Reminder of important clinical lesson

Extreme hyponatraemia with intact neurological outcome in a young child with Addison's disease

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Summary

The authors present the case of a 6-year-old boy with a good neurological outcome from extreme hyponatraemia caused by autoimmune hypoadrenalism. He presented with 1 week of reduced appetite, lethargy, vomiting and one episode of diarrhoea. He was described as being slightly unsteady on his feet. Clinically he was alert, although intermittently confused, with dry mucous membranes and sunken eyes. Serum sodium was 96 mmol/l with normal serum potassium and renal function. He was initially treated with 3% saline intravenously, and his serum sodium increased to 128 mmol/l by day 3. He developed slurred speech and ataxia on day 4, although MRI brain showed no evidence of pontine myelinosis, and the symptoms resolved over 1 week. A Synacthen test on day 10 confirmed a diagnosis of Addison's disease and he was commenced on hydrocortisone and fludrocortisone replacement therapy. At 5 months follow-up there are no obvious neurological or developmental sequelae.

BACKGROUND

Hyponatraemia is a relatively common diagnostic challenge in acute medicine. The presenting symptoms can be suggestive, or it can be an incidental finding. Whether it is acute or chronic, and associated with excessive, normal or reduced intravascular volume will help determine its cause and correct management. We present the case of a 6-year-old boy with severe hyponatraemia (initial sodium 96 mmol/l) caused by autoimmune hypoadrenalism, who made a good neurological recovery.

CASE PRESENTATION

A 6-year-old boy presented with just 1 week history of reduced appetite, lethargy, vomiting and one episode of diarrhoea. He was also described as being slightly unsteady on his feet. No contacts or family members had been unwell, and there was no history of fever. There was no significant family history. He was the youngest of four children, born at 36+2/40, and the pregnancy was complicated by maternal cholestasis. He had a simple febrile convulsion at 3 years, and an episode of tonsillitis at 4 years of age, during which his renal function and electrolytes were normal, including serum sodium 138 mmol/l. This suggests that the hyponatraemia was of relatively recent onset and had developed at some point between the ages of 4 and 6 years. Over recent months there had been no lethargy, although some concern as to progress in the first years of school.

On examination, he was alert, although intermittently confused, with dry mucous membranes and sunken eyes. His blood pressure was normal for age (99/68 mm Hg), weight 22.8 kg (50th centile) and height 118.5 cm (just above the 50th centile) and the remainder of the observations and examination were normal. He was estimated

as 10% dehydrated and commenced on 0.9% saline intravenously, while pathology results were awaited. These initial investigations are outlined on table 1 and show severe hyponatraemia, minimal hyperkalaemia and also hypochloridaemia. Liver function tests, full blood count, and C-reactive protein were normal. Once hyponatraemia was confirmed, intravenous fluids were changed to hypertonic (3%) saline. Table 2 shows subsequent investigations.

The patient's sodium level increased by 15 mmol/l in the first 24 h, and 14 mmol/l in the second 24 h, reaching 128 mmol/l on the 3rd day of admission. Ongoing intravenous fluid thereafter was 0.9% saline and he had persisting mild hyponatraemia in the 128–131 mmol/l range for several days thereafter. On day 4 of admission, he developed neurological symptoms—slurred speech, ataxia and clumsiness. MRI brain the following day showed no evidence of myelinosis in the pontine region, which is the more classically recognised abnormality in hyponatraemia. However the MRI did show diffuse basal ganglia increased signal (caudate and lentiform nuclei bilaterally), which may be attributable to his profound hyponatraemia.

Table 1 Initial investigations.

Parameter	Level	Reference range
Serum		
Sodium	96 mmol/l	133–146
Potassium	5.8 mmol/l	3.5–5.6
Urea	6.0 mmol/l	2.5–6.2
Creatinine	24 µmol/l	28–52
Chloride	69 mmol/l	95–105
Bedside		
Blood glucose	6.8 mmol/l	2.5–5.8

Table 2 Subsequent investigations.

Parameter	Level	Reference range
Capillary		
pH	7.42	7.35–7.45
pCO ₂	3.58 kPa	4.7–6.0
Base excess	–5.4 mmol/l	–2.0–2.0
Serum		
Cortisol (day 2)	283 nmol/l	
Cortisol (day 8)	607 nmol/l	
Cholesterol	4.1 mmol/l	
Osmolality	231 mOsm/kg	275–295
Antiadrenal antibodies	Positive	
Very long chain fatty acids	Normal	
Renin (day 4, when sodium 128)	1110 mu/l	4–85 mU/l
Urine		
Sodium	81 mmol/l	
Potassium	63 mmol/l	
Osmolality	489 mOsm/kg	

The cortisol level (283 nmol/l) at presentation was considered suspiciously suboptimal for degree of illness. Therefore, while a wider range of differential diagnoses (see below) were considered, plans were also made to investigate his adrenal axis further. Interestingly, a further random serum cortisol on day 8 was reassuringly normal (607 nmol/l), although hyponatraemia persisted (131 mmol/l). A Synacthen test on day 10 showed a flat response: serum cortisol 198 nmol/l (0 min), 196 nmol/l (30 min) and 212 nmol/l (60 min). This diagnosed adrenal insufficiency. An elevated adrenocorticotrophic hormone (ACTH) 314 ng/l indicated primary adrenal failure and an extremely elevated plasma renin indicated mineralocorticoid deficiency. Investigations into the cause of his primary adrenal failure excluded X linked adrenoleukodystrophy (normal very long chain fatty acids levels) and instead identified an autoimmune process with positive adrenal autoantibodies, indicative of Addison's disease.

INVESTIGATIONS

See table 1 and table 2.

DIFFERENTIAL DIAGNOSIS

See table 3

OUTCOME AND FOLLOW-UP

The patient made a good neurological recovery over the following week, and was discharged home on day 11 on oral hydrocortisone 10 mg/m² daily, fludrocortisone 100 micrograms daily and sodium supplements 30 mmol twice daily. Two weeks following his admission to hospital, his weight had increased by 2.6 kg, suggesting approximately 11% dehydration at presentation, consistent with initial clinical estimates. He was weaned off sodium supplements by 4 weeks postdiagnosis and has maintained normal serum sodium thereafter. At 5 months after initial presentation, he had a repeat MRI which showed resolution of the swelling and hyperintensity of the corpus striatum, although there was subtle minimal volume loss of the putamina bilaterally. Clinically, he is back to his normal self, progressing well at school, with no obvious neurological or developmental sequelae.

Table 3 Causes of hyponatraemia.

Category	Condition
Reduced body sodium	
Renal sodium loss	Prematurity; mineralocorticoid deficiency or resistance; diuretics; polyuric acute renal failure; salt wasting renal disease; renal tubular acidosis; cerebral salt wasting
Extrarenal sodium loss	Diarrhoea; vomiting; fistulae; laxative abuse; cystic fibrosis; excess sweating; burns; surgery; trauma; septic shock
Increased body water	
Excess water intake	Hypotonic intravenous fluids; psychogenic polydipsia
Reduced renal water excretion	Oliguric acute renal failure; chronic renal failure
Non-osmolar antidiuretic hormone (ADH) release	Cardiac failure; nephrotic syndrome; liver cirrhosis; glucocorticoid deficiency; hypothyroidism; antidiuretic drugs
Syndrome of inappropriate antidiuretic hormone (SIADH)	Central nervous system disease; respiratory disease

DISCUSSION

The young child described in this case had a most extreme degree of hyponatraemia. His case highlights a number of important principles of clinical management, first hyponatraemia in general and second the specifics of adrenal pathology.

First, detailed history and examination are essential to determine the chronicity of symptoms and biochemical changes. This boy's symptoms became apparent over a 1-week period. There was the suggestion of issues in school performance, raising the possibility of early encephalopathy, although they were subtle and their significance was uncertain. He had significant dehydration on presentation and we considered that an intercurrent gastroenteritis illness may have contributed. His admission plasma sodium level of 96 mmol/l suggests an acute-on-chronic situation, whereby there had been some degree of brain adaptation to chronic (>48 h) hyponatraemia. The high urine sodium and osmolality suggested renal sodium loss, either due to adrenal or renal pathology.¹ The differential diagnoses of hyponatraemia in children (table 3) are broadly categorised into those in which there is increased body water or reduced body sodium, causes of the latter often being accompanied by dehydration.² Children are at greater risk than adults of developing hyponatraemic encephalopathy, that is, at a lesser degree of hyponatraemia, due to reduced cranial capacity.³ The symptoms are well-described, of which headache, nausea and vomiting are the most consistent early features.⁴ It is suggested that in chronic hyponatraemia the sodium level should be corrected slowly to avoid osmotic demyelination.⁵ However, when encephalopathy is present the sodium level should be increased rapidly using hypertonic (3%) saline.³ Current guidance suggests limiting the sodium correction to <10–12 mmol/l in 24 h, <18 mmol/l in 48 h.

Initial laboratory investigations help elicit the cause, but it is important to appreciate that classical biochemical abnormalities are not universal, for example, the absence of hyperkalaemia in this case. Addison's disease has been termed the Great Masquerader, presenting subtly and

atypically and sometimes missed initially as a diagnosis. The autoimmune process destroys the adrenal cortex reducing glucocorticoid and mineralocorticoid production, the latter acting on the distal renal tubule to promote sodium reabsorption and potassium and hydrogen ion secretion. The resultant aldosterone lack would be expected to cause hyponatraemia accompanied by hyperkalaemia. Soule previously described that hyperkalaemia was present in only 53% of a cohort of 50 patients with Addison's disease.⁶ The proposed mechanisms for the absence of hyperkalaemia in Addison's disease include isolated hypocortisolism, poor potassium intake and excessive potassium loss through vomiting.¹ Important tests to consider where there is hyponatraemia and diagnostic uncertainty, include plasma electrolytes, creatinine, osmolality, albumin, glucose, thyroid function tests, renin, cortisol, urinary electrolytes and osmolality. It is important to consider, not just the absolute value of the serum cortisol, but whether it is inappropriately low for the clinical context. If there is any degree of doubt, undertaking an ACTH stimulation test (Synacthen test), is essential to diagnose or exclude adrenal failure. The commonest cause of primary adrenal failure, historically was tuberculosis, but is now autoimmune destruction. While that proved to be the cause in this boy, evidenced by positive antiadrenal antibodies, consideration of X linked adrenoleukodystrophy is important in boys and it is essential to assay very long chain fatty acids.

Learning points

- This case illustrates (a) the surprisingly young age at which autoimmune adrenal failure can present, (b) important principles of fluid resuscitation in extreme hyponatraemia, (c) differential diagnoses to consider and (d) that neither normal serum potassium nor detectable random serum cortisol exclude Addison's disease.

Competing interests None.

Patient consent Obtained.

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