

Osmotic demyelination syndrome in a 40-day-old infant

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ABSTRACT

Osmotic demyelination syndrome refers to the myelin destruction of various brain structures that follows osmotic stress. It affects myelinated brain; therefore, it is very rare in babies and it has not been reported in patients younger than 10 months of age. Herein, we present a 40-day-old infant with osmotic demyelination syndrome, along with imaging findings. Her pontine and thalamic lesions regressed during the 10-day treatment course, whereas demyelinated areas in the lentiform nucleus persisted. Magnetic resonance spectroscopy of the latter revealed decreased levels of all major metabolites. Imaging findings remained unchanged after that phase.

Key words: • *osmotic demyelination syndrome*
• *myelinolysis, central pontine and extrapontine*
• *infant* • *magnetic resonance imaging*

Osmotic demyelination syndrome (ODS) is a rare and acute demyelinating process that involves the pons (central pontine myelinolysis) and other locations of the central nervous system (extrapontine myelinolysis). This syndrome may follow osmotic stress and its neurological symptoms are caused by damage to the corticospinal and corticobulbar tracts. It was initially described by Adams et al. (1) as solitary, symmetrical demyelinating foci at the center of the pons, and is therefore called, central pontine myelinolysis. Similar lesions in other parts of the brain were subsequently called extrapontine myelinolysis (2). These 2 pathological lesions share a common histology and are known as ODS. The main causes of this disorder are alcoholism and chronic nutritional deficiency (1).

In the past, ODS gained attention only as a rare pathology and was observed only during autopsies. With the aid of modern imaging techniques, most notably magnetic resonance imaging (MRI), various causative factors and a wide range of patient characteristics have subsequently been identified (3). However, ODS is still only infrequently seen in infants. In the relevant literature, only 3 cases under the age of 2 years are described (4, 5). Another infant case was recently published (6). The novelty of the present case report is that this patient represents the youngest patient to present with these findings.

Case report

A 40-day-old unconscious female was referred to our institution. At 4 weeks following normal vaginal delivery, she developed nystagmus and progressive loss of movement. Her level of consciousness progressively diminished during the following week. She then received intravenous fluid replacement in a secondary care center in an attempt to correct her hyponatremia. She was referred to our tertiary care center upon the development of tonic and clonic seizures, and loss of consciousness.

At presentation her vital signs were as follows: blood pressure, 65/35 mmHg; heart beat, 140 per min; breathing frequency, 35 per min; body temperature, 37°C. She was 58 cm long and weighed 4,500 g. Her head circumference was 38 cm. These anthropometrical measurements were between the 3rd and 10th percentiles.

In neurological examination she responded to painful stimuli by crying and by flexing her extremities. An increase of deep tendon reflexes, bilaterally positive Babinski reflexes, and spastic quadriparesis were observed. Pupils were isochoric and light reflex was positive. Her anterior fontanel was 2 × 3 cm wide and had an abnormal bulge. Other systemic findings were normal.

In laboratory studies, her complete blood count and her routine biochemical tests were unremarkable. Her cerebrospinal fluid (CSF)

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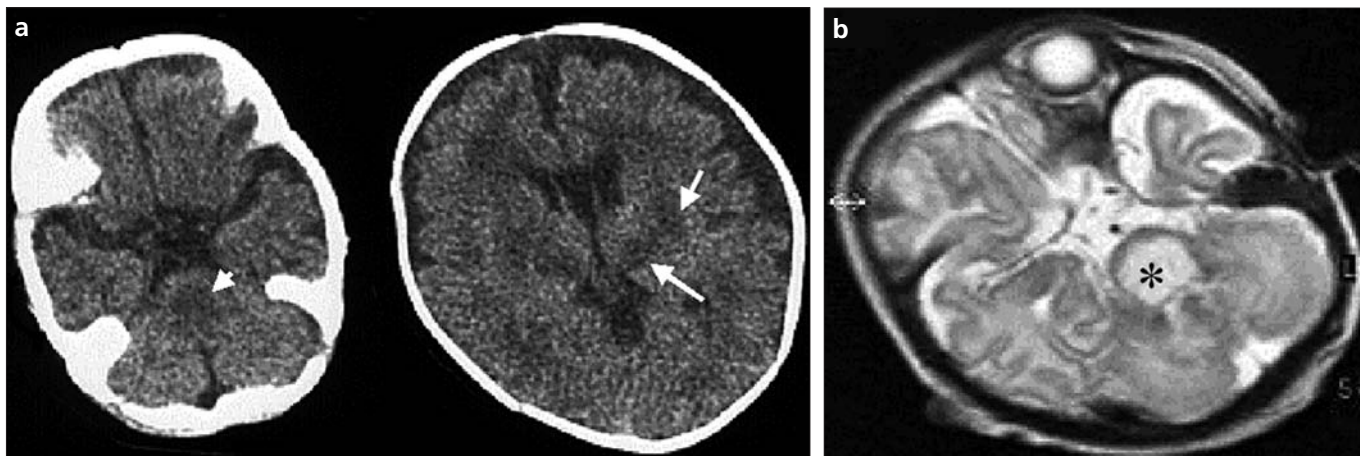


Figure 1. a, b. On early phase axial CT examination (a), prominent hypodense areas at the center of the pons (*arrowhead*), the center of thalami (*long arrow*), and posterior part of the lentiform nucleus (*short arrow*) are seen. Transverse T2-weighted MR image (b) shows centrally located pontine lesion (*asterisk*).

was free of cells. Her blood gases, serum lactate, and ammonia levels were normal.

Computed tomography (CT) examination during the acute phase revealed prominent hypodense areas at the pons, at the center of both thalami, and at the posterior parts of lentiform nucleus (Fig. 1a). On T2-weighted MR images, confluent hyperintense demyelinating areas were observed in these locations (Figs. 1b and 2). The center of the pons was affected, whereas its periphery was spared. The general level of myelination was normal. On the basis of pontine and extrapontine hyperintensities, the radiological diagnosis was ODS.

Her level of consciousness slightly improved on the 10th day of supportive and anticonvulsant therapy. On the follow-up MRI at 1.5 T, the pontine and thalamic hyperintensities regressed, whereas those of the lentiform nucleus persisted (Fig. 2). Single voxel spectroscopy was performed using a point-resolved spectroscopy sequence (PRESS) (TR/TE, 2000/136 ms) with 256 averages. Voxels ($15 \times 15 \times 15$ mm) were placed in the thalamus and lentiform nucleus. Prior to MR spectroscopy (MRS), shimming was performed to optimize field homogeneity and water suppression was optimized using automated routines. A chemical-shift selective saturation pulse suppressed the water signal. A spectral sweep width of 1,000 Hz was used with data size of 1,024 points. All data post processing was performed with software provided by the manufacturer. The magnitude spectra were

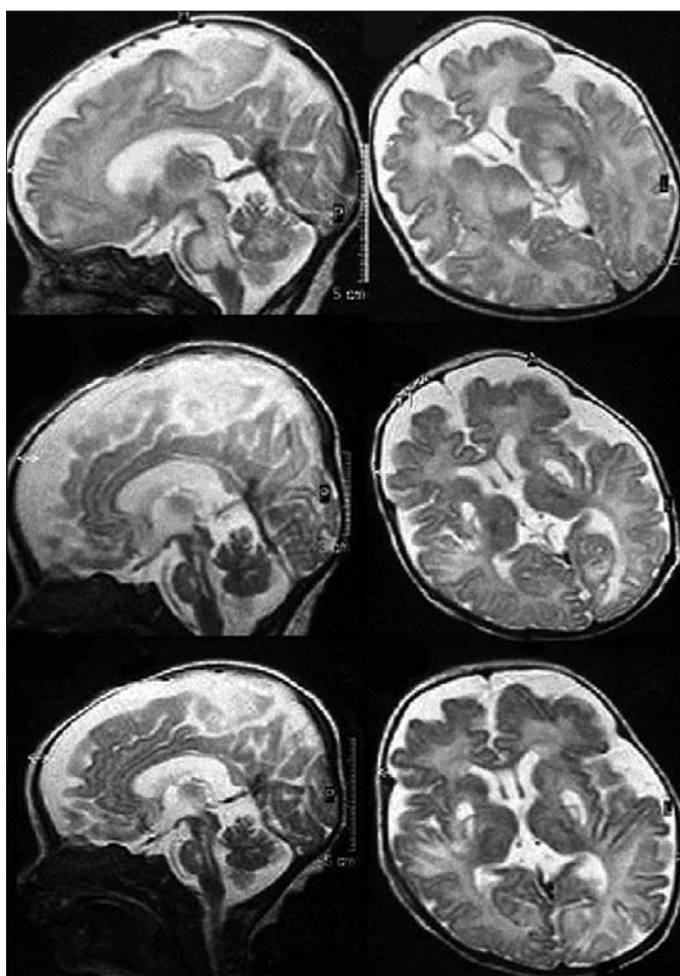


Figure 2. T2-weighted sagittal (*left column*) and transverse (*right column*) MR images. Serial imaging was performed upon presentation (*first row*), on the 10th day (*second row*), and the 20th day (*third row*). Please refer to the text for explanation.

processed automatically using baseline correction and curve-fitting procedures to determine the resonance areas of N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), and myoinositol. Reso-

nance peaks were assigned as follows: NAA, 2.0 ppm; Cr, 3.02 ppm; Cho, 3.2 ppm. Peaks were manually referenced to Cr. MRS of the lentiform nucleus revealed a diminished level for all 3

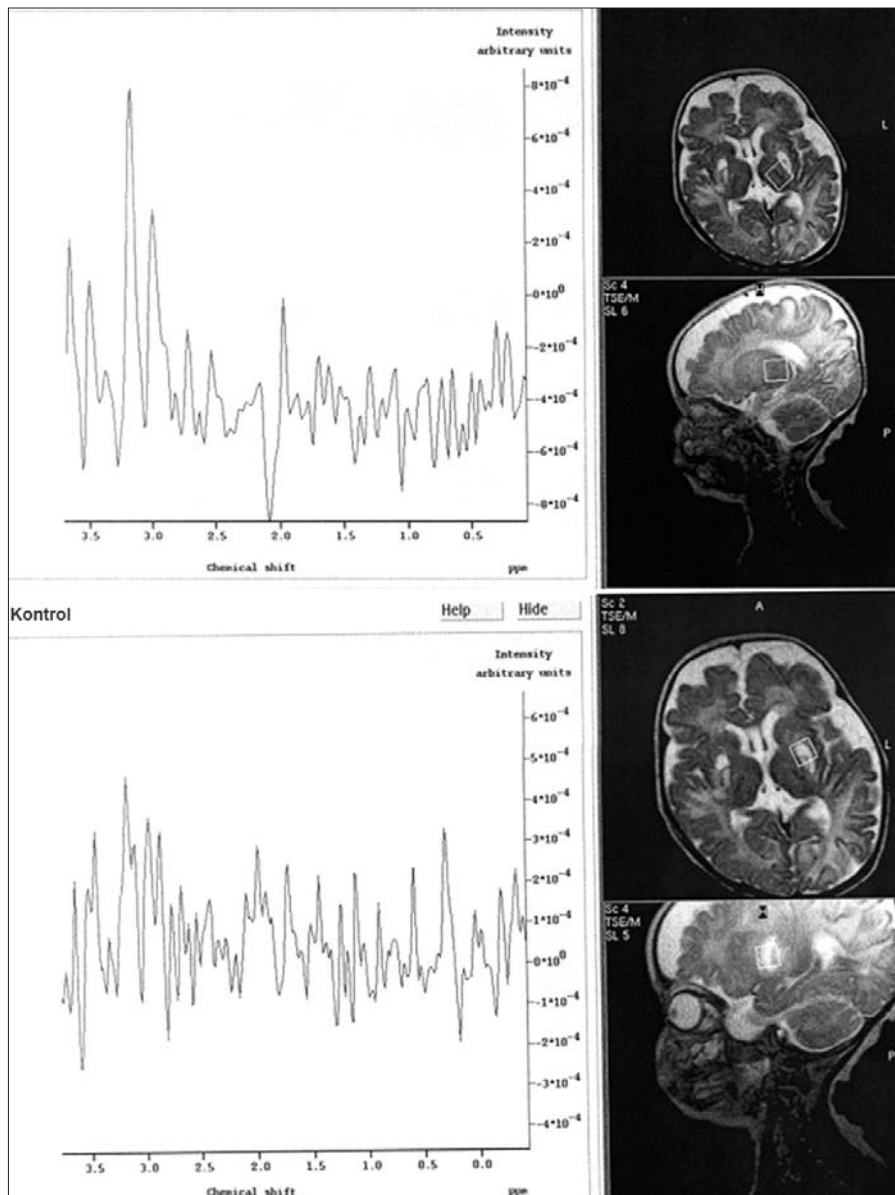


Figure 3. MR spectroscopy (TE, 136 ms) on the 10th day. Pathological signal area in the lentiform nucleus showed diminished levels of all metabolites, whereas that of the thalamus revealed a decreased level of N-acetyl aspartate (NAA) and an increased level of choline (Ch).

metabolites and that of the thalamus revealed a decreased level of NAA and an increased level of Cho (Fig. 3). The patient's clinical course paralleled the neuroradiological regression. On the 20th post treatment day, clinical findings improved, but MRI findings remained unchanged (Fig. 2).

Discussion

ODS is pathologically characterized by symmetrical demyelination. Myelinolysis is observed in the form of oligodendroglial loss and reactive astrogliosis. Inflammation is not a prominent feature, and axonal cylinders and

nerve cells are relatively preserved. Blood vessels remain unaffected (1, 7).

Clinically, ODS causes a wide spectrum of symptoms that range from mild loss of consciousness to lower cranial nerve palsies, pseudobulbar signs, and quadripareisis. The latter two are the most frequently encountered neurological findings and were also found in the presented case (3, 8).

ODS is known to develop in hyponatremic states, and is frequently caused by its rapid reversal at a rate greater than 12 mEq/l/24 h (9, 10). Debilitating conditions like chronic alcoholism, malnutrition, uremia, dialysis,

hepatocellular dysfunction, diabetes mellitus, electrolyte imbalances, organ transplantation, hypoxic-ischemic states, deep burns, intensive care treatment, and metabolic disorders are known predisposing factors (3–5, 7, 11). However, the exact etiology of ODS and its underlying pathophysiological mechanism are still unknown. Probably, myelotoxic factors, secreted from endothelial cells after the above-mentioned osmotic stresses, are responsible for the myelin damage (8).

ODS is very infrequently seen in babies. This rare occurrence is probably due to the ongoing process of myelination, which occurs under 2 years of age (4). Supratentorial white matter myelination occurs later than pontine myelination; therefore, extrapontine myelinolysis is even rarer. In their review of the relevant literature, Brown and Caruso (5) found only 35 pediatric ODS cases. Only 3 cases were younger than 2 years of age, and only 1 of them was younger than 1 year (10 months) (4, 5). As the youngest case, ours implies that ODS affects all age groups, albeit with differing frequencies.

With the increasing use of the neuroradiological methods, *in vivo* diagnosis and follow-up of ODS are now possible. CT, a modality of choice in neurological emergencies and in pediatric patients in whom anesthesia is not always possible, provides a quick diagnosis in some patients, as in the presented case; however, in many others it may not be successful in imaging the brain stem and in revealing early lesions because of the beam hardening effects in the posterior fossa (3). MRI, on the other hand, provides clear diagnostic data for pontine lesions and myelin destruction. In the acute phase, MRI reveals pontine and extrapontine hyperintensities on T2- and hypointensities on T1-weighted images. Although these changes may also be observed in some disorders like ischemia, multiple sclerosis, neoplasms, and metabolic disease, they are diagnostic of ODS when symmetrical. In diffusion weighted images, diffusional restriction is observed at the above-mentioned areas. In subacute and chronic phases, lesions become smaller (11). This evolving pattern probably reflects the regression of edema, demyelination, and the diminishing astrocytic response (12). The true demyelination can be shown only after the re-

gression of the lesions, which reach their peak size 1–2 weeks after initial symptoms. At that stage, extrapontine hyperintensities still persist; therefore, symmetrical basal ganglial hyperintensities mandate the consideration of ODS in the differential diagnosis. Initially, MRI findings may correlate to the clinical status; however, clinical improvement is independent of imaging; the former precedes the latter (12). In the presented case, MRI findings eventually stabilized, although there was a gradual clinical improvement. The complete resolution of MRI findings is very rare. Generally, residual focal signal changes representing scar formation, demyelination, and pontine atrophy is seen in advanced cases (13). It is reported that 50% of patients die within 2 weeks; whereas 90% die within 6 months. Survivors experience neurological deficits (14).

In the presented case, single voxel spectroscopy was used as a complimentary method to assess the status of myelination. Major MRS resonances of normal brain tissue include NAA, Cho, and Cr. Among them, NAA is the most sensitive central nervous system metabolite. It is an important predictor of neuronal dysfunction and abnormalities of neuronal structures, such as reduced neuronal density or viability, which lead to reductions in NAA. Cr, the second most important metabolite, plays an important role in cellular energy metabolism and it is mainly concentrated in glial cells. Except in trauma, stroke, tumor, parenchymal destruction, and Cr deficiency syndromes, Cr levels tend to remain relatively unchanged. Therefore, Cr is often used as a putative internal standard against which other metabolites can be compared. Cho is a constituent of the phospholipid metabolism of cell membranes. Major components of Cho resonance are choline-contain-

ing compounds with low molecular weight, such as phosphocholine and glycerophosphocholine, which form a pool involved in membrane synthesis and degradation. Therefore, increased Cho primarily reflects increased membrane synthesis and/or an increase in the number of cells. An increase in the Cho/Cr ratio may also indicate an inability to properly incorporate Cho-containing molecules into myelin. Loss or disruption of normal myelin also increases the availability of Cho-containing compounds. An increased Cho/Cr ratio, which could indicate increased membrane turnover and myelin breakdown, might correspond to glial cell proliferation. In the presented case the thalamus had a decreased level of NAA and an increased level of Cho. These were consistent with neuronal loss or dysfunction and membrane synthesis that develop after the demyelinating process. Conventional imaging with lower sensitivity than MRS was unable to reflect the involvement of this location. The lentiform nucleus, on the other hand, had diminished levels of all 3 metabolites. This finding was probably reflective of the consequent parenchymal destruction as discussed above.

The treatment of hyponatremia has more serious complications than the disease itself; therefore, specially trained personnel must conduct it. Spastic quadriparesis and pseudobulbar palsy that follow inappropriate treatment should warn physicians about ODS. In infants, an inadequate medical history and ambiguous findings may cause diagnostic difficulties; therefore, MRI, which reveals the characteristic findings (i.e., lesion at the center of the pons and the preservation of the periphery), is very important in the evaluation of infants who develop neurological disorders after electrolyte imbalance.

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