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Case Report

Water balance disorders after neurosurgery: the triphasic response revisited

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Abstract

Water balance disorders after neurosurgery are well recognized, but detailed reports of the triphasic response are scarce. We describe a 55-year-old woman, who developed the triphasic response with severe hyper- and hyponatraemia after resection of a suprasellar meningioma. The case illustrates how sudden and dramatic the changes in water balance after neurosurgery can be. The biochemical profile suggested central diabetes insipidus and the syndrome of inappropriate antidiuretic hormone secretion. The underlying pathophysiology was further analysed using fractional excretions, measurements of renin, aldosterone and vasopressin and a metyrapone test. Diagnostic, therapeutic and preventive strategies for these intriguing but complex cases are proposed.

Keywords: diabetes insipidus; hypernatraemia; hyponatraemia; meningioma; SIADH

Background

Water balance disorders after neurosurgery are well recognized and may give rise to hyponatraemia or hypernatraemia. Interestingly, water balance disorders can also develop in a biphasic or even triphasic fashion with reported incidences of 3.4 and 1.1%, respectively [1]. Here, we present the case study of a 55-year-old female who developed the triphasic response after a subfrontal resection of a suprasellar meningioma. Because detailed reports of the triphasic response are scarce [2,3], our objective was to analyse its natural course and emphasize the sudden changes in water balance. In addition, we investigate the underlying pathophysiology, and formulate strategies for the management of these cases.

Case report

A 55-year-old female (no previous medical history, no medication) was referred, because a central nervous system tumour was suspected after she experienced decreased acuity and blurring of her left eye. Physical examination was unremarkable (no Cushingoid or acromegalic appearance, normal female hair pattern). Serum sodium and endocrine parameters were normal. Magnetic resonance imaging showed a suprasellar mass that was anatomically distinct from the pituitary, compressed the chiasma opticum and was enhanced by gadolinium contrast. These findings suggested the lesion to be a meningioma. She was started on dexamethasone (4 mg four times daily), and surgery was scheduled. She underwent neurosurgery using a subfrontal approach to resect the meningioma and decompress the optical and chiasm nerves, while leaving the pituitary stalk intact (according to the surgical notes). The procedure was successful, although it involved manipulation of the pituitary stalk and posterior pituitary. Pathological examination confirmed a transitional meningioma (World Health Organization Grade I) with a low proliferation index of ∼1% (immunohistochemistry for MIB-1, a tumour proliferation marker).

Postoperatively, she developed two polyuric and one antidiuretic phases (Figure 1). Polyuria (372 mL/h) developed in the first hours after surgery and led to a negative fluid balance (−2 L) and hypernatraemia (157 mmol/L). The patient was not hyperglycaemic and did not receive mannitol. Desmopressin (4 μg intravenously q.d. for 2 days) reduced polyuria (117 mL/h), raised specific gravity (1024 kg/L) and, together with intravenous fluids (2 L of dextrose 5% water per day between Days 1 and 2) and *ad libitum* drinking, restored normonatraemia (Figure 1).

On the 6th postoperative day (<48 h after hypernatraemia), she developed hyponatraemia (serum sodium 128 mmol/L, urine sodium 109 mmol/L, urine osmolality 809 mOsm/kg). She was clinically euvolaemic, had a normal kidney function (41 μmol/L) and a low-normal haematocrit (36%). Additional parameters are shown in Table 1. Despite the institution of fluid restriction (1–1.5 L/day), her intake exceeded her marginal urine production (19 mL/h), producing a positive fluid balance (∼ +1.5 L) and a further fall in haematocrit (35%) and serum sodium to 121 mmol/L (Figure 1). Although gross symptoms of hyponatraemia (seizures, coma) were

Table 1. Laboratory measurements during antidiuretic and polyuric phase

Measurement	Parameters (unit, reference)	Antidiuretic phase (Day 6)	Polyuric phase (Day 14)
Pituitary hormones	TSH (mU/L) (0.4–4.3)	0.113	0.959
	LH (U/L) (15–90)	10.4	16.9
	FSH (U/L) (35–150)	15.4	40.8
	Prolactine (U/L) (0.06–0.93)	0.25	0.14
	IGF-1 (nmol/L) (11–31)	17	19.2
	Vasopressin (pg/mL) (0.20–4.7)[b]	0.50	0.31
Adrenal function	Renin (μU/mL) (10–60)	15.3	–
	Aldosterone (pg/mL) (50–250)	169	–
	Response to metyrapone	–	Normal[a]
Acid-base	pH (7.35–7.45)	7.48	–
	pCO_2 (mmHg) (36–49)	36	–
	Bicarbonate (mmol/L) (21–27)	26	–
	Base excess (−3 to +3)	3	–
Uric acid and urea	Uric acid (mmol/L) (0.12–0.34)	0.09	–
	FE uric acid (%) (~10%)	23	–
	FE urea (%) (varies)	41.8	–

[a]Low cortisol (51 nmol/L, reference 200–800 nmol/L), high adrenocorticotropic hormone (46.2 pmol/L, reference <11 pmol/L), high 11-deoxycortisol (745 nmol/L, reference after metyrapone >350 nmol/L).
[b]1 pg/mL corresponds with 1.08 pmol/L vasopressin.
FE, fractional excretion; TSH, thyroid stimulating hormone; FSH, follicle stimulating hormone; LH, luteinising hormone; IGF-1, insulin-like growth factor-1.

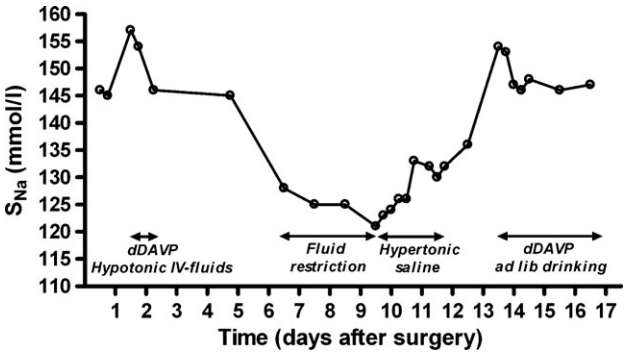

Fig. 1. Triphasic serum sodium course after neurosurgery. Abbreviation: dDAVP, desamino-D-arginine-vasopressin (synthetic vasopressin).

absent, she was confused, had headaches and unsteadiness of gait, which resulted in a fall. Because adrenal insufficiency and/or symptomatic hyponatraemia as a cause of the collapse could not be ruled out, dexamethasone (which had been tapered to 2.5 mg three times daily) was converted to hydrocortisone (10 mg b.i.d.), and treatment with hypertonic saline was commenced. After discontinuing hypertonic saline at 133 mmol/L, fluid restriction increased serum sodium further to 136 mmol/L (Figure 1). At this time, the patient again started producing hypotonic polyuria (specific gravity 1001, urine production 250 mL/h) for which desmopressin (0.1 mg orally) was administered once. Although this improved her urine concentration ability (urine osmolality 351 mOsm/kg), she became hypernatraemic overnight (serum sodium 154 mmol/L), while still remaining on fluid restriction. After desmopressin wore off, urine osmolality measured 130 mOsm/kg and urine sodium 22 mmol/L. *Ad libitum* fluid intake gradually decreased serum sodium to 147 mmol/L, while urine osmolality remained low (144 mOsm/kg). One year after surgery, she remains normonatraemic (serum sodium 142 mmol/L) with the use of desmopressin (0.1 mg b.i.d.). Discontinuation of desmopressin to evaluate if central diabetes insipidus still persists has not been tried. Magnetic resonance imaging showed no recurrence of meningioma, a normal aspect of the pituitary and its stalk, and a normal position of the chiasma opticum.

Discussion

This case illustrates the dramatic and sudden changes in water balance that may occur after neurosurgery. It appeared that mere manipulation of the pituitary stalk was sufficient to cause these perturbations, which has been shown before [4]. However, we cannot exclude the possibility that physical or vascular injury to the stalk occurred.

The pathophysiology of the triphasic response appears to be early hypothalamic dysfunction, subsequent release of vasopressin from the degenerating pituitary and, finally, depletion of vasopressin stores. Therefore, the two polyuric phases are consistent with central diabetes insipidus, for which the dDAVP-responsive hypotonic polyuria was additional evidence.

Hyponatraemia after neurosurgery is usually attributed to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), although hypocortisolism and cerebral salt wasting (CSW) have also been reported [4]. A number of observations favour SIADH in our case, including the positive fluid balance during the development of hyponatraemia, the tendency towards metabolic alkalosis [5] and the high fractional excretions of uric acid and urea. Transient hypopituitarism (see low pituitary hormones, Table 1) may have been present, although secondary adrenal insufficiency seems unlikely, because the patient received glucocorticoids throughout the postoperative course.

The fact that vasopressin was not suppressed during hyponatraemia suggests inappropriate secretion or

Table 2. Diagnosis and treatment of dysnatraemia after neurosurgery

Monitoring
A triphasic response (polyuria–antidiuresis–polyuria) can occur after neurosurgery
Urine output, specific gravity and/or osmolality should be monitored every 4–6 h in the early postoperative period
To prevent dysnatraemia, changes in urine output and tonicity should directly lead to appropriate intervention
Serum sodium should be checked between the 6th to 9th postoperative day for developing hyponatraemia
Diagnosis
In the absence of hyperglycaemia or mannitol, polyuria (3 L/day or 40 mL/kg) with a low urine osmolality (<250 mOsm/kg) is usually due to central DI, but can also be nephrogenic DI (especially after subfrontal surgery)
A rise in urine osmolality (100% if complete, 15–50% if partial) after dDAVP (10 μg nasally or 4 μg i.v.) confirms central DI
Hyponatraemia is usually caused by SIADH, but cerebral salt wasting and secondary adrenal insufficiency should also be considered
The presence of a metabolic alkalosis and a high $FE_{uric\ acid}$ (usually >12%) may help to differentiate SIADH from the other causes
Treatment
Central DI may require (temporary) treatment with dDAVP (initially 10–20 μg nasally 1–2x/day or 0.1–0.2 mg orally 3x/day), while monitoring serum sodium and urine osmolality
Hyponatraemia due to SIADH may be treated with fluid restriction, hypertonic saline or perhaps vasopressin-receptor antagonists (little experience)

dDAVP, desamino-D-arginine-vasopressin (synthetic vasopressin); DI, diabetes insipidus; FE, fractional excretion; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

leakage. However, urine osmolalities of around 800 mOsm/kg usually correlate with much higher vasopressin levels (~4 pg/mL) [6]. Therefore, precursors of vasopressin or other substances with antidiuretic properties may have been acting, as was previously reported in a patient with a macroprolactinoma [6]. In the future, the analysis of copeptin may be of value, because it is a stable marker of vasopressin release [7].

It is increasingly recognized that even patients without gross symptoms of hyponatraemia have central nervous system impairments that predispose to falls, which may warrant more aggressive treatment [8]. One option would be to fluid restrict the patients even more, although some authors advocate a low threshold for hypertonic saline, especially after neurosurgery [9]. A new treatment option are the vasopressin-receptor antagonists, for which the first successful results in neurosurgery were recently reported [10].

It has been difficult to identify patients at risk, but predisposing factors appear to relate both to the disease (macroadenoma [11], microadenoma, craniopharyngioma, Rathke cleft cyst [12]) and to the surgery (degree of manipulation [4], intraoperative cerebrospinal fluid leak [12]). Our case demonstrates that even frequent monitoring is sometimes unable to prevent severe dysnatraemia. Successful prevention probably involves a psychological switch by not waiting until frank dysnatraemia has developed, but to act as soon as urine output and tonicity change. This is even more important, because patients may have impaired thirst (also in this case: no complete normalization of hypernatraemia despite *ad libitum* drinking, Figure 1). This requires an index of suspicion for treating and consulting physicians and specific instructions to nursing staff, especially in non-intensive care settings. Our recommendation is to check for polyuria in the immediate postoperative period, for hyponatraemia between Days 6 and 9, and prolong monitoring if necessary for the delayed onset of central diabetes insipidus. These and other management strategies are summarized in Table 2; we also recommend two recent excellent reviews [13,14].

Conflict of interest statement. None declared.

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