Cytotoxic Lesion of the Corpus Callosum

Ian VanAntwerp DO

Jing Qi MD

Children's Wisconsin

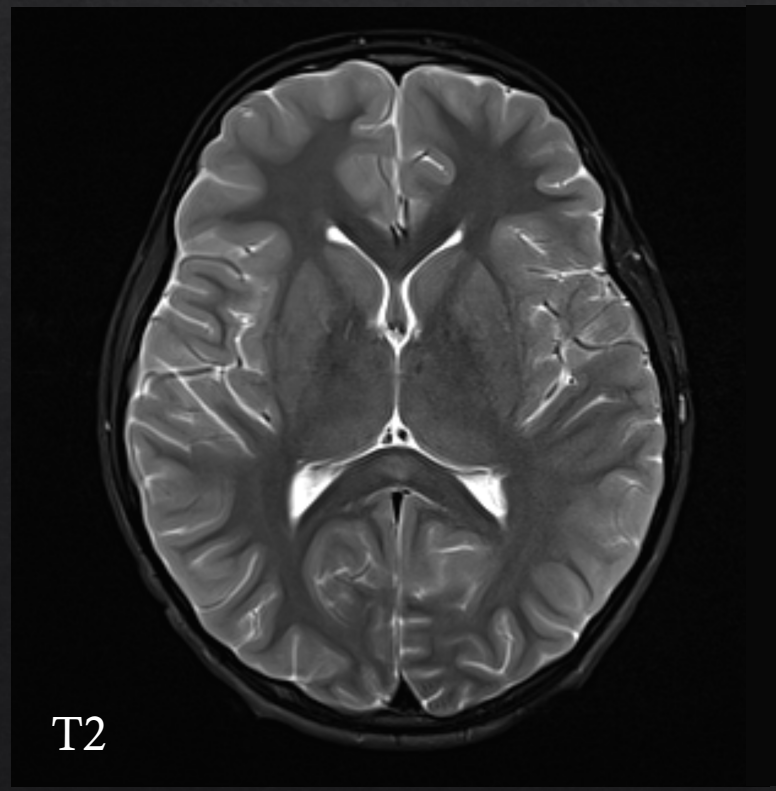
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Clinical Presentation

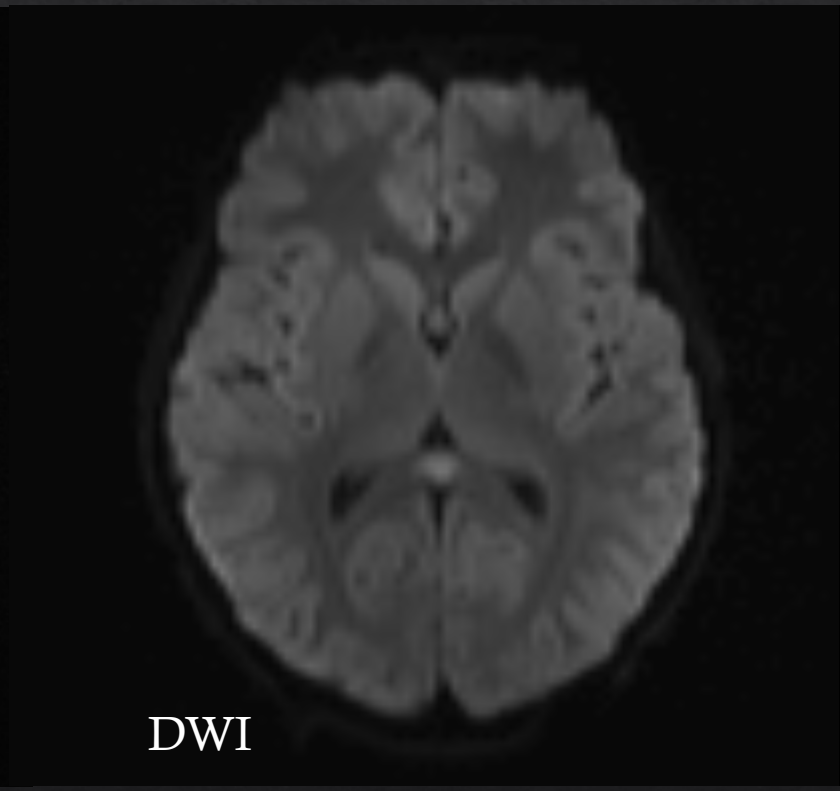
- An 8-year-old previously healthy female presented with fevers (Tmax of 102.8 F) and altered mental status
- Sore throat and abdominal pain with emesis for several days prior
- On the day of presentation, she had a witnessed episode of generalized body shaking for 1 minute concerning for seizure
- Concerns for encephalopathy vs meningitis on arrival given patient's clinical picture (ill-appearing, altered mental status, elevated inflammatory markers, and continued fevers)
- Admitted for further evaluation including long-term EEG monitoring, MRI brain, and lumbar puncture.

Initial Imaging

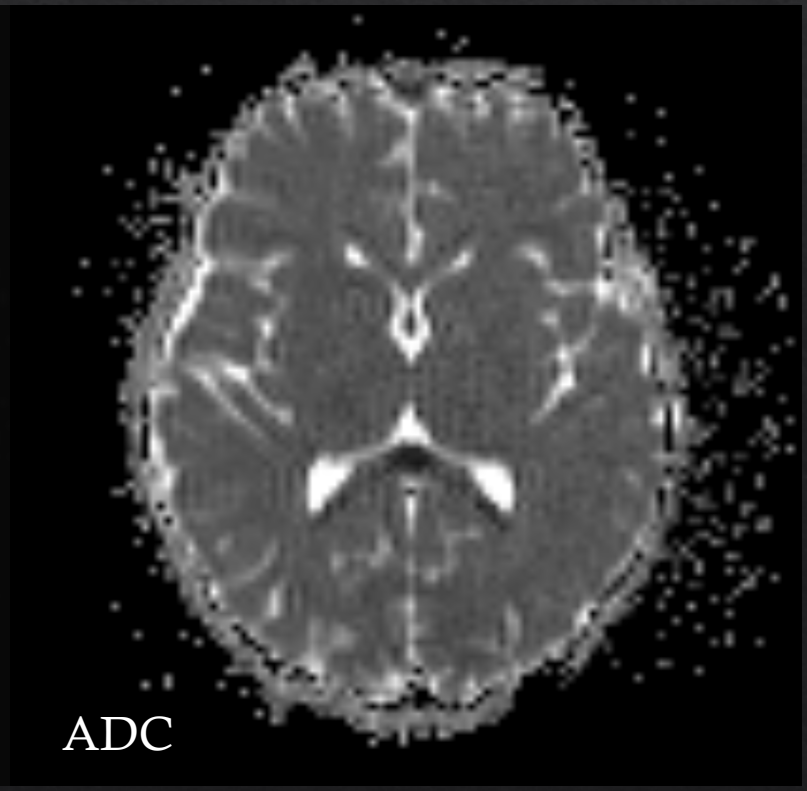
- MRI of the brain was preformed with contrast
- Small focus of long TR hyperintensity and restricted diffusion in the splenium of corpus callosum.



T2



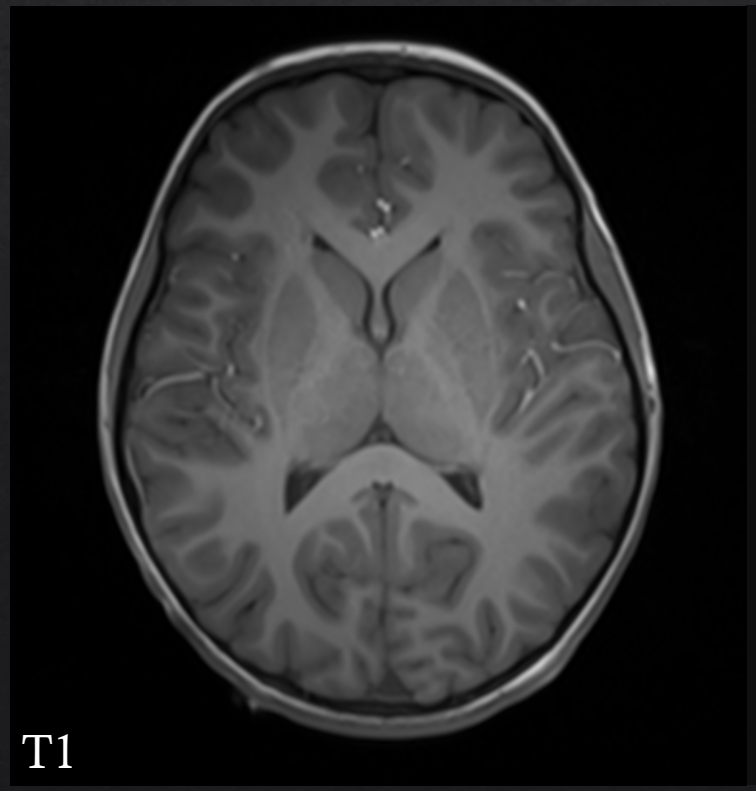
DWI

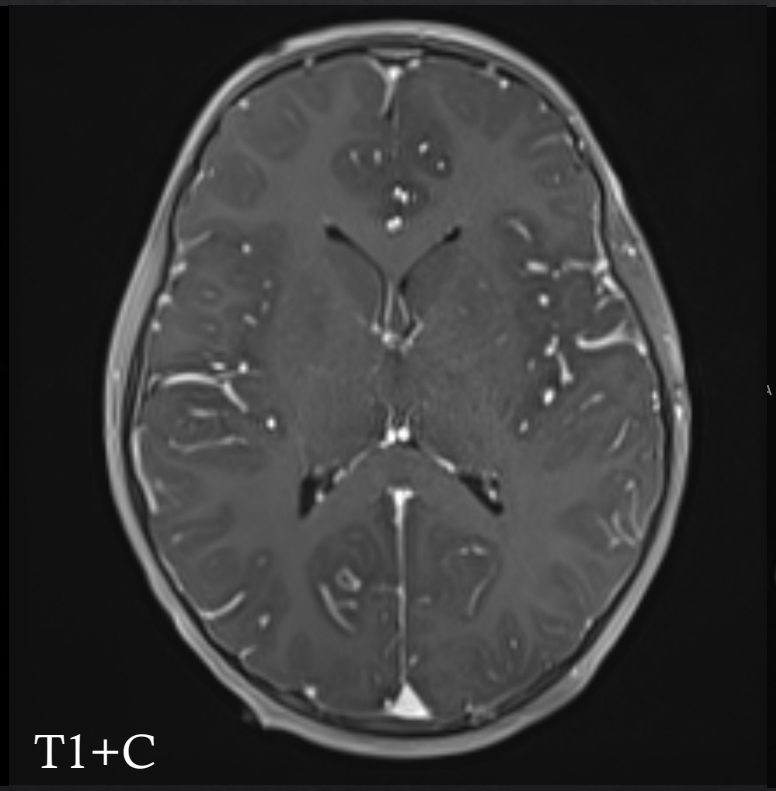


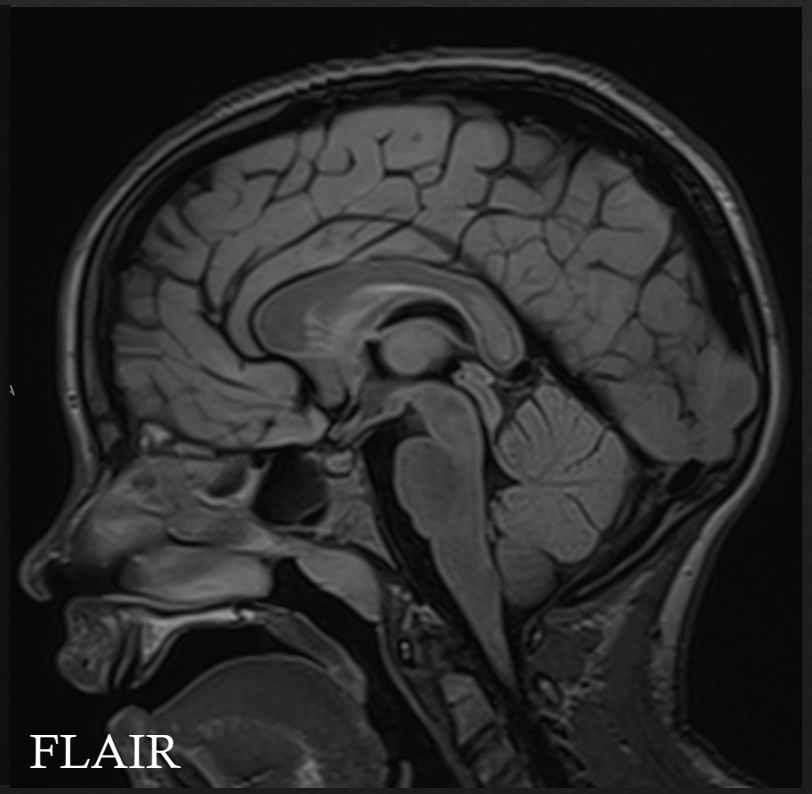
ADC

Initial Imaging

- FLAIR hyperintensity centered within the splenium
- No associated enhancement
- Initial differential considerations included postictal status, drug toxicity or antiepileptic drugs, mild encephalitis/encephalopathy (viral infection like influenza) and electrolyte imbalance


T1


T1+C

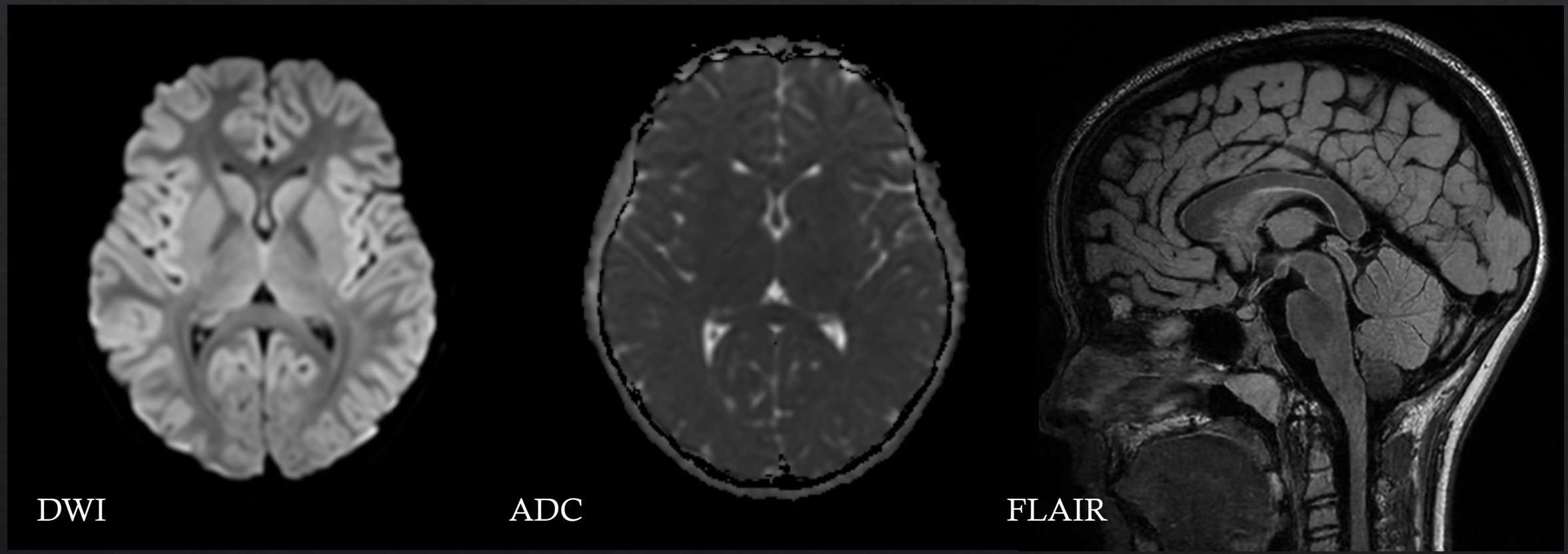

FLAIR

Management/Outcome

- Neurology and Infectious disease consult was obtained
- EEG was normal and there was resolution of encephalopathy over the course of 24 hours
- CSF, blood cultures, and urinalysis were negative for infection and the patient's fever resolved with Motrin
- Clinical improvement with supportive therapy and the patient was discharged with instructions for follow up imaging in 1 month

Follow-up Imaging

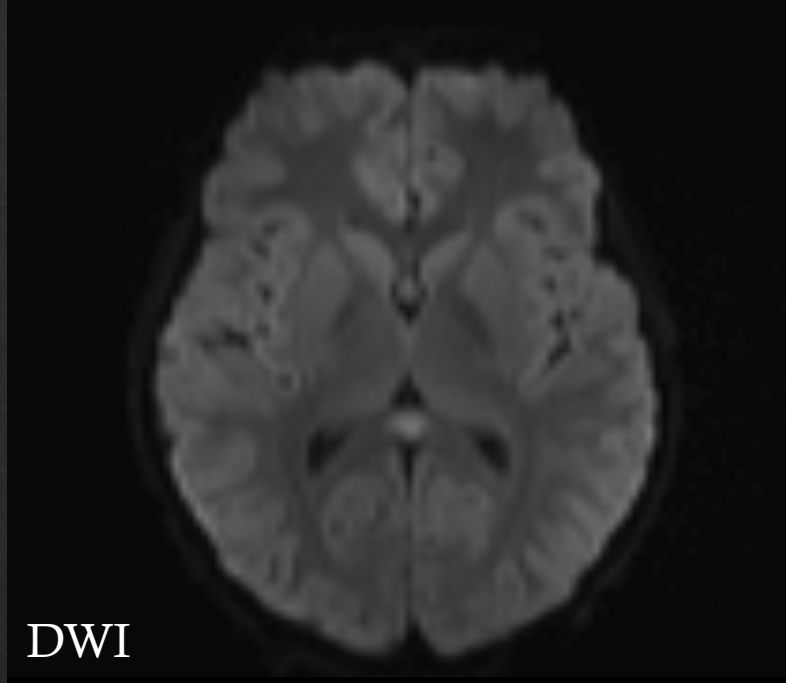
- Follow-up imaging 3 weeks later demonstrated complete resolution of imaging findings

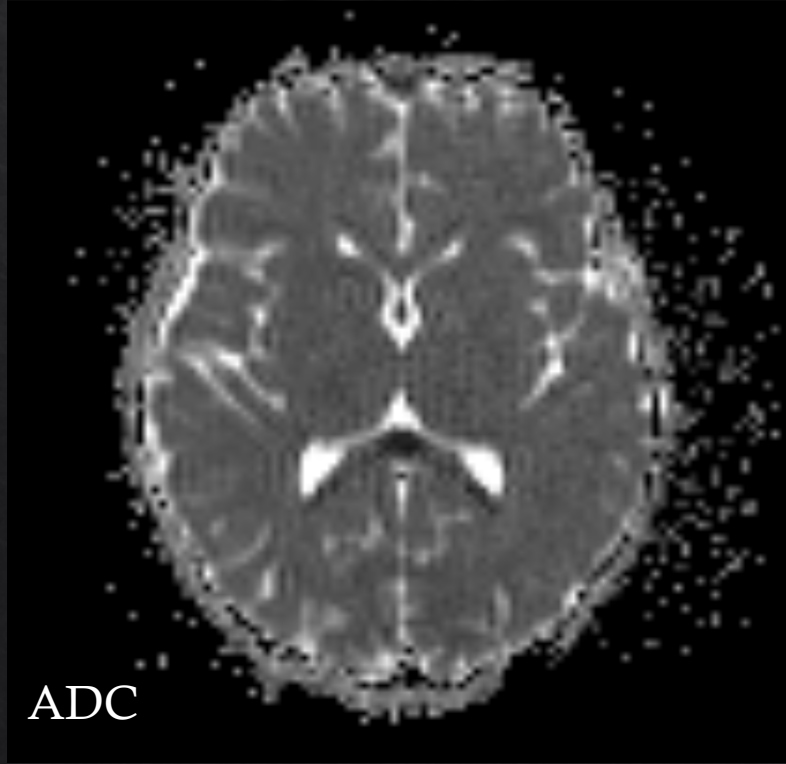


Cytotoxic Lesion of the Corpus Callosum

(CLOCC)

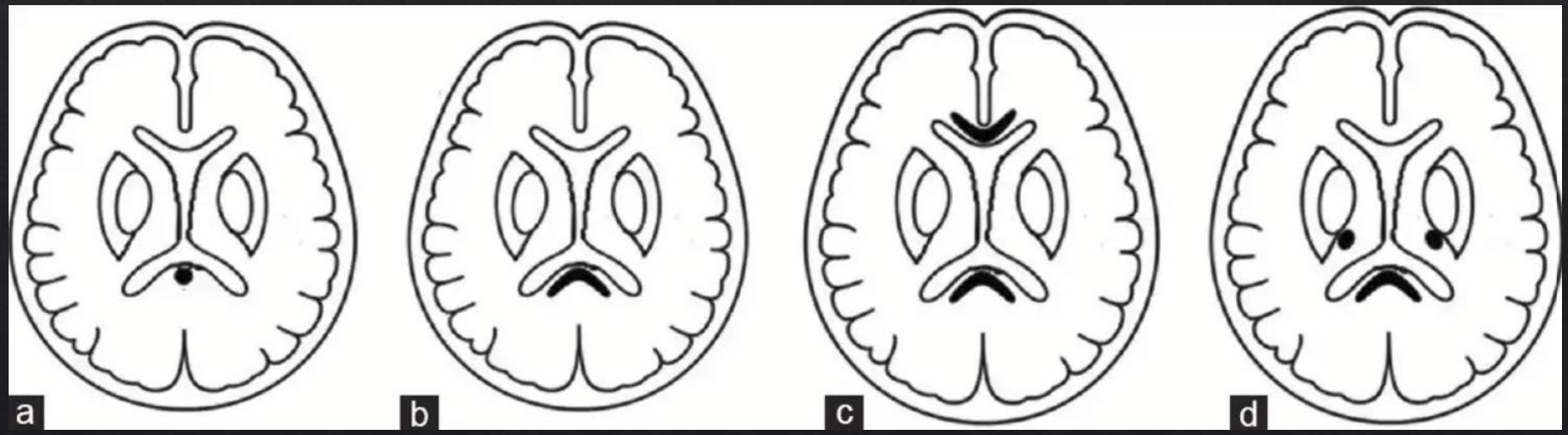
- Collection of conditions which cause features of cytotoxic edema within the splenium of the corpus callosum
- Clinical presentation relates to the underlying pathology rather than the imaging findings
- Felt to result from inflammatory cytokine response manifesting as cytotoxic edema preferentially involving the splenium due to high density of oligodendrocytes expressing glutamate-affected receptors
- Three distinct imaging patterns
  - Well-circumscribed, small, oval lesions within the midline splenium (most common)
  - Irregular lesions involving the splenium and extending into the cerebral hemispheres
  - Extension anteriorly into the body of the corpus callosum





Discussion

- Cytotoxic edema results from cells being unable to maintain ATP-dependent Na+/K+ pumps, as well as excitotoxic action of glutamate on NMDA receptors, AMPA receptors, and aquaporins
- Corpus callosum and splenium can be preferentially involved due to high density of receptors
- Imaging findings are often symmetric



Pictorial representation of CLOCCs. (a) Dot sign. (b) Boomerang sign. (c) Double boomerang sign. (d) Boomerang plus sign. CLOCCs: Cytotoxic lesions of the corpus callosum

- Wide variety of clinical settings and reported etiologies for CLOCC
- History and associated imaging findings can help narrow the differential

Type of CLOCC	Helpful Imaging Features	Helpful Clinical Features	Reported Causes
Drug-associated CLOCCs	Abnormality of the dentate nuclei with metronidazole therapy	History of seizure, antiseizure therapy (eg, carbamazepine), chemotherapy, or other recent drug therapy	Carbamazepine, cyclosporine, diet pills with a sympathomimetic stimulant, fluorouracil, glufosinate ammonium, intravenous immunoglobulin therapy, lamotrigine, methyl bromide, metronidazole, neuroleptic malignant syndrome (amitriptyline, clozapine), phenytoin, corticosteroids, withdrawal of antiseizure therapy
Malignancy-associated CLOCCs	Evidence of CNS malignancy, including mass lesions and leptomeningeal enhancement	History of malignancy or chemotherapy	Acute lymphocytic leukemia, esophageal cancer, leptomeningeal glioblastomatosis, spinal meningeal melanocytoma
Infection-associated CLOCCs	Abscess formation or leptomeningeal enhancement, imaging findings that vary widely with the infectious agent and localization	Fever, leukocytosis, nuchal rigidity, altered mental status, history of travel to endemic areas (malaria)	Adenovirus, aseptic meningitis or encephalitis, Epstein-Barr virus (EBV), *Escherichia coli*, herpes, influenza virus A (H1N1), influenza, *Legionella*, malaria, measles, *Mycoplasma*, mumps, rotavirus, *Salmonella*, *Staphylococcus*, *Streptococcus*, tick-borne encephalitis, varicella-zoster virus
SAH-associated CLOCCs	Extensive hemorrhage within the subarachnoid space, lack of vessel irregularity on angiograms	Thunderclap headache, "worst headache of life," loss of consciousness, seizures in a patient with hypertension	Aneurysm, arteriovenous malformation
Metabolic disorder–associated CLOCCs	Classic central lesion in central pontine myelinolysis; symmetric lesions in the medial thalami and the mammillary bodies and surrounding the third ventricle and cerebral aqueduct in Wernicke encephalopathy; "eye of the panda" sign in Wilson disease	Fluid-electrolyte imbalances; history of cirrhosis or hepatic dysfunction, liver transplantation, malnutrition, or AIDS that may predispose to osmotic demyelination; history of alcoholism or malnutrition in Marchiafava-Bignami disease or Wernicke encephalopathy; Kayser-Fleischer rings in Wilson disease	Acute renal failure, alcoholism, extrapontine myelinolysis, central pontine myelinolysis, hepatic encephalopathy, hyperammonemia, hypernatremia, hypoglycemia, hyponatremia, malnutrition, Marchiafava-Bignami disease, Wernicke encephalopathy, Wilson disease
Trauma-associated CLOCCs	Brain contusions; multifocal punctate lesions on FLAIR, diffusion-weighted, or susceptibility-weighted MR images at the gray matter–white matter junction or in the corpus callosum or brainstem	Trauma with immediate loss of consciousness and persistent coma, altered mental status, or seizures	Trauma of various causes
CLOCCs associated with other entities	Varies with the cause	Varies with the cause	Acute high-altitude sickness, anti–glutamate receptor antibody, anti–voltage-gated potassium channel antibody, eclampsia, hemolytic uremic syndrome, vaccination, Kawasaki disease, posterior reversible encephalopathy syndrome, postpartum cerebral angiopathy, seizure without drug therapy, status epilepticus

Starkey et al. Radiographics.

Take Home Points

- Cytotoxic lesion of the corpus callosum is an imaging pattern, classically an oval nonenhancing lesion with restricted diffusion centered in the splenium
- Presentation relates to the underlying pathology and warrants a search for systemic process
- Classically seen with seizures or cessation of antiseizure medications with additional common etiologies including viral infections, metabolic disturbance, drugs/toxins, inflammatory disease, and less commonly malignancy or vascular injury
- Reversible imaging features typically within 1 month, most within 1 week following neurologic recovery
- Prognosis follows the underlying disease

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Ian VanAntwerp DO

Contact: ivanantwerp@mcw.edu

Children's Wisconsin

Froedtert & Medical College of Wisconsin