Title page
Extrapontine myelinolysis associated with pituitrin: case report and literature review

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Abstract

Background: Hyponatremia is the most common electrolyte abnormality encountered in hospitalized patients, resulting from a varied spectrum of conditions. Both the primary disturbance and its correction can result in life-threatening neurological consequences. Extrapontine myelinolysis is one such complication and is associated with the rapid correction of hyponatremia. Here we describe a patient who developed extrapontine myelinolysis unexpectedly after the correction of hyponatremia involving the drug pituitrin.

Case presentation: A 24-year-old Chinese woman was transferred to our neurology department with the symptoms of dysarthria and quadriparesis developing one day after the correction of hyponatremia (from 118 mmol/L to 140 mmol/L), which followed with intravenous drip continuously of pituitrin for controlling of hemoptysis in the emergency room. During the course, she developed involuntary movement. Magnetic resonance imaging changes were consistent with extrapontine myelinolysis.

Conclusion: This present case describes the mechanism of profound hyponatremia involving pituitrin, and the subsequent development of extrapontine myelinolysis. Physicians may approach effective clinical management of patients through awareness of the adverse effect of pituitrin on serum sodium levels, and avoid rapid correction of hyponatremia in clinical practice.

Keywords

Pituitrin, hyponatremia, extrapontine myelinolysis

Background

Hemoptysis, is a common symptom in clinical practice, while can sometimes be a life-threatening situation and requires urgent management. Pituitrin is the best available drug for control of severe pulmonary hemorrhage or repeated hemoptysis with the ability of strong vasoconstriction[1]. Untoward effects of pituitrin, such as hyponatremia are often ignored by physicians, as most patients with hyponatremia are asymptomatic. Hyponatremia generally is defined as plasma sodium level of less than 135 mmol/L[2]. Although hyponatremia is a common and often underestimated problem, rapid correction of chronic hyponatremia can have devastating neurological consequences, i.e. central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM). CPM and EPM are two variants of osmotic demyelination syndrome, which is related to rapid osmotic changes, particularly an aggressive correction of hyponatremia[3]. EPM may involve the cerebellum, lateral geniculate body, basal ganglia and cerebral white matter with varied spectrum of symptom. Parkinsonism is common, while involuntary movements such as dystonia and myoclonus are less frequent[3, 4]. We report a case of iatrogenic EPM presenting with dysarthria, quadriplegia and involuntary movements following correction of hyponatremia associated with pituitrin.

Case presentation

A 24-year-old Chinese woman was transferred to our neurology department, presenting with dysarthria and weakness of all four extremities. The patient had a medical history of tetralogy of Fallot since infancy with resulting cyanosis. Corrective surgery was undertaken 4 years ago, and since then, she had been stable and functionally well. The episode began when the patient contracted repeated minor hemoptysis, she was seen by a doctor with conventional therapy with aminomethylbenzoic acid and etamsylate without efficiency. On the fifth day, she began to get a fever and was transferred to the emergency department in our hospital.

On admission, she showed a massive hemoptysis, and pituitrin was prescribed urgently to control bleeding. Pituitrin administered 18 U in 30 ml of saline was intravenous drip continuously at a rate of 2 ~ 3 ml/h via pump for six days. On the fourth admission day, she became nauseous and generalized weak and blood test reviewed
a profound hyponatremia with sodium 118 mmol/L. She was resuscitated with i.v. saline, and the sodium was 140 mmol/L four days later (Figure 1). Unfortunately, the next day she deteriorated once more, developing initially a dysarthria and quadriparesis. An immediate computed tomography (CT) of the head presented normal, and she was transferred to our neurology department. During the course, she developed involuntary movements, mainly paroxysmal oromandibular dystonia and myoclonus in the left upper limb. Magnetic resonance imaging (MRI) showed bilateral symmetric basal ganglia lesions consistent with EPM (Figure 2). She was treated mainly with corticosteroid, diazepam and hyperbaric oxygen therapy, and was discharged home with little residual symptoms (speaking in relative fluency and walking by her own without involuntary movements).

Conclusions
This patient developed EPM unexpectedly after the intravenous use of pituitrin for controlling of hemoptysis. Pituitrin, extracted from posterior pituitary, consists of oxytocin and vasopressin. The latter can activate type-1A receptors located in vascular smooth muscle cells resulting in vasoconstriction[5]. Thus, pituitrin has been used in gastrointestinal or pulmonary hemorrhage, and the result is almost as if forceps had been applied directly to the bleeding vessel. Besides, water reabsorption is mediated by vasopressin activation of type-2 receptors in the basolateral membrane of cells in the renal collecting ducts[5]. This patient developed hyponatremia as a result of that mechanism.

Hyponatremia can be classified into acute (< 48 h) and chronic (≥ 48 h) hyponatremia. When hyponatremia develops, the brain reduces the number of osmotically active particles within its cells (mostly organic solutes) in an attempt to adapt the osmotic change, which takes 48 h[6]. CPM and EPM are acquired metabolic disorders of acute central demyelination strongly associated with rapid correction of hyponatremia[7]. CPM typically involves the central pontine and EPM involves different brain regions, like cerebellum, thalamus, basal ganglia or subcortical white matter. EPM can manifest with movement disorders, such as parkinsonism, involuntary movements. Special populations seem vulnerable to the development of osmotic myelinolysis, including not only the alcoholics and malnourished patients, but also those with liver disease, sepsis, adrenal insufficiency and severe burns[8]. Studies showed that the chronicity of hyponatremia before correction is a critical risk factor for the development of osmotic myelinolysis[9, 10]. This patient developed chronic hyponatremia documented to exist for at least 48 h, and after a rapid increase of serum sodium from 118 mmol/L to 134 mmol/L in 24 h, there was a delay of one day before progressive neurological decline. Recommendations suggest that ideally hyponatremia be corrected with a limiting increase to not more than 8-10 mmol/L during every 24 h[11]. We identified three cases, each reporting a single case in which deamino arginine vasopressin, a kind of vasopressin analogue, was implicated as a possible contributory factor in the development of severe electrolyte imbalances that triggered the osmotic demyelination[12-14]. This case and literature review highlights that: 1) hyponatremia is the most frequent electrolyte disturbance observed in hospitalized patients. Drugs like pituitrin can cause profound hyponatremia, and should be considered in the differential diagnosis when approaching a patient with hyponatremia. 2) Osmotic myelinolysis is most frequently associated with rapid correction of hyponatremia. Prevention of CPM and EPM by caution in correction of hyponatremia, especially chronic hyponatremia, is more important than early diagnosis.

Consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.
List of abbreviations

CPM: Central pontine myelinolysis;
EPM: Extrapontine myelinolysis;
CT: Computed tomography;
MRI: Magnetic resonance imaging.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
Liying Zhuang contributed to manuscript writing and interpretation of the data. Ziqi Xu contributed to acquisition and interpretation of the data. Yaguo Li contributed to the critical revision of the manuscript for intellectual content. Benyan Luo contributed to the critical revision of the manuscript for intellectual content. All authors read and approved the final manuscript.

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References:


Illustrations and figures (figure legends)

Figure 1. Changes of the patient’s serum sodium concentration. Triangles showing the serum sodium gradually decreased with the use of pituitrin, the black arrow pointing out the day beginning use of hypertonic saline.

Figure 2. Brain magnetic resonance imaging. A, axial T1-weighted MRI showing low signal intensity of bilateral symmetric basal ganglia; B, axial T2-weighted MRI showing high signal intensity of bilateral symmetric basal ganglia; C, axial T2-weighted MRI showing no lesion in the pons (the red arrows pointing out the lesions).
Additional files

Additional file 1

Additional file 1.xls

Literature review of similar cases

Note: The literature review of similar cases shown in this table according to the editors’ requirement was consistent with the references 12-14 cited in the ‘conclusions’ section (line 119-122), so the table was not cited in the text.
Figure 1

Serum Sodium (mmol/L)

Admission day
Additional files provided with this submission:

Additional file 1: Additional file 1.xls, 14K
http://www.biomedcentral.com/imedia/1150272623134445/supp1.xls