CASE REPORT

Intensive care management of severe hyponatraemia in the context of group A streptococcal septicaemia

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SUMMARY

This case describes a 54-year-old woman with exudative eczema, who was admitted to the intensive care unit with a serum sodium concentration of 191 mmol/L, secondary to profound dehydration in the context of group A streptococcal septicaemia. Successful rehydration and electrolyte normalisation was achieved with continuous venovenous haemodiafiltration (CVVHDF), the replacement fluid of which was infused with hypertonic saline to limit the rate of sodium reduction. This case report comments on three areas of interest. First, hyponatraemia of this level is unusual. Second, the infusion of hypertonic saline into the replacement fluid of the CVVHDF filter is not common practice but successfully ensured a controlled reduction in serum sodium concentration while aggressively replacing a 9 L water deficit. Third, the notable physiological reserve demonstrated by the patient: despite an extraordinary serum sodium concentration in the context of overwhelming streptococcal septicaemia, she has made a full cognitive recovery.

BACKGROUND

Hyponatraemia, a serum sodium concentration >150 mmol/L, occurs either when osmotically active electrolytes (sodium and potassium) are retained without water or when water is lost without sodium (or a combination of the two). Normally, neither salt intake nor water loss results in hyponatraemia because the ensuing rise in plasma osmolality stimulates the release of both antidiuretic hormone and thirst, minimising further water loss and increasing water intake. However, if these losses are unreplaced, serum sodium concentration will rise. This rise in serum sodium initially causes fluid movement out of the brain, which leads to cerebral contraction. The physiological responses to this are twofold, with an acute and chronic phase. First, there is a rapid uptake of electrolytes, countering the decreasing cerebral volume. Following this, there is slower accumulation of organic osmolytes, in an attempt to maintain a steady brain volume. When correcting hyponatraemia, one must be aware of these acute and chronic changes, as major differences in serum osmolality can cause dramatic shifts in water movement, eventually leading to cerebral oedema and potentially death.¹

Correction of hyponatraemia requires the administration of dilute fluids to both correct the water deficit and replace ongoing water losses. In cases of chronic hyponatraemia (where the sodium

has accumulated over longer than 48 hours), it is generally accepted that careful correction of serum sodium concentration (8–10 mmol/24 hours) is important, so as to avoid dramatic shifts in water movement, and the subsequent cerebral oedema, which can eventually lead to significant neurological compromise or death.^{2–3} The goal is to correct the water deficit and electrolyte imbalance in a reasonable time frame, acknowledging that persistent hyponatraemia is itself associated with an increased mortality.⁴

The cause for this patient's hyponatraemia is also of great interest. Group A streptococcus (GAS) is an aerobic Gram-positive coccus, which can cause a diverse range of skin, soft tissue and respiratory tract infections. Occasionally, GAS can cause extremely severe infection, followed by multiorgan failure. When bacteria are isolated from a normally sterile body site, such as the blood, the infection is termed invasive GAS. Any GAS manifestation can lead to the development of streptococcal toxic shock. Mortality in patients diagnosed with GAS ranges from 25% to 48%, with shock being the most important predictor of mortality.^{5,6}

The importance of this case lies in a number of reasons. The unusual presentation of severe hyponatraemia in the context of a group A streptococcal septicaemia; the correction of this hyponatraemia with continuous venovenous haemodiafiltration (CVVHDF); the dialysate of which was infused with reducing volumes of hypertonic saline, so as to control the reduction of serum sodium concentration more tightly; and finally, the survival of this patient, with discharge at her normal cognitive baseline.

CASE PRESENTATION

The patient, a 54-year-old woman of Afro-Guyanese descent, was found by the police, collapsed in her home, having not been seen for 5 days. London ambulance service attended, who described extensive exudative excoriations across 70% of the patient's body surface area and severe dehydration. She was alert but weak and unable to complete sentences. She was disorientated with a Glasgow Coma Score (GCS) of 12 (E4V3M5).

A complex medical history included severe eczema, systemic lupus erythematosus (SLE) with no organ involvement, antiphospholipid syndrome, hypertension, hypercholesterolaemia, iron deficiency anaemia, a thrombotic stroke in 2006, upper gastrointestinal bleed in 2012 and subdural haematoma in 2013 (for which she had had a right sided

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Table 1 Serum sodium concentration, CVVHDF sodium concentration, fluid balance and serum urea over first 7 days of ICU admission

ICU day	Date	Na (serum)	Vol 30% NaCl added to dialysate	Na (dialysate)	Filter exchange rate	Daily fluid balance	Overall fluid balance	Serum urea
-1	18/09/2017 admission to ED	191	NA	N/A	N/A	Given 2.85 L in ED	9L deficit on admission	81
0	19/09/2017 admission to ICU	186	30 mL	170	16 mL/kg/hour	1.15 L+ve	4 L+ve	79
1	20/09/2017	170	20 mL	160	16 mL/kg/hour	3.5 L+ve	7.5 L+ve	56
2	21/09/2017	162	20 mL	160	16 mL/kg/hour	3.1 L+ve	10.6 L+ve	29
3	22/09/2017	154	10 mL	150	24 mL/kg/hour	1.8 L+ve	12.4 L+ve	18
4	23/09/2017	151	10 mL	150	24 mL/kg/hour	2.2 L+ve	14.6 L+ve	12
5	24/09/2017	147	0 mL	140	24 mL/kg/hour	1.8 L+ve	16.5 L+ve	12
6	25/09/2017	148	N/A	N/A	Filter off	1.6 L+ve	18.1 L+ve	11
7	26/09/2017	146	N/A	N/A	Filter off	0.4 L+ve	18.5 L+ve	13

CVVHDF, continuous venovenous haemodiafiltration; ED, emergency department; ICU, intensive care unit.

parietal craniectomy). She had a penicillin allergy and took once daily warfarin 2 mg, amlodipine 10 mg, bendroflumethiazide 2.5 mg and levetiracetam 250 mg. She lived alone, managing all activities of daily living independently. She had a close relationship with neighbours and had siblings who lived nearby. There was no significant family history of note.

On arrival to the emergency department at King's College Hospital, she was cardiovascularly stable, with a mean arterial pressure >65 mm Hg and a normal heart rate. She was afebrile. On catheterisation, she passed small volumes of concentrated urine. On examination, her chest was clear with equal air entry. She was tachypnoeic. Heart sounds were normal, but profound clinical dehydration was again commented on, alongside extensive, purulent skin break down.

An initial blood gas, taken while the patient was receiving oxygen via a 15 L non-rebreathe mask, demonstrated pH 7.241, partial pressure of carbon dioxide (pCO₂) 7.85, partial pressure of oxygen (pO₂) 9.14, serum bicarbonate concentration (HCO₃) 24.4, base excess (BE) -2.0, corrected serum potassium concentration (cK) 4.8, corrected serum sodium concentration (cNa) 196, corrected serum calcium concentration (cCa) 1.16, corrected serum chloride concentration (cCl) 154, anion gap (AG) 17.5, lactate 3.9 and glucose 5.9.

Her chest X-ray was clear, and a CT head demonstrated no acute findings but did show generalised involutinal changes and evidence of a previous stroke.

Her laboratory bloods confirmed a sodium of 191 mmol/L, up from a baseline of 142, taken 1 month previously. Potassium was 4.7, creatinine was 346 (from 85) and urea was 81.3 (from 5.1). Creatine kinase was 4092. Albumin was 33, globulin was 53, bilirubin was 8, alkaline phosphatase was 70, aspartate transaminase was 65 and gamma glutamyl transaminase was 8. C reactive protein was 54, white cell count was 25 (neutrophils 23), haemoglobin was 131 and platelet count was 138. Urinalysis demonstrated blood and protein. Plasma osmolality was 493, and urinary osmolality was 581. Her renal ultrasound scan was normal.

Consultant-led resuscitation was initiated in the emergency department, with slow infusion of 0.9% sodium chloride. Oxygenation was supported with high flow nasal cannulae. Broad spectrum intravenous antibiotics were commenced as per microbiology to cover for bacterial and viral causes (linezolid, ciprofloxacin, metronidazole and acyclovir), and admission to the intensive care unit was planned for respiratory support,

electrolyte management and in anticipation of likely cardiovascular collapse secondary to septicemia.

Further blood results demonstrated a GAS bacteraemia and a GAS positive skin swab. Subsequent virology results were all negative, including tests for hepatitis B and C, HIV, herpes simplex virus, varicella and enterovirus. SLE-specific investigations showed markers were at baseline.

DIFFERENTIAL DIAGNOSIS

These results supported the diagnoses of group A streptococcal septicaemia secondary to infected lichenified eczema; an acute kidney injury secondary to dehydration and rhabdomyolysis; and dehydration-related hypernatraemia. Consensus from the rheumatology multidisciplinary team meeting was that this presentation was unlikely to represent reactivation of lupus.

TREATMENT

On intensive care, the patient required less than 24 hours of respiratory support with high flow nasal cannulae oxygen, after which time she self-ventilated on room air, achieving adequate gas exchange independently. She never required vasopressor support. Intravenous acyclovir was stopped when negative Herpes Zoster Virus (HSV) swabs were confirmed; linezolid, metronidazole and ciprofloxacin were continued for 7 days. Linezolid was then switched to vancomycin (due to a mild but notable fall in platelet count), which was continued for a total of 7 days. Her infected eczema was treated topically until full resolution, and pain relating to this was managed initially with a low dose fentanyl infusion, followed by regular gabapentin. Her conscious level improved slowly; she was obeying commands on arrival to ICU, and her verbal response improved as she was rehydrated.

The main focus of her admission was fluid management and electrolyte correction.

Slow intravenous fluid was commenced to start correction of the estimated 9L water deficit, and renal replacement therapy was initiated with the hope of avoiding a rapid reduction in serum sodium concentration. It was assumed that this hypernatraemia had been present for longer than 48 hours, given the length of time that she had not been seen and the extent of her dehydration. To prevent any rapid sodium shift (>8–10 mmol/L), a protocol published by Guy's and St Thomas' Trust was followed, which describes the addition of hypertonic saline (30%) to the replacement fluid of the haemodialysis

filter.⁷ According to this guideline, the standard sodium concentration of a 5 L replacement fluid bag is 140 mmol/L. This concentration can be increased by infusing 5 mL aliquots 30% saline (25 mmol Na⁺); each 5 mL hypertonic saline increases the concentration of the replacement bag by 5 mmol/L. For this patient, a reducing regimen of hypertonic saline infused replacement fluid was used (see table 1). By day 5, she had a serum sodium of 147 mmol/L, and renal replacement therapy could be suspended. She was passing urine independently while on the filter, and this continued after renal replacement therapy was suspended. Biochemical markers, osmolarities and urine dip suggested recovery of renal function, and by day 10, her renal profile, including her serum sodium concentration, were back to baseline. By this time, the patient had made a full cognitive recovery. She was alert, orientated, conversational, sleeping well and communicating normally with her friends and family. An MRI scan of her brain showed no radiological evidence of intracranial complications secondary to her period of hypernatraemia and subsequent electrolyte correction.

OUTCOME AND FOLLOW-UP

After a 12-day stay on intensive care, the patient was discharged back to the ward under the care of the medical team, with regular input from dermatology. Although weak (presumed to be secondary to her period of critical illness), she continued to improve, and the focus of her ward-based stay was discharge planning. With regular physiotherapy and support from the occupational therapy team, she regained enough independence for discharge. She arrived back at home just 3 weeks after her admission. She continues to have community follow-up by rheumatology and dermatology.

DISCUSSION

A serum sodium concentration over 190 mmol/L in an adult patient is uncommon, and survival without neurological sequelae is even more so. The infrequency with which this presentation is encountered, and the dilemma posed by treatment strategies, contribute to the clinical difficulties of these cases: a fast correction rate risks cerebral oedema and its associated complications, while a slow correction rate promotes persistent hypernatraemia. Both are associated with increased mortality.¹⁴ Case reports that describe the successful management of severe hypernatraemia are therefore of clinical and scientific importance.

Learning points

- ▶ Continuous venovenous haemodiafiltration can be used to achieve successful re-equilibration of profound hypernatraemia.
- ▶ Adding hypertonic saline to the replacement bags of the filter dialysate allows for a slower rate of correction by creating a smaller electrolyte gradient.
- ▶ This appears to have been safe and effective and perhaps highlights an area for potential research in life-threatening electrolyte imbalance.
- ▶ Physiological reserve varies widely across patients. This case demonstrates this and serves as a reminder that the 'one size fits all' approach to sepsis ought to be adopted with caution.
- ▶ More research is required to elucidate the idiosyncratic responses to physiological compromise.

Most commonly, these reports describe an acute (<48 hours), iatrogenic rise in serum sodium concentration, which is rapidly corrected either by intravenous fluid administration or renal replacement therapy.^{8–10} Severe, chronic hypernatraemia secondary to dehydration has also been described, although less frequently.¹¹

Of the cases that describe the use of renal replacement therapy to correct the serum sodium, a small number of them describe the addition of hypertonic saline to the dialysate fluid, creating a smaller (and, importantly, adjustable) sodium concentration gradient, allowing for a more gradual re-equilibration.^{1 6 11} This case adds to the small number of reports that describe the successful correction of severe hypernatraemia using CVVHDF, with a reducing concentration of dialysate sodium: a serum sodium of 147 was achieved after 5 days of renal replacement therapy, with no adverse neurological sequelae encountered. This method seems to have been effective and safe, and perhaps adds weight to Nur *et al*'s¹ suggestion that the role of renal replacement therapy in the management of life-threatening hypernatraemia could be further explored.

Finally, despite invasive group A streptococcal bacteraemia often being associated with extreme states of physiological compromise and significant mortality, this patient never required vasopressor or other organ support, despite the additional compromise of severe renal injury and electrolyte imbalance. This perhaps demonstrates the variety with which patients can behave when faced with illness and may be an example of where greater understanding of individual data could lead to personal and precise treatment strategies and improved outcomes.

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