

# Cytotoxic lesions of the corpus callosum (CLOCCs) with a flow gap in straight sinus on magnetic resonance venography

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## ABSTRACT

Cytotoxic lesions of the corpus callosum (CLOCCs) are cytotoxic lesions observed in the splenium of the corpus callosum and are also called mild encephalitis or encephalopathy with reversible splenial lesions or reversible splenial lesion syndrome. It was first reported in patients with epilepsy and since then has been observed in a wide variety of diseases, including infections, trauma, metabolic disorders (hyperglycaemia, hypernatraemia and hyponatraemia), mountain sickness and cerebral venous sinus thrombosis. Here, we present a patient with CLOCCs accompanied by a flow gap in the straight sinus on magnetic resonance venography without any evidence of cerebral venous sinus thrombosis and discuss the possible clinical implications.

## CASE PRESENTATION

A 57-year-old man visited the emergency department with a 1-week history of general weakness and dysarthria. Prior to his visit, he had spent 3 days at a regional hospital, where he was diagnosed with hyperglycaemic hyperosmolar syndrome. After discharge, he experienced no improvement and came to the emergency department of our hospital. He denied any history of medical illness except newly diagnosed diabetes mellitus and moderate smoking (30 pack-years). Laboratory findings from the prior hospital indicated a serum sodium level of 162 mEq/mL, serum osmolality of 413 mOsm/kg and glycated haemoglobin of 12.9%. Initial brain diffusion-weighted (DW) MRIs performed immediately after the onset of the symptom revealed no abnormalities. However, the rescanned brain DW MRIs at our hospital (SIGNA Architect, 70 cm, GE HealthCare, USA) showed a boomerang-like high-signal intensity lesion in the splenium of the corpus callosum (SCC) [figure 1A](#). The apparent diffusion coefficient (ADC) map presented a cytotoxic lesion with low

intensity. Contrast-enhanced (CE) MRIs, three-dimensional time-of-flight MR arteriography (MRA) and venography (MRV) were performed the following day. There was no abnormality on MRA, but MRV showed an absence of the left transverse sinus, left sigmoid sinus and left internal jugular vein ([figure 1B](#)) and a flow gap at the junction of the straight sinus and the vein of Galen ([figure 1C](#)). CE T1-weighted MRIs revealed the flow gap shown in MRV was related to a large arachnoid granulation (AG) in the proximal segment of the straight sinus ([figure 1D](#)) and three additional AGs in the distal segment of the left transverse sinus ([figure 1E](#)). Fluid attenuated inversion recovery (FLAIR) axial MRIs presented a ring-like high signal intensity pattern in the left internal jugular vein ([figure 2A](#)) and an absent signal void in the left sigmoid and left transverse sinus ([figure 2B,C](#)). Following extensive intravenous hydration and appropriate medications to control his blood glucose levels, the patient's condition improved and he was discharged after 2 weeks. On the follow-up DW MRIs taken 1 week after the admission, the cytotoxic lesion disappeared ([figure 1F](#)). On the follow-up CE MRIs, MRA and MRV taken 1 month later, the absence of the left transverse sinus, left sigmoid sinus and left internal jugular vein changed to be hypoplastic ([figure 1G](#)) and the flow gap at the junction of the straight sinus and the vein of Galen was observed without change ([figure 1H](#)). The AGs seen on CE T1-weighted MRIs showed no significant difference ([figure 1I,J](#)). The FLAIR axial MRIs indicated a return to normal signal intensity in the left internal jugular vein ([figure 2D](#)) and an improved signal void in the left sigmoid sinus and left transverse sinus ([figure 2E,F](#)).

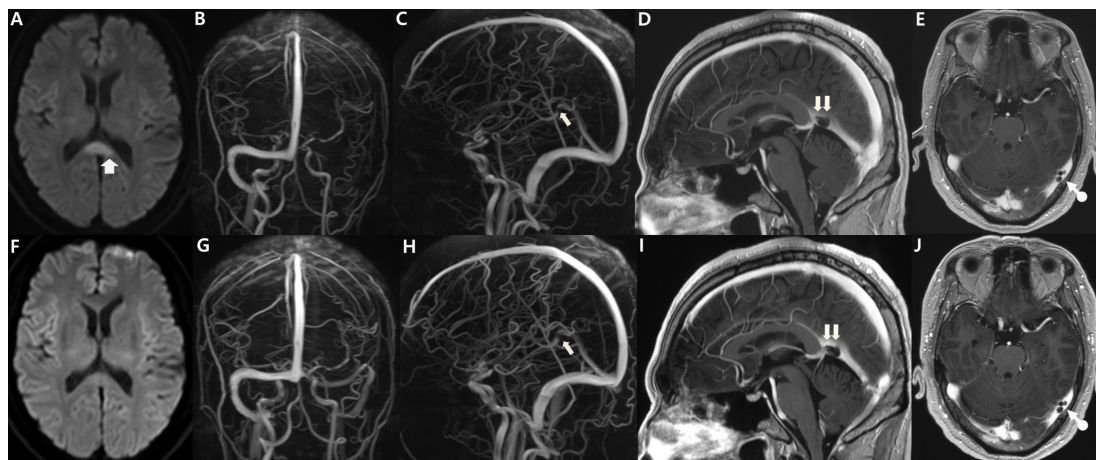


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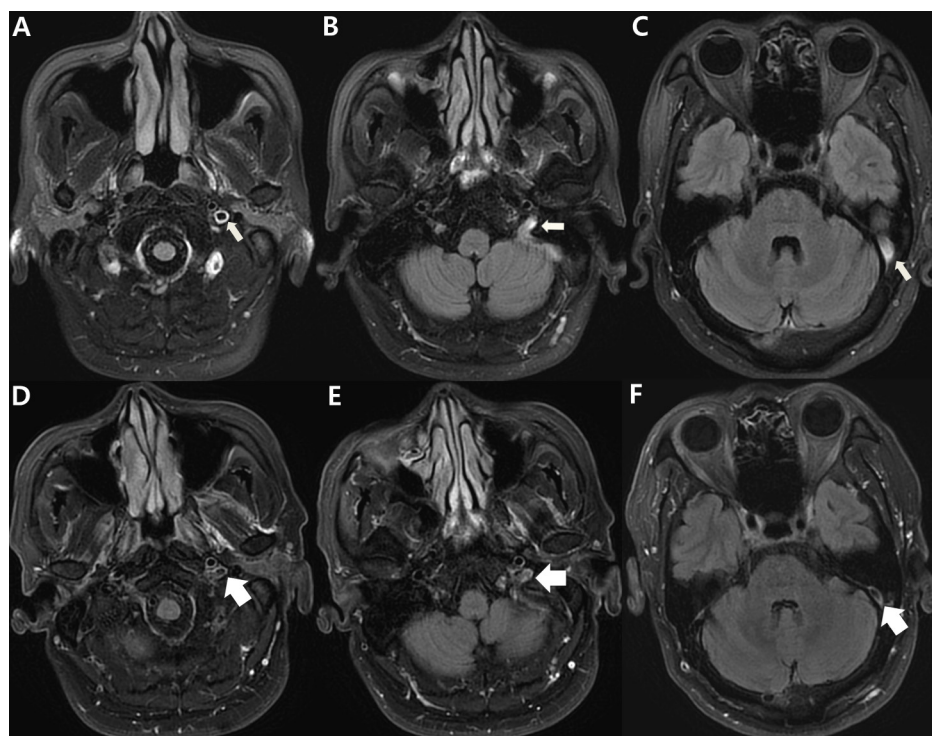


**Figure 1** MRI and magnetic resonance venography findings. (A) Boomerang-like restricted diffusion of the splenium of the corpus callosum on the diffusion-weighted image (thick arrow). (B) Absent left transverse sinus, left sigmoid sinus and left internal jugular vein on MRV. (C) A flow gap in the junction between the vein of Galen and the straight sinus (thin arrow). (D) Arachnoid granulation in the straight sinus on contrast-enhanced MRI (double arrow). (E) Arachnoid granulations in the left transverse sinus (round arrow). (F) Disappearance of restricted diffusion on a diffusion-weighted image after 1 week. (G) Hypoplastic left transverse sinus, left sigmoid sinus and left internal jugular vein after 1 month. (H) A flow gap in the junction between the vein of Galen and the straight sinus (thin arrow) after 1 month. (I) Arachnoid granulation in the straight sinus on contrast-enhanced MRI after 1 month (double arrow). (J) Arachnoid granulations in the left transverse sinus after 1 month (round arrow).

## DISCUSSION

Cytotoxic lesions of the corpus callosum (CLOCCs) are clinico-radiological syndromes and were called by diverse names in the past, such as mild encephalitis or encephalopathy with reversible splenic lesions and reversible

splenic lesion syndrome (RESLES), but (1) encephalopathy is not always mild, (2) the lesions are not always completely reversible and (3) the lesions sometimes extend to adjacent brain regions. It is generally agreed that callosal lesions with restricted diffusion and low



**Figure 2** Fluid attenuated inversion recovery axial MRI findings. (A) Ring-like high signal intensity change in the left internal jugular vein (thin arrow). (B) Absent signal void and high signal intensity in the left sigmoid sinus (thin arrow). (C) Absent signal void and high signal intensity in the left transverse sinus (thin arrow). (D) Normalised signal intensity in the left internal jugular vein (thick arrow). (E) Decreased signal intensity in the left sigmoid sinus (thick arrow). (F) Normalised signal void in left transverse sinus (thick arrow).

ADC values are caused by cytotoxic oedema; therefore, CLOCCs have been proposed as a proper nomenclature.<sup>1</sup> Infection, metabolic disorders (hypoglycaemia and hypernatraemia), trauma, malignancy, drugs, high-altitude cerebral ischaemia (mountain sickness) and cerebral venous sinus thrombosis were reported as CLOCCs-prone conditions.<sup>1–4</sup> Starkey *et al* proposed cytokinopathy and glutamate-induced excitotoxicity as the final common pathways of the CLOCCs based on autopsy data.<sup>1</sup> The SCC is vulnerable to cytokinopathy as a consequence of high levels of cytokine receptors, glutamate, other excitatory amino acid receptors, toxin receptors and drug receptors.<sup>1</sup> Based on the homogenous and reversible pattern on DW MRIs, persistent ischaemia was excluded as a causative mechanism. A similar pattern shown in CLOCCs occurs in hemiplegic migraine and venous occlusion<sup>2</sup> and may suggest a common pathogenesis. The corpus callosum has relatively simple arterial circulation through the anterior pericallosal artery branching from the anterior cerebral artery and the posterior pericallosal artery branching from the posterior cerebral artery. However, venous flow is complex, and the subependymal veins, anterior septal veins and medial atrial veins drain into the straight sinus via the internal cerebral vein and vein of Galen. Additionally, with accessory drainage, the anterior and posterior pericallosal veins (also called splenic veins) go to the straight sinus through various routes.<sup>5</sup> Therefore, the veins of Galen and the straight sinus are responsible for the main venous drainage of the corpus callosum, especially the splenium. Studies using MRV for CLOCCs are rare. Liu *et al* reported two RESLES cases with cerebral venous sinus thrombosis,<sup>4</sup> and Altunkas *et al* presented a patient with postpartum RESLES with normal MRV findings.<sup>6</sup>

In this case, a flow gap of the MRV was observed at the junction between the straight sinus and the vein of Galen. This flow gap might be related to a large AG at the proximal segment of the straight sinus on CE MRIs, despite the slight difference in the exact location. Interestingly, the invisible left transverse sinus, sigmoid sinus and internal jugular vein in the initial MRV changed to hypoplastic on the follow-up MRV performed 1 month later. On FLAIR axial MRIs, the prominent signal changes in the left internal jugular vein, left transverse sinus and left sigmoid sinus were nearly normalised (figure 2). No imaging findings indicated cerebral venous sinus thrombosis. In combination with the MRV and FLAIR axial MRI findings, we believe that there was abnormal venous circulation rather than thrombosis from the vein of Galen through the straight sinus, left transverse sinus, left sigmoid sinus and left internal jugular vein. The AGs in the straight and left transverse sinuses remained unchanged after 1 month. Double AGs (AG in the straight sinus and AG in the transverse sinus) may not cause a problem in the usual clinical setting, but in some critical circumstances for CLOCCs, such as infection and inflammation, they may provoke jeopardy in the deep venous circulation and ultimately cause splenic injury. AG in the straight sinus

is reported to be a very rare situation.<sup>7</sup> But a prospective CE 3D MRV study reported that AG of the cerebral dural sinus was observed in the superior sagittal sinus (46%), transverse sinus (27%) and straight sinus (23%).<sup>8</sup> Therefore, AG in the straight sinus may not be as uncommon as previously presumed.

Further data will help clarify whether the pathology of the vein of Galen and the straight sinus is an important prerequisite for the development of CLOCCs, if it merely increases the likelihood of occurrence as a triggering factor, or even if it is coincidental in this case. Therefore, performing CE MRI and MRV together would be helpful for understanding the pathophysiology of CLOCCs.

### Key points

- ⇒ Cytotoxic lesions of the corpus callosum (CLOCCs) are secondary lesions associated with various disease entities, and attention should be paid to their primary cause.
- ⇒ Mild encephalitis or encephalopathy with reversible splenic lesions and reversible splenic lesion syndrome are also known as CLOCCs.
- ⇒ Diffusion restriction with a low apparent diffusion coefficient value in the splenium of the corpus callosum (SCC) is a typical MRI finding and is caused by cytotoxic oedema through cytokinopathy and glutamate-induced excitotoxicity.
- ⇒ Straight sinus drain venous flow from the SCC and disturbed circulation may have a relationship with the pathogenesis of CLOCCs.
- ⇒ Magnetic resonance venography and contrast-enhanced MRIs can provide additional important clues for patients with CLOCCs.

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