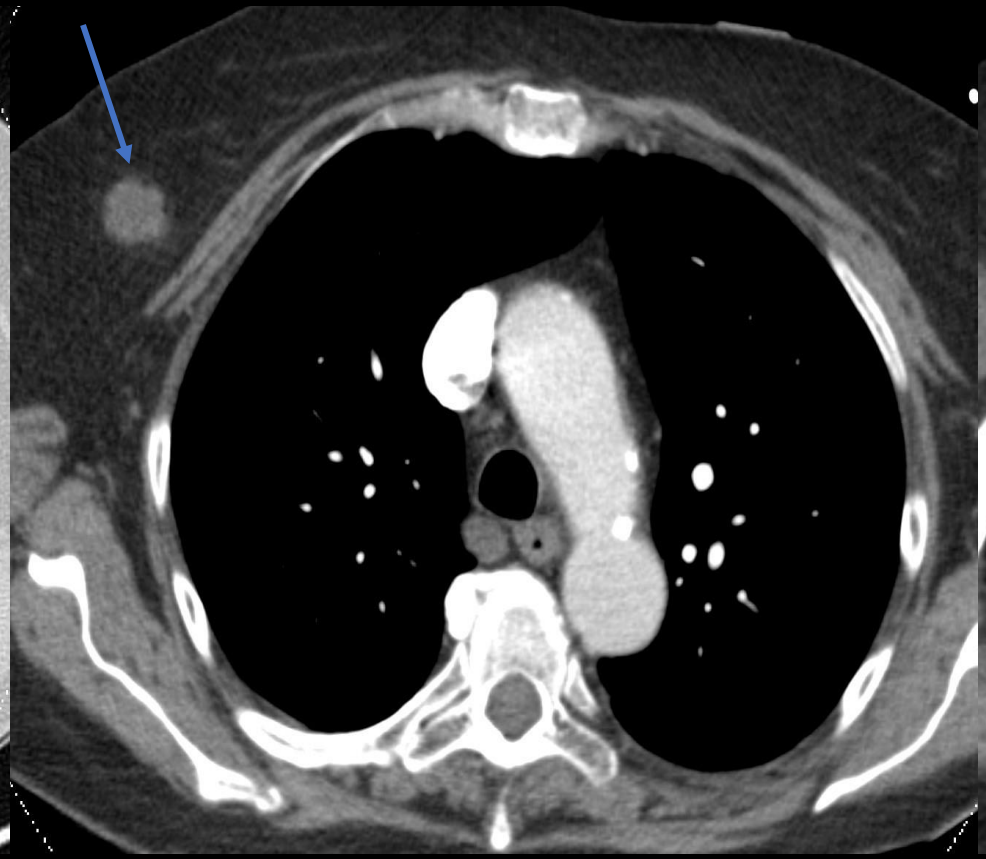
Moderate sized pericardial effusion

Soft tissue density peritoneal masses

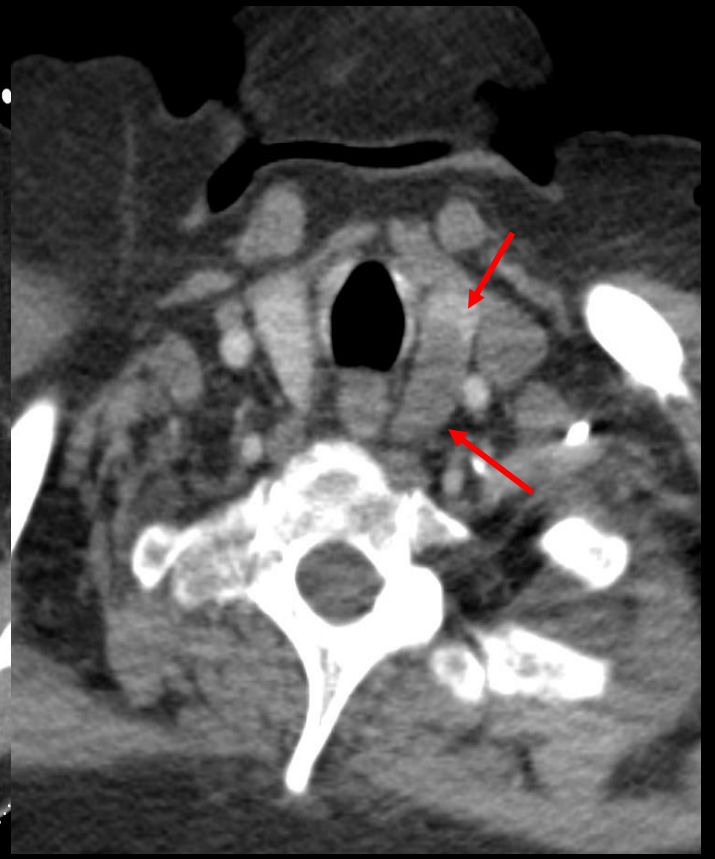
Findings (labeled)



Numerous bilateral pulmonary nodules



Soft tissue density lobulated mass in R breast



large hypodense nodule in L thyroid lobe

Interval History

- On hospital day (HD) 2, ultrasound-guided biopsy of the right breast lesions was performed with surgical pathology findings negative for carcinoma with evidence of necrosis with inflammatory changes. On HD 3, a stroke alert was issued due to sudden-onset left-sided facial droop, dysarthria and upper extremity pronator drift.

What Imaging Should We Order Next?

Select the applicable ACR Appropriateness Criteria

Variant 2: **Adult. Focal neurologic deficit. Clinically suspected acute ischemic stroke. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without IV contrast	Usually Appropriate	O
CT head without IV contrast	Usually Appropriate	☢☢☢
CTA head with IV contrast	Usually Appropriate	☢☢☢
CTA neck with IV contrast	Usually Appropriate	☢☢☢
US duplex Doppler carotid artery	May Be Appropriate	O
MRA head without IV contrast	May Be Appropriate	O
MRA neck without and with IV contrast	May Be Appropriate	O
MRA neck without IV contrast	May Be Appropriate	O
MRI head perfusion with IV contrast	May Be Appropriate	O
CT head perfusion with IV contrast	May Be Appropriate	☢☢☢
US duplex Doppler transcranial	Usually Not Appropriate	O
Arteriography cervicocerebral	Usually Not Appropriate	☢☢☢
MRA head without and with IV contrast	Usually Not Appropriate	O
MRI head without and with IV contrast	Usually Not Appropriate	O
MRV head without and with IV contrast	Usually Not Appropriate	O
MRV head without IV contrast	Usually Not Appropriate	O
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
CTV head with IV contrast	Usually Not Appropriate	☢☢☢

This imaging modality was ordered by the neurologist

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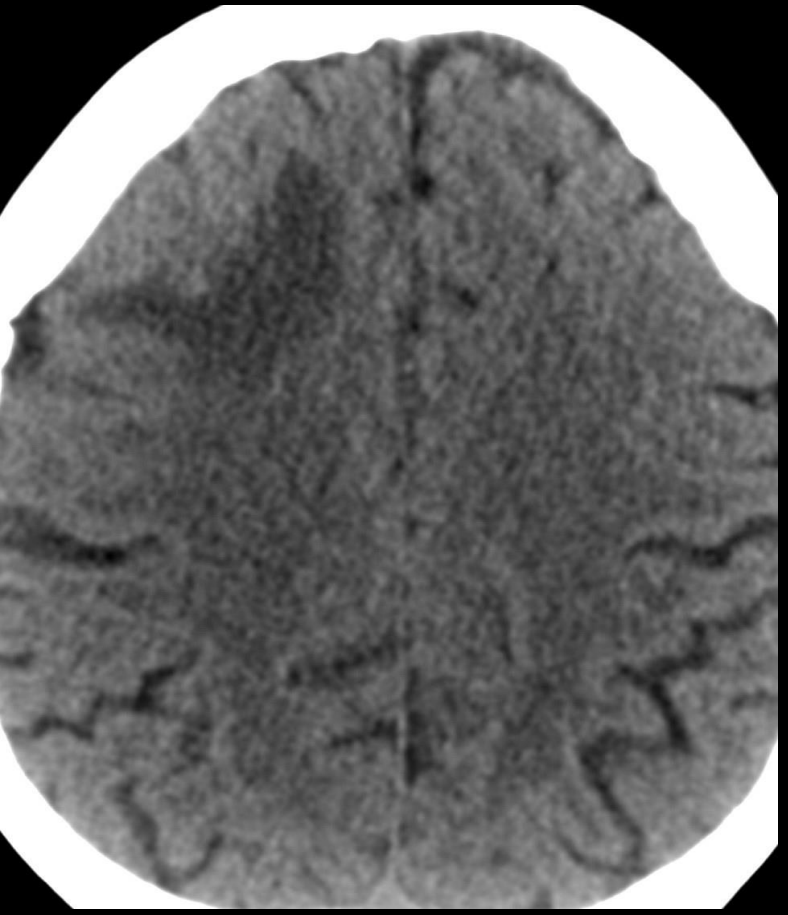
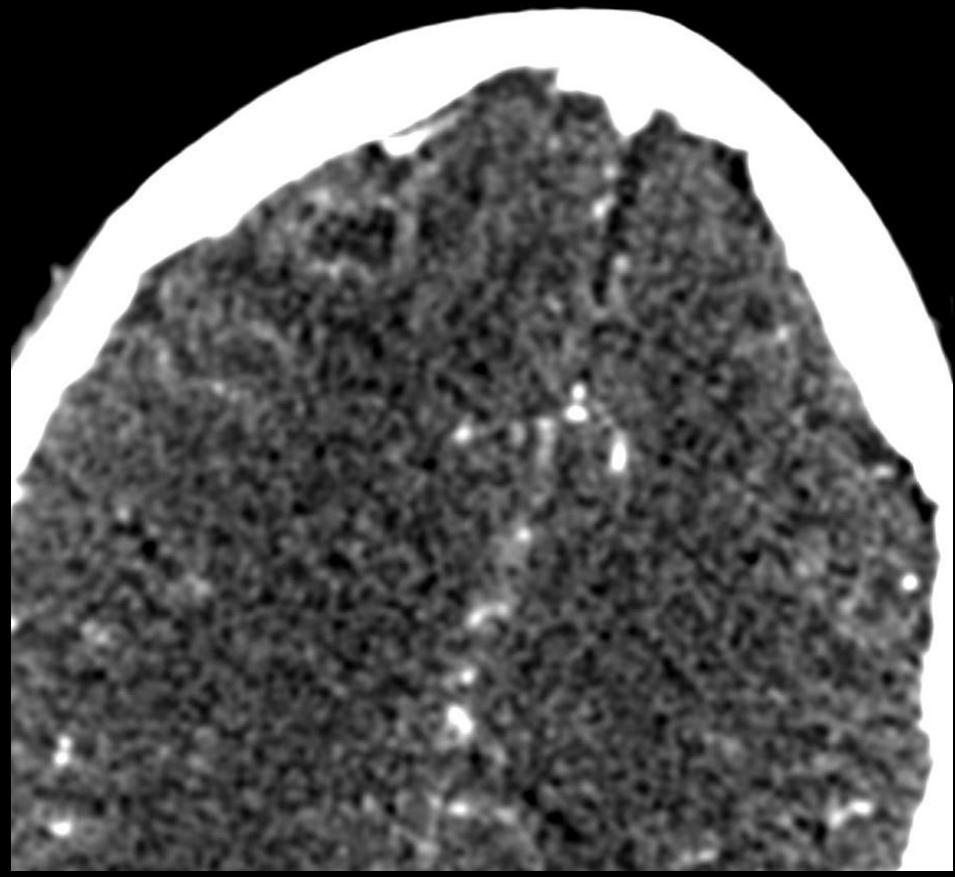
Findings (unlabeled)



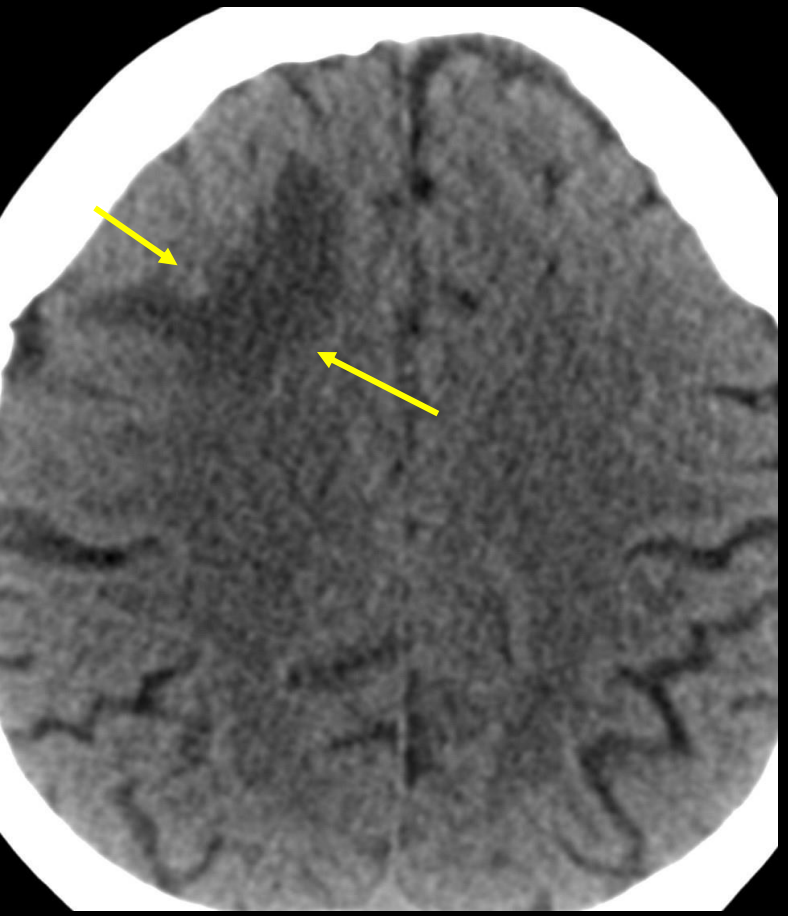
Axial Non-contrast head CT

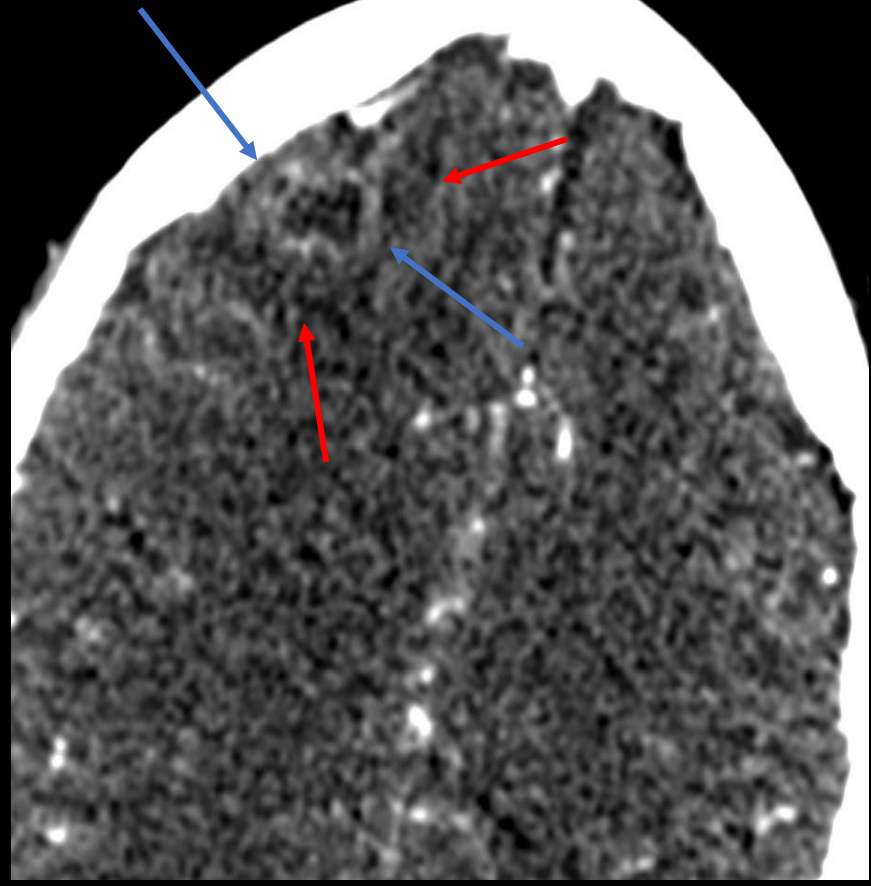
Axial Non-contrast head CT



Axial CTA Head

Findings (labeled)





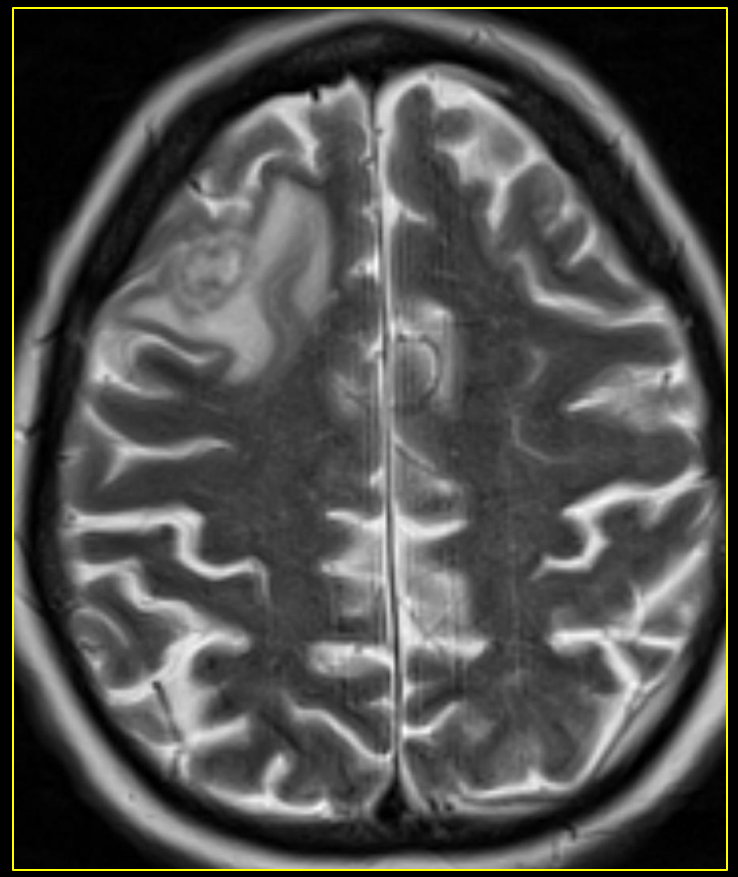
Hypodense areas in the R frontal and R inferior temporal lobes

Ring enhancing R frontal lobe lesion
with surrounding vasogenic edema

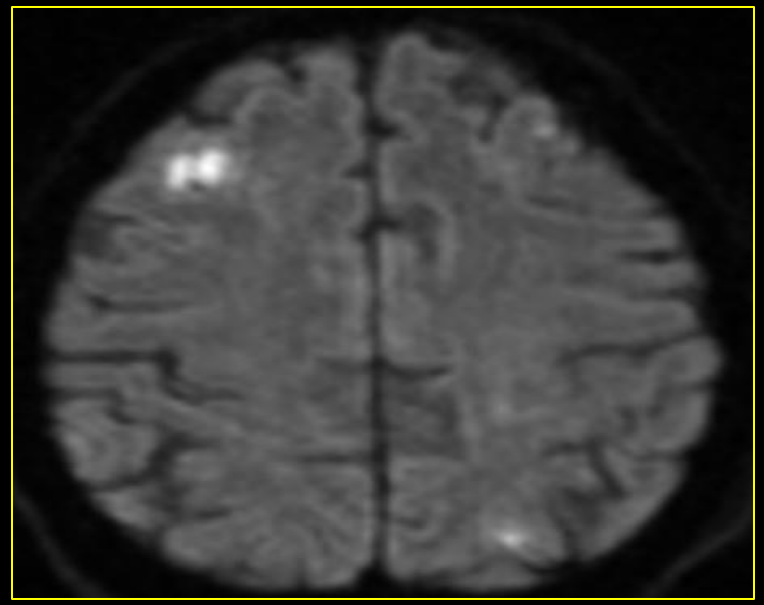
Interval History

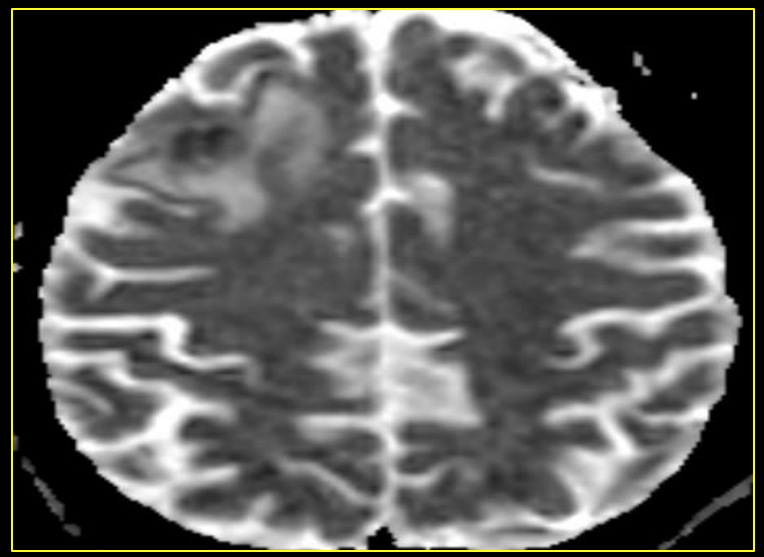
- Given the findings of focal areas of vasogenic edema and ring enhancing lesions on interval CT imaging, the patient's neurologist recommended further evaluation with MRI.

Findings (unlabeled)



Axial MR Brain T2





Axial MR Brain T1 Post Contrast

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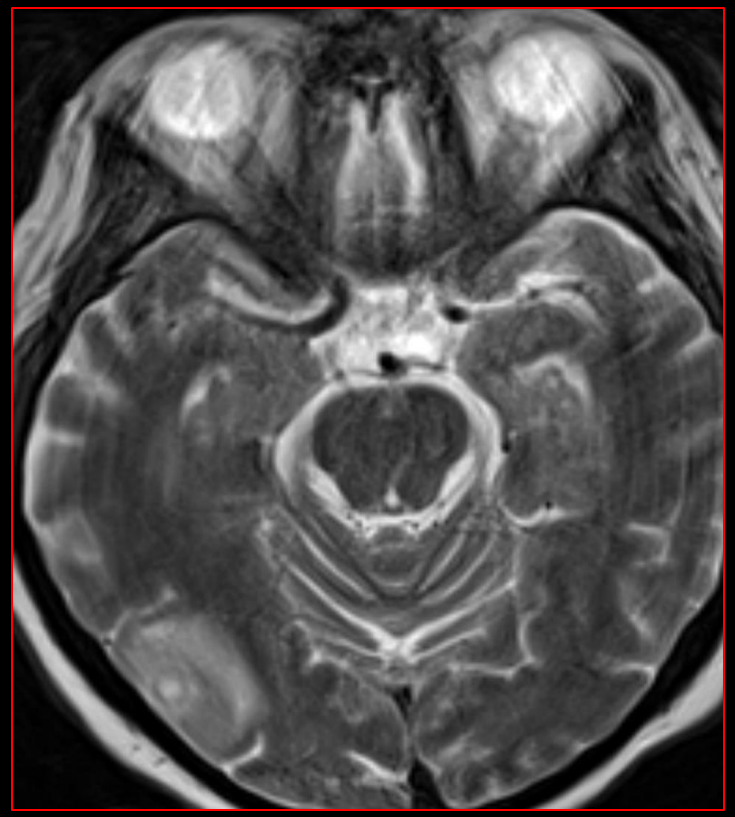
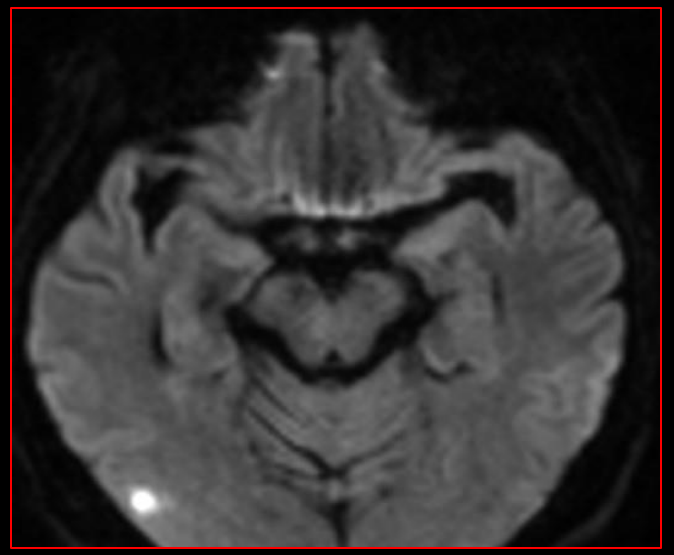
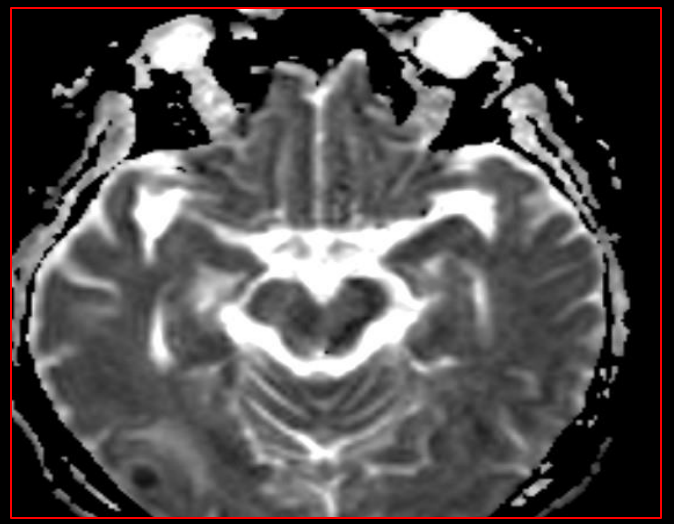
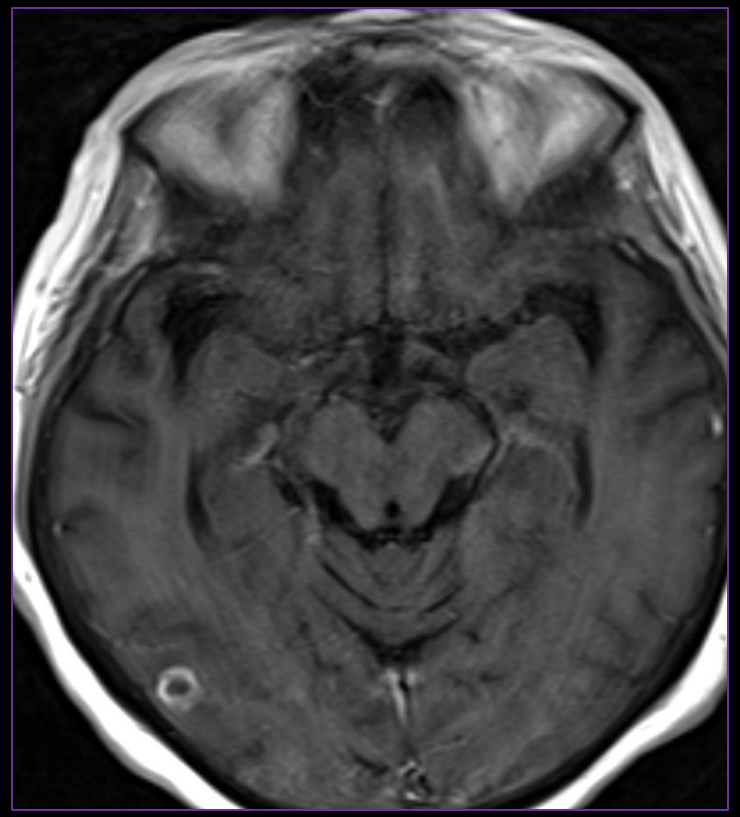
Findings (unlabeled)



Axial MR Brain T2







Axial MR Brain T1
Post Contrast

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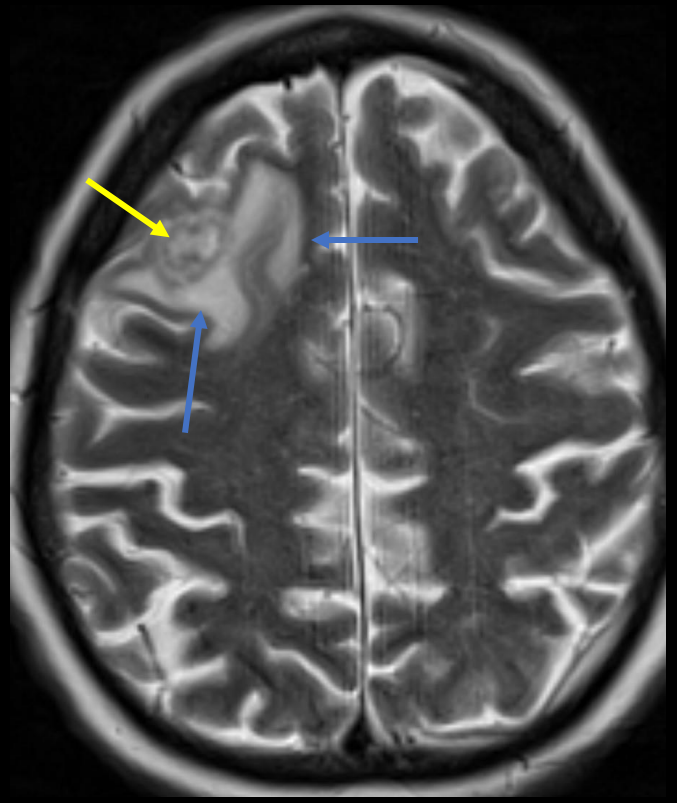
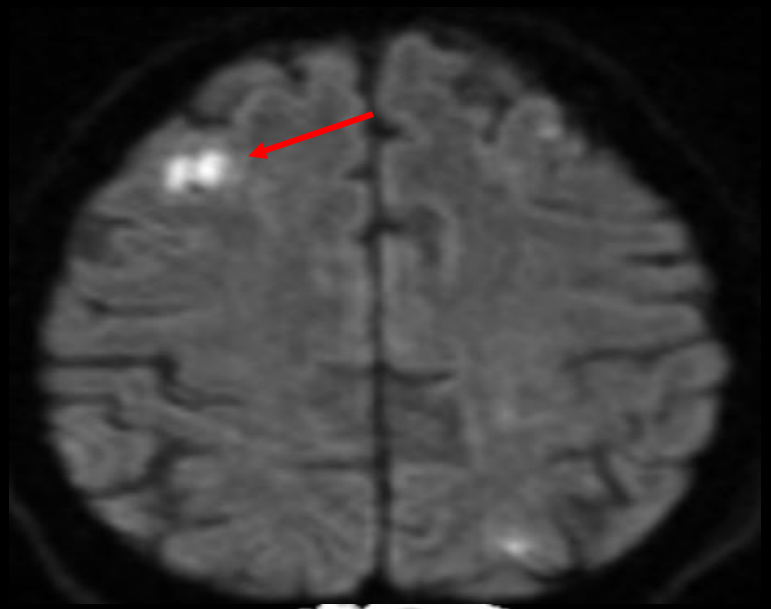
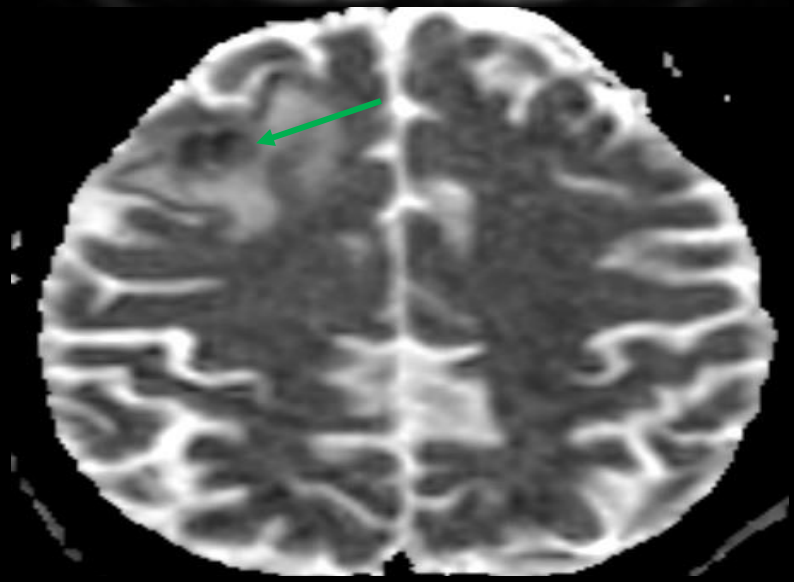
Findings (labeled)



central hyperintense lesion in the R frontal lobe with surrounding vasogenic edema and associated restricted diffusion on DWI/ADC maps





R frontal lobe lesion demonstrates significant peripheral enhancement

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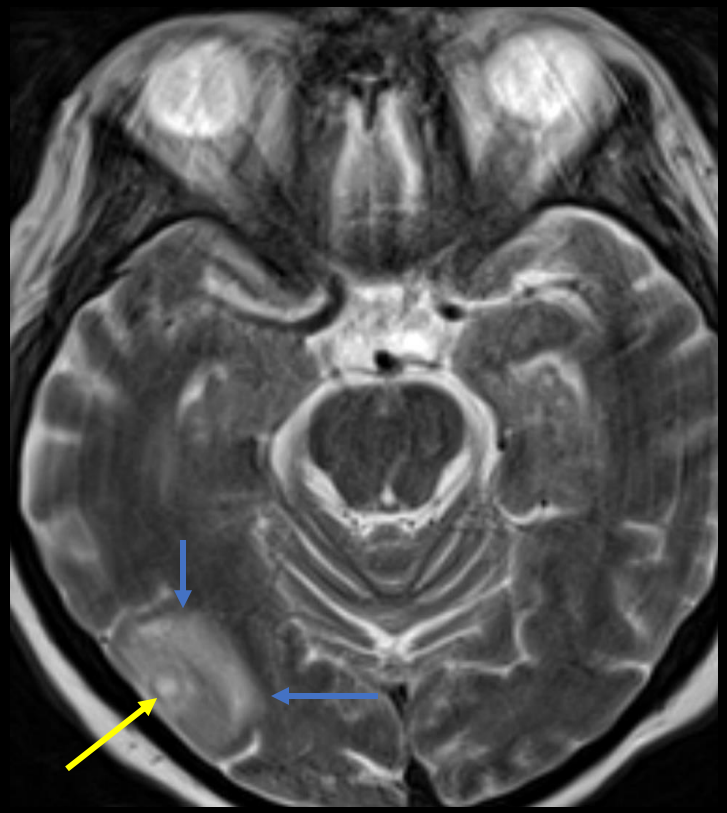
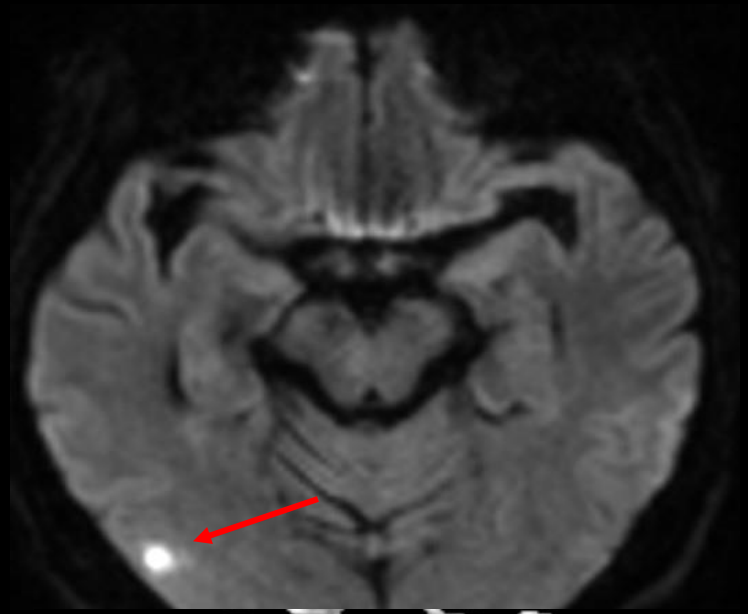
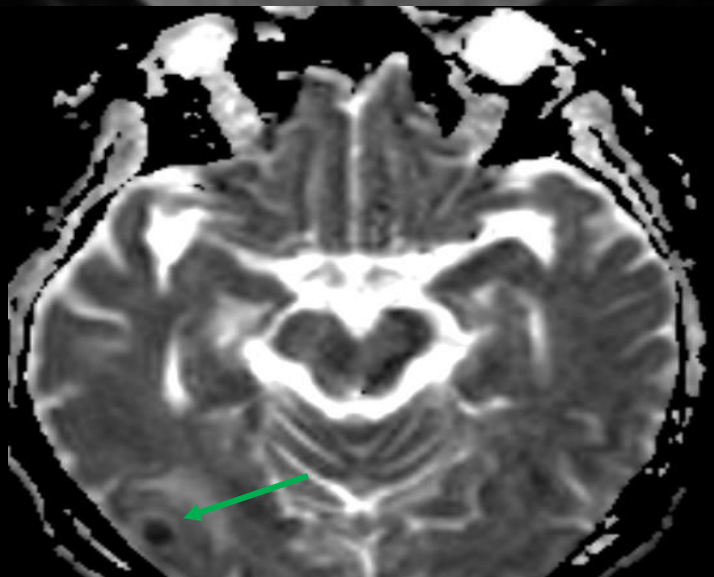
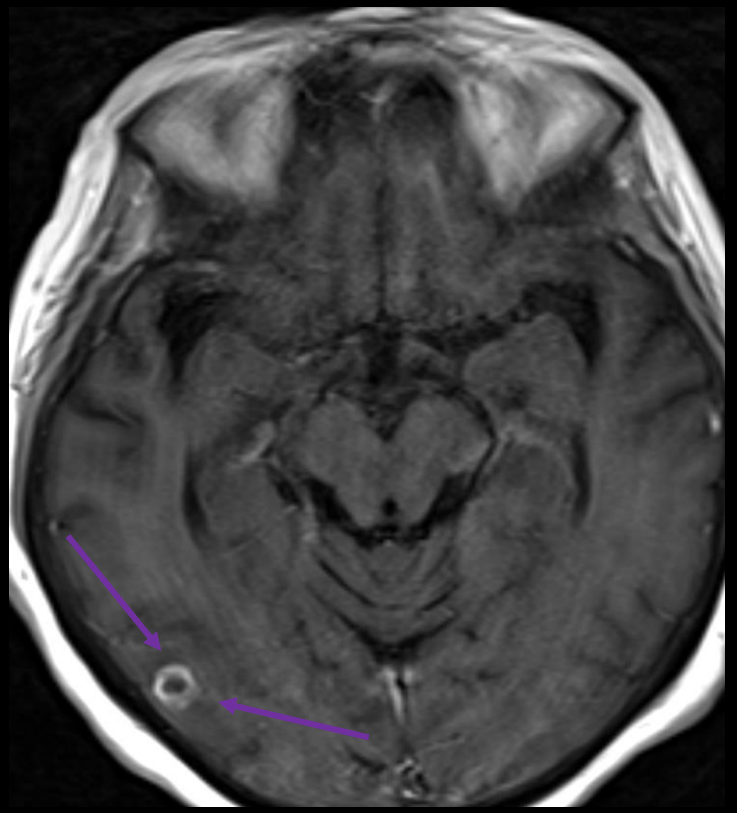
Findings (unlabeled)



central hyperintense lesion in the R inferior temporal lobe with surrounding vasogenic edema and associated restricted diffusion on DWI/ADC maps







R inferior temporal lobe lesion demonstrates significant peripheral enhancement

Interval History

- While the imaging findings of disseminated ring-enhancing lesions were concerning for underlying infection, metastatic disease could not be ruled out necessitating further diagnostic workup
- Due to a pericardial effusion found on echocardiography, the patient underwent pericardiocentesis with pericardial fluid cultures
  - These fluid cultures resulted for *Aspergillus fumigatus.*
- Additionally, serum studies found an elevated galactomannan and a positive 1,3-Beta-D-Glucan level, further supporting a fungal etiology
- Given the patient's underlying immunosuppression and rapid multisystem decompensation, the diagnosis of disseminated aspergillosis was ultimately confirmed

Final Dx:

Disseminated Aspergillosis

Case Discussion: Etiology of Aspergillosis

- Disseminated aspergillosis (DA) is a severe, often fatal manifestation of invasive aspergillosis (IA), defined by hematogenous dissemination of *Aspergillus* species from a primary site, typically the lungs, to noncontiguous organs
- This condition predominantly affects individuals with profound immunosuppression including patients with solid-organ transplants, neutropenia and prolonged use of corticosteroids
- DA is a medical emergency with mortality rates upwards of 90% in cases of cerebral dissemination

Case Discussion: Presentation and Diagnosis of Disseminated Aspergillosis

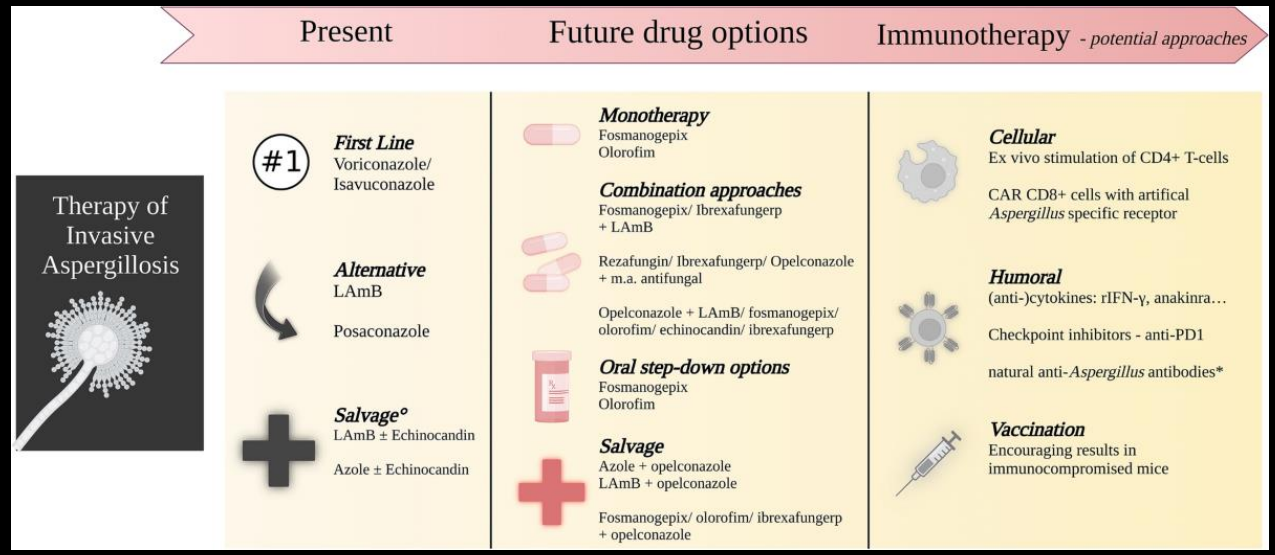
- History and Physical exam
  - Invasive pulmonary aspergillosis is commonly implicated as a precursor to DA, particularly in patients with long stays in the ICU with mechanical ventilation
  - Common presenting symptoms of invasive aspergillosis are non-specific, including fever, cough, chest pain,, malaise, and dyspnea.
  - Given the possibility of widespread organ involvement, physical examination may reveal multisystem deficits
- Imaging (Thorax)
  - Evaluation of DA typically includes the use of CT or MRI, which assist in detecting organ involvement and guiding tissue sampling
  - The initial modality of choice is typically CT chest, which frequently reveals multiple, bilateral pulmonary nodules representing invasive aspergillosis
  - Importantly, DA can mimic metastatic disease on imaging; however, certain features favor a fungal etiology of the lesions:
  - The halo sign describes a nodule with surrounding ground-glass opacity and is found in approximately 61% of patients with pulmonary aspergillosis.
  - Less frequent findings specific to fungal infection include cavitary lesions (20%) and the air crescent sign (10%) which describes a crescent-shaped lucency within a nodule representing necrosis or cavitation.
  - Importantly, the initiation of antifungal treatment with findings of the halo sign correlated with significantly better 12-week survival (71% vs. 53%) and treatment response (52% vs. 29%), emphasizing its diagnostic and prognostic value

Case Discussion: Presentation and Diagnosis of Disseminated Aspergillosis (cont'd)

- Imaging (Brain)
  - In the event of cerebral dissemination, MRI is the preferred imaging modality due to superior visualization of soft tissue and sensitivity for early abscesses/infarcts
  - The most distinctive central nervous system findings of DA are multiple ring-enhancing lesions with surrounding vasogenic edema and areas of diffusion restriction
  - these features overlap with bacterial abscesses, making distinguishing the etiology of such findings difficult
  - Fungal lesions may demonstrate more irregularity or partial ring enhancement along with a predilection for vascular invasion. Bacterial abscesses tend to present as more well-circumscribed lesions with completely enhancing rims
- Imaging (Cardiac)
  - Cardiac involvement may be discerned with transesophageal echocardiography or cardiac magnetic resonance imaging to evaluate for mobile intracavitary masses consistent with fungal endocarditis
- Unique features of this case
  - First, the pattern of dissemination included the lungs, pericardium, breast, thyroid, peritoneum, and brain—a distribution that radiographically mimicked metastatic malignancy.
  - While pulmonary and cerebral involvement are well-documented in IA, nodular involvement of the breast and thyroid is rare and may confound initial diagnostic impressions.
  - Second, the presence of a mobile mass on the left ventricular endocardium suggested cardiac aspergillosis, a rare and diagnostically challenging complication, often identified post-mortem

Case Discussion: Treatment and Prognosis of Disseminated Aspergillosis

- Management of disseminated aspergillosis typically involves prolonged course of combination antifungal therapy
- This patient was treated initially with a loading dose of intravenous voriconazole followed by maintenance therapy with oral voriconazole suspension at 250 mg every 12 hours. Concurrently, amphotericin B Liposomal 500 mg in dextrose 5% 250 mL was administered via IV piggyback.
- Micafungin 100 mg intravenous daily was added to the regimen to enhance coverage via synergistic activity with the other antifungals.
- Despite initiation of appropriate treatment, the patient's rapid neurologic decline and subsequent death reflect the aggressive course and high mortality rate of disseminated aspergillosis, particularly with CNS involvement.
- This outcome highlights the critical importance of early recognition with tools such as imaging, laboratory work and clinical assessment in order to initiate prompt treatment



Reference 1 (treatment of IA and future directions)

References:

1) Boyer J, Feys S, Zsifkovits I, Hoenigl M, Egger M. Treatment of Invasive Aspergillosis: How It's Going, Where It's Heading. *Mycopathologia*. 2023;188(5):667-681. doi:10.1007/s11046-023-00727-zFosses Vuong M, Hollingshead CM, Waymack JR. Aspergillosis. [Updated 2023 Feb 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482241/

2) Greene RE, Schlamm HT, Oestmann JW, et al. Imaging findings in acute invasive pulmonary aspergillosis: clinical significance of the halo sign. *Clin Infect Dis*. 2007;44(3):373-379. doi:10.1086/509917

3) Herbrecht R, Denning DW, Patterson TF, et al. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. *N Engl J Med*. 2002;347(6):408–415.

4) Kuhlman JE, Fishman EK, Burch PA, Khangure MS. Invasive pulmonary aspergillosis in acute leukemia. *Radiology*. 1988;166(2):357–361.

5) Marr KA, Carter RA, Crippa F, Wald A, Corey L. Epidemiology and outcome of mould infections in hematopoietic stem cell transplant recipients. *Clin Infect Dis*. 2002;34(7):909–917.

6) Marr KA, Schlamm HT, Herbrecht R, et al. Combination antifungal therapy for invasive aspergillosis: a randomized trial. *Ann Intern Med*. 2015;162(2):81–89.

7) Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the IDSA. *Clin Infect Dis*. 2016;63(4):e1-e60.

8) Schwartz S, Thiel E. Update on the treatment of cerebral aspergillosis. *Ann Hematol*. 2004;83 Suppl 1:S42-S44. doi: 0849-8

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