Multifaceted hyponatraemia: a case of changing aetiologies

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Introduction

Hyponatraemia is the most common electrolyte disturbance encountered both in the community and hospitalised patients, with a prevalence of 8% in the community and a particular risk among the geriatric population. The aetiology of hyponatraemia is multifactorial, with drugs and a poor diet being among the most common causes. Syndrome of inappropriate antidiuretic hormone secretion and endocrinopathies are less frequent aetiologies. This case report presents a patient with symptomatic severe hyponatraemia with an initial serum sodium level of 97mmol/litre, with recurrence following 10 days of hospitalisation. The change in aetiology, corroborated by investigations and response to treatment, are discussed in detail as thiazide-associated hyponatraemia and syndrome of inappropriate anti-diuretic hormone are described.

Discussion

True hyponatraemia is defined as a serum sodium level of less than 135 mmol/litre in hypotonic plasma, ie a serum osmolality of less than 275 mOsm/kg. Biochemically,

Case report

An 82-year-old woman, known to suffer from hypertension and anxiety, presented to the emergency department with a 2-day history of headache, nausea with retching and fluctuating alertness. A collateral history from her daughter revealed a 1-week history of decline with decreased oral intake. She had recently been started on indapamide to treat high blood pressure. No other new medications had been prescribed. She had previously been independent with no history of cognitive impairment.

On initial physical examination, the patient was alert and oriented with no focal neurological deficits. She had dry mucous membranes with mildly reduced skin turgor. There was no postural hypotension and the rest of the clinical examination was unremarkable. Initial investigations revealed a profound hyponatraemia of 97 mmol/litre and a hypokalaemia of 2.72 mmol/litre. Serum electrolytes taken 2 months previously were normal. **Table 1** summarises the initial investigation results.

The patient was admitted to a high dependency unit under constant cardiac monitoring and was initially started on 0.9% saline with supplemental potassium. Treatment was reviewed and indapamide was stopped. Within a few hours of admission, the patient became increasingly confused and fell from her bed, sustaining a head injury and a right maxillary fracture. Her Glasgow coma scale score was 3 and hypertonic saline (3% saline) was administered in two successive infusions.

An initial rise in serum sodium level from 97 to 118 mmol/litre was observed. Serum sodium levels were taken at 2-hourly intervals with respective changes in intravenous fluid administration, as outlined in **Figure 1**. The patient's serum sodium level continued to improve until normalisation. The patient's general condition also improved, as she became more alert and oriented with a normal Glasgow coma scale score. She also started eating and drinking, causing intravenous fluids to be stopped at day 7 of admission. However, serum sodium level was noted to decrease again at day 11. This was initially ascribed to poor oral intake, resulting in the administration of oral rehydration sachets and 0.9% saline. Despite this, serum sodium level continued to decrease further to 118 mmol/litre. Repeat investigations were consistent with a diagnosis of syndrome of inappropriate anti-diuretic hormone (**Table 1**). Fluid restriction to 1.5 litres per day was ensured. Serum sodium levels improved once again, normalising before the patient was discharged to a rehabilitation hospital.

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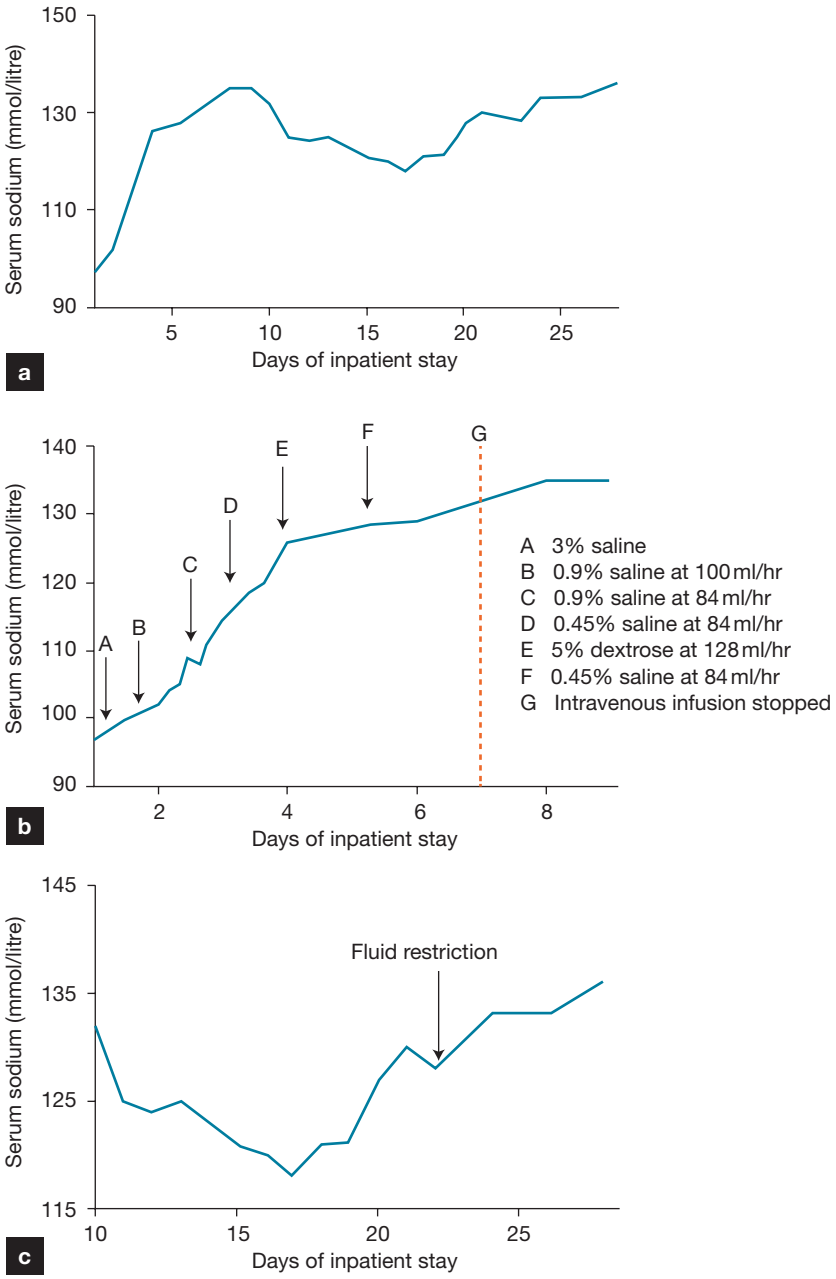

Figure 1. a. Serum sodium levels during inpatient stay. b. Hyponatraemia management and response between day 1 and 8. c. Hyponatraemia management and response between day 10 and 30.

hyponatraemia can be mild (serum sodium level between 130 and 135 mmol/litre), moderate (serum sodium level between 125 and 129 mmol/litre) or severe (serum sodium level <125 mmol/litre). Clinically, moderately severe hyponatraemia is characterised by confusion, headaches and nausea, whereas severe hyponatraemia is characterised by a reduced level of consciousness (a Glasgow coma scale score of 8 or below), significant lethargy, seizures, vomiting or cardiopulmonary distress. Hyponatraemia is considered chronic 48 hours since its initial development.

In this case, the patient presented with a biochemically severe hyponatraemia. Hypertonic saline was administered secondary to the development of clinically severe hyponatraemia, as per European Society for Endocrinology guidelines (Spasovski et al, 2014). At presentation, laboratory investigations revealed a low serum osmolality and normal glucose, protein and cholesterol levels, thus confirming a diagnosis of true hyponatraemia. Based on the patient's hypovolaemic state and the presence of high urinary sodium (64 mmol/litre), thiazide-associated hyponatraemia secondary to indapamide was the most likely diagnosis.

Table 1. Investigation results on admission at day 1 and day 11

	Result (day 1)	Result (day 11)	Normal ranges
Serum sodium	97 mmol/litre	121 mmol/litre	136–145 mmol/litre
Serum potassium	2.72 mmol/litre	3.8 mmol/litre	3.5–5.1 mmol/litre
Serum osmolality	232 mOsm/kg	256 mOsm/kg	282–300 mOsm/kg
Urine sodium	64 mmol/litre	41 mmol/litre	54–190 mmol/litre
Urine osmolality	522 mOsm/kg	189 mOsm/kg	50–1200 mOsm/kg
Cortisol	1754 nmol/litre	991 nmol/litre	145–619 nmol/litre
Thyroid-stimulating hormone	1.394 mIU/ml	1.377 mIU/ml	0.3–3 mIU/ml
Free thyroxine	22.78 pmol/litre	20.1 pmol/litre	11.9–20.3 pmol/litre
Prolactin	Not considered necessary during initial assessment	239 mIU/litre	56–619 mIU/litre*
Follicle-stimulating hormone	Not considered necessary during initial assessment	61.3 U/litre	21.7–153 U/litre*
Luteinizing hormone	Not considered necessary during initial assessment	14.7 U/litre	11.3–39.8 U/litre*
Oestradiol	Not considered necessary during initial assessment	49 pmol/litre	0–118 pmol/litre*

**Hormone range for postmenopausal women*

A normal random cortisol level (1754 mmol/litre) excluded mineralocorticoid deficiency. The low potassium level at presentation and the improvement in the serum sodium level following the cessation of indapamide further supported this diagnosis.

The diagnosis of thiazide-associated hyponatraemia depends on the improvement of serum sodium levels following the cessation of the thiazide diuretic, with no recurrence (Filippone et al, 2020). However, the hyponatraemia recurred, putting the initial diagnosis into question. The patient was clinically euvolaemic at the time. Repeat investigations showed a low serum osmolality of 255 mOsm/Kg with normal glucose, protein and cholesterol levels, categorising the patient as having hypotonic hyponatraemia with euvolaemic status. Initiation of intravenous fluids and oral rehydration solution aggravated the hyponatraemia. Laboratory findings showed the presence of a relatively high urinary sodium excretion (40 mmol/litre), a normal cortisol level and a normal thyroid and renal function. Urinary osmolality was less than maximally dilute (189 mOsm/kg) and in the absence of diuretics, syndrome of inappropriate secretion of antidiuretic hormone was this time the likely diagnosis.

The antecedent cause for syndrome of inappropriate secretion of antidiuretic hormone is thought to have been the head injury on admission. Traumatic brain injury is frequently associated with hypopituitarism and acute hyponatraemia. This is usually transient with very few reported cases of chronic or recurrent hyponatraemia. It is thought to be caused by transient damage to the pituitary stalk or posterior pituitary and consequent hypersecretion

Learning points

- Being multifactorial, hyponatraemia, especially in older patients, may be challenging to diagnose. Investigations of serum and urine, together with the clinical picture, are crucial in understanding the aetiology of hyponatraemia.
- Drug-induced hyponatraemia is easily reversible and should always be part of the initial differential diagnosis.
- The occurrence of two separate causes of hyponatraemia within 10 days has not been documented in the literature.
- The aetiology of hyponatraemia should not be assumed but investigated, as seen in this case with recurrence of hyponatraemia secondary to syndrome of inappropriate secretion of antidiuretic hormone.

of antidiuretic hormone (Dick et al, 2015). The improvement in serum sodium levels following fluid restriction further confirmed this diagnosis.

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