CASE REPORT

Syndrome of inappropriate antidiuretic hormone secretion: a story of duloxetine-induced hyponatraemia

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SUMMARY

Hyponatraemia is the most commonly encountered electrolyte abnormality in clinical practice. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) accounts for nearly 60% of all hyponatraemias. Selective serotonin reuptake inhibitors (SSRIs) are well known to have side effects of SIADH. There have been few reported cases of serotonin norepinephrine reuptake inhibitors (SNRIs) causing SIADH-induced hyponatraemia. Duloxetine is one type of SNRI used to treat several conditions, including depression and diabetic neuropathy. We present a case of a 76-year-old woman with a history of fibromyalgia who had recently been prescribed duloxetine for her condition. On admission to the hospital, her sodium decreased to a low of 118 mmol/L. Evaluation for other causes of hyponatraemia yielded negative results. Duloxetine was discontinued and after 3 days the patient's sodium increased to 130 mmol/L. The purpose of this case report is to highlight the importance of having suspicion for rare but real side effects of medications such as duloxetine.

BACKGROUND

Hyponatraemia, defined as a serum sodium level less than 135 mmol/L, is the most commonly encountered electrolyte abnormality in clinical practice. Hospitalised patients and the elderly are at increased risk of developing hyponatraemia.¹ Although often found incidentally on laboratory results, patients with hyponatraemia can manifest with headache, change in mental status, seizures or loss of consciousness. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) accounts for nearly 60% of hyponatraemia by some studies.² SIADH is characterised by clinical euvolemia, low serum osmolality, inappropriately elevated urine osmolality and urine sodium greater than 40 mmol/L. Other types of euvolemic hyponatraemia causes, such as thyroid dysfunction and adrenal insufficiency, must be excluded. Some of the most common causes of SIADH include medications such as antiepileptics and antidepressants. A case-control study found that serotonergic antidepressants increase the risk of hyponatraemia fourfold.³

CASE PRESENTATION

We present a case of a 76-year-old woman with a history of debilitating fibromyalgia, diet-controlled type II diabetes and hypertension. She presented to the emergency department with abdominal pain

and constipation. On presentation, the patient had symptoms of nausea but had not vomited. She denied loss of sensation, weakness, difficulty with memory and other neurological symptoms. She also denied any shortness of breath, chest pain and other pulmonary symptoms. The patient's medications on admission included aspirin, pantoprazole, polyethylene glycol and quinapril, as well as 30 mg duloxetine, daily. She was not on any diuretic. On physical examination, she appeared euvolemic, without signs of dehydration or volume overload. An abdominal X-ray revealed adynamic ileus. During initial evaluation, she was found to have serum sodium of 124 mmol/L.

INVESTIGATIONS

The patient's serum osmolality was 254 mmol/L and her urine osmolality was 415 mmol/L. Urine sodium was found to be 150 mmol/L. Her sodium continued to decline to as low as 118 mmol/L. Thyroid-stimulating hormone (TSH) was found to be normal at 2.25 μ IU/mL and early morning free cortisol was 1.50 μ g/dL. Free T3 was low at 2.7 pmol/L but free T4 was normal at 1.46 ng/dL. Haemoglobin was 13.9 g/dL and potassium was 4.3 mmol/L.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis in the setting of the history and laboratory findings included adrenal insufficiency and hypothyroidism-induced hyponatraemia. However, with a cortisol level of 1.50 μ g/dL, adrenal insufficiency was less likely. Regarding hypothyroidism, it appeared that the patient's hypothyroidism was under control, with a normal TSH level. She had also carried this diagnosis for a long time with stable sodium. The combination of

Figure 1 The progression of the patient's serum sodium in relation to duloxetine administration.

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Figure 2 Algorithm for the differential diagnosis and approach to a patient with euvoletic hyponatraemia.

normal TSH, decreased T3 and a higher than expected cortisol level in the setting of hypothyroidism corresponds with euthyroid sick syndrome and not a true hypothyroid state. A true hypothyroid state usually has a low cortisol level. Other differentials to consider in euvoletic hyponatraemia are diuretics use and other causes of SIADH such as traumatic brain injury, some cancers and other medications. Our patient was not on diuretics and had not had an injury to the brain. She was also not on other medications that result in SIADH except for the duloxetine. It is worth mentioning that hypothyroidism has been reported to be a cause of paralytic ileus. Our patient's hypothyroid state was due to euthyroid sick syndrome and could have certainly contributed to her ileus.

TREATMENT

The patient was restricted to 1 L of water per day for 6 days. She was also administered 0.5 mg sodium chloride tablets twice a day for 5 days. This was increased to three times a day after no improvement was seen with the former. When a further three days passed without improvement, the dose was increased to 1 mg three times daily. On further evaluation, it was discovered that duloxetine had been started 2 days prior to admission. Prior to start of the medication the patient's serum sodium was 132 mmol/L. The duloxetine was discontinued three days after the patient's serum sodium had slowly risen from 118 mmol/L to 129 mmol/L (figure 1).

Regarding her ileus, the patient had minimal relief from polyethylene glycol alone so Senna was added to the regimen. In addition to medications, the patient was turned frequently and encouraged to ambulate. A repeat abdominal X-ray showed resolved ileus.

OUTCOME AND FOLLOW-UP

The patient was discharged at a later date with serum sodium of 130 mmol/L.

DISCUSSION

This case emphasises the diagnostic criteria for SIADH, including euvolectmia, in the setting of elevated urine osmolality and low serum osmolality (figure 2). Physicians must be aware that medications that interact with serotonergic pathways commonly cause SIADH.⁴ There have been several case reports of duloxetine-induced SIADH, some of which suggest that the elderly population is at particularly high risk of drug-induced hyponatraemia.⁵ It is suggested that SSRIs and SNRIs such as duloxetine cause SIADH by increasing ADH secretion via stimulation of α adrenergic and serotonergic receptors in the hypothalamus.⁶ Until 2012, previous case reports showed that most duloxetine-induced SIADH were in women.^{7–9} This was the case in our patient. However, in 2012, Choi *et al*¹⁰ reported a case of duloxetine-induced SIADH in a middle-aged male. In most of the cases reported, hyponatraemia resulted after 2–3 days of starting medication. Our patient had started the medication 2 days prior to admission. Treatment of SIADH includes removing the inciting agent and restricting fluids. In more extreme cases, salt tablets and hypertonic saline may be used.¹¹

Learning points

- Consider rare side effects of medications when work ups for suspected conditions are normal.
- Medications that interact with serotonergic pathways commonly cause syndrome of inappropriate antidiuretic hormone secretion (SIADH).
- Treatment for SIADH includes removing the inciting agent and restricting fluids.

Competing interests None declared.

Patient consent Obtained.

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