The triple-phase response – problems of water balance after pituitary surgery

RS Lindsay, JR Seckl, PL Padfield

Summary

A 29-year-old woman presenting with persistent headache and oligomenorrhoea was found to have a pituitary adenoma which was treated surgically. Postoperatively she developed diabetes insipidus which resolved on treatment with desmopressin acetate. She represented 11 days post surgery with nausea and vomiting and inappropriate antidiuresis was diagnosed in an infectious diseases unit. On re-admission to our unit cranial diabetes insipidus was confirmed by water deprivation. This case demonstrates the need for careful monitoring of patients after pituitary and suprasellar surgery or head injury.

Keywords: pituitary surgery, diabetes insipidus, inappropriate antidiuresis syndrome, water balance

Diabetes insipidus¹ and syndrome of inappropriate antidiuresis² are uncommon but important complications of pituitary surgery and of head injury. Despite the fact that they represent the opposite ends of the spectrum of water balance problems they may occur serially in the same patient after pituitary trauma^{3,4} making the management of such cases more complex.

Case report

The patient was referred at the age of 24 years to an infertility clinic with failure to conceive for two years. She was of normal weight for her height and her only significant past medical illness had been an episode of pelvic inflammatory disease eight years previously. Routine biochemistry was normal apart from a slightly raised prolactin at 503 U/l (reference range 60–360 U/l). Laparoscopy was performed and was normal with patent fallopian tubes. She was treated with clomiphene but failed to

conceive and did not attend for further investigations or management.

At the age of 29 she complained of persistent headache and had developed oligomenorrhoea. Serum prolactin level was raised at a level of 2520 U/l. She was further investigated with a computed tomography (CT) scan which displayed a low density lesion within a normal pituitary fossa reported as being consistent with a pituitary adenoma.

The patient was treated with a course of bromocriptine but despite the gradual introduction of this drug she suffered from nausea and it had to be discontinued. After discontinuation she became amenorrhoeic and was referred for pituitary surgery.

Transsphenoidal adenomectomy was carried out. Peri-operatively she was treated with hydrocortisone in a dose of 100 mg tid. On the first postoperative day she passed 4.5 l of dilute urine (specific gravity < 1.005) and was found to have a raised plasma sodium (Na 149 mmol/l (132–144), K 3.7 mmol/l (3.3–4.7), CO₂ 25 mmol/l (24–30) and urea 1.5 mmol/l (2.5–6.6)). A diagnosis of postoperative diabetes insipidus was made. She was treated with 4 µg of desmopressin acetate (DDAVP) daily on three of the next four days which was associated with a fall in her urine output and correction of plasma sodium to 141 mmol/l on the fourth postoperative day.

Her recovery was otherwise uneventful, glucocorticoid replacement was gradually reduced to 25 mg of cortisone acetate orally twice daily. She was mobilised and allowed home on the 8th postoperative day. Sodium on the 7th postoperative day had fallen to 132 mmol/l despite no DDAVP having been administered for 48 hours.

She was seen by her general practitioner 11 days following surgery with a two-day history of nausea and vomiting such that she had been unable to take her glucocorticoid replacement. She was referred to an infectious diseases unit with a putative diagnosis of gastroenteritis and was found to be hyponatraemic (Na 113 mmol/l, K 3.5 mmol/l, CO₂ 24 mmol/l, urea 3.4 mosm/kg, plasma osmolality 238 mosm/kg, urine, osmolality 697 mosm/kg). A diagnosis of syndrome of inappropriate antidiuresis was made, she was treated with fluid restriction, demeclocycline (200 mg tid) and parenteral glucocorticoid (hydrocortisone 100 mg tid). After two days her sodium had risen to 143 mmol/l and at that stage she was referred to our unit for further assessment.

Features of the triple response

The triple response describes a sequence of problems of water balance observed in patients after head injury or pituitary surgery. Early diabetes insipidus is followed by inappropriate antidiuresis at 4–7 days prior to a return either to normal or to diabetes insipidus

Department of
Medicine, University
of Edinburgh, Western
General Hospital,
Edinburgh EH4 2XU,
UK
RS Lindsay
JR Seckl
PL Padfield

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Box 1

On arrival in our unit demeclocycline was discontinued. Anterior pituitary function was assessed and was found to be satisfactory (thyroxine 133 nmol/l; short synacthen test, basal cortisol 476 nmol/l and 30 min 747 nmol/l; prolactin 445 U/l, luteinising hormone 5.9 U/l and follicle-stimulating hormone 5.0 U/l) and glucocorticoid replacement was discontinued. By the second day her urine output was once again rising and a formal water deprivation test provoked a rise in plasma osmolality from 295 mosm/kg to 300 mosm/kg over seven hours while urine osmolality failed to rise above 179 mosm/kg. Urine volume was over 150 ml at the end of the test. In response to 1 µg of DDAVP urine osmolality rose to 408 mosmol/kg. A diagnosis of cranial diabetes insipidus was made and she was started on intranasal DDAVP, after which water balance returned to normal.

The patient has been maintained on DDAVP since that time and her anterior pituitary function has remained normal. Her periods subsequently returned and she has since become pregnant.

Discussion

The diagnosis of postoperative diabetes insipidus depends upon the demonstration of several features (boxes 2 & 3).⁵ Diabetes insipidus has occurred in as many as 5–20% of adult patients after transsphenoidal pituitary surgery in some series,¹ usually has its onset within 24 hours and is transient in the majority of cases.⁶ Signs of recovery after a few days should be treated with caution however, as this may indicate a 'triple response'.^{3,4} In this response initial postoperative diabetes insipidus gives way after 4–8 days to a remission or even a period of clinical inappropriate antidiuresis before eventual recurrence of the diabetes insipidus. This triple response has been observed after both pituitary surgery^{3,4} and head injury and can lead to a false assumption that the diabetes insipidus has been transient as in our patient and slower recognition of further water balance problems.

Diabetes insipidus

Demonstrated by hypotonic (< 300 mosm/kg) polyuria (> 2 ml/kg hourly) together with increased plasma osmolality (> 300 mosm/kg) after excluding glycosuria, mannitol administration or renal failure

Box 2

Syndrome of inappropriate antidiuresis

Demonstrated by inappropriately concentrated urine (> 100 mosm/kg) in the presence of both euvolaemia and low plasma osmolality (< 275 mosmol/kg)

Box 3

The hyponatraemia observed in this case on the 11th postoperative day might have three possible aetiologies. Glucocorticoids play a permissive role in the generation by the kidney of a dilute urine and hyponatraemia is a feature of glucocorticoid deficiency.⁶ The patient had been unable to take oral glucocorticoid replacement for two days prior to her second admission. In the event, as her pituitary–adrenal function later proved to be normal and as her symptoms preceded her inability to tolerate oral glucocorticoid it seems unlikely that glucocorticoid deficiency was the cause of her illness and hyponatraemia.

The second possibility might be a continued action of the administered DDAVP. The doses used were larger than those routinely used in our unit for the postoperative management of cranial diabetes insipidus but by the time of her admission to the infectious diseases unit no DDAVP had been administered for six days. Intranasal DDAVP produces 8–20 hours of antidiuresis⁷ although the plasma half-life is far shorter than this, therefore continued biological action of DDAVP seems an unlikely explanation for her hyponatraemia at this stage.

The biochemistry on admission to the infectious diseases unit was in keeping with a syndrome of inappropriate antidiuresis and the subsequent demonstration of cranial diabetes insipidus by water deprivation indicates a triple response. The transient resolution of the diabetes insipidus seen in this triple response is thought to represent nonspecific release of antidiuretic hormone by degenerating posterior pituitary tissue⁸ and following this there is usually a reversion to a permanent state of cranial diabetes insipidus. With its onset in the second week after surgery when postoperative monitoring may be less intense and the usually vague symptoms associated with hyponatraemia syndrome of inappropriate antidiuresis is easy to miss but may carry considerable morbidity for the patient.²

The hyponatraemia of syndrome of inappropriate antidiuresis should be corrected with fluid restriction. The use of hypertonic saline infusions is only indicated if severe central nervous system symptoms are present⁹ and then only with caution and careful monitoring. Hyponatraemia is associated with the catastrophic complication of central pontine myelinolysis¹⁰ but it is now appreciated that this complication relates to the overrapid correction of usually chronic hyponatraemia and most authorities would recommend that plasma sodium levels do not rise by more than 12 mmol in 24 hours.¹¹ Demeclocycline has no place in the acute management of syndrome of inappropriate antidiuresis.

Learning points

Water balance may be complex after both surgery and head injury with sequential diabetes insipidus and inappropriate antidiuresis in the same patient

Box 4

More patients are undergoing pituitary and suprasellar surgery. Careful monitoring of such patients is necessary to avoid the morbidity associated with both diabetes insipidus and with syndrome of inappropriate antidiuresis. Such electrolyte problems are most likely to be

seen by specialist neurosurgical or endocrine units but may be of relevance to other specialities as this can also occur after head injury. In our patient's case, presentation was to an infectious diseases unit.

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Figure 1 Venogram of the right leg showing extensive occlusion of the deep veins of the calf with lateral displacement and stricture of the popliteal vein

Department of
Medicine, York
District Hospital,
Wigginton Road,
York, UK
EM Scott
FJ White
PE Jennings

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Popliteal vein thrombosis associated with femoral osteochondroma and popliteal artery pseudoaneurysm

EM Scott, FJ White, PE Jennings

Summary

Deep vein thrombosis is a common condition thought to be caused by impaired venous blood flow or hypercoagulable blood states. However, often no predisposing cause can be found. We describe a deep vein thrombosis formed in association with femoral osteochondroma and popliteal artery pseudoaneurysm. It is an interesting combination that has only been described once before.

Keywords: deep vein thrombosis, femoral osteochondroma, popliteal artery pseudoaneurysm

Case report

A 37-year-old office worker was admitted with an acutely swollen, painful right calf. She had been taking the oral contraceptive pill since the birth of her child two and a half years previously and was otherwise fit and well. She was a keen horse-rider but had no history of trauma. On examination the right calf was significantly swollen, hot, tense, and tender. The popliteal fossa was noted to be very hard but the knee had a full range of movement. Peripheral pulses were normal. A diagnosis of deep vein thrombosis was made. Venography (figure 1) confirmed extensive occlusion of the deep veins of the calf but those of the thigh and

pelvis were not involved. The popliteal vein was noted to be displaced laterally by an osteochondroma and there appeared to be a tight localised stricture at the junction of the popliteal vein with the deep femoral vein. An ultrasound scan of the popliteal fossa revealed a large (6×2.5 cm) popliteal pseudoaneurysm arising from the posterior aspect of the popliteal artery. A plain radiograph of the knee showed the presence of several femoral exostoses just above the knee joint, surrounding the pseudoaneurysm. The knee joint itself looked normal. An arteriogram (figure 2) confirmed the popliteal pseudoaneurysm and its relation to the osteochondroma. It arose at the junction of the superficial femoral artery with the popliteal artery and contained a large amount of thrombus.

She underwent ligation of the popliteal artery and bypass grafting using the long saphenous vein, from which she has made a good recovery.

Discussion

Osteochondroma is a cartilage-capped bony exostosis. It is the commonest benign tumour of bone. The lesion may be single or multiple and may arise in any bone formed by endochondral ossification, but the long bone metaphyses are the commonest sites. They are usually asymptomatic, but recognised comp-