CASE REPORT

Hyponatraemia secondary to cerebral salt wasting syndrome following routine pituitary surgery

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Hyponatraemia is a common complication of transsphenoidal surgery, occurring several days postoperatively; women and patients with Cushing’s syndrome may be more prone to its development (1, 2). It has been suggested that leakage of antidiuretic hormone (ADH) from surgically damaged posterior pituitary nerve terminals is a likely mechanism, and the recommended treatment is that of fluid restriction with or without glucocorticoid therapy (1, 2).

Case report

A 53-year-old housewife presented with a history suggestive of an epileptiform seizure 4 months previously, with memory loss and headaches since that time. She had a history of hypertension treated with 2.5 mg of bendrofluazide daily. Examination, including visual field assessment, was unremarkable and her blood pressure was 140/80 mmHg. Haematological and biochemical parameters were normal. Thyroid function tests (TSH, 1.2 mIU/l; free thyroxine, 15 pmol/l) and prolactin (385 mIU/l) were normal. A computed tomography (CT) scan showed a suprasellar lesion abutting the optic chiasm for which surgical transsphenoidal excision was undertaken. The lesion was shown histologically to be a Rathke’s cyst. Postoperative recovery was uncomplicated and she was discharged home 6 days after surgery on 2.5 mg of bendrofluazide daily. A biochemical profile at discharge showed a sodium content of 131 mmol/l, but was otherwise normal. She presented 10 days after discharge (16 days postoperatively) with headache, nausea and vomiting. A CT scan showed no new abnormality and a biochemical profile was not performed. On day 2 of admission she had clinically improved, but on day 3 she suffered two tonic clonic fits and became unrousable. Her blood pressure was 90/60 mmHg. Biochemical investigation showed profound hyponatraemia (sodium 120 mmol/l), hypokalaemia (potassium 2.8 mmol/l) and hypo-osmolality (serum 213 mOsmol/kg, normal range 275–325; urine 405 mOsmol/kg, normal range 300–1000), with a urine sodium (“spot” sample) excretion of 13 mmol/l. A diagnosis of the syndrome of inappropriate antidiuretic hormone (SIADH) was made and intravenous hypertonic saline (3.6%) was infused at 125 ml per hour. In addition, intravenous frusemide (40 mg), hydrocortisone (100 mg four times daily) and phenytoin (100 mg three times daily) were also initiated. Six hours later a central venous pressure measurement was found to be 9 cmH2O, leading to a re-evaluation of the diagnosis of SIADH and a change in her management. Hypertonic saline and frusemide therapy were discontinued and normal saline was infused slowly (1 litre, 12-hourly) to correct the fluid deficit. Her serum sodium had increased to 121 mmol/l within 12 h. After 24 h (day 4 of admission) her biochemistry revealed: sodium, 120 mmol/l; potassium, 2.8 mmol/l; urea, 2.9 mmol/l; urinary sodium, 80 mmol/l; plasma osmolality 259 mOsmol/kg; urine osmolality, 304 mOsmol/kg. Her central
venous pressure measurements were between +2 and +8 cmH₂O after 36 h of treatment. A retrospective cortisol measurement on day 1 prior to hydrocortisone administration was 900 nmol/L, excluding ACTH insufficiency. By day 5 of admission she was alert, oriented and obeying commands. Her sodium had risen to 131 mmol/L and thyroid function tests were reported as normal. On day 6 her sodium was 138 mmol/L and all other biochemical parameters were within the normal range and remained so thereafter. On day 7 she became unresponsive, with laboured respiration, and developed generalized spasticity of her limbs. An MRI scan showed bilateral basal ganglia lesions with no pontine involvement, which was compatible with a diagnosis of extrapontine myelolysis. Over a 10-month period she has remained bio-chemically stable, but the generalized spasticity remains and she has frequent prolonged grand mal epileptiform seizures.

Discussion

Hyponatraemia following transsphenoidal surgery is common, occurring in 12 of 52 patients studied in one series (1) and 32 of 91 patients in another (2). Patients with Cushing’s syndrome may be more at risk from developing postoperative hyponatraemia than other pituitary adenoma subtypes and women appear more prone to develop the condition (1, 2). The onset of hyponatraemia occurs 6–8 days postoperatively, resolves on average after 5 days but may range from 1 to 13 days (2). The phenomenon may be unrecognized and may remit spontaneously (1, 2). No residual neurological morbidity or mortality secondary to late-onset hyponatraemia following transsphenoidal pituitary surgery has been reported until now (1).

Hyponatraemia associated with an increased extracellular volume is seen in congestive cardiac failure, liver cirrhosis and SIADH secretion, the latter resulting from a dilutional hyponatraemia secondary to increased renal water resorption. However, no clinically demonstrable increase in extracellular volume can be seen in SIADH, unlike that seen in cardiac failure, cirrhosis and nephrotic syndrome. Conversely, hyponatraemia with extracellular volume depletion is seen in renal failure, Addison’s disease and diuretic therapy, all of which were excluded here. In cerebral salt wasting syndrome (CSWS), extracellular volume reduction and hyponatraemia result from a progressive natriuresis with a concomitant diuresis (3–5). Cerebral salt wasting syndrome is associated with cerebral insults such as subarachnoid haemorrhage (3–5). However, very rarely has CSWS been documented following transsphenoidal pituitary surgery (6). The biochemical picture may be identical in CSWS and SIADH; both present with hyponatraemia, a low serum osmolality, elevated urinary sodium excretion and an inappropriately concentrated urine osmolality (5). However, they may be distinguished by the extracellular volume expansion in SIADH and the extracellular volume depletion in CSWS, determined easily by central venous pressure measurement. Other non-diagnostic measurements include creatinine clearance (normal or increased in SIADH; normal or decreased in CSWS), urine volume (normal or decreased in SIADH; normal or increased in CSWS) and blood urea (normal or decreased in SIADH; normal or increased in CSWS). A central venous pressure measurement will establish the diagnosis and guide treatment of either water restriction in the SIADH or the replacement of both the sodium and water deficit in CSWS. However, in this case hyponatraemia with hypotension and a low urine sodium are not features of SIADH (7), and therefore central venous pressure measurement may not have been necessary if the diagnosis of CSWS had been made immediately. The initial urinary sodium content of 13 mmol/L was misleadingly low and was probably secondary to the marked total sodium depletion that had occurred by that time, with a more representative urinary sodium content of 80 mmol/L being recorded when sodium replacement was begun.

The aetiology of the extracellular volume depletion and concomitant urinary sodium excretion in CSWS is still unclear, but atrial natriuretic peptide (ANP) secretion has been implicated (3–5). In a study of 14 patients following subarachnoid haemorrhage both ANP and ADH were elevated (3), whilst in a study of two patients following transsphenoidal surgery both ANP and ADH measurements were within the normal range (6). In addition to ANP, it has been suggested that ouabain-like factors secreted from the hypothalamus in response to sodium and water retention inhibit the cell membrane sodium/potassium pump in the renal tubules, leading to a natriuresis (8, 9).

This patient showed hyponatraemia with extracellular volume depletion and a natriuresis characteristic of the cerebral salt wasting syndrome. It is likely that the condition had started to develop at the time of her discharge 6 days postoperatively, when her serum sodium was retrospectively noted to be 131 mmol/L, with a further progression over the 10-day period until she represented. The 2.5 mg of bendrofluazide that she was taking for hypertension would have been a contributory factor for the development of the hyponatraemia, but it would have been unlikely to cause the sodium loss so quickly. The SIADH secretion was thought to be the cause of her hyponatraemia and, because of its severity fluid restriction was supplemented with hypertonic saline and diuretic therapy. This management strategy would have resulted in an exacerbation of the existing fluid depletion. The cause of the neurological complications following hyponatraemia can be accounted for by the rate of sodium repletion, which appears to occur if the rate of sodium repletion is greater than 12 mmol Na/L per day (10, 11). Emergency treatment of symptomatic severe hyponatraemia may safely be initiated by
infusion 3% saline at 1–2 ml/kg per hour for 2 to 3 h: once the emergency has passed, conservative measures so that the overall rate of correction does not exceed 12 mmol Na/l per day can be substituted (12). However, the neurological sequelae of hyponatraemia may occur by a number of mechanisms. It has been suggested that it is the presence of a cerebral insult rather than the level or rapidity of sodium correction that accounts for the development of myelinolysis (13). However, animal models suggest that it is the initial rapid fall in serum sodium that causes the primary insult, whilst others suggest that any rapid serum sodium osmolality shifts may precipitate the onset of myelinolysis, especially those precipitated by rapid iatrogenic correction (4, 10, 11, 14).

In two large series of hyponatraemic patients following transsphenoidal surgery, it was thought that the mechanism of hyponatraemia was due to ADH secretion, and water restriction was suggested as an effective and safe method to correct the hyponatraemia (1, 2). In both series, standard laboratory criteria for diagnosis were used: in one series, ADH was measured in a subset of patients and found not to differ before and after surgery (2). Without measurement of the intravascular volume, CSWS cannot be excluded as a possible cause for the hyponatraemia in some of these patients. Whilst intravascular volume measurement is probably not necessary or justified in the majority of hyponatraemic patients, we suggest that the insertion of a central venous pressure line should be undertaken in ill patients with severe symptomatic hyponatraemia, to distinguish between SIADH and CSWS and guide the appropriate management.

In conclusion, cerebral salt wasting syndrome is very rare following transsphenoidal pituitary surgery but should be considered in the differential diagnosis if subsequent postoperative hyponatraemia occurs. Cerebral salt wasting syndrome cannot be distinguished from the SIADH on standard biochemical criteria alone, but, in the absence of hypotension, measurement of the central venous pressure will differentiate between the two conditions, allowing appropriate treatment. Treatment is directed towards reduction of the extracellular volume in SIADH; conversely, replacement of both extracellular volume and the sodium deficit is necessary in CSWS. Cautious serum sodium correction may prevent the irreversible neurological sequelae of pontine and extrapontine myelinolysis.

References


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