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Resolving MR Features in Osmotic Myelinolysis (Central Pontine and Extrapontine Myelinolysis)

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Summary: Osmotic myelinolysis is a distinctive clinical syndrome with characteristic MR features in the central pons (central pontine myelinolysis) and in other locations (extrapontine myelinolysis). We describe the resolving MR features in an adolescent who has experienced complete neurologic recovery. Regions of involvement manifested increased T2 signal intensity. The extrapontine involvement was noted to resolve earlier with interim-increased T1-weighted signal. The mechanism for the variable appearance of increased T1 signal intensity is discussed.

Index terms: Brain stem, magnetic resonance; Degenerative brain disease; Demyelinating disease

Osmotic myelinolysis (OM) is a demyelinating disease classically of alcoholic, malnourished, or chronically debilitated adults with an autopsy incidence of 0.25% (Cleveland, Ohio) (1) to 1.1% (Hamburg, Germany) (2). OM is hallmarked clinically by spastic quadriparesis and pseudobulbar palsy that rapidly deteriorates to a pseudocoma state ("locked-in" syndrome) within 2 weeks and usually death within 8–12 weeks. Pathologically, demyelination is typically evidenced in the pons (central pontine myelinolysis or CPM) but may occur in other locations (extrapontine myelinolysis or EPM) (1–4).

We describe the characteristic magnetic resonance (MR) features of OM in a patient with clinical recovery. The patient's prolonged survival afforded the opportunity to evaluate the resolution of both CPM and EPM.

Case Report

A 17-year-old girl underwent elective colectomy for asymptomatic familial polyposis. Her postoperative period was remarkable only for increased ostomy output, occasional emesis, and hyponatremic fluid replacement with diet soft drink. One month following surgery, she presented with orthostatic hypotension and brief disorientation. Laboratory examination revealed a serum sodium of 105 mmol/L. Vigorous fluid resuscitation with Ringer's lactate and D5 1/2 NS intravenous solutions resulted in the increase of her serum sodium to 124 mmol/L by 24 hours and to 132 mmol/L by 48 hours. Although her hydration status dramatically improved, she continued to have mild disorientation, emotional lability, and the perseveration of ideas.

On the seventh day, however, her clinical course began to deteriorate with worsened disorientation, decreased vocalization, and decreased physical activity. By the 10th day, she manifested pseudobulbar features to include dysarthria, dysphagia, facial diplegia, and emotional lability. Additionally, she developed a mild spastic quadriparesis. By the 12th day, she had progressed to a near complete "locked-in" syndrome consisting of a severe spastic quadriparesis, inability to speak or swallow, facial diplegia, and a retained ability to track visually in all directions. Cerebrospinal fluid evaluation was remarkable only for a protein of 53 mg/dL (normal range 15–45 mg/dL). Of note, the patient had not experienced any episodes of hypoxia, prolonged hypotension, hypoglycemia, or exposure to carbon monoxide, methanol, or cyanide.

Computed tomography (CT) evaluation performed on the ninth day revealed hypodensity in the region of the pons and suggestion of basal ganglia hypodensity. On the 12th day, MR imaging on a 1.5-T GE Signa scanner better demonstrated these pontine and extrapontine lesions. T2-weighted images (spin echo (SE) 2800/80/2 (TR/TE/excitations)) revealed hyperintense signal in the central pons (Figs. 1A and 1B) and the basal ganglia (Fig. 1D). On T1-weighted sequences (SE 650/20/4 (TR/TE/excitations)), abnormal hypointense signal was noted in the same regions (basal ganglia, Fig. 1C). These MR features coupled with

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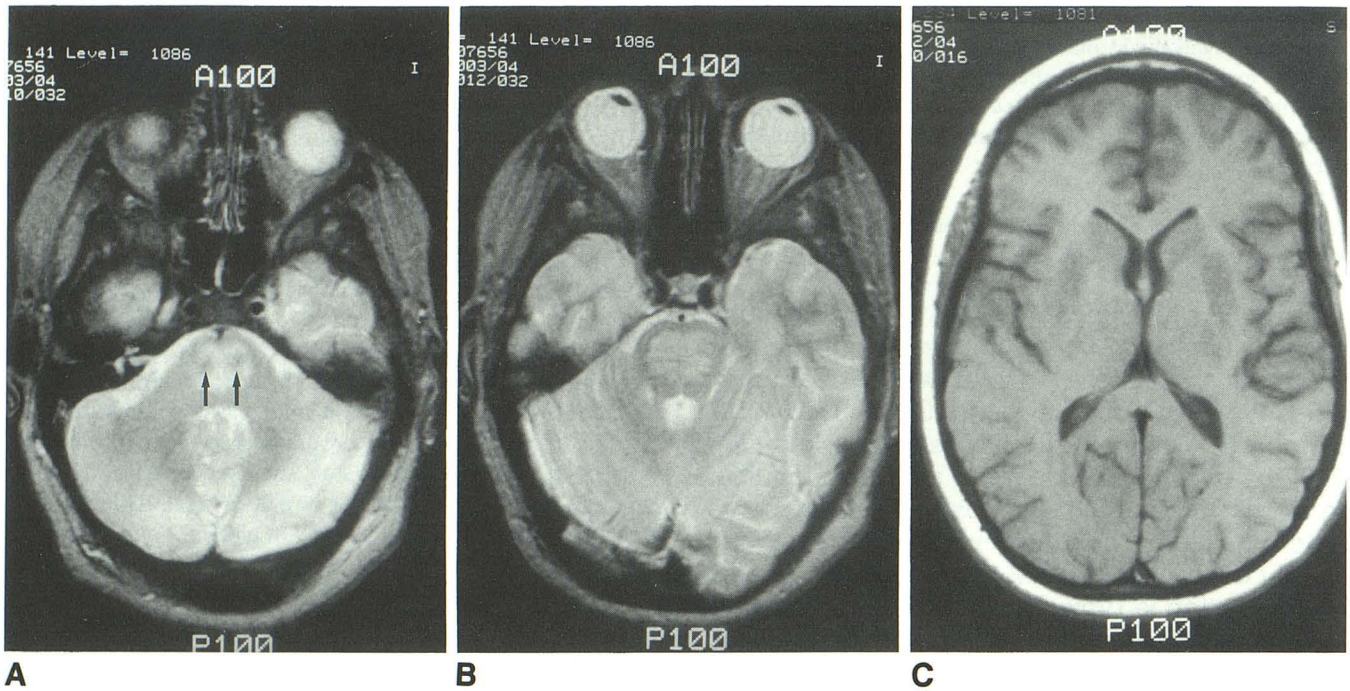
the patient's clinical presentation were characteristic for CPM and EPM.

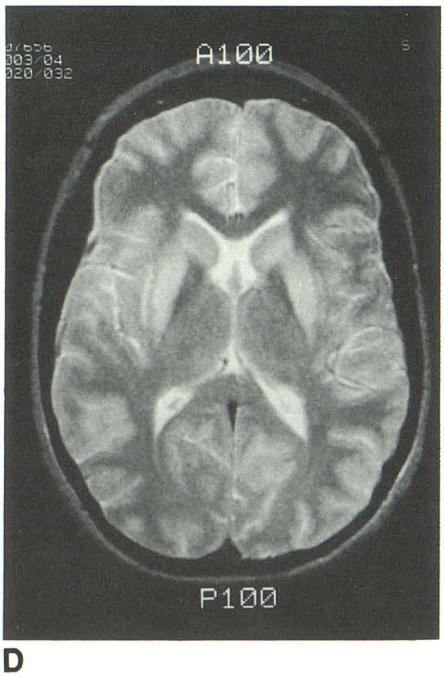
One month following her initial presentation, the patient began to recover, gradually regaining the motor control of her face, neck, shoulders, and legs. By 4 months, her neurologic state had returned to its premorbid state. MR evaluation at that time revealed persistent hyperintensity in the pons on T2-weighted images (Figs. 2A and 2B) but normal T2 signal in the basal ganglia (Fig. 2D). On T1-weighted sequences, however, the extrapontine lesions had developed abnormal hyperintense signal (Fig. 2C). At 10 months, the patient was still without complaints and MR imaging at that time revealed persistence of the pontine lesion (Fig. 3A) but normal signal characteristics in the basal ganglia, particularly on T1-weighted images (Fig. 3B).

Discussion

OM was first described by Adams et al (3) in 1959 as a "disease occurring in alcoholic and malnourished patients." Since then, over 200 cases of OM have been reported in association with a variety of other conditions to include:



A B C



D

Fig. 1. The initial MR evaluation revealed the characteristic hyperintense pontine lesion of CPM on T2-weighted images (*A* and *B*, axial (SE 2800/80/2)). The pontine involvement is central with sparing of the longitudinal fibers of the descending corticospinal tracts (*A*, *arrows*) and a thin peripheral rim (*B*). On T1-weighted images (*C*, axial (SE 650/20/4)), symmetric hypointense abnormalities were identified in the caudate nuclei, putamina, and globus pallidi. T2-weighted images (*D*, axial (SE 2800/80/2)) showed these regions to be hyperintense. The MR appearance of the central pons and the extrapontine lesions was consistent with edema characteristic for osmotic myelinolysis.

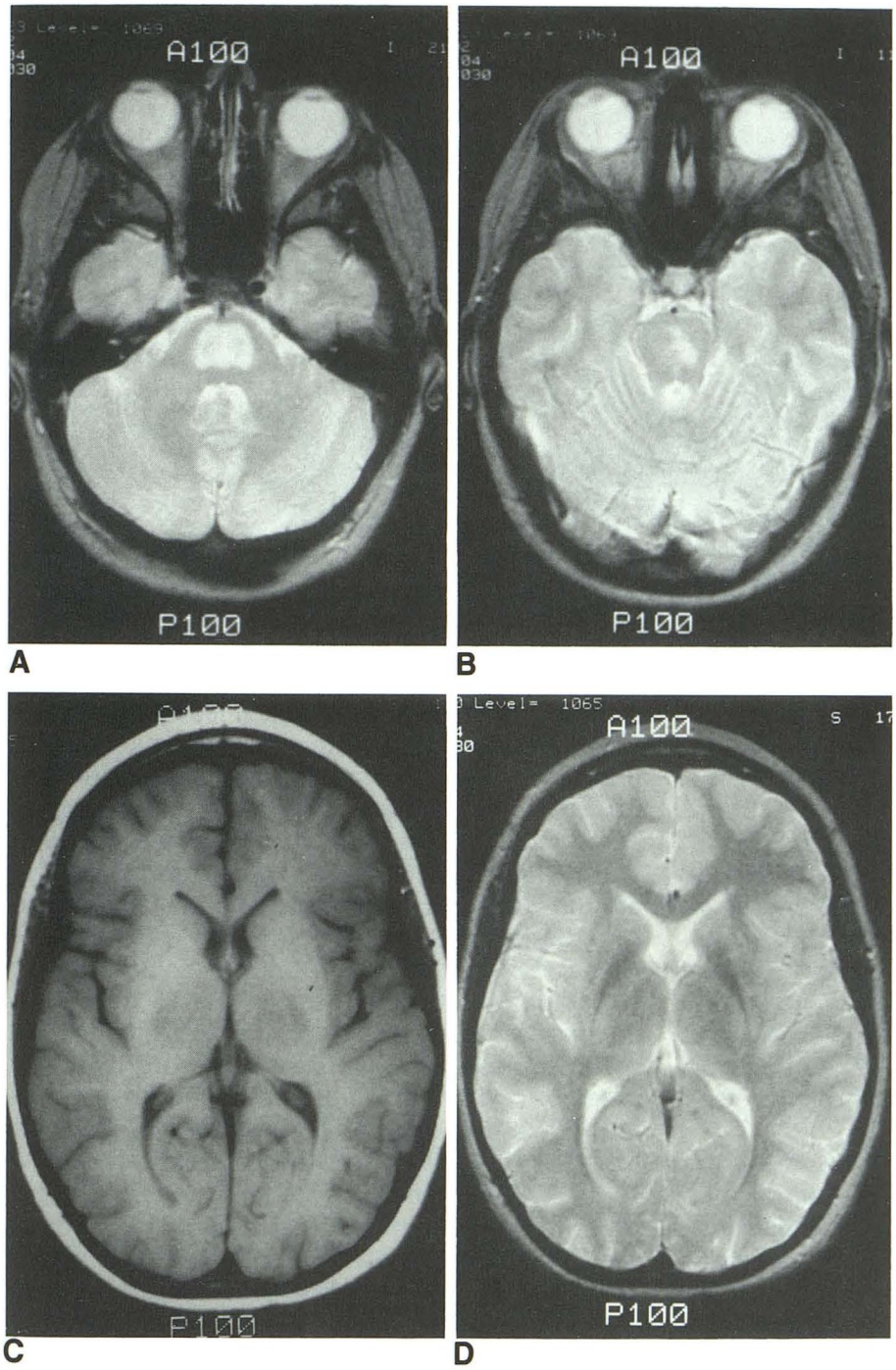


Fig. 2. MR 4 months later with patient's clinical recovery.

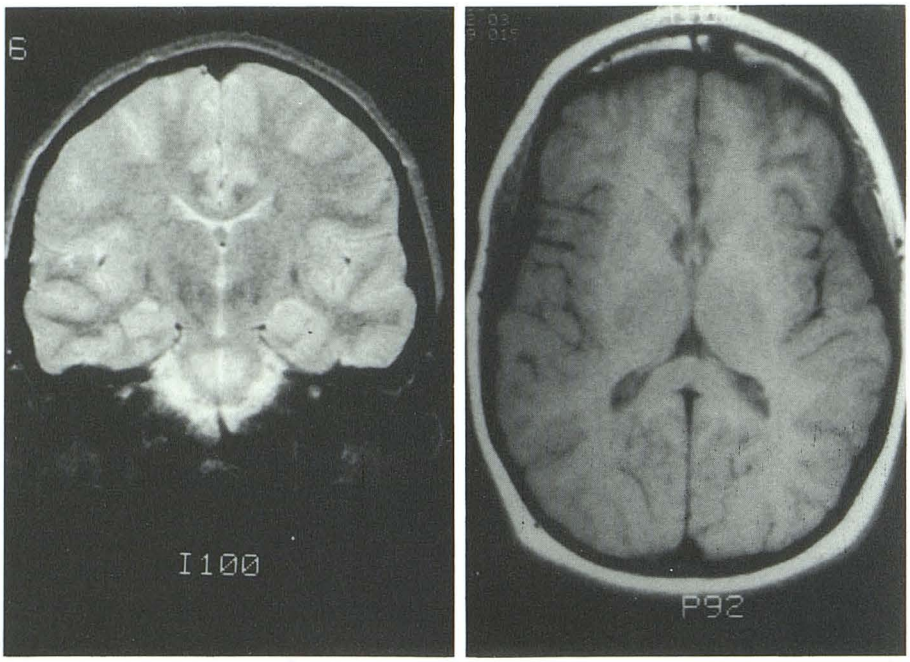
A and *B*, T2-weighted axial (SE 2800/80/2). Pontine abnormalities persist.

C and *D*, The resolving basal ganglia lesions are now evident as hyperintensities on T1-weighted sequences (*C*, axial (SE 650/20/4)) with normal T2-weighted signal (*D*, axial (SE 2800/80/2)).

chronic renal failure, hepatocellular dysfunction, dehydration, diabetes mellitus, syndrome of inappropriate antidiuretic hormone secretion, and electrolyte imbalances (1–10).

Pathologically, OM is characterized by the loss of myelin (myelinolysis) with relative sparing of the nerve cells and axis cylinders. Lesions occur typically in the midline of the basis pontis (CPM). However, OM may involve other locations (EPM): most notably, the basal ganglia, thalami, brain stem, and cerebral and cerebellar gray-white matter junctions. CPM and EPM may occur in conjunction or as isolated entities (1–4).

Recent clinical reviews and animal experiments have found a high correlation between the development of OM and the rapid correction of hyponatremia (5–7). Inasmuch as patients with OM may be hypernatremic and chronically hypona-



A B

Fig. 3. MR 10 months after the patient's initial presentation.

A, T2-weighted coronal (SE 2800/80/2). Abnormally high signal intensity persists in the central pons.

B, T1-weighted axial (SE 650/20/4). Complete resolution of the basal ganglia lesions has occurred.

tremic patients may not develop OM, Norenberg et al suggested that the rate rather than the absolute serum sodium level was the most important factor in the pathogenesis of OM (5). In fact, one patient in their series who was chronically hyponatremic developed OM only following rapid sodium correction. Similarly, Stern et al found a good correlation between the development of OM and the correction of serum sodium greater than 12 mmol/L/day (or 0.5 mmol/L/hour) (6). The occurrence of OM in younger patients, albeit uncommon with fewer than 30 cases reported, further supports the role of electrolyte correction (4, 5).

Norenberg et al theorized that the rise in serum sodium exerts an osmotic endothelial injury that leads to the release of myelinotoxic factors, mainly derived from the more vascular gray matter (5). The high gray-white matter apposition found in the pons provides the suitable environment for the development of OM. The absence of involvement in the pure white matter tracts such as the internal capsule and corona radiata support this contention. For this reason, Stern et al (6) suggested the term "osmotic demyelination syndrome" for central pontine myelinolysis; however, we prefer the simpler term of osmotic myelinolysis.

Patients with OM present with a variety of symptoms which can be mild (weakness, confusion, and dysarthria) or severe (seizures and coma). Initially, patients may improve following intravenous hydration therapy. However, invariably they develop spastic quadriparesis, mutism, and pseudobulbar palsy that progresses within 3–10 days to a pseudocoma ("locked-in" syndrome). Although some recovery may be evidenced, OM is usually fatal within 2–3 months. In our review of the medical literature, survival beyond 6 months has been reported in only 5%–10% of cases (1–10).

Radiographically, OM manifests as regions of increased water content. On CT, areas of involvement are seen as hypodensity, and on MR, as areas of hypointensity on T1-weighted scanning and hyperintensity on T2-weighted imaging (7–10). The involvement of the central pons should suggest OM in the acute setting, especially in the presence of sodium correction. Pontine involvement is primarily of the transverse fibers and may spare the longitudinal fibers of the descending corticospinal tracts (2, 4, 8) as demonstrated in our patient (Fig. 1A). Furthermore, the concomitant involvement of the basal ganglia is fairly specific for OM. The differential considerations for pontine and basal ganglia involvement include hypoxia, Leigh disease, and Wilson disease; however, differentiation based on clinical grounds is usually possible.

In surviving patients, pontine abnormality usually persists on MR imaging (7–10). EPM, however, has been reported to resolve following clinical improvement or recovery (10). The presence of both CPM and EPM in our patient allowed us

to observe the relative earlier resolution of EPM to CPM.

Transient symmetric hyperintense T1 signal as evidenced in the basal ganglia of our patient (Fig. 2C) has never been reported in resolving or fatal OM. The precise explanation for this finding is uncertain as pathologic data on surviving patients is not available for correlation. This phenomenon may result from OM's preferential destruction of myelin and the regional release of myelin byproducts (principally cholesterol) that have short T1 relaxation times (11). Alternatively, OM may promote the mixing of free (axonal) and bound (myelin) waters, a process also associated with T1 shortening (12). The T1 signal contribution of myelin-bound waters with its short T1 relaxation time is normally limited by the tightly wrapped myelin structure. During OM, an unwrapping of the myelin sheath may occur that would preferentially admix the myelin-bound waters with that of axonal free waters and result in a shortened T1 time. These phenomenon may only be apparent on MR during the healing phase following the resolution of the more dominant T1 signal of the edema noted acutely (Fig. 1C).

Recently, hepatocellular dysfunction, systemic lupus erythematosus, and total parenteral nutrition have also been reported to be associated with symmetric hyperintense T1 signal in the basal ganglia (13, 14). Mirowitz et al postulated that, in the case of total parenteral nutrition, the shortened T1 signal may be attributable to the deposition of "paramagnetic trace elements, especially manganese, and/or an astrogliotic reaction to such deposition" (13). A similar phenomenon may be occurring during the resolution of OM. Additional explanations for the shortened T1 signal in our patient include transient calcification (15) or even microhemorrhage. Although the exact reason for the transient T1 shortening is obscure, its presence may be appreciated only in surviving patients, as it was in our case.

In conclusion, OM represents a distinctive clinical syndrome with reversible neurologic features. Radiographic findings are characteristic on MR. The combination of central pontine and basal ganglia lesions should suggest a diagnosis of OM. OM is not universally fatal and long-term survival can be seen. Despite clinical recovery, MR features may persist, especially those in the pons.

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