

AMSER Case of the Month

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41 year old female with altered mental status

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Patient Presentation

- 41-year-old woman with paraneoplastic dermatomyositis and recently diagnosed left breast carcinoma s/p partial mastectomy and chemotherapy was admitted to the MICU for dermatomyositis flare, respiratory failure, and immunomodulation.
- Hospital course complicated by altered mental status, concern for seizure, severe thrombocytopenia, intermittent fevers, diffuse alveolar hemorrhage, pancytopenia, and suspected hemophagocytic lymphohistiocytosis / macrophage activation syndrome.

Pertinent Workup

- EEG showed diffuse slowing without epileptiform activity.
- Blood Labs: WBC 1.7 K/ μ L, hemoglobin 7.0 g/dL, platelets 38 K/ μ L; peak ferritin >25,000 ng/mL, triglycerides 275 mg/dL, AST 454 U/L, IL-2R 1315.2 pg/mL
- Infectious workup was broadly unrevealing
- Initial CT head/CTA head and neck showed no acute intracranial abnormality

What Imaging Should We Order?

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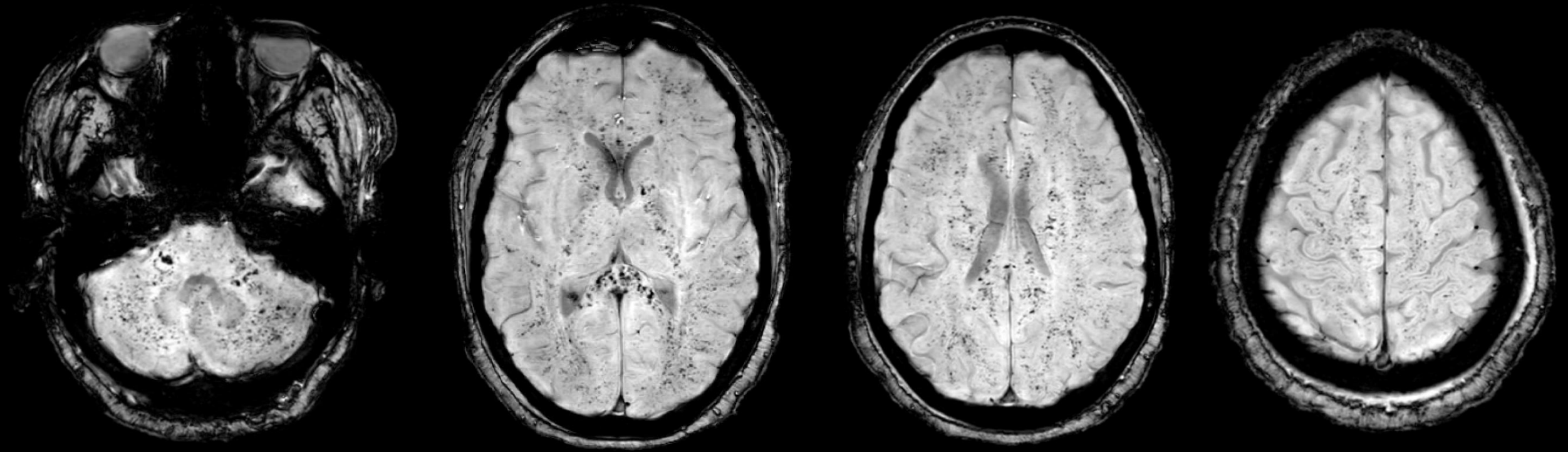
ACR Appropriateness Criteria: Altered Mental Status, Coma, Delirium, and Psychosis

Variant: 1 Adult. Altered mental status. Suspected intracranial pathology or focal neurologic deficit. Initial imaging.

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

MRI with and without contrast was ordered following a negative CT head

MRI (SWI) - Unlabeled

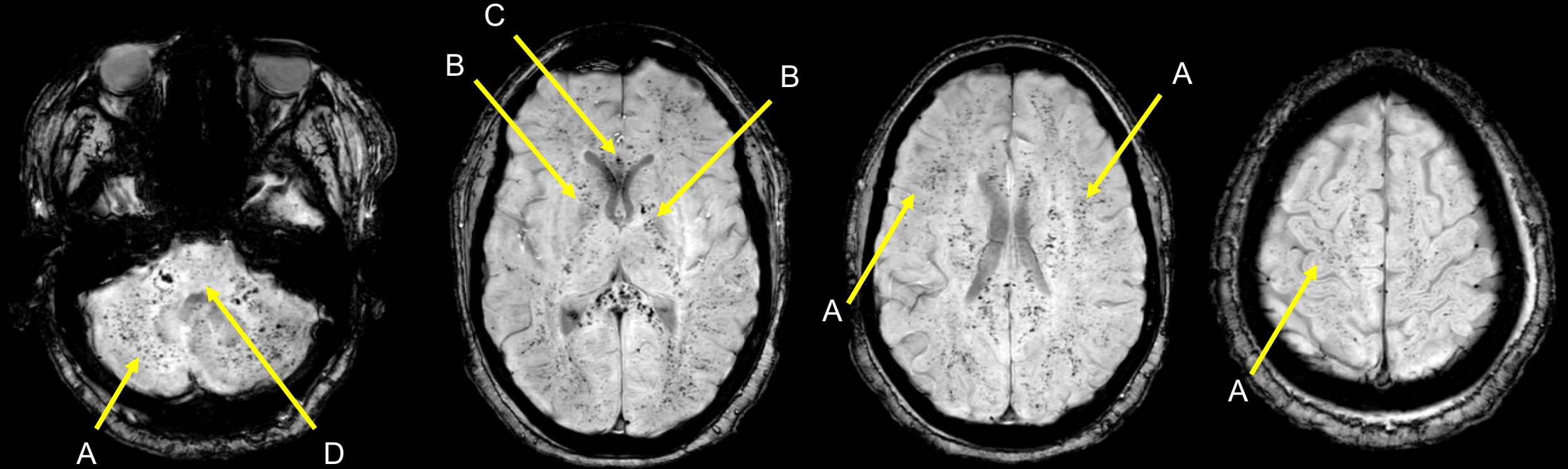


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MRI (SWI) - Labeled



Axial SWI MRI of the brain at multiple levels shows innumerable punctate foci of susceptibility artifact throughout the cerebral and cerebellar hemispheres (A), basal ganglia (B), corpus callosum (C), and brainstem (D), predominantly in the juxtacortical and subcortical white matter, consistent with diffuse microhemorrhages. DWI/FLAIR abnormalities also seen, but not visualized on this sequence.

Differential Diagnosis

- HLH/MAS with CNS involvement: Given microbleeds and diffusion restriction as well as patient's previous immunosuppression, 3-line cytopenias, elevated ferritin, elevated triglycerides, and transaminitis
- Critical illness associated cerebral microbleeds: Given respiratory failure, mechanical ventilation, thrombocytopenia, and a classic juxtacortical/corpus callosal microbleed distribution.
- Hemorrhagic infectious emboli or fungal infection: Less favored due to lack of enhancement and unrevealing infectious evaluation
- CNS vasculitis or hemorrhagic leukoencephalitis: Less likely as imaging showed no enhancement, vascular occlusion, or venous thrombosis
- Metastatic disease: Less likely given brain lesions did not enhance; PET/CT showed no osseous or solid-organ metastatic disease before admission.

Additional Imaging

- CTA chest / CT abdomen-pelvis: no pulmonary embolus; no acute abdominal or pelvic abnormality; spleen grossly unremarkable; no suspicious osseous lesion.
- Spine MRI: diffuse heterogeneous T1 hypointense/T2 hyperintense marrow signal with heterogeneous enhancement, initially concerning for metastases but later favored reactive marrow change in multidisciplinary clinical context.
- PET/CT three months earlier: intensely FDG-avid biopsy-proven left lower axillary/axillary tail malignancy, but no scan evidence of osseous, solid-organ, abdominal, or pelvic metastatic disease.
- Bone marrow biopsy was not pursued

Leading Dx:

Hemophagocytic lymphohistiocytosis /
macrophage activation syndrome with
possible critical illness associated cerebral
microbleeds

Case Discussion

HLH is a severe hyperinflammatory syndrome driven by uncontrolled immune activation, cytokine overproduction, and multiorgan injury. In adults, common triggers include infection, malignancy, and autoimmune/autoinflammatory disease.^{1 2}

Diagnosis is clinical and laboratory based. The HLH-2004 framework requires either a compatible molecular diagnosis or at least 5 of 8 criteria: fever, splenomegaly, cytopenias, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis, low/absent NK-cell activity, ferritin elevation, and elevated soluble IL-2 receptor.¹

CNS involvement may manifest with encephalopathy, seizures, coma, diffusion abnormalities, hemorrhage, and poor neurologic prognosis, and may appear on MRI as cerebral microhemorrhages on SWI as well as non-specific lesions of high T2/FLAIR signal in the cerebral and cerebellar hemispheres.³

Case Discussion

While microhemorrhages and DWI/FLAIR abnormalities were seen on brain MRI, they are not pathognomonic for any specific diagnosis. Our initial differential included HLH/MAS, infection/septic emboli, vasculitis, hemorrhagic leukoencephalitis, and metastases.

HLH/MAS was our leading diagnosis given patient's previous immunosuppression, 3-line cytopenia, elevated ferritin, elevated triglycerides, and transaminitis, which resulted in an H-score of 165 translating into a 40-54% probability of HLH⁴

Other diagnoses were less favored as broad infectious workup was unrevealing, brain lesions were nonenhancing, and PET/CT showed no osseous or solid-organ metastases before admission

Critical illness-associated cerebral microbleeds remained plausible given patient's respiratory failure, mechanical ventilation, thrombocytopenia, and callosal/juxtacortical distribution.^{5 6}

Clinical Follow Up

Following supportive critical care, and treatment with steroids and anakinra for HLH/MAS, patient's systemic markers improved, but remained with a poor neurologic examination.

Serial MRI demonstrated partial interval improvement in cortical/subcortical restricted diffusion and FLAIR abnormality, however widespread microhemorrhages were persistent possibly due to the critical illness associated microbleeds.

The patient failed eventual extubation attempt due to upper airway stridor and secretion burden. Given poor neurologic prognosis, a goals of care meeting was held, and the family elected to continue with comfort measures with palliative extubation, and the patient passed away.

References:

1. Henter JL, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, et al. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48(2):124-131. doi:10.1002/pbc.21039.
2. La Rosée P, Horne A, Hines M, von Bahr Greenwood T, Machowicz R, Berliner N, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. *Blood*. 2019;133(23):2465-2477. doi:10.1182/blood.2018894618.
3. Anderson TL, Carr CM, Kaufmann TJ. Central nervous system imaging findings of hemophagocytic syndrome. *Clin Imaging*. 2015;39(6):1090-1094. doi:10.1016/j.clinimag.2015.07.013.
4. Fardet L, Galicier L, Lambotte O, Marzac C, Aumont C, Chahwan D, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. *Arthritis Rheumatol*. 2014;66(9):2613-2620. doi:10.1002/art.38690.
5. Fanou EM, Coutinho JM, Shannon P, Kiehl TR, Levi MM, Wilcox ME, Aviv RI, Mandell DM. Critical Illness-Associated Cerebral Microbleeds. *Stroke*. 2017 Apr;48(4):1085-1087. doi: 10.1161/STROKEAHA.116.016289. Epub 2017 Feb 24. PMID: 28235962.
6. Greenberg SM, Vernooij MW, Cordonnier C, Viswanathan A, Al-Shahi Salman R, Warach S, Launer LJ, Van Buchem MA, Breteler MM; Microbleed Study Group. Cerebral microbleeds: a guide to detection and interpretation. *Lancet Neurol*. 2009 Feb;8(2):165-74. doi: 10.1016/S1474-4422(09)70013-4. PMID: 19161908; PMCID: PMC3414436.