

Case Report



Cytotoxic Lesions of the Corpus Callosum Preceding Osmotic Demyelination Syndrome in Hypernatremia and Hyperosmolar Hyperglycemic State: A Case Report

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ABSTRACT

Osmotic demyelination syndrome (ODS) is a rare neurological disorder associated with osmotic imbalances. Traditionally, ODS has been known to occur following the rapid correction of hyponatremia; however, ODS has also been reported concerning hypernatremia and hyperglycemia. Cytotoxic lesions of the corpus callosum (CLOCC), identified using transient magnetic resonance imaging, can arise from various causes, including drugs, vascular diseases, infections, and metabolic disturbances such as electrolyte imbalances and dysglycemia. The simultaneous occurrence of ODS and CLOCC is extremely rare. Here, we report a case whereby a 57-year-old male initially developed CLOCC via severe hypernatremia and hyperosmolar hyperglycemic state (HHS) was also subsequently identified with ODS. Physicians should know CLOCC may be an early radiologic finding in ODS associated with severe hypernatremia and HHS. Therefore, proactive brain imaging should be considered in these patients to facilitate the early detection of neurological complications.

Keywords: Consciousness; Corpus callosum; Hyperglycemia; Hypernatremia; Magnetic resonance imaging

INTRODUCTION

Generally, hypernatremia and hyperglycemia can lead to brain damage, including cerebral edema, hemorrhage, and thrombosis [1]. Meanwhile, osmotic demyelination syndrome (ODS) and cytotoxic lesions of the corpus callosum (CLOCC) have been identified using brain imaging methods in relation to these conditions.

ODS, which includes both central pontine myelinolysis and extrapontine myelinolysis, is characterized by acute demyelination lesions occurring in brain cells [2]. Traditionally, ODS has been described in patients with rapid osmotic shifts, especially rapid correction of hyponatremia or severe hypernatremia [3]. However, several case reports have documented the occurrence of ODS, even in hyperglycemia [4].

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Conflicts of interest

All authors have no conflicts of interest to declare.

Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

Supervision: CSK. Writing - original draft: HJP, SHS¹. Writing - review & editing: SHS², HSC, EHB, SKM, SWK, CSK. All authors read and approved the final manuscript.

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CLOCC is a transient signal alteration on magnetic resonance imaging (MRI), typically involving the splenium of the corpus callosum (SCC). CLOCC exhibits hyperintensity on diffusion-weighted imaging (DWI) sequences with corresponding hypo-intensity on apparent diffusion coefficient (ADC) maps. Various diseases and conditions have been associated with CLOCC, including trauma, drug-related, infections, vascular diseases, and metabolic disorders [5]. CLOCC caused by electrolyte imbalance is commonly observed hyponatremia, whereas it is relatively rare in hypernatremia [6]. These lesions usually recover within one to several weeks after correcting the underlying cause [5].

We report an exceptionally rare case of CLOCC initially manifested in a patient with concurrent hypernatremia and hyperosmolar hyperglycemic state (HHS), followed by the subsequent development of ODS.

CASE REPORT

A 57-year-old man presented to the emergency department with confusion and irritability. The patient also complained of anorexia and vomiting for 2 weeks before the visit, and had a weight loss of approximately 10 kg over the past six months. He denied any history of trauma or alcohol use. The patient had no known underlying medical conditions and was not taking any medications. However, he did report a habitual excessive intake of dietary sugar.

On admission, the patient appeared confused, producing incomprehensible sounds. His vital signs were measured: blood pressure of 130/60 mmHg, heart rate of 97 beats/min, body temperature of 36.2°C, and oxygen saturation of 100% on room air. A physical examination revealed a dry tongue and decreased skin turgor, which suggested severe dehydration. His laboratory results were as follows: serum creatinine, 2.4 mg/dL (0.5–1.3 mg/dL); serum sodium, 176 mEq/L (136–146 mEq/L); serum potassium, 3.2 mEq/L (3.5–5.1 mEq/L); serum magnesium, 2.5 mg/dL (1.6–2.6 mg/dL); serum inorganic phosphorus, 3.0 mg/dL (2.5–4.5 mg/dL); serum osmolality, 401 mOsm/kg (280–295 mOsm/kg); urine osmolality, 353 mOsm/kg (300–900 mOsm/kg); hemoglobin A1c, 15.1% (4.4–6.4%); blood glucose, 525 mg/dL (60–100 mg/dL). The corrected serum sodium level was 186 mEq/L. The serum pH was 7.40 (7.35–7.45), and the bicarbonate level was 26.6 mmol/L (21–28 mmol/L), indicating an absence of acidosis. The ketone body level was mildly elevated at 155.7 μmol/L (28–120 μmol/L). A detailed summary of the patient's laboratory findings on the first hospital day is presented in **Table 1**.

Brain MRI was performed to evaluate the altered mental status of the patient and demonstrated a diffusion-restricted lesion in the SCC, appearing hyperintense on DWI and fluid-attenuated inversion recovery (FLAIR) sequences, with corresponding hypointensity on the ADC maps (**Fig. 1**).

The patient was treated using hypotonic fluids and continuous intravenous insulin infusion to correct hypernatremia and hyperglycemia. Hypernatremia was gradually corrected over several days to prevent overcorrection. Insulin therapy for glycemic control was transitioned from continuous infusion to multiple daily injection regimens, followed by oral hypoglycemic agents—metformin and linagliptin. We included a summary table to illustrate the daily trends in serum sodium, glucose, osmolality, potassium, blood urea nitrogen, and creatinine during the early course of hospitalization (**Table 2**). On the 14th day of hospitalization, the patient did not fully recover consciousness despite serum sodium levels and osmolality

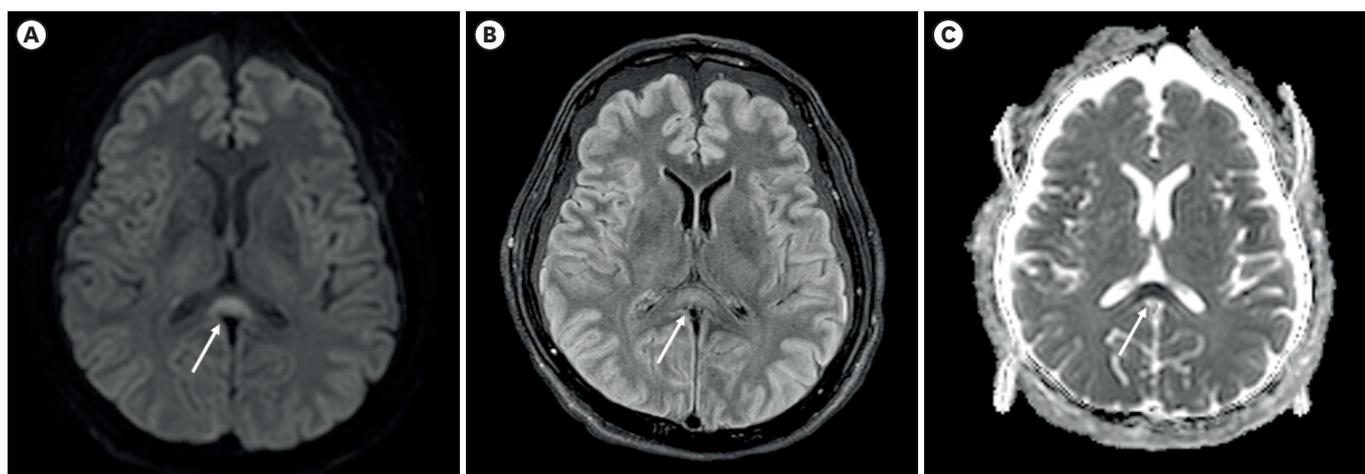


Fig. 1. Magnetic resonance imaging findings in cytotoxic lesions of the corpus callosum. (A) Diffusion-weighted imaging and (B) fluid-attenuated inversion recovery show high signal intensity. (C) The apparent diffusion coefficient map shows hypointense signals in the same lesion, indicating restricted diffusion (arrow).

Table 1. Laboratory findings on the first hospital day

| Laboratory parameter | Result | Reference range |
|--|--------|-----------------|
| White blood cell count (μL) | 6,100 | 4,000–10,000 |
| C-reactive protein (mg/dL) | 0.78 | 0–0.3 |
| Aspartate aminotransferase (U/L) | 31 | 13–39 |
| Alanine aminotransferase (U/L) | 54 | 7–52 |
| Serum albumin (g/dL) | 3.5 | 3.5–5.2 |
| Serum creatinine (mg/dL) | 2.4 | 0.5–1.3 |
| Serum sodium (mEq/L) | 176 | 136–146 |
| Serum potassium (mEq/L) | 3.2 | 3.5–5.1 |
| Serum magnesium (mg/dL) | 2.5 | 1.6–2.6 |
| Serum inorganic phosphorus (mg/dL) | 3.0 | 2.5–4.5 |
| Serum osmolality (mOsm/kg) | 401 | 280–295 |
| Urine osmolality (mOsm/kg) | 353 | 300–900 |
| Hemoglobin A1c (%) | 15.1 | 4.4–6.4 |
| Blood glucose (mg/dL) | 525 | 60–100 |
| Serum pH | 7.40 | 7.35–7.45 |
| Bicarbonate (mmol/L) | 26.6 | 21–28 |
| Ketone bodies ($\mu\text{mol/L}$) | 155.7 | 28–120 |

Table 2. Daily laboratory results during hospitalization

| Laboratory parameter | HD 1 | HD 2 | HD 3 | HD 7 | HD 14 |
|----------------------------|------|------|------|------|-------|
| Serum sodium (mEq/L) | 176 | 168 | 161 | 145 | 142 |
| Serum glucose (mg/dL) | 525 | 391 | 222 | 171 | 163 |
| Serum osmolality (mOsm/kg) | 401 | 385 | 350 | 294 | 293 |
| Serum potassium (mEq/L) | 3.2 | 3.0 | 3.9 | 3.7 | 4.1 |
| BUN (mg/dL) | 43.0 | 37.4 | 22.1 | 21.9 | 18.7 |
| Creatinine (mg/dL) | 2.42 | 2.08 | 1.76 | 0.90 | 0.79 |

BUN, blood urea nitrogen; HD, hospital day.

appearing normalized. A follow-up brain MRI showed a resolution of the SCC lesions; however, new lesions consistent with ODS were revealed, affecting the external capsules, thalami, hippocampi, and pons (**Fig. 2**). After one month, the patient had fully regained consciousness.

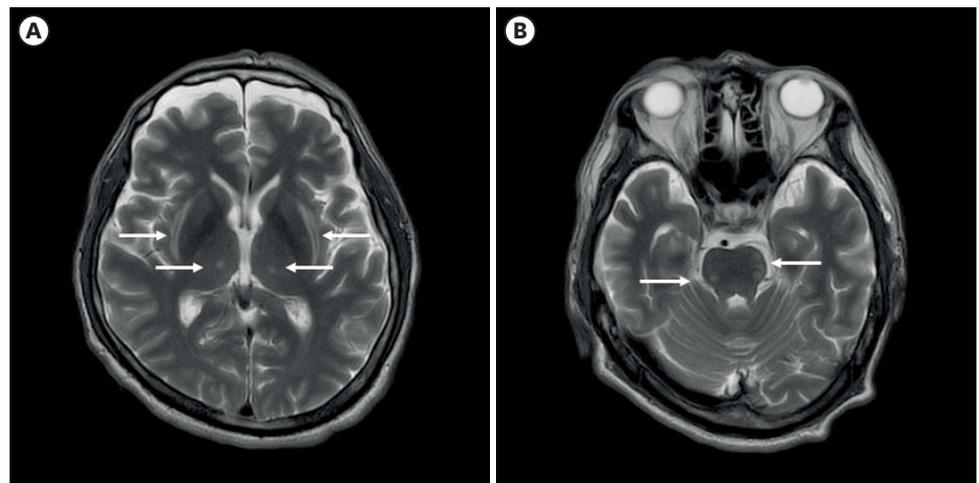


Fig. 2. A follow-up brain magnetic resonance imaging (hospital day 14). Symmetrical T2 hyperintensities in the (A) external capsules, thalami, (B) hippocampi, and peripheral pons. These findings suggest metabolic encephalopathy, such as osmotic demyelination syndrome (arrows).

Ethics statement

This study was approved by the Chonnam National University Hospital (study approval number: CNUH-EXP-2025-099).

DISCUSSION

We present a case in which ODS was subsequently identified in a patient who developed CLOCC as a result of hypernatremia and HHS. ODS is a rare neurological disorder characterized by demyelination of brain cells, encompassing both central pontine myelinolysis and extrapontine myelinolysis [2]. The most widely recognized precipitating factor in clinical practice is the rapid correction of chronic hyponatremia, but in some cases, its association with hypernatremia and hyperglycemia has also been revealed [3,4]. In ODS, seizures or encephalopathy may manifest initially. As the disease progresses, dysarthria, dysphagia, oculomotor dysfunction, and variable degrees of quadriplegia may develop. Radiological findings on brain MRI are hyperintense lesions in the central pons or associated extrapontine structures on T2-weighted and FLAIR sequences with corresponding hypointensity on T1-weighted sequences. While ODS has historically been considered a condition with a poor prognosis, recent studies indicate favorable recovery is not uncommon [2].

The term CLOCC was first proposed by Starkey et al. [7] in 2017. Prior to this, these lesions were referred to as mild encephalitis/encephalopathy with reversible splenial lesion, reversible or transient splenial lesions, and reversible splenial lesion syndrome. MRI shows these lesions exhibit hyperintensity on T2-weighted imaging, FLAIR, and DWI while demonstrating hypointensity on ADC. On T1-weighted imaging, these lesions exhibit either hyperintensity or isointensity. In most cases, contrast enhancement is not observed. Clinical manifestations are usually nonspecific and varied. Meanwhile, fever and headache are commonly observed, while cognitive impairment, behavioral change, confusion, seizures, and loss of consciousness can also occur. CLOCC is associated with diverse causes, including trauma, drugs, viral or bacterial infections, vascular diseases, and metabolic disorders such as electrolyte disturbances and dysglycemia. The exact mechanism underlying splenial

lesions remains unclear, but the high density of excitatory amino acid receptors in the corpus callosum may contribute to its vulnerability to cytokine-mediated injury. These lesions generally resolve within a few weeks following correction of the underlying cause [5].

In our patient, we hypothesized that diabetes mellitus developed but remained untreated, leading to uncontrolled hyperglycemia. Moreover, as no findings were observed on the computed tomography scan of the neck, chest, and abdomen that indicated the existence of malignant tumors, the 10 kg weight loss over six months was thought to be a manifestation of diabetes mellitus. Osmotic diuresis was induced afterward, and hypernatremia is presumed to have worsened due to polyuria and inadequate oral intake. Although most cases of CLOCC are linked to hyponatremia [6], CLOCC has also been reported in the context of hypernatremia and hyperglycemia [8-10]. Thus, we suggest that hypernatremia and hyperglycemia contributed to the development of CLOCC in this case. A follow-up MRI performed three weeks later revealed imaging findings consistent with ODS. To our knowledge, the simultaneous occurrence of CLOCC and ODS is extremely rare, with only a single case previously reported by Zhang et al. [10] in 2024, in which CLOCC and ODS were induced by hypernatremia. In that case, the patient recovered consciousness within five days; in our case, complete recovery required several weeks. We hypothesized the reasons for this occurred in two ways. Since our patient presented to the emergency department, determining the baseline sodium level and continuously monitoring the levels was challenging. Additionally, the exact timing of deterioration was unclear, leading to a delayed diagnosis of hypernatremia and HHS. Another reason is related to the coexistence of hypernatremia and hyperglycemia. Both serum sodium and glucose play essential roles in regulating serum osmolality, and their coexistence leads to delayed recovery from ODS, as the condition is influenced by changes in serum osmolality.

In conclusion, CLOCC lesions are important radiologic findings and may be observed early in ODS caused by severe hypernatremia and HHS. Therefore, physicians should consider performing proactive brain imaging, and further research is needed to explain the pathological mechanisms associated with CLOCC and ODS.

REFERENCES

1. Meena A, Singh A, Goyal VK, Gupta N, Payal V, Chaturvedi K. Brain injury patterns in neonates with hypernatremic dehydration: single center experience. *Indian Pediatr* 2021;58:947-950. [PUBMED](#) | [CROSSREF](#)
2. Singh TD, Fugate JE, Rabinstein AA. Central pontine and extrapontine myelinolysis: a systematic review. *Eur J Neurol* 2014;21:1443-1450. [PUBMED](#) | [CROSSREF](#)
3. Han MJ, Kim DH, Kim YH, Yang IM, Park JH, Hong MK. A case of osmotic demyelination presenting with severe hypernatremia. *Electrolyte Blood Press* 2015;13:30-36. [PUBMED](#) | [CROSSREF](#)
4. Kusumoto K, Koriyama N, Kojima N, Ikeda M, Nishio Y. Central pontine myelinolysis during treatment of hyperglycemic hyperosmolar syndrome: a case report. *Clin Diabetes Endocrinol* 2020;6:23. [PUBMED](#) | [CROSSREF](#)
5. Tetsuka S. Reversible lesion in the splenium of the corpus callosum. *Brain Behav* 2019;9:e01440. [PUBMED](#) | [CROSSREF](#)
6. Takanashi J, Tada H, Maeda M, Suzuki M, Terada H, Barkovich AJ. Encephalopathy with a reversible splenial lesion is associated with hyponatremia. *Brain Dev* 2009;31:217-220. [PUBMED](#) | [CROSSREF](#)
7. Starkey J, Kobayashi N, Numaguchi Y, Moritani T. Cytotoxic lesions of the corpus callosum that show restricted diffusion: mechanisms, causes, and manifestations. *Radiographics* 2017;37:562-576. [PUBMED](#) | [CROSSREF](#)

8. Cagnin A, Manara R, Piron L, Dam M, Hemmings HC. Hyponatremia-induced limbic system damage. *Anesthesiology* 2011;114:175. [PUBMED](#) | [CROSSREF](#)
9. Kaino K, Kumagai R, Furukawa S, et al. Reversible splenic lesion syndrome with a hyperosmolar hyperglycemic state and neuroleptic malignant syndrome caused by olanzapine. *J Diabetes Investig* 2017;8:392-394. [PUBMED](#) | [CROSSREF](#)
10. Zhang YX, Zhang TY, Zhou JP, Liu ZR. Concurrent reversible splenic lesion syndrome and extrapontine osmotic demyelination syndrome associated with hyponatremia. *QJM* 2024;117:595-596. [PUBMED](#) | [CROSSREF](#)