CASE REPORT

An unusual case of osmotic demyelination syndrome without electrolyte changes in a patient with diabetes

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Abstract

Central pontine myelinolysis (CPM) is a demyelinating disease of the pons which is also associated with the demyelination of extrapontine areas of the central nervous system. Although the aetiology and pathogenesis are unclear, CPM is usually associated with hyponatremia or its rapid correction. Malnutrition and chronic alcoholism are also the common underlying conditions. Herein, we report a rare presentation of ODS, secondary to hyperosmolar hyperglycaemic state. We observed a 37-year-old female with diabetes type 1 and hypertension who presented with ataxia, dysarthria and pseudobulbar effect which evolved over a duration of few weeks at home with no evidence of hyponatremia or its rapid correction and no history of alcohol abuse or malnutrition.

Key words: Central pontine myelinolysis, diabetes mellitus, extrapontine myelinolysis, hyperosmolar hyperglycaemic state, osmotic demyelination syndrome

INTRODUCTION

Central pontine myelinolysis (CPM) is a non-inflammatory demyelinating disorder of the central portion of pons, first described by Adams *et al*.[1] It is commonly associated with electrolyte imbalance is commonly associated with electrolyte imbalance, rapid correction of hyponatremia, chronic malnutrition, alcoholism, burns, chronic renal failure with dialysis and post-liver transplantation.[2-8] Pontine and extrapontine myelinolysis (EPM) in patients with type 1 diabetes without electrolyte changes are usually rare and underdiagnosed. We report a case of a 37-year-old female with type 1 diabetes who developed osmotic demyelination syndrome (ODS) after rapid correction of osmolarity with normal serum electrolyte levels. This would be the first report of ODS in diabetic patient, associated with hyperosmolar hyperglycaemic state (HHS) with normal serum electrolytes.

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CASE REPORT

A 37-year-old female with a history of type 1 diabetes mellitus (DM) and hypertension was admitted with a history of dysarthria, ataxia, behavioural changes which were gradual in onset and progressive with Glasgow Coma Scale (GCS) 12/15 (E4V4M4). Her neurological examination revealed normal cranial nerves, with grade 5/5 power in all 4 limbs with ataxic gait. Detailed history revealed progressively increasing ataxia with dysarthria, clumsiness with emotional lability and

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bilateral dysmetria which were progressively worsening over the last 10–14 days, knee and ankle jerks were present and flexor plantar response. Computed tomography scan brain was done within an hour and revealed normal study. Arterial blood gas analysis showed normal acid-base and lactate values. Laboratory investigations revealed white blood cells count of 11430/mm^3, serum creatinine 0.59 mg/dL, blood urea nitrogen 30.5 mg/dL, Hb1Ac 8.8%, random blood sugar 482 mg/dL and serum osmolality of 327.66 mOsm/kg. Serum levels of sodium, potassium, calcium and magnesium were 140 mmol/dL, 3.35 mmol/L, 8 mg/dL and 1.9 mg/dL, respectively. Urine analysis showed the presence of glucose without ketone bodies

Patient was managed initially on the line of hyperglycaemic hyperosmolar state with 0.9% normal saline at 1 l/h and insulin therapy at 0.15 U/kg as intravenous (IV) bolus and 0.1 U/kg/h as infusion. Serial blood sugar and osmolality monitoring were done to avoid rapid shift in sugar level and osmolality. The serum osmolality fell to 300 mOsm/kg after 12 h of management and blood sugar level was controlled in the range of 200–280 mg/dL. However, after 6 h of initiating treatment, patient's sensorium deteriorated until GCS reached 4/15 (E2V1M1). The patient was then immediately shifted to Intensive Care Unit (ICU). Neurological examination revealed bilateral loss of knee jerk, ankle jerk and plantar reflex. Pupils were normal in size and responding to light stimuli, power was 1/5 in all the four extremities. Sensory assessment could not be performed due to poor GCS. Examination of cardiovascular and respiratory system was normal. Chest X-ray and electrocardiogram findings were within normal limits. In spite of SpO_2 100%, PaO_2 90 mmHg and $PaCO_2$ 38 mmHg, patient was intubated with 7.5 mm cuffed endotracheal tube primarily for airway protection. Oxygen at a flow rate of 6 L/min was delivered through T piece. Magnetic resonance imaging (MRI) of the brain revealed the T2 and fluid-attenuated inversion recovery hyperintensities in pons and right superior cerebral peduncle as well as bilateral caudate nuclei suggestive of pontine and extrapontine myelinosis [Figures 1 and 2]. Hyperintensities were noted in bilateral periventricular white matter and bilateral corona radiata in diffusion weighted images which on apparent diffusion coefficient map shows reduced signal intensities suggestive of cytotoxic oedema [Figures 3 and 4]. Cerebrospinal fluid (CSF) analysis was normal with clear in appearance with glucose 150 mg/dL, CSF/blood sugar ratio 0.7, chloride 120 mEq/L, no lymphocytes and protein 20 mg/dL.

Treatment modalities included control of blood sugar between 200 and 280 mg/dL, through IV infusion of insulin as per sliding scale. Acid-base status and electrolytes never fluctuated significantly during the course of treatment and sodium remained in between

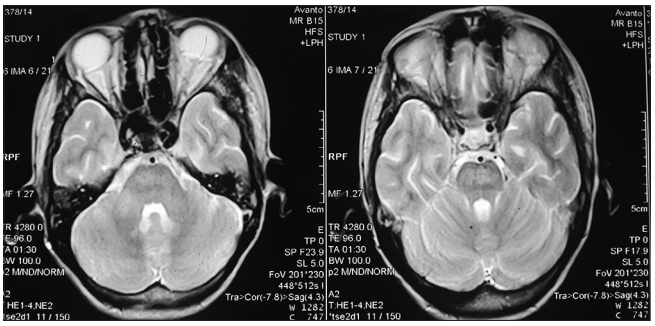

Figure 1: Hyperintensities were noted in bilateral periventricular white matter and bilateral corona radiata in diffusion-weighted images which on apparent diffusion coefficient map shows reduced signal intensities suggestive of cytotoxic oedema

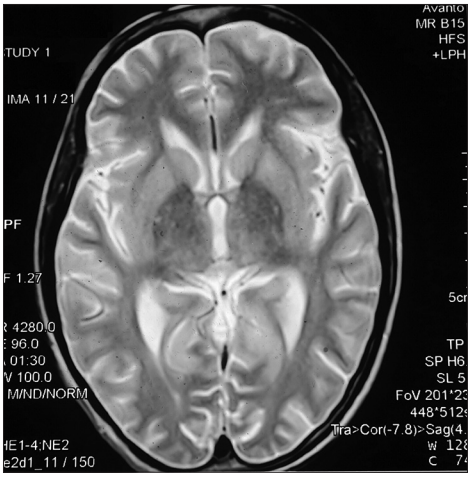

Figure 2: Magnetic resonance imaging of brain revealed the T2 and fluid-attenuated inversion recovery hyperintensities in pons and right superior cerebral peduncle as well as bilateral caudate nuclei suggestive of pontine and extrapontine myelinolysis

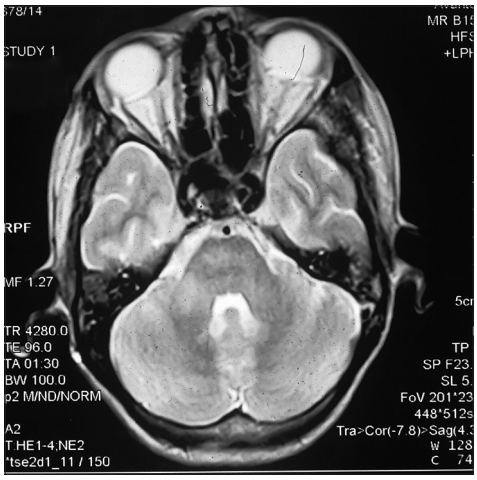

Figure 3: Hyperintensities were noted in bilateral periventricular white matter and bilateral corona radiata in diffusion-weighted images which on apparent diffusion coefficient map shows reduced signal intensities suggestive of cytotoxic oedema

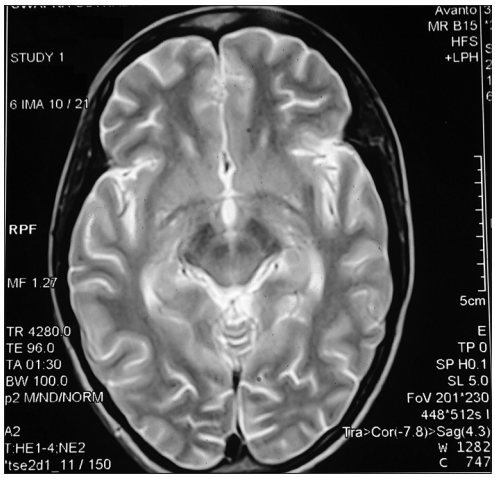

Figure 4: Hyperintensities were noted in bilateral periventricular white matter and bilateral corona radiata in diffusion-weighted images which on apparent diffusion coefficient map shows reduced signal intensities suggestive of cytotoxic oedema

140 and 145 mmol/L. Patient remained afebrile all throughout. On the 7th day of ICU admission, percutaneous tracheostomy was done. However, the neurological status never actually improved even until the 10th day. Follow-up MRI of brain was done and did not show any improvement in size and intensity of the area involved. However, the patient expired on the 15th day.

DISCUSSION

The concept of CPM was extended from 1962, with the recognition that lesions can occur outside the pons, so-called EPM. In 1976, a link between these disorders and the rapid correction of sodium in hyponatremic patients was suggested.[1-4] The pathophysiology of CPM has not been well-understood, but it has become clear that CPM relates to the physiologic imbalance of osmoles in the brain.[9] Histological studies have shown that oligodendroglial cells are most susceptible to CPM-related osmotic stresses, with the distribution of CPM changes paralleling the distribution of oligodendroglial cells that normally embed large neurons within the central pons, thalamus, cortex, putamen, lateral geniculate and other extrapontine sites.[2,9-11] The transverse pontocerebellar fibres are most frequently involved, followed by long rostrocaudal tracts. Histologically, there is the preservation of neurons and axons, differentiating this process from a central pontine infarct.[12] In malnourished states like in diabetic and alcoholic patients, due to lack of sufficient energy reserve causes imbalance in energy supply-demand results in pro-apoptotic drive which finally leads to demyelination of cells.[13] Therefore, CPM results from multifactorial process and different mechanisms may also account for variable clinical courses observed among patients with CPM. The clinical course of CPM has been classically described as biphasic,[14] beginning with a generalised encephalopathy due to hyponatremia, which usually transiently improves following initial elevation of sodium. This is followed by a second neurologic syndrome, which occurs 2–3 days following correction or overcorrection of hyponatremia caused by myelinolysis. This latter phase is classically characterised by spastic quadriparesis and pseudobulbar palsy.

There are few reports documented about CPM occurring in diabetic patients[15,16] without electrolyte changes. Casey *et al*.[15] reported two cases of CPM as an unusual complication of diabetes showing asymptomatic or subclinical pontine lesions in long-standing poorly controlled diabetic patients. Yun *et al*.[17] reported the asymptomatic EPM in a diabetic women. Furthermore, a case of asymptomatic CPM after severe hypoglycaemia without electrolyte changes has been reported by Chun *et al*. in the year 2005.[18] Earlier CPM cases were reported in patients with hyperglycaemia with concomitant ketoacidosis, abnormality in serum sodium, or occurrence after treatment of the hyperglycaemic hyperosmolar state.[19-21] Burns *et al*.,[19] Guerrero *et al*.[20] and O'Malley *et al*.[21] reported the cases of pontine myelinolysis and complication associated with it after being treated for hyperglycaemia. There is a case report of EPM associated with hyperosmolar hyperglycaemic syndrome and hypernatremia by Koh *et al*.[22] A case of CPM occurring secondary to hyperglycaemic hyperosmolar state and not secondary to the treatment of the hyperglycaemic hyperosmolar state is reported by Saini *et al*.[23] The cause of pontine lesions in poorly controlled diabetic patients is probably due to renal dysfunction and osmolar shifts and high glucose levels induced cerebral oedema due to disruption of cerebral autoregulation, endothelial cells and blood brain barrier which leads to plasma leakage.[24-26] There is no specific treatment for CPM and management is largely supportive. In our case, the patient was having long-standing poorly controlled type 1 DM with increased serum osmolality without electrolyte imbalance.

The present case is unique in some aspects such as the patient was presented with HHS without concomitant ketoacidosis or electrolyte imbalance. The symptoms of ODS were evolved gradually over the preceding 10–14 days long before she was hospitalised, suggests that patient presented as a complication of uncontrolled DM and not as a complication of treatment of HHS as shown by many previous studies. Furthermore, the clinical outcome in our case was worse and patient rapidly deteriorated and died, contrary to the previous studies by Burns *et al*.,[19] Guerrero *et al*.[20] and O'Malley *et al*.[21] which showed a good recovery and prognosis.

In nutshell, the case report emphasises on long-standing uncontrolled DM as rare aetiology of ODS and highlights hyperosmolar hyperglycaemia as a cause of demyelination of brain cells. DM should be included as a grave aetiology of ODS.

CONCLUSION

Although CPM is a condition typically associated with rapid correction of hyponatremia, the syndrome might be clinically underdiagnosed in long-standing poorly controlled DM patients. Clinicians should be aware of the possibility of CPM when treating diabetic patients with neurologic disorders even if serum sodium or osmolality has not changed significantly.

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Conflicts of interest

There are no conflicts of interest.

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