

Case Report

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Severe Headache and Fever in a Young Woman - Cytotoxic Lesion of the Corpus Callosum

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ABSTRACT

Introduction: Cytotoxic lesion of the corpus callosum (CLOCC) is a reversible clinic-radiologic entity associated with a wide range of infectious, metabolic, toxic, and inflammatory conditions. Recognition of its characteristic imaging appearance is essential to avoid misdiagnosis and guide appropriate management.

Case Presentation: A 19-year-old woman presented with fever and severe headache. Initial computed tomography of the brain was normal. Forty-eight hours after admission, she developed worsening fever, headache, neck stiffness, hypertension, and mild confusion. Laboratory investigations, including complete blood count, electrolytes, and renal function, were normal. Lumbar puncture demonstrated no pleocytosis, and microbiologic and viral studies were negative. Brain MRI revealed an isolated, non-enhancing lesion in the splenium of the corpus callosum with T2 hyperintensity and restricted diffusion, consistent with CLOCC.

Differential diagnoses, including meningitis, multiple sclerosis, and complex migraine, were excluded based on clinical, laboratory, and imaging findings. A follow-up MRI performed five days later demonstrated near-complete resolution of the lesion.

Discussion: CLOCC is an imaging finding with diverse etiologies, including infection, metabolic disturbances, seizures, and drug toxicity. In this patient, infectious and metabolic causes were excluded, making amitriptyline toxicity the most likely precipitating factor. The characteristic transient splenial lesion and rapid radiologic resolution supported the diagnosis. Management is directed at the underlying cause, and prognosis is generally favorable with appropriate treatment.

Conclusion: This case highlights the importance of considering CLOCC in young patients presenting with acute encephalopathic symptoms and characteristic MRI findings. Early recognition can prevent unnecessary investigations, facilitate targeted management, and avoid misdiagnosis of demyelinating or infectious disorders.

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Introduction

A 19-year-old female presented to the emergency department with fever and severe headache.

Results/Observations

Initial unenhanced computed tomography of the brain was normal, with no acute cortical infarction or intracranial hemorrhage (Figure 1). The patient was admitted for further evaluation.

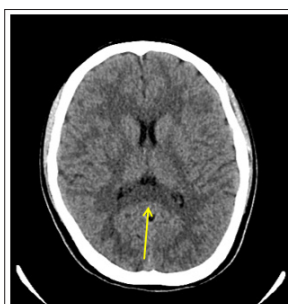


Figure 1: Axial non-contrast CT of the head demonstrates no acute finding. Note that the splenium is normal in appearance (arrow)

During the initial 2 days, the patient was clinically stable and under close observation. She was monitored supportively, until she experienced an acute clinical deterioration approximately 48 hours after admission. This was characterized by symptoms of fever, headache, neck stiffness and hypertension.

There was a significant past medical history of depression. Patient was currently being treated with amitriptyline 75mg PO. The patient denied use of tobacco, alcohol and recreational drugs. On physical examination, the patient was slightly confused to time and place. Patient looked well otherwise. There is no motor weakness or sensory symptoms. Reflexes were normal. Laboratory analysis revealed normal Complete blood count (CBC), electrolytes, and renal function.

A lumbar puncture was performed and showed no leukocytosis or cells. Microbiology and all viral serology was negative.

An MRI of the brain was performed (Figure 2) and demonstrated a focal region of edema (bright T2 signal) within the splenium of the corpus callosum in the midline. This lesion was dark on T1 and showed no enhancement following intravenous contrast administration. Diffusion-weighted imaging showed bright signal with corresponding dark signal on ADC map, consistent with restricted diffusion (Figure 3).

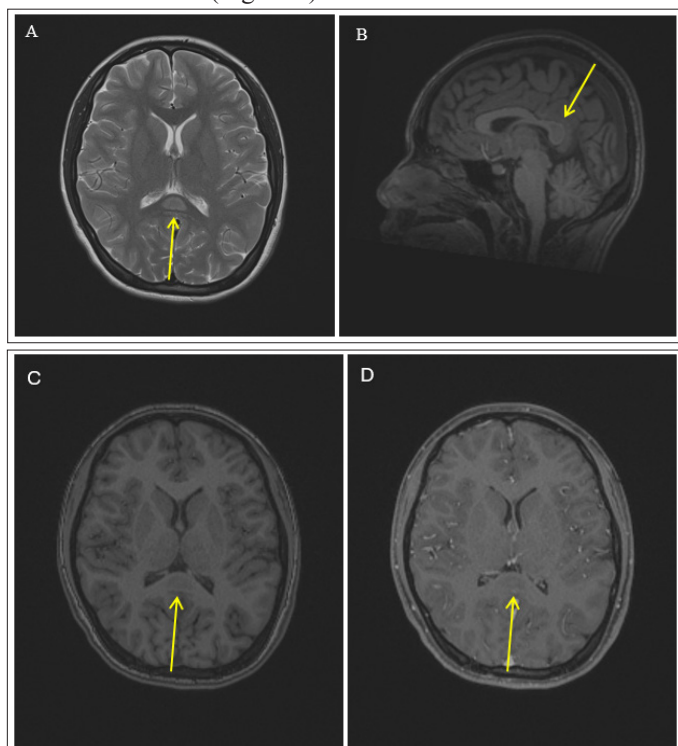


Figure 2: Focal region of edema (bright T2 signal) within the splenium of the corpus callosum in the midline (arrow) on axial T2 (A). This lesion was dark on T1 (arrows) (B, C) and showed no enhancement following intravenous contrast administration (arrow) in D. The rest of the brain was normal.

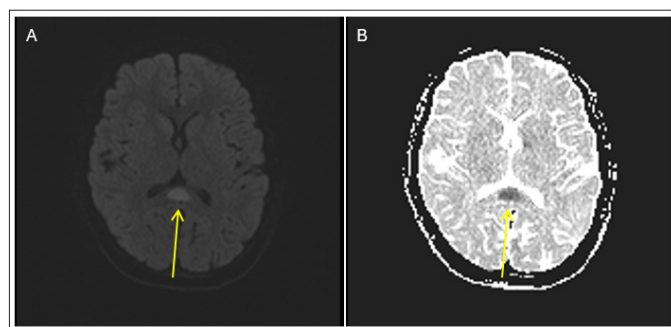


Figure 3: Axial diffusion-weighted imaging (A) showed bright signal in the splenium of the corpus callosum (arrow) with corresponding dark signal on ADC map (B) consistent with restricted diffusion.

The diagnosis was cytotoxic lesion of the corpus callosum (CLOCC). Although the patient is a young female, multiple sclerosis was unlikely given the lack of dissemination in time and space on MRI and the overall clinical picture. There was only one lesion as well, which makes this unlikely. Complex migraine was considered unlikely due to the absence of a migraine history and focal neurological deficits. Meningitis was ruled out due to a normal lumbar puncture with no leukocytosis and negative microbiology.

A follow-up MRI performed 5 days later showed improvement with near complete resolution of the cytotoxic lesion of the corpus callosum (CLOCC) seen on the previous examination (Figure 4).

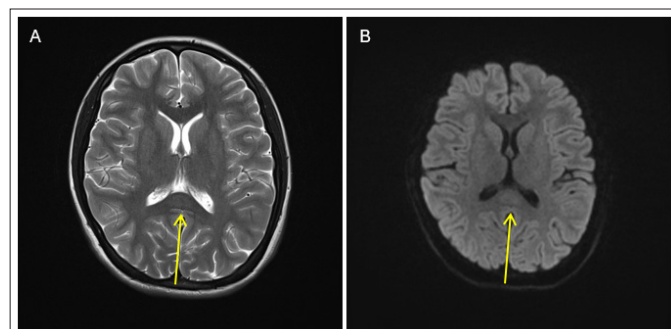


Figure 4: Axial T2 (A) and axial diffusion-weighted imaging (B) on MRI performed 5 days later reveal near complete resolution of the cytotoxic lesion of the corpus callosum (CLOCC) (arrows) seen on the previous examination.

Discussion

Cytotoxic lesion of the corpus callosum is a common magnetic resonance imaging finding [1] and it has various etiologies. Its prevalence is unknown, due to its variability in presentation [2]. Some patients are asymptomatic and do not necessitate neuroimaging. Symptoms are usually related to the etiology of the cytotoxic lesion of the corpus callosum more than the neuroanatomical territory itself [1]. Typical symptoms usually include fever, headache, confusion, and altered mental status [3].

Etiologies of cytotoxic lesion of the corpus callosum in this case could have been drug toxicity (antidepressants, antiepileptic, antipsychotics, or pesticide ingestion), seizures, metabolic disturbance (electrolyte imbalance, hemolytic-uremic syndrome, hypoglycemia, osmotic demyelination, or Wernicke's encephalopathy), or viral infection (influenza measles, herpes, mumps, adenovirus, rotavirus, SARS-CoV-2). Other causes

include bacterial infections, malignancy, chemotherapy and subarachnoid hemorrhage [4].

The typical workup includes complete blood count and electrolytes to rule out a metabolic disturbance, a lumbar puncture, and neuroimaging if clinically indicated. In this case, an initial Computed Tomography of the brain was ordered to rule out any causes of increased intracranial pressure. Two days later, the patient had neck stiffness, so a lumbar puncture was performed to rule out meningitis.

The pathophysiology of the condition is an initial trigger that causes macrophages to release inflammatory cytokines. All of this leads to a large buildup of glutamate outside cells, which then results in water entering astrocytes and neurons, causing cytotoxic edema. The splenium of the corpus callosum is particularly affected because it contains many oligodendrocytes with a high number of glutamate-sensitive receptors [4].

In terms of treatment, some studies suggest the use of methylprednisolone and intravenous immunoglobulin to stop the cytokine storm [5]. However, no clinical benefit has been demonstrated. The typical treatment depends on the etiology of the cytotoxic lesion of the corpus callosum. For example, in patients with subarachnoid hemorrhage, treatment includes clipping or endovascular coil embolization [6].

A drug overdose with amitriptyline is suspected due to the patient's history of depression. Other potential causes, such as infectious or metabolic etiologies, have been ruled out. Amitriptyline is the only plausible agent responsible for the toxicity, as the patient does not take any other medications and does not use any substances. The correct answer is sodium bicarbonate, as it is the standard of care for tricyclic antidepressant toxicity [7].

It improves cardiac conduction and hypotension. Once the patient is medically stable, a psychiatry consultation is essential for optimizing treatment and assessing suicide risk. High-flow nasal cannula could have been appropriate in the context of respiratory compromise secondary to a viral or bacterial infection. Fluid therapy may play a role in dilution and clearance, but it is mainly used in the context of acute resuscitation (e.g., sepsis, hemorrhage)

and for maintaining homeostasis. Finally, activated charcoal is used in cases of poisoning and is most effective when administered within a short window after toxin ingestion, particularly when no specific antidote exists.

Prognosis is dependent on the etiology. Typically, with appropriate treatment, there is both clinical and radiologic resolution of disease.

This case highlights the importance of considering CLOCC in young patients presenting with acute encephalopathic symptoms and characteristic MRI findings. Early recognition can prevent unnecessary investigations, facilitate targeted management, and avoid misdiagnosis of demyelinating or infectious disorders.

References

1. Moors S, Nakhostin D, Ilchenko D, Kulcsar Z, Starkey J, et al. (2024) Ineichen BV Cytotoxic lesions of the corpus callosum: a systematic review. *Eur Radiol* 34: 4628-4637.
2. Soares M, Rosa S, Bettencourt S, Ferreira R, Sardinha M, et al. (2024) Cytotoxic lesions of the corpus callosum due to FOLFIRINOX chemotherapy, *Brain Disorders* 15: 2666-4593.
3. Procaccini L, Mincuzzi E, Bernardini A, Franchi P, Voicu IP, et al. (2022) "Reversible cytotoxic lesion of the corpus callosum following SARS-CoV-2 mRNA vaccine administration: a finding to be aware of" *Neuroradiol J* 35: 758-762.
4. Gaillard F, Sharma R, Campos A, et al. Cytotoxic lesions of the corpus callosum (CLOCCs). Reference article, *Radiopaedia*. org <https://doi.org/10.53347/rID-26390>.
5. Takanashi J, Shiihara T, Hasegawa T, Takayanagi M, Hara M, et al. (2015) Clinically mild encephalitis with a reversible splenial lesion (MERS) after mumps vaccination *J Neurol Sci* 349: 226-228.
6. Toi H, Yagi K, Matsubara S, Hara K, Uno M (2021) Clinical Features of Cytotoxic Lesions of the Corpus Callosum Associated with Aneurysmal Subarachnoid Hemorrhage. *AJNR Am J Neuroradiol* 42: 1046-1051.
7. Odigwe CC, Tariq M, Kotecha T, Mustafa U, Senussi N, et al. (2016) Tricyclic antidepressant overdose treated with adjunctive lipid rescue and plasmapheresis. *Proc (Bayl Univ Med Cent)* 29: 284-287.