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Therapeutic Effect of Steroids in Osmotic Demyelination of Infancy

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Abstract

An 11-month-old male presented with acute gastroenteritis, seizures, and altered mental status. Laboratory workup revealed serum sodium of 177 mmol/L. Magnetic resonance imaging of the brain showed reduced diffusion in the supratentorial white matter, T2 hyperintensities in the left central pons and midbrain, subacute stroke in the right occipital lobe, and bilateral cerebellar hemorrhagic infarcts. The child was presumed to have hypernatremia-induced central pontine and extrapontine myelinolysis. He received 5 days of high-dose methylprednisolone for persistent encephalopathy and spastic quadriparesis with rapid recovery of his cognitive function and neurological examination. The child remained seizure-free and achieved normal development at 3-month and 2-year follow-ups. Osmotic demyelination of infancy may leave children with a significant neurological deficit. For favorable neurological outcome, early steroids should be considered.

Keywords

central pontine myelinolysis, extrapontine myelinolysis, methylprednisolone

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Osmotic demyelination syndrome is an acute demyelination process which usually occurs several days following a rapid rise in serum osmolality and presents as spastic quadriparesis, pseudobulbar palsy, and pseudobulbar affect. It was originally described by Adams et al¹ in 1959, where they recognized a peculiar and unique demyelination occurring in central pons in individuals with alcoholism and malnutrition and labeled it as central pontine myelinolysis. Since its original description, the demyelination process following osmotic stress involving other locations outside of pons, including thalamus, internal capsule, deep cerebral cortex, and cerebellum, is termed as extrapontine myelinolysis.² As both central pontine myelinolysis and extrapontine myelinolysis share a common histology, they are known as osmotic demyelination syndrome.

Osmotic demyelination syndrome is rare in infants. It is frequently seen with sodium dysregulation such as rapid correction of hyponatremia.^{3,4} Few cases of osmotic demyelination syndrome secondary to hypernatremia have also been reported in adults.⁵ Here, the author presents a case of osmotic demyelination syndrome in infancy secondary to hypernatremia and its response to the steroids.

Case Summary

An 11-month-old male, developmentally appropriate for his age, presented with a history of vomiting, diarrhea, and fever

for 4 days, altered mental status, and multiple generalized tonic-clonic seizures on the day of admission. There was no history of rash, cough, sick contact, or trauma. The family was giving him concentrated oral rehydration solution for hydration at home. On examination, he had a temperature of 41.1°C, a pulse of 180/minute, respiratory rate of 40/minute and stuporous and responded to painful stimuli by crying and flexion of extremities. In neurological examination, an increase in deep tendon reflexes, axial hypotonia, bilateral positive Babinski reflex, and spastic quadriparesis was observed. Pupils were equal and reactive to light, and no neck stiffness was noted.

The child initial laboratory workup revealed hemoglobin 8.5 g/dL, white blood cell count 13 600 cells/ μ L, platelets 513 000 cells/ μ L, serum sodium 177 mmol/L, potassium 4.2 mmol/L, chloride 149 mmol/L, and bicarbonate 8 mmol/L. The rest of his serum chemistries, transaminases, lactate dehydrogenase, C-reactive protein, lactate, urine organic acid, and urinalysis was in the normal range. Rotavirus stool antigen was positive.

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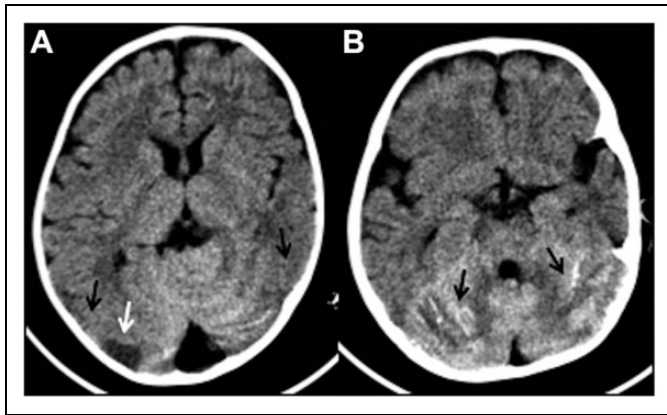


Figure 1. Computed tomography (CT) of the head noncontrast on day of admission: (A) right occipital hypodensity (white arrow) and bilateral occipital sulcal effacement (black arrows) and (B) bilateral cerebellar hemorrhagic infarcts (black arrows).

The child was found to have subclinical status epilepticus on electroencephalogram and was treated with intravenous phenobarbital, midazolam drip, and levetiracetam.

A noncontrast computed tomography of the head obtained on admission showed bilateral occipital sulcal effacement, right occipital subacute infarct, and bilateral cerebellar hemorrhages (Figure 1). The child hyponatremia was corrected with intravenous fluids over 72 hours. After serum sodium correction, the child remained encephalopathic with continuous crying, moaning, and inability to recognize family members. On examination, he continued to have axial hypotonia, increased deep tendon reflexes, and spastic quadriparesis.

Brain magnetic resonance imaging (MRI) with and without contrast was obtained on day 5 of admission, which showed (Figure 2A-D) diffuse hyperintense supratentorial white matter on diffusion-weighted images with isointense apparent diffusion coefficient, a patchy area of restricted diffusion in the right parieto-occipital region, and small hemorrhagic infarcts in the bilateral cerebellar hemispheres. T2-weighted image showed hyperintensities in the left central pons and midbrain with isointense diffusion-weighted images/apparent diffusion coefficient. Contrast enhancement was noted in the bilateral cerebellar hemisphere and vermis. The patient was presumed to have hyponatremia-induced central pontine myelinolysis and extrapontine myelinolysis.

Due to persistent encephalopathy and to rule out meningitis, a lumbar puncture was obtained on day 6, which showed zero cell counts, normal glucose, and protein. Following this, the child was started on intravenous high-dose methylprednisolone (30 mg/kg/d) for 5 days. Immediate improvement in infant's cognition, irritability, muscle tone, and reflexes was noted. At discharge, on day 10, he was able to sit unassisted, move all extremities, stand with support, eat by mouth, and interact with family members.

A follow-up MRI brain imaging at 3 months showed T2 hyperintensities in the bilateral posterior periventricular white matter, a cortical area of encephalomalacia and gliosis in the

right occipital region, and hemosiderin staining in the bilateral cerebellar hemisphere (Figure 2E and F). At 3-month and 2-year follow-ups, the child remained seizure-free, had a normal neurological examination, and achieved normal developmental milestones.

Discussion

Osmotic demyelination syndrome is a rare acute demyelination process with a prevalence of 0.25% to 0.5% in the general population. Its occurrence in infancy is extremely rare. Ranger et al³ identified 76 pediatric patients with osmotic demyelination syndrome between 1960 and 2009, and of them, only 5 (6.5%) were younger than 1 year.

Osmotic demyelination is known to develop following a rapid rise in serum sodium, usually greater than 12 mEq/mL in a 24-hour period.⁴ Our patient with rotavirus gastroenteritis also developed osmotic demyelination syndrome, likely due to hyperosmotic oral rehydration solution, which he received at home.

Clinically, osmotic demyelination syndrome may present with a wide range of symptoms, including spastic quadriparesis, altered mental status, emotional lability, pseudobulbar palsy, dysarthria, dysphagia, dystonia, ophthalmoplegia, ataxia, nystagmus, and cranial nerve palsies. Severe cases may present as “locked-in” syndrome or death.^{6,7} The first 2 symptoms are most frequently encountered symptoms and were also found in our case.

Therapeutic effects of steroid in osmotic demyelination syndrome has been reported in adults in few case reports.^{8–10} In animal studies also, dexamethasone has been shown to have a beneficial response in osmotic demyelination syndrome.¹¹ Other alternative potential therapeutic maneuvers with limited evidence as observed in rats model or adults include use of minocycline, myo-inositol, and lovastatin.^{12–14} The author presents the first case of steroid use in osmotic demyelination syndrome in infancy and its response to a rapid improvement in neurological function and normal developmental outcome.

Disruption of the blood–brain barrier is thought to be one of the underlying pathogenesis of osmotic demyelination syndrome. Rapid correction of hyponatremia or an increase in serum sodium causes water to move into the extracellular space, causing shrinking and dehydration of brain vascular endothelial cells and glial cells, thereby causing disruption of blood–brain barrier tight junctions and axonal shear damage. Disruption of blood–brain barrier allows access to cytokines, lymphocytes, complement proteins, and vasoactive amines to central nervous system tissue which may later lead to inflammatory demyelination. Steroids are known to regulate the blood–brain barrier permeability and thus prevent blood–brain barrier disruption induced by hyperosmolality.^{11,15}

In pediatric osmotic demyelination syndrome, a normal neurological outcome is expected in 20% of patients, almost 23% may have mild-to-moderate neurological deficit, and more than 50% may die of their disease within days to weeks of the onset of neurological symptoms.³ In this index case with extensive

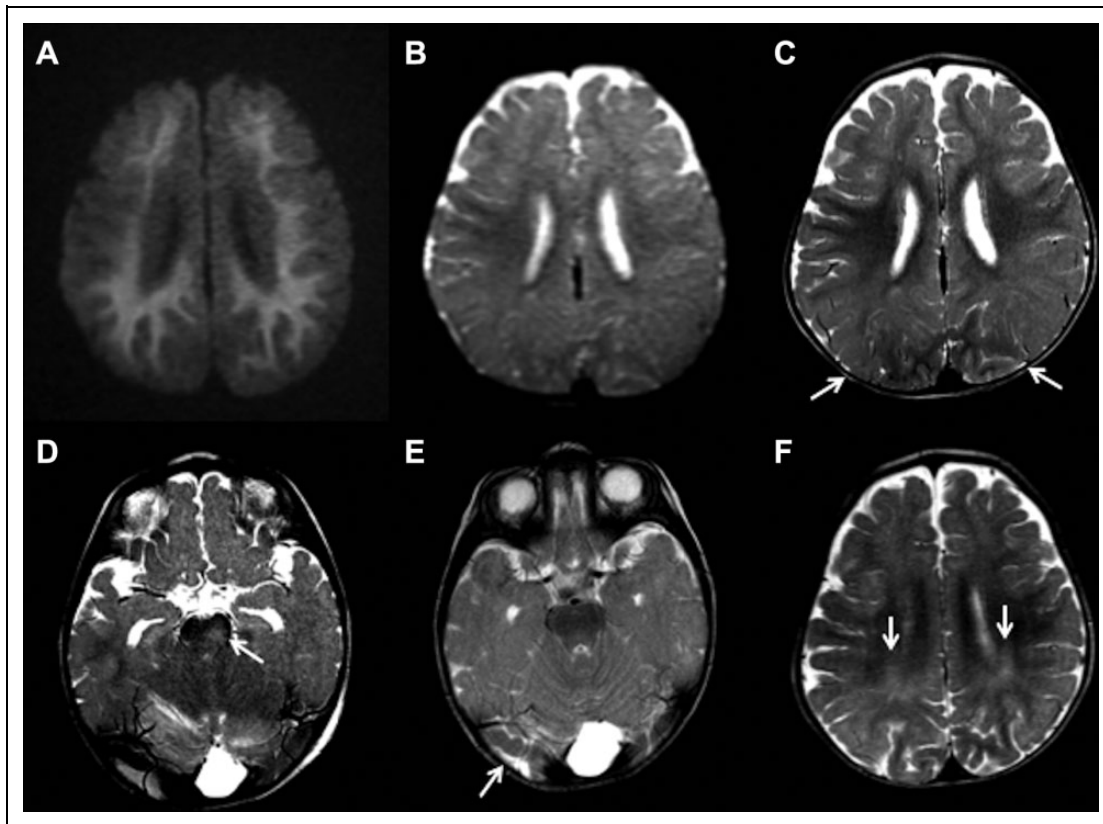


Figure 2. Magnetic resonance imaging (MRI) of the brain at supratentorial level (A-C) revealing (A) diffuse hyperintense white matter on diffusion-weighted images, (B) isointense apparent diffusion coefficient, and (C) sulcal effacement over bilateral posterior quadrant (arrow). D, T2 axial at level of pons showing hyperintensities in left central pons (arrow) and bilateral cerebellum hemispheres. At 3-month follow-up (E-F): (E) T2 axial showing right occipital encephalomalacia (arrow) and resolution of left central pons hyperintensity and (F) T2 axial showing bilateral posterior periventricular white matter hyperintensities (arrow).

neuroradiological changes, it is difficult to predict what would have been the outcome if no steroids were given. With steroid use, the child showed rapid improvement in neurological function, with normal development at both short- and long-term follow-ups. Early use of steroids in children with osmotic demyelination syndrome should be considered for good neurological outcomes.

Authors' Note

The case has not been presented in any meeting. No added assistance was taken from anyone else for writing this manuscript beyond the listed author.

Author Contributions

LRB contributed to literature search, manuscript writing, and revision. Also, he took care of this patient.


Declaration of Conflicting Interests

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Ethical Approval

The author has seen and approved the submission of this version of the manuscript and takes full responsibility for the manuscript.

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