An unusual cause of confusion and hyponatraemia in an elderly patient

R Greer, J Rahman & V Parfitt

Abstract

A large proportion of patients presenting on the acute medical take are frail and elderly and a significant proportion of these will have symptoms such as confusion, reduced mobility and electrolyte disturbances. These symptoms are typically attributed either to the iatrogenic effects of prescribed medications, disturbances in fluid balance and possible infective causes. We describe the case of a gentleman who presented with delirium, reduced mobility and hyponatraemia who was subsequently found to have pituitary failure secondary to pituitary apoplexy.

Keywords

Apoplexy, Hyponatraemia, Pituitary.

Learning Points

- An early morning cortisol should be checked in all patients presenting with confusion and hyponatraemia where there is no clear precipitant
- A normal ACTH stimulation test does not exclude the possibility of ACTH deficiency
- Appropriate treatment of pituitary failure should result in rapid resolution of the symptoms

Case Study

A 94 year old man with a background of type 2 diabetes, cerebrovascular disease and benign prostatic hypertrophy was admitted to the Acute Medical Unit (AMU) with fluctuating confusion, slurred speech and urinary incontinence. His medication comprised aspirin, metformin and tamsulosin. He was an ex-smoker and did not drink alcohol. He lived in the annexe of his daughter's house, and was able to manage basic activities of daily living, only requiring help with domestic tasks.

He had been admitted 3 months earlier with an episode of confusion and pyrexia at which time investigations revealed a normal serum sodium, mildly elevated CRP and neutrophilia (see table 1); he was treated for a urinary tract infection and his confusion improved, although his daughter reported that his mobility and appetite had been less good since then.

On this admission, he was apyrexial. Cardiovascular, respiratory and abdominal examinations were unremarkable. His blood pressure was 108/62, with no postural measurements recorded due to his unsteadiness. His abbreviated mental test (AMT) score was 4/10 with no focal neurological deficit on peripheral or cranial nerve examination.

Blood tests revealed a normal white cell count, with C-reactive protein of 47mg/L (<10mg/L). Serum sodium was low at 123mmol/L and potassium normal at 4.5mmol/L. TSH was 0.93mu/L (0.27-4.2mu/L). Chest x-ray was unremarkable, the electrocardiogram showed normal sinus rhythm and urinalysis was negative for leucocytes and nitrites. Cranial CT scan showed age-related generalised involutional changes and patchy ischaemic white matter change, with no evidence of intracranial haemorrhage.

Despite intravenous fluid administration, repeat sodium levels two days later had fallen (see table 1). Serum osmolality was low at 258mOsm/kg (normal range 275-295mOsm/kg), urine osmolality and urine sodium levels were appropriate at 322 mOsm/kg, and15mmol/L respectively.Serum cortisol level measured at 9am was low at 52nmol/L.

An ACTH stimulation test (short Synacthen test, SST) and full pituitary function tests were requested. Free T_4 levels were low at 4.0pmol/L (12.0-22.0pmol/L) and the SST showed a normal response. Testosterone level was low at 0.3 nmol/L, with normal prolactin, FSH and LH levels.

The findings of persistent hyponatraemia, low cortisol with normal SST, and low-normal TSH with low FT_4 were suggestive of pituitary pathology. Hydrocortisone was commenced at a dose of 20mg pre-breakfast, 10mg midday and 10mg evening. MRI of the pituitary gland revealed a focus of high intensity within the anterior lobe of the pituitary, suggestive of haemorrhage. (See Figure 1.)

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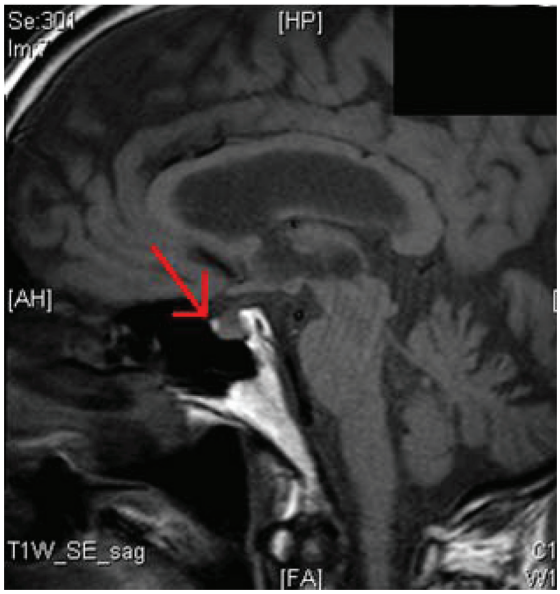

Figure 1. MRI pituitary suggestive of anterior pituitary haemorrhage.

The diagnosis of hypopituitarism secondary to pituitary haemorrhage was confirmed and oral hydrocortisone was continued at a dose of 10mg pre-breakfast, 5mg midday and 5mg in the evening. He was also started on levothyroxine 50 micrograms. With treatment, his AMT score improved to 6/10, mobility increased and he was discharged sixteen days after admission.The patient was followed up in endocrinology outpatient clinic six weeks after discharge and continues to show improvement.

Discussion

We describe the case of a gentleman who presented with delirium, reduced mobility and hyponatraemia who was subsequently found to have pituitary failure secondary to pituitary apoplexy. Delirium (acute confusional state) is a common condition, affecting up to 30% of all older patients admitted to hospital[2] and can be precipitated by a number of causes.[3] Electrolyte disturbances, are also common in older patients presenting to hospital with acute confusion. Hyponatraemia is commonly caused by dehydration or diuretic use and may itself be a cause for delirium; alternatively it may occur in the presence of another explanation for confusion, such as infection, particularly respiratory tract infections complicated by the syndrome of inappropriate ADH (SIADH). In this case there were no apparent sources of infection,the patient was not taking diuretics or other culprit medications, paired serum and urine osmolalities were not suggestive of SIADH and there was no response to intravenous rehydration. These factors alerted the clinical team to the possibility of an endocrine explanation.

We advocate checking a morning cortisol in patients presenting with confusion and hyponatraemia where there is no clear precipitant.

Box 1. Summary of recommendations for the management of patients with suspected pituitary apoplexy.[1]

Clinical Assessment

- Detailed history should focus on symptoms of pituitary dysfunction such as hypogonadism, followed by a thorough physical examination including cranial nerves and visual fields.
- In haemodynamically unstable patients, intravenous hydrocortisone should be administered immediately after baseline endocrine tests have been taken. Do not delay for short synacthen testing.

Radiological Assessment

- Urgent MRI scan must be done if pituitary apoplexy is suspected to confirm diagnosis (Pituitary CT can be done if MRI is contraindicated).

Management

- Careful assessment of fluid and electrolyte balance, replacement of corticosteroids, and supportive measures to ensure haemodynamic stability.
- Patients with pituitary apoplexy, who are haemodynamically unstable, should be commenced on empirical steroid therapy. Hydrocortisone 100-200mg as an intravenous bolus is appropriate, followed either by 4-6mg per hour by continuous intravenous infusion or 50-100mg six hourly by intramuscular injection, after drawing blood samples to check renal and liver function, clotting screen, full blood count, random cortisol, prolactin, fT4, TSH, IGF1, GH, LH, FSH, testosterone (men) and oestradiol (women).
- For patients not fulfilling these criteria, consider steroids if 9am cortisol < 550nmol/L.
- Conservative management is indicated for patients without neuro-ophthalmic signs or those with mild, stable signs and symptoms (as in this case).
- Surgical management is considered for patients with severe neuro-ophthalmic signs such as severely reduced visual acuity, severe and persistent or deteriorating visual field defects or deteriorating level of consciousness.

Furthermore, if hypoadrenalism is suspected, random blood cortisol and ACTH levels should be taken immediately prior to starting steroids. The laboratory should receive the ACTH sample on ice for storage, only to be tested if the cortisol level is found to be low. Box 1 summarises the recommended management of a patient with suspected pituitary apoplexy. It is important to recognise that a low cortisol level in an unwell patient, even if it is a random sample, indicates a failure to mount a normal stress response to illness due to insufficiency in the hypothalamo-pituitary-adrenal axis.

It should be noted that, despite a low early morning cortisol and subsequent diagnosis of pituitary apoplexy, this patient had a normal response to SST. It is recognised that the adrenal glands

Box 2. Precipitating factors in pituitary apoplexy.

- Systemic hypertension (26%)
- Major surgery, in particular coronary artery bypass surgery
- Dynamic pituitary function tests with GNRH,TRH and CRH
- Anticoagulation therapy
- Coagulopathies
- Oestrogen therapy
- Initiation or withdrawal of dopamine receptor agonist
- Radiation therapy
- Pregnancy
- Head trauma

atrophy following a 4 – 6 week lack of stimulation from ACTH, thereby inhibiting the adrenal response to SST. However the fact that this gentleman had a normal SST would suggest a relatively acute onset of apoplexy.This is supported by the normal sodium levels noted at the time of his previous hospital admission. Acute physicians should be aware that, in the presence of a low early morning cortisol, a normal SST does not exclude the possibility of a pituitary cause.

Pituitary apoplexy is a rare but potentially life-threatening condition caused by haemorrhage or infarction of the pituitary gland.[4]Peak incidence is in the fifth decade, but can affect all age groups.[5,6] In 65 – 95% of cases, a pre-existing pituitary adenoma is present.[7] Other common precipitants are listed in Box 2. Patients usually present with sudden onset, severe headache, visual defects or ophthalmoplegia, confusion or altered state of consciousness and are found to have variable endocrine deficits. However, up to 20% of pituitary apoplexy cases may be silent, or sub-clinical, with radiological and pathological evidence of a haemorrhagic infarction but no acute symptoms, as was the case in our patient.Most patients presenting with apoplexy have hypopituitarism with decreased levels of all or several pituitary hormones, resulting in confusion and a decreased level of consciousness.[7] A sudden lack of cortisol, seen in 70% of cases of pituitary apoplexy due to a lack of adrenocorticotropic hormone (ACTH) secretion from the anterior pituitary gland,results in adrenal or Addisonian'crisis'. This may present acutely to the medical team with collapse, postural hypotension, hypoglycaemia and hyponatraemia, requiring immediate medical attention.

Insulin tolerance testing (ITT) is considered to be the Gold Standard for assessing function of the hypothalamo-pituitary-adrenal axis.[8]Insulin induces hypoglycaemia and, as part of the stress response, ACTH is released which subsequently stimulates cortisol secretion. However, this test can be unpleasant and potentially life-threatening for the patient. Side-effects range from minor symptoms, such as sweating and palpitations, to more serious sequelae such as seizures and coma due to hypoglycaemia. In individuals with severe, acute adrenal insufficiency, there is the risk of precipitating an Addisonian crisis and ITT would therefore not be advocated. In the case of our patient, we had already established that his short Synacthen test was normal, and in view of his age, frailty and co-morbidities, it was deemed inappropriate to pursue ITT.

Declaration of competing interests: nothing to declare

Table 1. Blood test results.

	Admission 1	Admission 2 Day 1	Admission 2 Day 3	Outpatient Clinic
White Cell Count	16.8 x10^9/L	4.9 x10^9/L	5.1 x10^9/L	6.2 x10^9/L
C-reactive protein	24mg/L	47mg/L		
Serum Sodium	135mmol/L	123mmol/L	121mmol/L	137mmol/L
Serum Potassium	4.7mmol/L	4.5mmol/L	4.4mmol/L	
TSH (0.27-4.2mu/L)	3.3 mu/L	0.93mu/L		0.05mu/L
Free T4 (12.0 - 22.0pmol/l)			4.0pmol/l	16.6pmol/l

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