Central pontine myelinolysis due to rapid correction of hyponatremia induced by excessive water intake

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ABSTRACT

We report a 25-year-old female with a recent diagnosis of gastric B-cell lymphoma based on imaging and pathological findings. She was discharged against medical advice after it was recommended to her, by an “alternative medicine practitioner,” to restrict her diet to excessive ingestion of the “Holy water Zamzam” (natural well water in Makkah). She presented back with altered level of awareness and severe, new-onset hyponatremia. The hyponatremia was corrected rapidly and her condition improved. Six days later, she developed the classical pyramidal and extrapyramidal features of central pontine myelinolysis, documented by MRI. The patient succumbed to her original disease 3 months later.

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Central pontine myelinolysis (CPM) was first described by Adams et al. in 1959 as a clinicopathologic syndrome affecting alcoholics and the malnourished, and characterized by quadripareisis, pseudobulbar palsy, and a symmetric lesion in the center of the basis pontis. Although Zamzam water is well known to the Muslim community to have a therapeutic modality for many disorders, in this case the excessive drinking of Zamzam lead to severe, symptomatic hyponatremia. The objective of this report is to increase awareness of this unique neurological complication of rapid correction of hyponatremia.

Case Report. A 25-year-old Saudi female with a recent diagnosis of gastric B-cell lymphoma presented with abdominal pain, nausea, vomiting, asthenia, and an epigastric mass. The diagnosis was established by abdominal imaging including, CT, MRI, and gastroscopy with gastric biopsy. Her history was otherwise non-contributory. On her initial examination, she had evidence of the epigastric mass and was neurologically normal. Twenty days after her initial hospital discharge, she presented with new-onset deterioration of her level of awareness, but without any fever, or seizures. While at home, she had been restricting her diet to the holy water, Zamzam, as recommended by an alternative medicine practitioner. She was gradually becoming more lethargic until her second hospital admission when she became very ill with failure to thrive. Her examination this time showed a very ill looking person with stable vital signs and systemic examination. She was drowsy with a Glasgow Coma Scale of 11/15. There was no cranial nerve or long tract signs. In the emergency room, her sodium (Na) was 109 mmol/L (normal range 135-145). The other electrolytes, complete blood count, liver function test, glucose, amylase and lipase were normal. Her urea was high at 11 mmol/L (3.5-7.2 mmol/L) with normal creatinine. Initial brain MRI was completely normal. The patient was managed in the intensive care unit (ICU) and was given normal saline infusion to correct her dehydration and hyponatremia. Her Na became 136 mmol/L 36 hours later. Her general
condition, including higher mental function improved, and she was transferred to the floor. She was started on soft diet with improvement of her general wellbeing. Six days later, her level of consciousness deteriorated and she developed spastic quadriplegia, with hypertonia, clonus, bilateral Babinski sign, and extra-pyramidal signs in the form of rigidity and tremor. Her repeat MRI, one week after the initial one, showed classical central pontine and extrapontine myelinolysis (EPM) (Figure 1). She was transferred back to the ICU where she was intubated and mechanically ventilated. She received total parenteral nutrition, physiotherapy, and occupational therapy. When her general condition improved, she received aggressive chemotherapy and radiotherapy for her underlying B-cell lymphoma. Unfortunately, she died 3 months later due to a combination of the underlying gastric B-cell lymphoma and the iatrogenic myelinolysis.

Discussion. Central pontine myelinolysis is a well-recognized clinicopathologic, demyelinating disorder of the CNS first described by Adams et al in 1959. Originally, the disease was seen in association with chronic alcoholism, malnutrition, and liver disease. Other associations include renal failure, diuretic usage, Addison's disease, and severe electrolyte imbalance. Shortly after the original report, a body of evidence began to grow that linked myelinolysis with the rapid correction of hyponatremia. Sterns et al confirmed this hypothesis. Their review of the literature included 51 cases of individuals with serum Na concentrations below 106 mmol/L. They found that patients who develop CPM have had their hyponatremia corrected by more than 12 mmol/L per day. In our case, the cause of CPM was rapid correction of hyponatremia induced by drinking Zamzam water to excess. It is unclear why the rapid correction of hyponatremia causes this disease. Osmotic changes in the cerebral microenvironment with subsequent alterations in water and electrolyte balance may injure oligodendrocytes or damage the myeline itself. In addition, osmotic changes may lead to opening of the blood-brain-barrier resulting in vascular injury with subsequent edema and demyelination. The exact incidence of CPM is unknown, however, a study by Singh et al illustrated that CPM was present in 29% of postmortem examination of liver transplant patients. In another study in Japan, the estimated incidence was 37 cases in 1,000 consecutive autopsies.

Although the demyelination was first described within the pons, subsequent reports have indicated that the lesions can occur outside the pons (EPM) in up to 10% of cases. The EPM may occur in the cerebellum, lateral geniculate body, putamen, thalamus, and/or the caudate nuclei. Microscopically, there is destruction of myeline with relative sparing of neurons, axis cylinders, and blood vessels. There may be associated glial cytoplasmic swelling, nuclear pyknosis of the glial cells, and neuronal shrinkage or even neuronal death. The CPM is characterized clinically by spastic quadriplegia, pseudobulbar palsy, dysarthria, or mutism, hyperreflexia, seizures and varying degrees of encephalopathy or coma. The patients may be in a “locked-in” state, communicating by eye blinking and vertical gaze. Extrapontine myelinolysis can present with ataxia, visual field defects or movement disorders such as Parkinsonism, choreoathetosis, or dystonia. Some patients may require mechanical ventilation and ionotropic support.

An MRI is the diagnostic, and most sensitive modality of neuroimaging for myelinolysis. Lesions appear hypointense on T2-weighted images and hypointense in T1-weighted images. The pontine lesion is symmetrically centered in the basis of pontis, while

![Figure 1 - Axial FLAIR (fluid attenuated inversion recovery) sequence (a & b), axial T2 weighted images (c & d) showing increased signal intensity in central portion of upper pons (a & c), bilateral lentiform nuclei and head of caudate nuclei (b & d) (arrows). Notice the symmetric involvement of the basal ganglia.](image-url)
the extrapontine lesions are seen in the thalamus and neostriatum. Myelinolytic lesions do not typically enhance with gadolinium initially, but later enhancement may occur.9 Our case showed the classical pontine and EPM with hyperintense lesions on T2-weighted images and hypointense lesions on T1-weighted images with no gadolinium enhancement.

Prevention of myelinolysis includes the judicious correction of hyponatremia, discontinuation of diuretic therapy, correction of associated metabolic abnormalities, and prevention of medical complications. Based on clinical data and animal studies, there is a low incidence of myelinolysis if the increase in serum Na is less than or equal to 12 mmol/L in 24 hours.9 Reports on small case series or single case reports of therapy, including steroids, plasmapheresis, intravenous immunoglobulins, and thyrotropin releasing hormone, have all shown good outcomes. However, these results are of limited value given the types of studies. The general therapeutic measures conducted initially in the ICU, include adequate caloric intake, correction of water and electrolyte imbalance, anti-edema therapy, and prophylaxis against pneumonia, thrombosis, and decubitus ulcer. The prognosis of the osmotic demyelination syndrome has long been regarded as bleak, however, due to advances in neuroimaging and medical care, the patient survival rate is potentially better. Most patients, who survive, develop permanent neurological damage. Neither clinical features nor extent of radiological change is predictive of outcome.10 Our case developed CPM induced by rapid correction of hyponatremia, which was induced by strictly drinking Zamzam holy water.

References