Reminder of important clinical lesson

Isolated extra pontine myelinolysis presenting as acute onset parkinsonism

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Summary

A 50-year-old woman was brought to the emergency department with complaints of altered mental status, her serum sodium at that time was 103 mmol/l. Slow correction of hyponatraemia was started but despite every effort serum sodium rise was rapid. Although the patient improved initially, after 4 days she presented with features of parkinsonism. MRI brain was done and it was suggestive of features of EPM. She responded well to levodopa plus carbidopa therapy.

BACKGROUND

Osmotic demyelination syndromes are known to be caused due to rapid correction of hyponatraemia. Central pontine myelinolysis (CPM) and extra pontine myelinolysis (EPM) are osmotic demyelination syndromes; they are pathologically similar entities that can occur together or in isolation. As the name suggests CPM involves the central pons whereas EPM involves the basal ganglia, thalami and cerebellum. Usual clinical features of CPM are dysphagia, dysarthria, quadriparesis and 'locked in' state, whereas EPM presents generally with movement disorders like choreoathetosis, parkinsonism, postural limb tremors, ataxia, catatonias and mutism. We present the case of 50-year-old woman who developed acute onset parkinsonism due to EPM. We will also discuss briefly the clinical features, MRI findings, treatment and prognosis of CPM/EPM.

CASE PRESENTATION

A 50-year-old woman was brought to the emergency department with the complaints of vomiting 8–10 episodes followed by altered mental status in the form of drowsiness and not able to recognise her relatives for last 24 h, her medical history was significant for hypertension since last 3 years for which she was taking ramipril 5 mg and hydrochlorothiazide 12.5 mg regularly. There was no history of fever, convulsions and weakness of any limb or ear discharge. On examination her pulse rate was 80/min regular, blood pressure was 130/80 mm Hg, respiratory rate was 20/min and temperature was 98.4 °F; there were no signs of dehydration and were no pallor, icterus, clubbing or pedal oedema, jugular venous pressure was not raised. Neurological examination revealed that she was drowsy and not oriented to time, place and person. There were no cranial nerve palsies and plantar response was flexor bilaterally, tone and power in all the four limbs was normal, deep tendon reflexes were intact and no involuntary movements were observed in any limb, also there

were no signs of meningeal irritation. On investigations she was found to have haemoglobin 12 gm/dl, total leucocyte count 8000/mm³ and differential leucocyte count P78 L22. Blood sugar, blood urea, serum creatinine were within normal limit, chest radiograph revealed no abnormality. Her serum sodium was 103 mmol/l; serum potassium 4.1 mmol/l and serum calcium was 9.5 mg/dl. Serum osmolality was 240 mOsm/l. Cerebrospinal fluid examination revealed no abnormality.

Based upon these findings she was diagnosed to be a case of metabolic encephalopathy due to hyponatraemia, the cause of hyponatraemia was presumed to be diuretic use and vomiting. Hypertonic saline (3% NaCl) infusion was started, with the aim to raise serum sodium slowly and not more than 8 mmol/l/day. Hypertonic saline was administered according to calculations but repeat serum sodium at 6 h was 115 mmol/l, then hypertonic saline was stopped and 0.9% saline infusion was initiated but serum sodium at 12 h was 122 mmol/l so we switched to 0.45% saline and dextrose infusion and serum sodium at 24 h was 128 mmol/l. Despite our best efforts the rise of sodium was 25 mmol/l in 24 h. However, the patient improved a lot with the rise of serum sodium, she became fully, conscious oriented and alert.

After 4 days the patient started to experience tremors in her hands, difficulty in walking, slowness of movements and difficulty in speech. On repeat neurological examination patient was fully conscious, cooperative and oriented to time, place and person. Her speech was dysarthric and memory was intact. All the cranial nerves were normal, power in all the four limbs was normal, there was cog wheel type of rigidity in all four limbs, coarse pill rolling type of tremors were observed in the upper limbs, plantar response was flexor bilaterally.

INVESTIGATIONS

Repeat serum sodium was 131 mmol/l, potassium was 4.2 mmol/l and Calcium was 8.9 mg/dl. MRI was done

Figure 1 (A and B) Axial T2-weighted and fluid attenuated inversion recovery images at the level of atrium of lateral ventricle showing bilaterally symmetrical hyperintensities involving head and body of caudate nucleus (black arrow) and putamen (white arrow) with relative sparing of globus pallidus (red arrow).

the next day, which revealed bilaterally symmetrical hyperintensities involving caudate nucleus and putamen with relative sparing of globus pallidus (figure 1). The lesions showed evidence of mild restriction on diffusion-weighted imaging (DWI) sequence (figure 2). However, pons of the patient was found to be normal (figure 3).

On the basis of documented hyponatraemia, history of rapid correction of hyponatraemia, parkinsonian features and typical MRI findings she was diagnosed as a case of EPM.

TREATMENT

Patient was started on levodopa and carbidopa combination.

OUTCOME AND FOLLOW-UP

Patient's symptoms started to show improvement on this treatment. She is on follow-up since 4 months now her tremors and rigidity are significantly reduced.

DISCUSSION

CPM and EPM are osmotic demyelination syndromes that are now known to be caused due to rapid correction of hyponatraemia.

Adams *et al*¹ first described CPM in alcoholic and malnourished patients. But it was by 1982 that the connection between these disorders and rapid correction of

hyponatraemia was established.² Pathologically CPM and EPM are similar processes which can occur together or in isolation.² Gocht *et al*, in their study, found isolated CPM in about 50% of patients, CPM along with EPM in about 30% patients and isolated EPM in about 20% of cases.^{2 3} The exact pathogenesis of myelinolysis is not completely understood and the reason why particular areas of brain are affected more than others is poorly understood. Pathologically there is sparing of neurons and axons but only myelin is destroyed. Classically central pons is most affected hence the name CPM was given to this condition. If other areas like basal ganglia, thalami, cerebral or cerebellar grey-white matter junction is affected the condition is known as EPM. In both CPM and EPM bilateral and symmetrical involvement is usually the rule.^{2 4} The above-described patient had bilateral and symmetrical involvement of basal ganglia.

Classically a biphasic clinical course is described for osmotic demyelination syndromes; the first phase is the phase of encephalopathy due to hyponatraemia which improves with restoration of normal sodium levels to be followed by a second phase. Second phase in CPM is characterised by dysphagia, dysarthria, quadriplegia and locked-in state.² The clinical features of EPM include mutism, catatonia, ataxia and various movement disorders like dystonia, postural limb tremors, choreoathetosis and parkinsonism. Few cases of isolated EPM presenting as parkinsonism had been described in the literature.⁵⁻¹² As discussed above our patient also followed a biphasic course she was brought to the hospital due to altered mental status, she had hyponatraemia at that time (Na=103 mmol/l) with the correction of hyponatraemia she regained consciousness but later developed features of parkinsonism in the form of bradykinesia, rigidity and tremors.

MRI is the imaging investigation of choice for CPM and EPM.² Hyperintense lesions are seen on T2 and hypointense lesions are seen on T1-weighted images. The lesions are not contrast enhancing.² CPM typically causes trident shaped signal changes in the pons on T2 images. Central pons is involved sparing a rim at the periphery. EPM presents as bilateral and symmetrical hyperintensities in basal ganglia, thalami, cerebellum and white matter. Sparing of globus pallidus had been described in EPM.¹³ There is no correlation between extent of

Figure 2 (A and B) Diffusion-weighted images (DWI) taken the same level as in figure 1 with evidence of mild restriction on DWI sequence.

Figure 3 (A and B) Axial T2-weighted and fluid attenuated inversion recovery images showing normal signal intensity of the pons.

abnormalities on MRI and the outcome of patients.¹⁴ DWI can detect changes of osmotic demyelination syndrome before they can be demonstrated by conventional MRI.¹⁵ Restricted diffusion has been demonstrated in CPM within 24 h of onset of symptoms.¹⁵ MRI of our patient also demonstrated bilateral symmetrical hyperintensities on T2-weighted images, also there was relative pallidum sparing. DWI of our patient were suggestive of mild restriction on DWI sequence. Also pons was normal in our patient, thus suggesting isolated EPM.

Treatment of EPM and CPM is mainly supportive and symptomatic. Case reports and various case series have documented the use of steroids, intravenous immunoglobulins and thyrotropin releasing hormones to be beneficial, but there had been no large clinical trials to support the use of such treatments.² The movement disorders in EPM are potentially treatable, especially the parkinsonian features are reported to respond well to dopaminergic treatment.² The parkinsonian features of our patient also responded well to levodopa and carbidopa therapy.

Historically the prognosis of osmotic demyelination syndromes was thought to be very poor, but a recent study by Menger and Jorg¹⁴ on 34 patients showed only two deaths, while 10 patients were left dependent, 11 patients had some deficits but were independent and 11 patients recovered completely.

Correction of hyponatraemia should be done slowly, and the correction rate should not exceed >8 mmol/l/day. But the major difficulty in managing hyponatraemia is precisely controlling the rate at which serum sodium should increase.¹⁶ Rate of administration of hypertonic saline is generally calculated by calculating an excess of total body water. However, the rate at which serum sodium will increase depends not only on rate of administration of saline but also on the rate at which free water is excreted.¹⁶ Therefore, if a patient is excreting dilute urine, the rate of increase in serum sodium can exceed that calculated from the rate of hypertonic saline infusion.¹⁶ We also calculated the rate of correction of hyponatraemia by calculating total body water and aimed at correcting not more than 8 mmol/l/day, but as stated above if the patient is excreting free water the increase in serum sodium can be more than expected, this can be the cause of rapid increase in serum sodium in our patient. Unfortunately facility for measuring urine osmolality was not available at our centre.

Thus, to conclude as there is no documented treatment for osmotic demyelination syndromes it is better to

prevent them rather than to treat them, the only way of prevention is by slow correction of hyponatraemia, most recent consensus is not to correct more than 8 mmol/l/day. Despite that the problem is compounded as the treating physician has only indirect control over the rate of sodium rise which may correct faster despite their best intentions.²

Learning points

- ▶ Extra pontine myelinolysis (EPM) can occur as an isolated entity even in the absence of central pontine myelinolysis (CPM).
- ▶ Hyponatraemia should be always corrected slowly, although slow correction can be difficult at times despite physician's best effort.
- ▶ MRI is the investigation of choice for diagnosis of EPM.
- ▶ Biphasic clinical course in the setting of hyponatraemia should alert the treating physician about the possibility of EPM/CPM.
- ▶ Prognosis of CPM/EPM may be not as bad as previously thought.
- ▶ Parkinsonian features of EPM shows good response to dopaminergic treatment.

Competing interests None.

Patient consent Obtained.

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