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Case Report

Cytotoxic Lesion of the Corpus Callosum (CLOCC) in a Chinese Girl: A Case of Mycoplasma Meningoencephalitis

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Abstract Cytotoxic lesion of the corpus callosum (CLOCC), in the past is known as mild encephalitis/encephalopathy with reversible splenial lesion (MERS), reversible splenial lesion syndrome, or transient splenial lesions. CLOCC is a new normenclature which describes cytotoxic injury on the corpus callosum secondary to various aetiologies. Magnetic resonance imaging of brain demonstrates lesions with characteristic high-signal intensity on T2-weighted images with restricted diffusion in diffusion-weighted images over corpus callosum which are often reversible. Early recognition of CLOCC and treatment of the underlying aetiology leading to good neurological recovery in most cases. Proper counselling of CLOCC with good prognosis may lessen parental anxiety.

Key words Cytotoxic lesion of the corpus callosum (CLOCC); IVIG; Meningoencephalitis; Mycoplasma

Case Report

A 12 years old Chinese girl with good past health and normal development was admitted to a tertiary hospital via emergency department for fever and confusion in June 2024. She presented with 6 days of fever, right side otalgia and coryzal symptoms. She was diagnosed to have right acute otitis media (AOM) and was given courses of oral cefuroxime and Augmentin by private doctor. She then developed generalised band-like headache, light-headedness and recurrent vomiting. Subsequently she had confusion and auditory hallucination on the night before admission. There was no seizure, weakness nor neck pain.

Physical exam on admission showed afebrile and stable vitals, she was oriented with Glasgow Coma Scale (GCS) at 15/15 but was slow in response and tired looking. There were no signs of meningism nor focal neurological deficits. Her right ear tympanic membrane was dull. Other systemic examinations were unremarkable. Our clinical diagnosis on admission was possible encephalitis/acute disseminated encephalomyelitis (ADEM) with partially treated AOM.

She was empirically covered with ceftriaxone, acyclovir, oseltamivir and doxycycline and was transferred to paediatric intensive care unit (PICU) for further management. She had progressive agitation, irritability, fluctuation of consciousness with the lowest GCS at 13/15. A course of intravenous immunoglobulin (IVIG) at 2 gram/kg was given since day of admission for possible autoimmune encephalopathy, levocarnitine was supplemented while waiting for metabolic and possible influenza nasopharyngeal result.

Her initial blood test showed normal cell counts, electrolytes, venous gas. There was mild elevated C-reactive protein at 13.7 mg/L (reference </=5). Lumbar puncture showed raised opening pressure at 24 cm H_2O. Cerebral spinal fluid (CSF) white cell count was elevated to 110/mm^3 with 96.4% mononuclear cell with elevated protein at 0.6 g/L (reference 0.15-0.45). Chest X-ray was normal. Nasopharyngeal aspirate (NPA) yielded mycoplasma pneumoniae. Blood culture, CSF bacterial culture, viral study, acid-fast bacilli, lactate, and glucose were unremarkable. Polymerase chain reaction analysis or antibody detection of mycoplasma in the CSF was not

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available. Subsequent blood and CSF encephalitis panel including NMDAR was negative. Metabolic workup was unremarkable. Serum interleukin-6 was elevated at 8.35 pg/ml (reference <1.25).

CT brain on admission showed bilateral mastoid effusion. Urgent MRI brain and brainstem on same day showed diffuse thin leptomeningeal enhancement with two band-like and cresenteric shaped T2 hyperintense and T1 hypointense signal over right paramedian and midline of splenium of corpus callosum. They show restricted diffusion with low apparent diffusion coefficient (ADC) values. The features are in favour of cytotoxic lesions of the corpus callosum (CLOCCs) (Figure 1 a-c). Electroencephalogram (EEG) showed generalised slow background without epileptiform discharges. Features are compatible with acute meningoencephalitis with CLOCC, associated with mycoplasma infection.

A course of 7-day ceftriaxone and 10-day doxycycline was given. Antivirals were stopped upon yielding negative viral result. The girl's neurological status improved drastically and became fully conscious since day 2 of admission with resolution of hallucination and irritability after treatment with antibiotic and IVIG. She had mild impairment in executive functions (e.g. working memory, calculation) which improved gradually during hospital stay. Nasopharyngeal aspirate repeated on day 5 was negative for mycoplasma. She has recovered back to premorbid state and function since day 11, repeated lumbar puncture showed improved white cell count at 37/mm^3 with normal biochemistry. She was discharged on day 14.

Follow up MRI brain 1 month later showed substantial improvement of previous T2 hyperintense lesion with restricted diffusion at splenium as well as the leptomeningeal enhancement (Figure 1 d-f). Repeated EEG was normal. She demonstrated complete recovery and adapted well in school on outpatient clinic follow up.

Discussion

This case report presented a girl with meningoencephalitis with mycoplasma infection. Initial MRI Brain showed features of CLOCC which showed drastic clinical and radiological recovery upon antibiotic treatment and immunotherapy with IVIG.

Mycoplasma pneumoniae is a common organism for community acquired pneumonia, with neurological symptoms being the most common extrapulmonary complications, up to 7% of hospitalised patients may have neurological symptoms.[1] Common neurological diseases related to mycoplasma includes encephalitis, meningitis, polyradiculitis, and myelitis etc. Mycoplasma accounts for 5-30% of all of the reported encephalitis cases.[1] Yet, the exact pathogenesis is still unclear. The postulated pathogenesis involves either direct invasion of the nervous system, neurotoxin or immune-mediated inflammatory response induced by the acute infection.[1,2] Despite mycoplasma infection are quite common in Hong Kong, there were no reported local case report of *M. pneumoniae*-associated encephalopathy with CLOCC in children to date.

Cytotoxic lesions of the corpus callosum (CLOCCs) are lesions described to be oval, small and reversible lesion in corpus callosum usually at midline with restricted diffusion restriction on MRI which has T2 enhanced signal intensity.[3,4] Previously this disease is also known as mild encephalitis/encephalopathy with reversible splenial lesion (MERS), reversible splenial lesion syndrome (RESLES), or transient splenial lesions (TSL). However, the cytotoxic lesions may not always be reversible, involve splenium nor associated with encephalopathy.[3] The new terminology of CLOCC is more accurate term to describe clinical and radiological presentation as well as pathophysiologic hypothesis of vulnerability of corpus callosum to excitotoxic injuries.[3] The corpus callosum, especially the splenium is most susceptible as they have abundant neurotransmitters such as cytokine, glutamate, toxin, drug and other excitatory receptors in neurons, astrocytes, and oligodendrocytes compared to other parts of brain.[3]

There are various proposed aetiologies for CLOCC which include infections (e.g. influenza, rotavirus, Epstein-Barr virus, measles, mumps, varicella-zoster, adenovirus, herpesvirus, COVID-19, Salmonella, mycoplasma and Legionnaire's disease), metabolic (e.g. hyponatraemia, hypoglycaemia, and hyperammonaemia), epilepsy, drug-related (e.g. abrupt withdrawal of anti-epileptics, use of chemotherapeutic agents, metronidazole), trauma, vascular, malignancies etc.[3,5-8] Infection was one of the commonest aetiology.[5,6] Around 97.7% of CLOCC were present with prodromal symptoms of infection.[6] Viral infection (e.g. influenza and rotavirus) contribute the largest proportion (75%) in paediatric patients, followed by bacterial infection (7%), and seizures or epilepsy (4%).[5] Mycoplasma was the commonest causative agent for bacterial cause.[5,6] The infection induced a cascade of complex inflammatory cytokines (IL-1 and IL-6) and stimulated cell reactions.

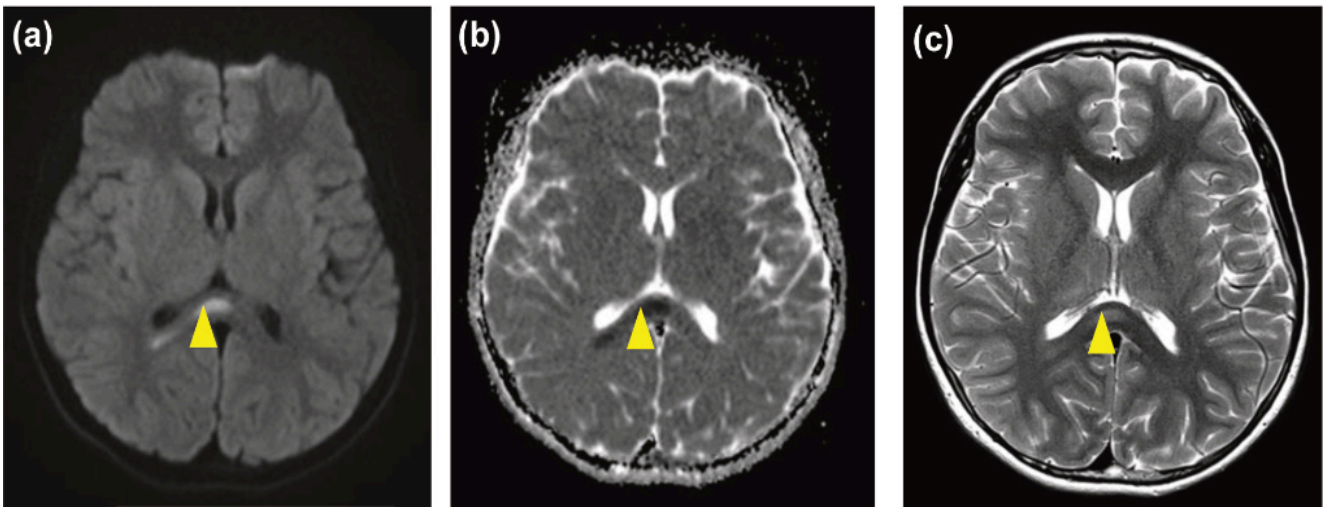

Figure 1 a-c Axial MRI brain of patient on day of admission. MRI showed leptomeningeal enhancement with two band-like and cresenteric shaped lesions at paramedian and midline of the splenium of corpus callosum. They showed restricted diffusion with (a) hyperintensity on diffusion-weighted image, (b) hypointensity on ADC map and (c) hyperintensity on T2-weighted image.

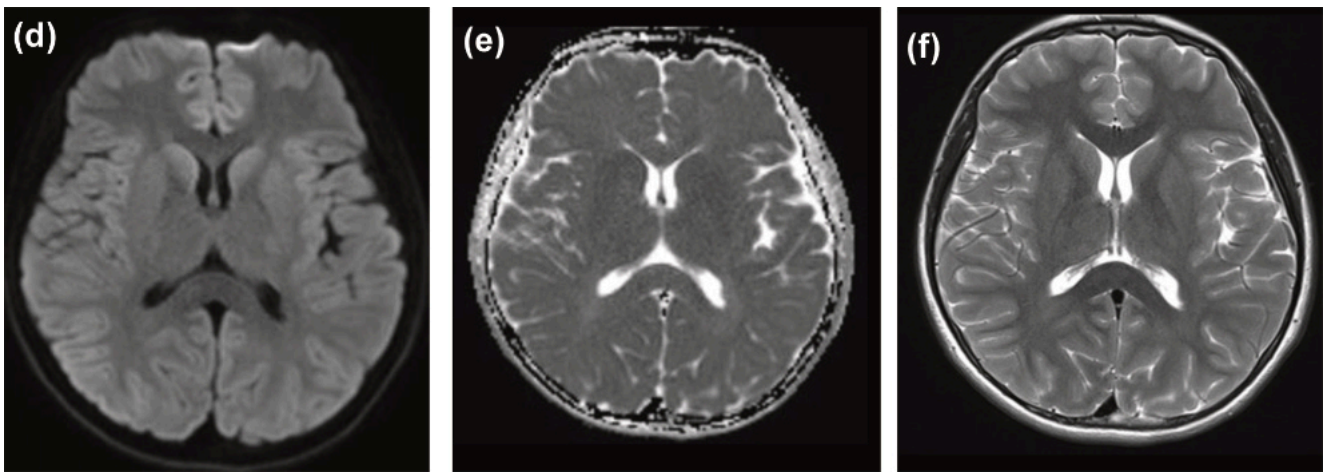

Figure 1 d-f Axial MRI brain of patient on 37 days after initial scan. MRI showed substantial resolution of abnormal signals at the splenium of corpus callosum on (d) diffusion-weighted image, (e) ADC map and (f) T2-weighted image.

These cell-cytokine interactions drastically increased cytokines and glutamate levels which cause excitotoxicity and dysfunction of cells with influx of water, result in cytotoxic oedema.[3,7] From our case, the plasma IL-6 level was elevated ~6 times of baseline which demonstrated the active inflammatory process. This may also support the postulated theory of cytokine-induced injury to the corpus callosum.

Clinical manifestations of CLOCC mimics ADEM/ encephalitis include seizures, confusion, delirium, ataxia, drowsiness, headache and even coma which could be distressing. Most common presentation was seizure (81.5%), followed by headache or dizziness (29.2%) and disturbance on consciousness (23.1%), other less common symptoms include ataxia, abnormal behaviour, limb weakness etc.[6]

However, with the radiological findings of CLOCC, we are more confident to predict the prognosis and clinical outcome. Unlike other encephalitis and ADEM, patients with CLOCC usually have good prognosis and most showed complete recovery in few days to within 1 month.[6,8,9] A large paediatric case series showed resolution of lesion in MRI in all cases with normal neurodevelopment.[6] Resolution of MRI lesions usually lag behind neurological recovery for 1

week onwards. Some cases even resolved without specific treatment.[9] Rarely, there were isolated reported cases with longer recovery period with need for ICU support or having persistent neurological deficit with comatose or bedridden state.[9] The therapeutic regimens varies from conservative approach to treatments include antimicrobials, anti-epileptic drugs, correction of electrolytes, corticosteroids, and IVIG.[6,9] Use of mannitol was implemented in case with raised intracranial pressure.[6] Currently there are no consensus on the standard treatment for CLOCC due to heterogeneity of aetiologies. Though on postulation, immunotherapy may play a role to hasten inflammation and hence further damage to the brain.

There are several differential diagnoses of CLOCC to be considered, like ADEM, as few patients can present with isolated splenium lesion in early stage, associated with encephalopathy, which also shared similar clinical presentations and recover after immunomodulatory therapy. MRI in ADEM usually shows multiple foci of T1 and T2 image with enhancement in bilateral or asymmetric subcortical white matters, which usually evolve over weeks to months and lesions disappear after several months.[9] Autoimmune encephalitis e.g. anti-N-methyl-D-aspartate receptor encephalitis also share similar clinical presentations. Corpus callosum infarction could be another mimic, which tend have multifocal areas of diffusion restriction, more subcortical involvement, with lateralised splenial lesion rather than midline involvement.[10] It is rare, due to the abundant collateral supply of blood from anterior and posterior circulation. Integrating the clinical, laboratory and radiographic characteristics can help to deduce the correct diagnosis.

Conclusion

CLOCC is a rare clinical radiological syndrome in paediatric populations which describes the cytotoxic injury to corpus callosum especially the splenium. Radiological finding of oval, small lesion in corpus callosum usually at midline with restricted diffusion on MRI with T2 enhanced signal intensity, which are often reversible on follow up scan may hint us to the diagnosis. Most reported cases have good recovery. Increasing awareness of this disease entity can allow physicians to provide accurate prognostic information to parents to aid counselling as well as guiding treatment regimen and management.

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Declaration of Interest

None

Table for summary of CLOCC

Presenting clinical features	Seizure, confusion, delirium, ataxia, drowsiness, weakness, headache, and coma
MRI features	Oval, small lesion in corpus callosum usually at midline with typical high T2 signal, low T1 signal, restricted diffusion, and lack of contrast enhancement. Lesions are often reversible within few days to several weeks on follow up scan
Investigations	Workup to look for aetiologies such as infection, metabolic, epilepsy, drug-related, traumatic, vascular, autoimmune and malignancy
Treatment	Depends on aetiology, varies from supportive to specific treatments like antimicrobials, anti-epileptic drugs, correcting electrolytes, corticosteroids, and IVIG etc.
Prognosis	Generally favourable

References

1. Guleria R, Nisar N, Chawla TC, Biswas NR. Mycoplasma pneumoniae and central nervous system complications: a review. J Lab Clin Med 2005;146:55-63.
2. D'Alonzo R, Mencaroni E, Di Genova L, Laino D, Principi N, Esposito S. Pathogenesis and treatment of neurologic diseases associated with Mycoplasma pneumoniae infection. Front Microbiol 2018:9:2751.
3. Starkey J, Kobayashi N, Numaguchi Y, Moritani T. Cytotoxic Lesions of the Corpus Callosum That Show Restricted Diffusion: Mechanisms, Causes, and Manifestations. Radiographics 2017;37:562-76.
4. Tada H, Takanashi J, Barkovich AJ, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. Neurology 2004;63:1854-8.
5. Moors S, Nakhostin D, Ilchenko D, et al. Cytotoxic lesions of the corpus callosum: a systematic review. Eur Radiol 2024;34:4628-37.
6. Chen H, Yu X, Chen Y, et al. Reversible splenial lesion syndrome in children: a retrospective study of 130 cases. Front Neurol 2023:14:1241549.
7. Gallucci M, Limbucci N, Paonessa A, Caranci F. Reversible focal splenial lesions. Neuroradiology 2007;49:541-4.
8. Uzunhan TA, Genç HM, Kutlubay B, et al. Cytotoxic lesions of the corpus callosum in children: etiology, clinical and radiological features, and prognosis. Brain Dev 2021;43:919-30.
9. Zhu Y, Zheng J, Zhang L, et al. Reversible splenial lesion syndrome associated with encephalitis/encephalopathy presenting with great clinical heterogeneity. BMC Neurol 2016:16:49.
10. Stamm B, Lineback CM, Tang M, et al. Diffusion Restriction in the Splenium: A Comparative Study of Cytotoxic Lesions of the Corpus Callosum (CLOCCs) versus Lesions of Vascular Etiology. J Clin Med 2023;12:6979.