AMSER Case of the Month December 2025

26-year-old female with headache and weakness

Natalie Sarafian MS4, UC San Diego School of Medicine
Luke Wojdyla DO, UC San Diego Department of Radiology
Nikdokht Farid MD, UC San Diego Department of Radiology

UC San Diego Health Sciences

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Patient Presentation

- 26-year-old female with a history of B-ALL referred to the ED from her chemotherapy infusion center for weakness, cough, headache, fever and tachycardia
- Vitals:
  - BP 124/97
  - Pulse 116
  - Temp 97.9 °F (36.6 °C)
  - Resp 16
  - SpO2 100%

Pertinent Labs

CBC

- WBC 0.5 (ref: 4.0 - 10.0 1000/mm3)
- Hgb 6.3 (ref: 11.2 - 15.7 gm/dL)
- Plt Count 15 (ref: 140 - 370 1000/mm3)
- ANC-Manual Mode 0.0 (ref: 1.6 - 7.0 1000/mm3)

Lactate:

- 3 -> 1.7 after fluid bolus

Hospital Course

- The patient developed recurrent fevers and diarrhea. A Code Sepsis was activated.
  CT chest and CT abdomen/pelvis were unremarkable except for minimal, nonspecific colonic wall thickening.
- Subsequently, the patient developed new right-sided facial weakness and left-sided ptosis. A Code Stroke was activated.
  CT head and CTA were unremarkable.
- Given the persistent facial weakness and ptosis, there was increasing concern for alternative etiologies of bilateral cranial neuropathies, including cerebrovascular events, infectious, neoplastic, or inflammatory leptomeningeal processes.

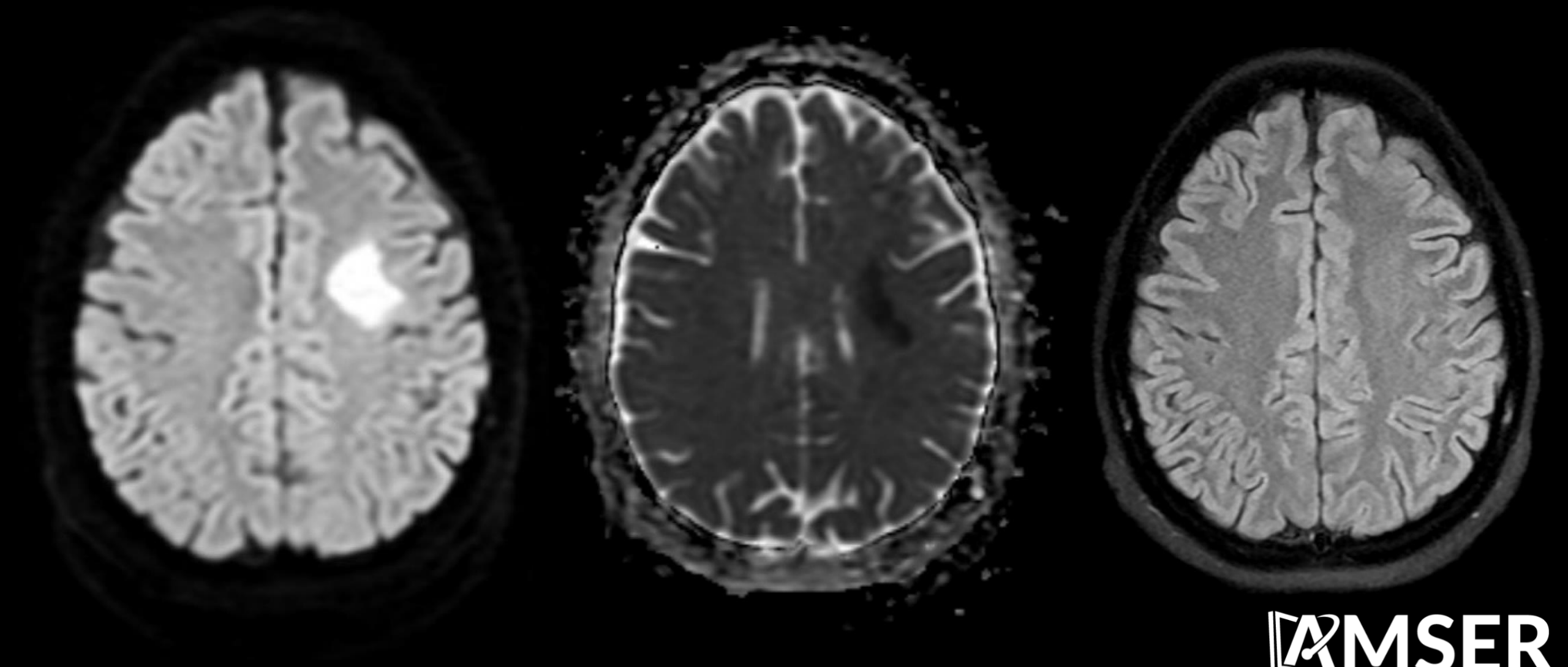
What Imaging Should We Order?

Select the applicable ACR Appropriateness Criteria

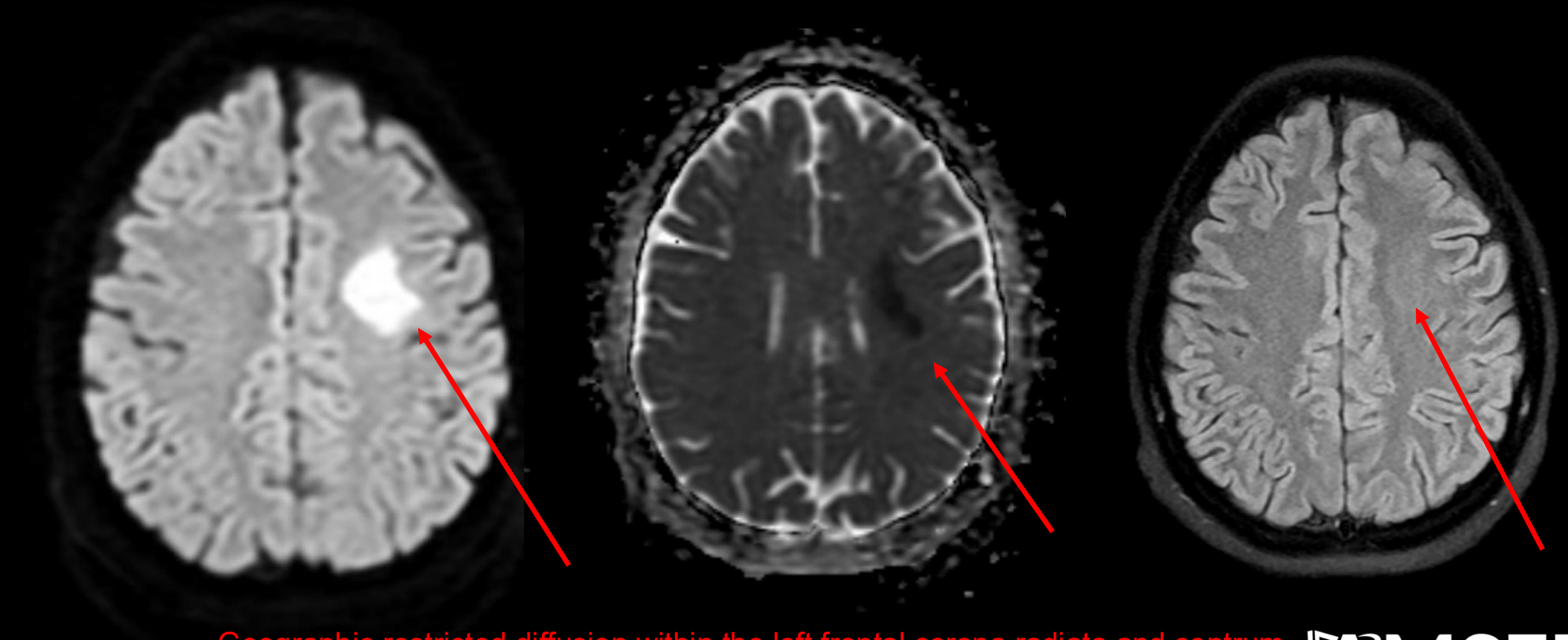
Brain tumor metastatic, screening, extracranial malignancy	3198610	MRI head without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually appropriate
		MRI complete spine without and with IV contrast	0 mSv O	0 mSv [ped] O	May be appropriate
		MRI head without IV contrast	0 mSv O	0 mSv [ped] O	May be appropriate
		MR spectroscopy head without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI complete spine with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI complete spine without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI functional (fMRI) head without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI head perfusion with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI head perfusion without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI head with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		MRI head without IV contrast with DTI	0 mSv O	0 mSv [ped] O	Usually not appropriate
		CT head with IV contrast	1-10 mSv ☢☢☢	0.3-3 mSv [ped] ☢☢☢	Usually not appropriate
		CT head without and with IV contrast	1-10 mSv ☢☢☢	3-10 mSv [ped] ☢☢☢☢	Usually not appropriate
		CT head without IV contrast	1-10 mSv ☢☢☢	0.3-3 mSv [ped] ☢☢☢	Usually not appropriate

This imaging modality was ordered by the Neurology team

MRI W/O Contrast Findings: (unlabeled)



MRI W/O Contrast Findings: (labeled)



Geographic restricted diffusion within the left frontal corona radiata and centrum semiovale. DDx includes CNS involvement of lymphoma or acute infarct.

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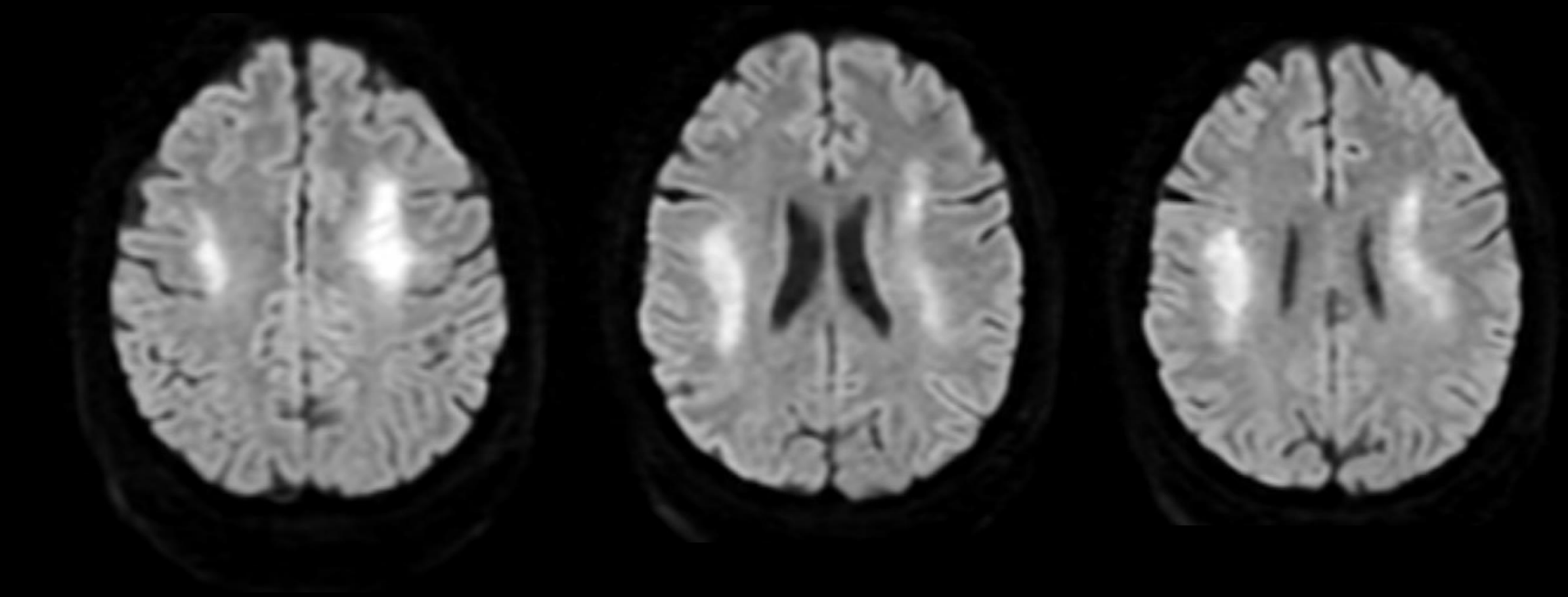
Hospital course (continued)

Differential diagnosis based on MRI and clinical findings included neoplastic involvement and acute infarct.

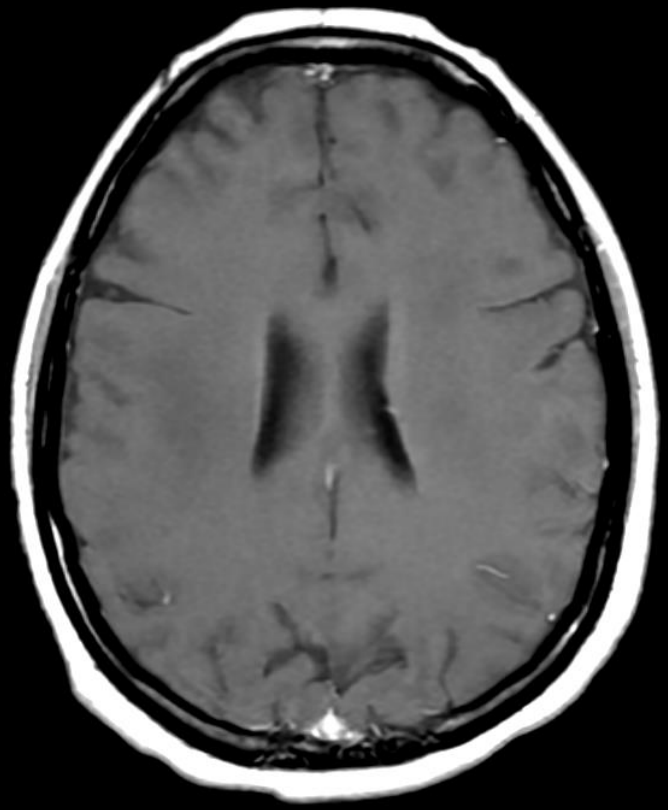
Within 12 hours, a Code Stroke was reactivated due to concern for altered mental status. The patient was found to be in respiratory failure and was subsequently intubated.

A repeat MRI was obtained

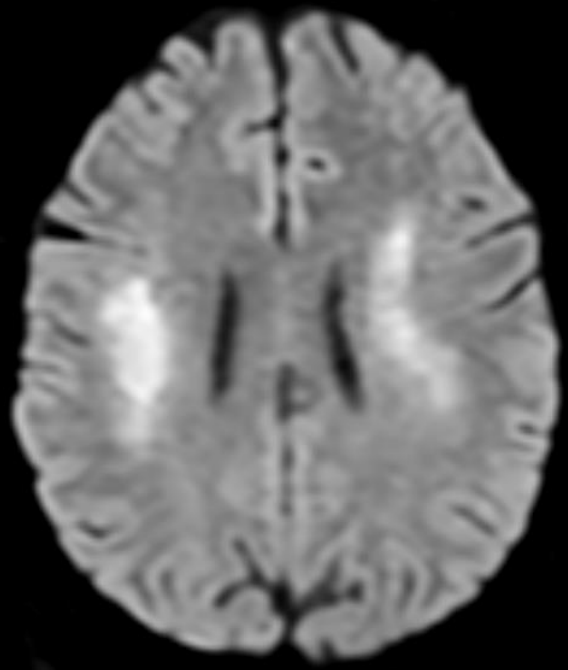
MRI W/ and W/O contrast Findings: (unlabeled)



MRI W/ and W/O contrast Findings: (unlabeled)



T1 post-contrast



DWI

MRI W/ and W/O Contrast Findings: (labeled)

Compared to the brain MRI performed earlier today, increased restricted diffusion within the left frontal centrum semiovale extending into the corona radiata and now involving the right centrum semiovale and right corona radiata.

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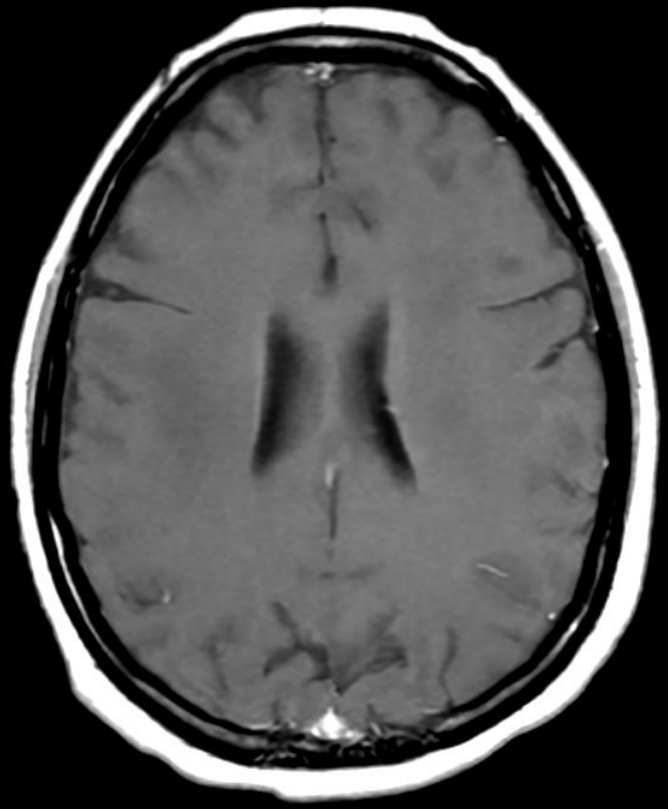
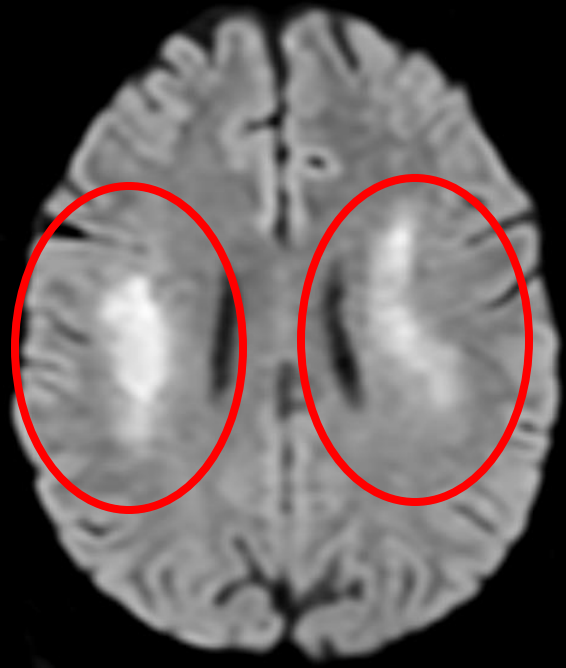
MRI W/ and W/O contrast Findings: (labeled)



T1 post-contrast



DWI

No abnormal post-contrast enhancement

Final Dx:

Methotrexate-Associated Leukoencephalopathy

Methotrexate (MTX)

- Methotrexate is a competitive inhibitor of dihydrofolate reductase; this folate antagonism reduces purine and pyrimidine synthesis, inhibiting cellular proliferation[1]
- In high-dose protocols, administering reduced folic acid in the form of folinic acid 24 hours after methotrexate can offset its toxicity in rapidly dividing cells[2]
- In patients with normal renal function, high-dose methotrexate can be safely administered with vigorous alkalization, hydration, and leucovorin rescue[3]

Neurotoxicity

- Subacute MTX neurotoxicity presents as transient stroke-like symptoms, encephalopathy, seizures, or aphasia around 2-14 days after MTX administration[4]
- In this case, the patient developed neurologic findings 7 days after her most recent MTX dose
- MRI findings are variable but may show transient high signal in the centrum semiovale and diffusion restriction[5]
- Acute episodes are treated supportively, and while most patients' symptoms resolve without medication, dextromethorphan or aminophylline can be used[6]
- Episodes typically resolve within 1 week[5] and patients can typically be rechallenged with MTX without recurrent symptoms [4]

References:

1. Chan, E. S., & Cronstein, B. N. (2010). Methotrexate—how does it really work?. Nature Reviews Rheumatology, 6(3), 175-178.

2. Hesdorffer, C. S., & Longo, D. L. (2015). Drug-induced megaloblastic anemia. New England Journal of Medicine, 373(17), 1649-1658.

3. Widemann, B. C., & Adamson, P. C. (2006). Understanding and managing methotrexate nephrotoxicity. The oncologist, 11(6), 694-703.

4. Bhojwani, D., Sabin, N. D., Pei, D., Yang, J. J., Khan, R. B., Panetta, J. C., Krull, K. R., Inaba, H., Rubnitz, J. E., Metzger, M. L., Howard, S. C., Ribeiro, R. C., Cheng, C., Reddick, W. E., Jeha, S., Sandlund, J. T., Evans, W. E., Pui, C., & Relling, M. V. (2014). Methotrexate-induced neurotoxicity and leukoencephalopathy in childhood acute lymphoblastic leukemia. Journal of clinical oncology, 32(9), 949-959.

5. Panicker, V. V., Radhakrishnan, S. E., Kuruttukulam, G. V., Bose, J. A., Favas, T. T., & Bose, J. (2024). Methotrexate-induced leukoencephalopathy as a clinical and radiological mimicker of acute ischemic stroke leading to thrombolysis. Cureus, 16(1).

6. Bhojwani, D., Bansal, R., & Wayne, A. S. (2021). Managing therapy-associated neur
children with ALL. Hematology, 2021(1), 376-383.

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