

CASE REPORT

Central pontine myelinolysis: not just a low sodium issue

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ABSTRACT

Osmotic demyelination syndrome is a rare complication following treatment of chronic hyponatraemia. We describe a case of a middle-aged man known with hypertension and hypothyroidism who presented with a reduced level of consciousness and a generalised convulsion. Laboratory results revealed severe hyponatraemia and hypokalaemia. Following rapid overcorrection of the serum sodium concentration, his level of consciousness remained unchanged, and he developed quadriplegia. Magnetic resonance imaging of the brain revealed central pontine myelinolysis (CPM). The patient died 3 weeks after hospitalisation. Other than rapid overcorrection of chronic hyponatraemia, this case also highlights the important role of potassium in the pathogenesis of CPM. Therefore, when severe chronic hyponatraemia is accompanied by hypokalaemia, the latter should be corrected first to further reduce the risk of CPM.

Keywords: hyponatraemia; osmotic demyelination syndrome; hypokalaemia.

INTRODUCTION

Osmotic demyelination syndrome (ODS) was first described in 1959 [1]. The term encompasses central pontine myelinolysis (CPM) and extrapontine myelinolysis. The most common risk for ODS is rapid overcorrection of chronic hyponatraemia, especially when the serum sodium concentration is <120 mmol/L [2]. Additional high-risk comorbidities include chronic alcoholism, malnutrition, advanced liver disease, diuretic use, hypokalaemia and hypophosphataemia [2,3]. There is a wide range of clinical features, including confusion and drowsiness, dysphagia, dysarthria, varying degrees of quadriplegia and coma or locked-in syndrome [4]. We describe a case of a middle-aged man who was found to have severe, symptomatic hyponatraemia and, following rapid overcorrection, developed CPM.

CASE PRESENTATION

A 50-year-old man known with hypothyroidism was diagnosed with hypertension and was initiated on indapamide and perindopril. According to his wife, he was otherwise in good health and was of sober habits.

Three months later, he became confused and was taken to another hospital by a co-worker. It was noted that his confusion was preceded by five days of severe headaches, nausea, diarrhoea and malaise. During hospitalisation, he had a generalised convulsion, which was aborted with intravenous clonazepam. Clinical examination revealed a reduced level of consciousness with a Glasgow Coma Scale of 5/15. His blood pressure was 141/107 mmHg, he was afebrile and his oxygen saturation was 90% on ambient air. Hydration was thought to be normal. Crackles and bronchial breath sounds were audible in the lower lung zones. The rest of the clinical examination was unremarkable. A chest radiograph revealed symmetrical mid and lower lung zone patchy infiltrates and a computed tomogram (CT) of the chest revealed bilateral lobar consolidation. Laboratory results on admission revealed a sodium concentration of 114 mmol/L (normal range: 136–145 mmol/L); potassium concentration of 2.2 mmol/L (normal range: 3.5–5.1 mmol/L) and a capillary glucose concentration of

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14.1 mmol/L. See Table 1. The patient was administered supplemental oxygen at 3 L per minute and oxygen saturation improved to 100%. Owing to his low level of consciousness and convulsions, acute hyponatraemia was considered. The patient was treated with two ampoules of 10% sodium chloride solution intravenously. The following day the sodium concentration was 126 mmol/L; however, his level of consciousness remained unchanged. As a result, a contrasted CT of the brain was performed, which was reported to be normal. Polymerase chain reaction for SARS-CoV-2 was positive.

Fifteen days following hospitalisation, the patient was transferred to our hospital. On arrival, he was drowsy but responded to a pain stimulus, pupils were equal and reactive to light, he had a gaze preference to the right, tone was reduced in the lower limbs but was normal in the

upper limbs, reflexes were brisk with the exception of reduced ankle jerks, and testing of power was limited but he was not moving all limbs symmetrically. Magnetic resonance imaging was performed 30 days after his initial presentation and revealed features consistent with CPM. See Figure 1. The patient remained comatose and required a tracheostomy. He died 3 weeks after admission at our hospital.

DISCUSSION

Our discussion focuses on the evolution of our patient's hyponatraemia and risk factors leading to CPM. He was recently prescribed indapamide for hypertension, which caused chronic hyponatraemia. Indapamide, a thiazide-like diuretic, has been reported to cause severe hyponatraemia and mild hypokalaemia [5]. Mechanisms responsible for thiazide-associated hyponatraemia include impaired free water clearance due to poor distal nephron solute delivery and hypovolaemia-induced antidiuretic hormone (ADH) secretion [5]. A meta-analysis reported that thiazide-associated hyponatraemia typically developed in elderly women (age >75 years) with a normal body mass index [6]. The mean time to its development was 19 days; however, it may occur months later, as was found in our case.

Hypothyroidism has been linked to the development of hyponatraemia, especially during myxoedema coma [7]. Mechanisms include a reduced cardiac output, which triggers baroreceptors leading to the release of ADH, poor water delivery to the diluting segments of the nephron and poor solute intake [7]. Our patient's thyroid function tests at hospital admission indicated poor control, possibly exacerbating his chronic hyponatraemia.

The syndrome of inappropriate ADH secretion induced by the pneumonia was another likely contributor [8]. Our patient also had a history of diarrhoea. The latter caused hypovolaemia, further stimulating both ADH release as well as thirst. Continued water intake along with an inability of the kidneys to excrete a water load likely caused an acute component of the chronic hyponatraemia.

CPM occurred in our patient for the following reasons. Although the initial concern was that he may have had acute, severe hyponatraemia and thus cerebral oedema, the overzealous correction of the serum sodium concentration to nearly normal using hypertonic saline was a major factor. Clinically, it may be very difficult to decide whether hyponatraemia is only acute or acute-on-chronic. For this reason, it may be more prudent to raise the serum sodium concentration by an amount that is safe while simultaneously reducing intracranial pressure, usually ~4–6 mmol/L [2]. Our patient's serum sodium concentration was increased by 12 mmol/L within 24 hours. During

Table 1. Results during initial hospitalisation.

Results	Reference range	Day of admission	24 hours later
Sodium (mmol/L)	136–145	114	126
Potassium (mmol/L)	3.5–5.1	2.2	2.4
Urea (mmol/L)	2.5–6.4	8.6	2.7
Creatinine (μmol/L)	62–124	198	96
TSH (mIU/L)	0.27–4.20	32.24	–
T4 (pmol/L)	2.0–22.0	7.8	–

Abbreviations: TSH, thyroid stimulating hormone; T4, thyroxine.

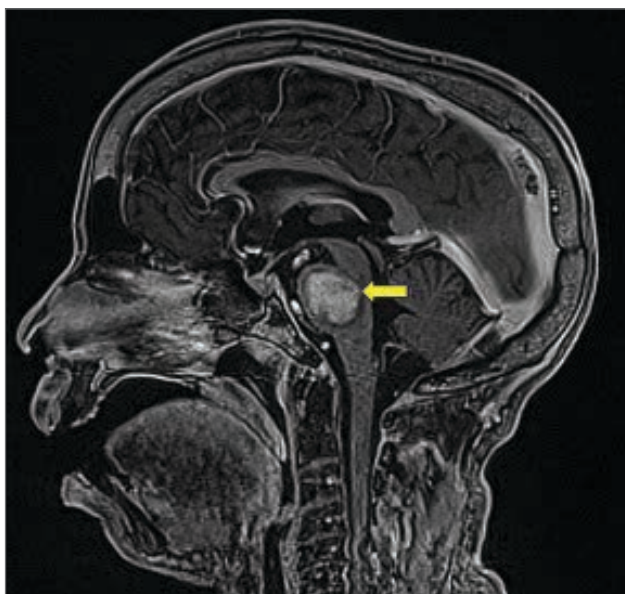


Figure 1. T2-weighted magnetic resonance imaging (sagittal view), indicating central pontine myelinolysis (yellow arrow).

chronic hyponatraemia, the recommended increase in serum sodium concentration should not exceed 8 mmol/L per day [2]. The reason for this is to allow neurons to import osmoles. In response to changes in serum osmolality, neurons have the unique ability to adapt by exporting osmoles when cells are swollen [9]. These osmoles consist of electrolytes, predominantly potassium, the major intracellular cation, which move rapidly, and organic osmoles, which move more slowly. This adaptation takes about 48 hours [2]. Once serum sodium begins to return to normal, neurons must reimport osmoles [2]. Since potassium constitutes most of the imported electrolyte osmoles, patients with hypokalaemia are at high risk of ODS [10]. Autopsy or MRI-confirmed cases of ODS were found in patients with simultaneous hypokalaemia and hyponatraemia in which the sodium concentration was corrected by more than 10 mmol/L within 24 hours [2]. Central pontine myelinolysis has also been reported in a patient with isolated hypokalaemia [11]. Therefore, since potassium plays a pivotal role in ODS [10], overlooking even relatively mild hypokalaemia may have devastating consequences if it is not addressed during the management of chronic, severe hyponatraemia.

The mechanism by which hypokalaemia predisposes to ODS remains unknown. It is speculated that there is an inability of brain vascular endothelial cells and/or glial cells to regulate their volume when hyponatraemia is accompanied by hypokalaemia [10]. The sodium/potassium-ATPase (Na/K-ATPase) located in the cell membrane is important for the regulation of cell volume. Cellular expression of this pump in glial and endothelial cells of the brain may be reduced in the presence of hypokalaemia, as has been demonstrated in skeletal muscle [12]. Therefore, during rapid increases in serum osmolality, these cells cannot rapidly adapt because of the low potassium availability as well as a lack of Na/K-ATPase pumps. It has been recommended that correction of hypokalaemia should be attained prior to correcting the hyponatraemia to reduce the risk of ODS [10].

Recently, it has been reported that hypokalaemia is a common finding in patients with COVID-19 infection [13]. SARS-CoV-2 gains entry to its host by binding to the angiotensin-converting enzyme 2 (ACE2) receptor and reduces ACE2 expression. This causes increased angiotensin II concentrations, resulting in secondary hyperaldosteronism with subsequent renal potassium wasting and ultimately hypokalaemia [13]. A recent study reported that 95 of 175 patients (55%) admitted with COVID-19 had hypokalaemia at the time of hospitalisation [13]. They also found that renal potassium excretion was higher in patients with hypokalaemia, indicating renal potassium wasting. Our

patient's hypokalaemia was likely due to multiple mechanisms that included diarrhoea, renal losses due to thiazide-like diuretic use as well as the effect of COVID-19 on renal potassium homeostasis.

CONCLUSIONS

Other than rapid overcorrection of chronic hyponatraemia, this case also highlights the important role of potassium in the pathogenesis of CPM. Therefore, when severe chronic hyponatraemia is accompanied by hypokalaemia, the latter should be corrected first to further reduce the risk of CPM.

Ethical considerations

Consent to publish this case report was granted by the Human Research Ethics Committee of Stellenbosch University (reference number C20/07/004_COVID-19, project number 17161).

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