

Cortical Laminar Necrosis Caused by Rapidly Corrected Hyponatremia

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ABSTRACT

Cortical laminar necrosis (CLN) is radiologically characterized by hyperintense cortical lesions on unenhanced T1-weighted images. Hypoxia is the representative cause of CLN; however, the rapid correction of hyponatremia has also been suggested as another possible cause. We present a patient who developed CLN and a permanent neurologic sequel following the rapid correction of hyponatremia without hypoxic insult, and discuss the characteristics of CLN lesions in view of osmotic demyelination syndrome based on magnetic resonance (MR) image findings.

Keywords: Cortical laminar necrosis, osmotic demyelination syndrome, hyponatremia.

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Introduction

Cortical laminar necrosis (CLN) is most commonly encountered in cases of severe hypoxic brain damage, and it is radiologically characterized by hyperintense cortical lesions on unenhanced T1-weighted magnetic resonance (MR) images, especially during the subacute stage.^{1,2} Delayed cortical atrophy is the characteristic MR imaging (MRI) finding during the chronic stage.¹⁻³ In addition to hypoxic brain damage, metabolic insults, infarction, seizure, and drugs are also known to be associated with CLN.²⁻⁶ However, the MRI finding of CLN developed by rapidly corrected hyponatremia has rarely been reported.^{4,5} We present a patient who developed CLN and a permanent neurologic sequel following the rapid correction of hyponatremia without hypoxic insult.

Case Report

A 27-year-old man with a history of congenital panhypopituitarism was admitted to our institution with a 3-day history of melena and hematemesis. He had no history of hypoxic insult, hypoglycemia, malnutrition, trauma, central nervous system infection, renal disease, alcohol abuse, or drug intoxication. His vital signs were normal. Routine blood laboratory tests were unremarkable with the exception of mild anemia (Hemoglobin [Hb] 8.2 g/dL), which had been a stationary level for him at the outpatient clinic. A thorough gastrointestinal evaluation revealed esophageal varix and cryptogenic liver cirrhosis. He was alert and cooperative through the first 9 days of admission. However, he complained of nausea and showed mildly drowsy mentality on hospital day (HD) 10. A profound hyponatremia (105 mmol/L) was detected, and inadvertently corrected to 140 mmol/L within 1 day. His mental

status deteriorated to stupor on HD 12. His vital signs were stable constantly, however, a neurologic examination revealed trace movement to painful stimuli and increased deep tendon reflex in all extremities thereafter. An urgent brain MRI with gadolinium enhancement revealed empty sella, mild cortical atrophy, and associated ventriculomegaly without a brain parenchymal lesion (not shown). On HD 13, the patient's serum sodium level further increased to 157 mmol/L. His mental status gradually deteriorated to coma over the next 3 days. A follow-up MRI was performed on HD 30 under the tentative diagnosis of osmotic demyelination syndrome (ODS). Diffuse hyperintense lesions in the cerebral cortex along the gyral distribution and lentiform nucleus were shown on T1- and T2-weighted images accompanied by a marked contrast enhancement. On T2-weighted images, some portions of hypointensity were seen in the white matter subjacent the hyperintense cortex, which represents a typical finding of CLN (Fig 1).¹ The thalamus, caudate nucleus, dorsal midbrain, and pons showed hyperintensities on T2-weighted images and hypointensities on T1-weighted images without contrast enhancement (Fig 1). The patient has remained in a comatose state to date (HD 90).

Discussion

ODS, a demyelinating disorder caused by a rapid increase in serum tonicity, especially in patients with hyponatremia, is clinically characterized by consciousness deterioration following the rapid correction of hyponatremia.⁷⁻⁹ The most common pathology of ODS is central pontine myelinolysis (CPM) or extra pontine myelinolysis (EPM).⁷⁻⁹ CLN was also rarely

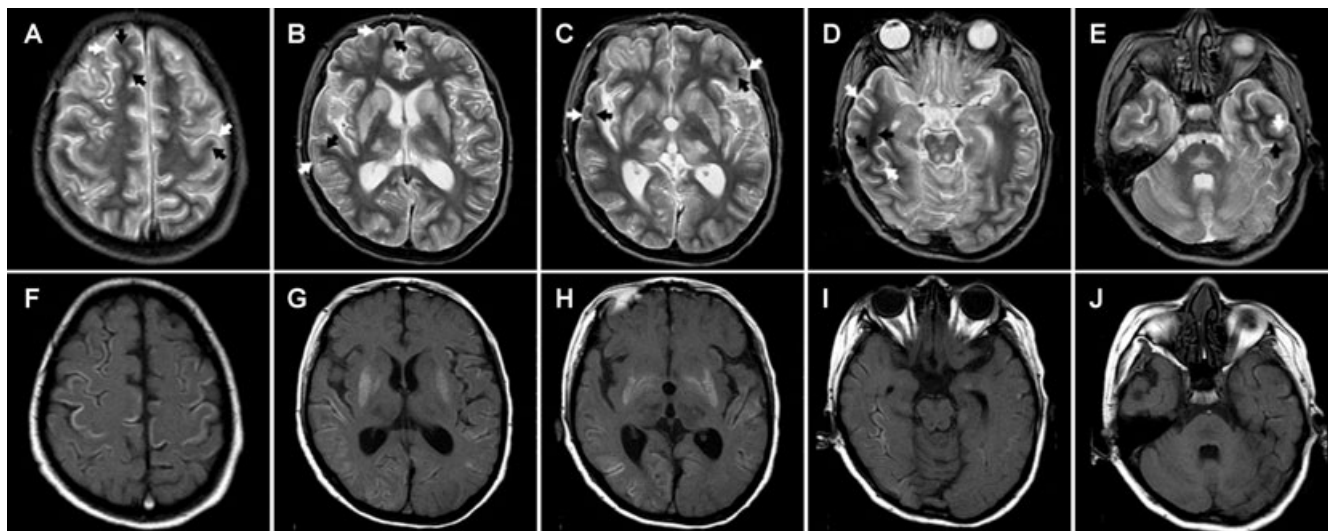


Fig 1. T2-weighted axial (A-E) and unenhanced T1-weighted axial (F-J) images of the patient taken on HD 30 (subacute stage). T2-weighted (A-E) images show high signal intensities of the cerebral cortex along the sulci (white arrow). Some portions of hypointensity were seen in the white matter subjacent the hyperintense cortex (black arrow), which represents a typical finding of CLN. T1-weighted (F-H) images show high signal intensities over the cortical lamina with enhancement (not shown). T2-weighted (B, C) images show high signal intensities in the caudate nucleus, lentiform nucleus, and thalamus. T1-weighted (G, H) images show high signal intensities in the lentiform nucleus, however, there are slightly low signal intensities over the caudate nucleus and thalamus without enhancement (not shown). T2-weighted image shows high signal intensities in the dorsal midbrain, cerebellar vermis (D), and midpons (E). T1-weighted images show low signal intensities over the dorsal midbrain, cerebellar vermis (I), and midpons (J) without enhancement (not shown). The image of the midpons shows the characteristic trident-shaped lesion of the central pontine myelinolysis (E, J).

described as the consequence of rapidly corrected hyponatremia, regardless of the presence of EPM or CPM.^{4,5,10-12}

A pontine lesion in the CPM is known to show a slightly lowered signal intensity on T1-weighted images and high signal intensity on T2-weighted images during the subacute stage.⁸ The lesions are pathologically characterized by the loss of myelin, the presence of macrophages filled with myelin debris, reactive astrocytosis, and the loss of oligodendroglial cells.¹³

The EPM lesions involve bundles of myelinated fibers in the gray matter, including the basal ganglia and thalamus. The lesions also invade the white matter surrounded by massive gray matter, such as the white matter of the cerebral gyri, internal, external, and extreme capsules.⁷ These characteristic distributions of EPM lesions support the pathophysiology introduced by Norenberg.¹⁴ He suggested that the myelinotoxic factors derived from the richly vascular gray matter could interact with adjacent bundles of white matter and result in demyelination. He also suggested that the demyelination was caused by a breakdown of the blood-brain barrier.¹⁴ A recent report suggested that the outward movement of the organic osmolytes from the brain during hyponatremia, which remained in the extracellular space, could result in the net shrinkage of the brain and the demyelination of vulnerable areas.⁸

These pathophysiologic evidences have been introduced in the interpretation of MR cortical signal changes in patients with ODS. Rapid correction of sodium in chronic hyponatremia induces a significant dehydration of the brain, and it makes the myelin sheath stripped from the axon and the oligodendrocytes damaged.⁹ In addition, the concomitant disease or hypoxic event may cause damage to the astrocytes and os-

motric change in the intracellular space, as well. These osmotic changes eventually lead to vasogenic edema and myelinotoxic substances leaking from the vessels.^{9,14} As for T2 prolongation in the early phase of ODS, blood-brain barrier breakdown and associated vasogenic edema has been proposed; whereas, for the T1 shortening in the subacute phase of ODS, the accumulation of cellular debris after demyelination has been proposed.^{4,14}

CLN caused by hypoxia usually involves the third cortical layer, whereas CLN associated with ODS encroaches on the inner layer of the cortex adjacent to the white matter.^{1,13} However, the pathogenesis, including the breakdown of the blood-brain barrier, macrophage deposition, demyelination, and the site of injury, is common between CLN and ODS lesions. Calakos et al. recently suggested that hyponatremia may increase the brain tissue susceptibility to the hypoxic insult.⁴ Conversely, he also proposed that hypoxia could impair the normal compensatory mechanisms of the brain to the hyponatremia.⁴ The pathologic findings previously reported in cortical lesions of the ODS included necrosis, demyelination, and gliosis.^{4,15} These findings seem to suggest some similarity between the CLN and ODS lesions and, at least, the possibility of the co-occurrence of both lesions in some circumstances.

Most previous case reports of CLN in ODS had an episode of hypoxic insult in addition to hyponatremia.¹⁰⁻¹² To our knowledge, only 3 cases have been published concerning the MRI findings of CLN in cases of rapidly corrected hyponatremia without hypoxia.^{4,5} The findings are consistent with CLN caused by hypoxia; however, there was no detailed explanation of their relationship to the presumably combined EPM

and CPM lesions. Inadvertently corrected hyponatremia-ODS was considered to be the most likely cause of CLN in our patient. The anemia could contribute to the CLN, but the compensatory mechanisms might preserve adequate tissue oxygenation in case of chronic steady anemia. However, as the pathophysiology underlying the cortical lesions in ODS, the possible contribution of chronic anemia could not be completely excluded for the development of CLN.⁴ As for the panhypopituitarism, his blood sugar level was stable, and thyroid functions were also in normal range with medication (levothyroxin sodium 50 µg/day). In the previous reports of CLN with other chronic disease, the rapid correction of hyponatremia or additional hypoxic insults rather than the underlying disease was the cause of the CLN and ODS.^{4,5,10-12} Therefore, we considered that the stable underlying disease (panhypopituitarism) of him did not have major influence on the course of disease.

The cortex showed high signal intensities in both the T1- and T2-weighted images and enhancement by gadolinium, which suggests the presence of CLN. Meanwhile, the caudate nucleus, thalamus, dorsal midbrain, and pons lesions showed low signal intensities on the T1-weighted image and high signal intensities on the T2-weighted image without enhancement, which suggest the presence of ODS lesions.

Although more pathologic study is needed to clarify the relationship between CLN and ODS, the present case suggests that CLN may develop via a similar pathogenesis as ODS.

References

1. Takahashi S, Higano S, Ishii K, Matsumoto K, Sakamoto K, Iwasaki Y, Suzuki M. Hypoxic brain damage: cortical laminar necrosis and delayed changes in white matter at sequential MR imaging. *Radiology* 1993;189:449-456.
2. Siskas N, Lefkopoulou A, Ioannidis I, et al. Cortical laminar necrosis in brain infarcts: serial MRI. *Neuroradiology* 2003;45:283-288.
3. Komiya M, Nishikawa M, Yasui T. Cortical laminar necrosis in brain infarcts: chronological changes on MRI. *Neuroradiology* 1997;39:474-479.
4. Calakos N, Fischbein N, Baringer JR, et al. Cortical MRI findings associated with rapid correction of hyponatremia. *Neurology* 2000;55:1048-1051.
5. Lebrun C, Thomas P, Chatel M, et al. Cortical sclerosis presenting with dementia as a sequel of rapid correction of hyponatraemia. *J Neurol Neurosurg Psychiatry* 1999;66:685-686.
6. Donaire A, Carreno M, Gomez B, et al. Cortical laminar necrosis related to prolonged focal status epilepticus. *J Neurol Neurosurg Psychiatry* 2006;77:104-106.
7. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. *J Neurol Neurosurg Psychiatry* 2004;75(suppl 3):22-28.
8. Brown WD. Osmotic demyelination disorders: central pontine and extrapontine myelinolysis. *Curr Opin Neurol* 2000;13:691-697.
9. Lampl C, Yazdi K. Central pontine myelinolysis. *Eur Neurol* 2002;47:3-10.
10. Shoji M, Kimura T, Ota K, et al. Cortical laminar necrosis and central pontine myelinolysis in a patient with Sheehan syndrome and severe hyponatremia. *Intern Med* 1996;35:427-431.
11. Susa S, Daimon M, Morita Y, et al. Acute intermittent porphyria with central pontine myelinolysis and cortical laminar necrosis. *Neuroradiology* 1999;41:835-839.
12. Kinoshita T, Takahashi S, Ishii K, et al. Reye's syndrome with cortical laminar necrosis: MRI. *Neuroradiology* 1996;38:269-272.
13. Ruzek KA, Campeau NG, Miller GM. Early diagnosis of central pontine myelinolysis with diffusion-weighted imaging. *Am J Neuroradiol* 2004;25:210-213.
14. Norenberg MD. A hypothesis of osmotic endothelial injury. A pathogenetic mechanism in central pontine myelinolysis. *Arch Neurol* 1983;40:66-69.
15. Wright DG, Lauren R, Victor M. Pontine and extrapontine myelinolysis. *Brain* 1979;102:361-385.