CASE REPORT

Hyponatraemia-induced rhabdomyolysis complicated by anuric acute kidney injury: a renal replacement conundrum

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SUMMARY

Hyponatraemia-induced rhabdomyolysis is a rare, but reported phenomenon, particularly in patients with chronic schizophrenia on depot antipsychotics prone to psychogenic polydipsia. To the best of our knowledge, there are no reported cases of hyponatraemia-induced rhabdomyolysis complicated by oligo-anuric acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT). The initiation of CRRT is complicated in severe hyponatraemia, predominantly due to the need to avoid rapid changes in tonicity associated with rapid changes in sodium. We report a case of severe hyponatraemia (104 mmol/L) complicated by oligo-anuric rhabdomyolysis-induced AKI and our management of the renal prescription.

BACKGROUND

Hyponatraemia is an unusual, but documented, cause of rhabdomyolysis that is in and of itself worth reporting. However, when complicated by oligo-anuric acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT), an additional complexity is introduced, namely the need to slowly correct the severe hyponatraemia. The degree of control which this necessitates could not be achieved with traditional renal prescriptions and modifications to the solution used for replacement therapy are required. Here, we present our solution to a rare complication of an unusual presentation.

CASE PRESENTATION

A 50-year-old indigenous man presented to a rural hospital reporting weakness and pain all over his body and was found to have a severe hyponatraemia. Previous medical history includes chronic schizophrenia for which he received 3 weekly paliperidone depot, intellectual impairment possibly related to an acquired brain injury, a history of alcohol abuse (abstinent for ~6 months) complicated by several episodes of alcoholic pancreatitis and a history of poor engagement with health services. Over the preceding 6 months, there had been five emergency department presentations at the rural hospital with hyponatraemia secondary to psychogenic polydipsia, all of which were successfully managed with fluid restriction. His most recent documented sodium was 131 mmol/L ~5 weeks prior to this presentation.

On this presentation, he was found to have a hypotonic (234 mmol/kg) hyponatraemia (104 mmol/L)

complicated by an AKI with a serum urea of 15 mmol/L and a creatinine of 487 μ mol/L from a baseline creatinine of 67 μ mol/L 2 months prior. He was reportedly passing 5–10 mL/hour of extremely dark urine. Urinary sodium was 23 mmol/L, urinary potassium was 46 mmol/L and urine osmolality was 224 mmol/kg.

He was at baseline mental state (indeed nursing notes indicate that he was sitting up in bed eating dinner), and there had been no history of seizures or seizure-like activity. He had no neurological findings on examination. Despite this, a 60 mL bolus of hypertonic (3%) saline was administered on the advice of a general physician while aero-medical retrieval to our hospital was arranged.

On arrival to Alice Springs following an uneventful transfer, his mental state and serum sodium were unchanged. He had, however, progressed to anuric renal dysfunction, with a corresponding rise in his serum creatinine to 617 μ mol/L, while creatine kinase was significantly elevated at 564 015 U/L.

INVESTIGATIONS

Extensive investigation of the possible cause of his presumed rhabdomyolysis was unremarkable. Autoimmune screen, recreational drug screen, metabolic screen, venom detection screen and a rhabdomyolysis genetic panel were normal. There was no clinical evidence of either trauma, neuroleptic malignant or serotonin syndrome. Prior to intubation, there was no focal muscle pain to suggest a widespread myositis, and he was mobilising to and from the toilet without assistance to pass stool. C reactive protein was mildly elevated at 86 mg/L but white cell count was normal, and he had been afebrile since his initial presentation 16 hours earlier. Ultrasound examination failed to show diffuse muscle oedema or signs of necrosis.

Urine microscopy revealed <10 leucocytes per high-powered field (HPF), >100 erythrocytes/HPF (with normal red cell morphology) and only scanty granular casts.

Further investigations of the hyponatraemia were similarly unremarkable with normal thyroid function tests and normal serum cortisol. Although serum tonicity suggested a hypotonic hyponatraemia, blood glucose, lipids and serum protein were undertaken which were also all within normal limits.

TREATMENT

Continuous veno-venous haemofiltration (CVVHF) was initiated using a modified commercial

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replacement fluid in order to allow a slow increase in sodium (table 1). He required intubation and mechanical ventilation to facilitate this due to his intellectual impairment.

OUTCOME AND FOLLOW-UP

By day 5, his biochemistry had largely normalised (figure 1, panels A–G) allowing a change to continuous veno-venous haemodiafiltration (CVVHDF), and he was making small amounts of urine (5–30 mL/hour). His clinical course was remarkable only for the development of a ventilator-associated pneumonia on day 4 of his admission, which was treated according to local guidelines. He was extubated on day 11 with relatively preserved power (5/5 all limbs) and a similar mental state as on arrival. He required several episodes of intermittent haemodialysis for biochemical indications while his native renal function improved, and he was discharged to the ward on day 21 of his admission.

DISCUSSION

Hyponatraemia-induced creatine kinase increases (presumably associated with rhabdomyolysis) have been reported in the literature—often as case studies or small case series.^{1–6} They have universally been in patients with chronic schizophrenia, often prescribed depot antipsychotics and in whom hyponatraemia was precipitated by psychogenic polydipsia. This is the first case in the published literature to the best of our knowledge in which hyponatraemia-induced rhabdomyolysis has been complicated by a severe oligo-anuric AKI (RIFLE–F) requiring continuous renal replacement therapy with a successful outcome.⁷ What is equally remarkable in this case is that there were no neurological signs despite a serum sodium of 104 mmol/L.

The pathophysiology underlying hyponatraemia-induced rhabdomyolysis has not been elucidated, and an animal model has failed to replicate the process.⁸ Most evidence has come from observational studies of elite athletes and previous case studies from which three theories have been postulated.^{1–6 9 10} One relates to an impaired ability for cells to extrude calcium via the sodium–calcium exchanger located in the cell wall of myocytes due to a reduced transcellular gradient.^{11 12} The

subsequent increase in intracellular calcium results in activation of proteases and lipases resulting in myocyte injury. A second hypothesis relates to so-called osmotic shock. Cell swelling due to changes in tonicity and fluid shifts are associated with increased reactive oxygen species, which in turn trigger localised increases in cytosolic calcium.^{10 13} The unregulated increase in intracellular calcium subsequently activates calcium-dependent proteases leading to myocyte breakdown.¹⁰ Previous studies have suggested that this process is initiated following correction of hyponatraemia, however, in the case reported here the creatine kinase was elevated when hyponatraemia was at its nadir. A third hypothesis is that intracellular hypokalaemia, induced by the need for the cell to extrude potassium to maintain cellular volume in the setting of hypotonicity, is the cause of myocyte injury.¹² This mechanism may explain why the serum potassium in this man was not also elevated despite his severe AKI, the potassium being excreted prior to the onset of oliguria.

Faced with an AKI of a severity which prevented endogenous normalisation of sodium homeostasis, the decision to initiate CRRT was made to correct his severe hyponatraemia and remove the presumed trigger of his rhabdomyolysis. It seems likely that this event would have been terminal without CRRT. However, patients with severe hyponatraemia and AKI pose a unique therapeutic challenge. Hypertonic saline is not indicated when there are no neurological complications arising from hyponatraemia, yet sodium homeostasis is unlikely to be restored in the setting of oliguric renal injury. Pharmacotherapy (loop diuretics or V2 receptor antagonists) are not likely to be successful at reduced glomerular filtration rates, while correction of the hyponatraemia must be at a rate that avoids the risk of osmotic demyelination syndrome. Current guidelines recommend a rise in serum sodium of no more than 8 mmol/L/day in the setting of chronic hyponatraemia.¹⁴

CRRT was chosen in preference to an intermittent mode (iHDx) in order to maintain tighter control over fluid and electrolyte shifts and, in particular, to avoid a rapid increase in the serum sodium concentration and the associated risk of osmotic demyelination syndrome. The intermittent haemodialysis machines in use at our facility (which incorporates the largest

Table 1 Effect of either removing replacement fluid and replacing with sterile water, or adding sterile water on electrolyte concentrations

	Total volume of replacement fluid* (L)	Final concentration (mmol/L)						
		Na ⁺	K ⁺	Ca ²⁺	Mg ²⁺	Cl [−]	HCO ₃ [−]	C ₃ H ₆ O ₃
Volume removed and replaced with sterile water (mL)								
0	5.00	140.0	0	1.75	0.50	109.5	32.0	3.0
250	5.00	133.0	0	1.66	0.48	104.0	30.4	2.9
500	5.00	126.0	0	1.58	0.45	98.6	28.8	2.7
750	5.00	119.0	0	1.49	0.43	93.1	27.2	2.6
1000	5.00	112.0	0	1.40	0.40	87.6	25.6	2.4
1250	5.00	105.0	0	1.31	0.38	82.1	24.0	2.3
1500	5.00	98.0	0	1.23	0.35	76.7	22.4	2.1
Volume of sterile water added (mL)								
0	5.00	140.0	0	1.75	0.50	109.5	32.0	3.0
250	5.25	133.3	0	1.67	0.48	104.3	30.5	2.9
500	5.50	127.3	0	1.59	0.45	99.5	29.1	2.7
750	5.75	121.7	0	1.52	0.43	95.2	27.8	2.6
1000	6.00	116.7	0	1.46	0.42	91.3	26.7	2.5
1250	6.25	112.0	0	1.40	0.40	87.6	25.6	2.4
1500	6.50	107.7	0	1.35	0.38	84.2	24.6	2.3

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C₃H₆O₃, lactate; Ca²⁺, calcium; Cl[−], chloride; HCO₃[−], bicarbonate; K⁺, potassium; Mg²⁺, magnesium; Na⁺, sodium.

Figure 1 Biochemistry changes over the first 7 days of the ICU admission. Day-1 represents his presentation to a remote hospital, and day 0 represents his admission to intensive care.

(A) Serum potassium; (B) serum bicarbonate; (C) serum chloride; (D) serum urea; (E) serum creatinine; (F) serum creatine kinase; (G) serum sodium. CVVHF, continuous veno-venous haemofiltration; CVVHDF, continuous veno-venous haemodiafiltration; ICU, intensive care unit.

haemodialysis centre in the Southern Hemisphere) are only able to dialyse down to a sodium concentration of 120 mmol/L, and this would have precipitated too rapid a rise in serum sodium. The use of CRRT in preference to iHDx has considerable support in the literature for these reasons.¹⁵ Furthermore, it was thought that iHDx would have been particularly difficult for this patient given his acquired brain injury.

The mode of CRRT chosen in the first instance was ultrafiltration in which a transmembrane pressure forces liquid through a semipermeable membrane relying on solvent drag to clear small-sized and middle-sized molecules.¹⁶ It was thought that ultrafiltration, in preference to haemodialysis, or the more commonly used haemodiafiltration, would allow tighter control over electrolyte balance, an approach supported in the literature.¹⁷ Ultrafiltration, however, requires the use of replacement fluid, and there are no commercial fluids which are hypotonic with low concentrations of sodium. The commercial solution available in our remote intensive care unit is Haemosol, which was diluted with sterile water to reduce the sodium concentration to allow a slow correction of the established hyponatraemia. Table 1 shows the volume of fluid to be removed and replaced with sterile water (or simply sterile water added) to the replacement fluid to achieve the desired concentration of sodium. It is obvious, but important to note that there is concurrent dilution of the other electrolytes contained in the replacement fluid and that strict aseptic techniques are necessary to reduce the risk of nosocomial blood stream infection.

Although previous reports have suggested adding sterile water to the standardised commercial bags of replacement fluid/dialysate, diluting the sodium sufficiently would have necessitated adding up to 1.3 L of sterile water to the existing bags potentially exceeding the volume capacity of the original bag and adding to the risk profile to nursing staff of lifting heavier bags of fluid.^{17–20} Instead electrolyte-rich fluid was removed from the bags and sterile water added in order to target slow sodium increases, initially using replacement fluid with a sodium concentration of 107 mmol/L for the first 8 hours and assessing the response with hourly arterial blood gasses. Over subsequent days, the concentration of sodium in the replacement fluid was slowly increased until the serum sodium was >125 mmol/L, at which time the mode of CRRT was changed to the more traditional CVVHDF in order to optimise his biochemical profile, remove excess free water and prepare him for extubation. He was successfully extubated on day 11 but required several sessions of intermittent haemodiafiltration which he tolerated while awake.

Learning points

- Hyponatraemia as a result of psychogenic polydipsia can result in rhabdomyolysis and acute kidney injury.
- Renal replacement therapy prescription must be altered when severe hyponatraemia is present.
- Clinicians must be aware of the electrolyte composition of commercial replacement fluids used for CRRT, and these must be altered to allow a slow correction of the serum sodium concentration to avoid demyelination syndrome.

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