CASE REPORT

Osmotic demyelination syndrome in type 1 diabetes in the absence of dyselectrolytaemia: an overlooked complication?

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SUMMARY

Central pontine myelinolysis (CPM) is a demyelinating disorder of central nervous system which involves central portion of the pons and sometimes extrapontine areas also. It is commonly reported in settings of hyponatraemia or its rapid correction, but in the last few years it has also been reported in patients with diabetes in the absence of electrolyte disturbances or correction of serum osmolality. Here we report a case of a 20-year-old female patient, with a known history of type 1 diabetes mellitus, who presented with acute onset spastic quadriparesis with dysarthria and mild ataxia which evolved over 2 weeks. Her MRI brain showed well-defined, bilateral symmetric hyperintense lesion involving central pons showing area of diffusion restriction which was consistent with CPM. Patient was treated conservatively and improved over a period of few weeks. To diagnose more number of cases, we should not overlook CPM in patients with diabetes.

INVESTIGATIONS

Her investigations revealed high fasting blood sugar (402) and postprandial (after 2 hours) blood sugar (556) with absent urine ketone bodies. On admission, serum electrolytes (serum sodium 142 mEq/L and serum potassium 4.2 mEq/L) and other renal function tests were normal. Her blood investigations including serum electrolytes done in previous 7 days were also normal. Serum osmolality was 318 mOsm/kg. HbA1c was found to be very high (14.2%), suggestive of a very poorly controlled diabetes. MRI brain showed T2-weighted and fluid-attenuated inversion recovery hyperintensities in central pontine region with diffusion restriction at similar site with absence of involvement of extrapontine sites (figures 1 and 2). Lumbar puncture was done and cerebrospinal fluid (CSF) was sent for examination which showed raised protein with normal cells and sugar. It was tested for all common CNS infections and was negative for all of them.

BACKGROUND

We decided to report this case to heighten awareness of diagnostic possibility of central pontine myelinolysis (CPM)/extrapontine myelinolysis (EPM) in patients of poorly controlled diabetes mellitus who can have varied clinical presentation, and it is obvious to miss such cases if careful attention is not paid. CPM may be one of the rare and preventable complications of uncontrolled diabetes mellitus.

CASE PRESENTATION

A 20-year-old female patient with a known history of type 1 diabetes mellitus, on irregular treatment with insulin, presented with 15 days history of acute onset dysarthria followed by weakness of all four limbs without bowel or bladder disturbance, which was progressive for the next 5 days followed by static course. She did not have any sensory complaints. She was ambulatory at the time of admission. Her neurological examination revealed spastic type quadriparesis (power 4/5) with bilateral lower motor neuron type of facial palsy with gait ataxia in the absence of other cerebellar signs with normal sensorium. She has neither had any symptoms suggestive of hyponatraemia (like confusion, behavioural change, etc) nor received any intravenous treatment in the last 15 days.

DIFFERENTIAL DIAGNOSIS

However, it was difficult to make the diagnosis of CPM clinically in this patient with such atypical presentation, neuroimaging helped us to conclude. She was diagnosed as having osmotic demyelination syndrome, which is rarely described in the literature in patients with diabetes.

TREATMENT

Her blood glucose level was controlled with long-acting and short-acting insulin. Patient was kept under observation; management remained supportive only.

OUTCOME AND FOLLOW-UP

She had gradual and parallel improvement in dysarthria and gait disturbance, so that she had complete recovery when she came for follow-up after 30 days.

DISCUSSION

Adams and his colleagues first described CPM in 1959, while the concept of EPM was evolved in 1962. The association between development of CPM and rapid correction of hyponatraemia was suggested in 1972 and later established in 1982.¹⁻³ Astrocytes are early target in osmotic brain injury which triggers apoptosis of astrocytes first followed

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Figure 1 (A) Fluid-attenuated inversion recovery axial image shows bilateral symmetrical hyperintensities in central pontine area and (B) diffusion-weighted image shows diffusion restriction at the same site.

by loss of trophic communication between astrocytes and oligodendrocytes.⁴ The distribution of pathological changes in CPM parallels the distribution of oligodendroglial cells that normally embed large neurons within the central pons, thalamus, cortex, putamen, lateral geniculate and other extrapontine sites. Malnourished patients like diabetics and alcoholics are particularly susceptible to develop CPM due to lack of enough energy reserves to meet demands resulting in proapoptotic drive and ultimately demyelination of neurons.⁵

Classical clinical presentation of CPM has biphasic course⁶: the first phase consists of encephalopathy (in which seizures, altered sensorium can occur) resulting from hyponatraemia; second phase occurs after 2–4 days as serum sodium level is corrected and it consists of dysarthria, dysphagia and quadriplegia. Oculomotor abnormalities may occur; consciousness level may be affected ('locked in syndrome') if large lesion in this site occurs. Neuropsychiatric features like behavioural and personality disturbances and involuntary movements can occur in EPM.

There are only few reports of documented CPM or EPM occurring in patients with diabetes^{7,8} without electrolyte changes. Casey *et al*⁸ reported two cases of CPM in patients with long-standing poorly controlled diabetes. Earlier, CPM

were reported in patients with hyperglycaemia with concomitant ketoacidosis, abnormality in serum sodium or occurrence after treatment of the hyperglycaemic hyperosmolar state. While Burns *et al*,⁹ Guerrero *et al*¹⁰ and O'Malley *et al*¹¹ reported the cases of pontine myelinolysis in relation with treatment for hyperglycaemia, Saini *et al*¹² described a case of CPM secondary to hyperglycaemic hyperosmolar state (HHS) but not secondary to its treatment or correction. Although explanations for development of CPM/EPM in patients with diabetes are still a matter of debate, a few hypotheses have been described in earlier literature. In patients with poorly controlled diabetes, hyperosmolarity resulting from increased blood glucose with greater osmolar shifts might cause brain oedema due to disruption of blood–brain barrier and eventual plasma leakage. In contrast to old concept of blood–brain barrier rupture in CPM, in recent years a new concept has emerged. Maintenance of osmotic homeostasis is vital for cell viability but in chronically uncontrolled diabetes, osmotic stress induces protein damage and aggregation in oligodendrocytes of brain which may be responsible for demyelination.¹³ It has been postulated that osmotic stress induced by serum hyperosmolarity causes release of nitric oxide and other inflammatory mediators may cause damage to tight junctions. In addition, toxic substances released by endothelial cell damage may attack oligodendrocytes. These may be the possible pathogenic mechanisms responsible for demyelination in CPM.

There is no effective treatment for CPM and supportive treatment should be provided to all patients for at least 6–8 weeks before making conclusion about its irreversibility. Although not established, plasma exchange may have beneficial role in CPM cases associated with rapid correction of hyponatraemia. Bibl *et al*¹⁴ described three cases of young female with CPM who improved after extensive therapeutic plasma exchange and their neurological symptoms took 2–12 months for improvement. Clinical improvement in these cases is believed to be caused by removal of high molecular weight myelin toxic substances by plasma exchange.

Learning points

- ▶ Central pontine myelinolysis (CPM) may have atypical clinical presentations, varied course and prognosis.
- ▶ Patients with poorly controlled diabetes are at risk of developing CPM/extrapontine myelinolysis (EPM).
- ▶ CPM/EPM can occur in patients with poorly controlled diabetes in the absence of electrolyte disturbance or its correction and ketoacidosis.

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Competing interests None declared.

Patient consent Obtained.

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Figure 2 (A) Fluid-attenuated inversion recovery coronal image and (B) T2-weighted sagittal image show hyperintense signals in central pontine area.

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