Not just another fall in the elderly

Bilateral adrenal lymphoma presenting with adrenal insufficiency causing weakness

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Case history

Mr R L, 86 years of age, was admitted to a regional hospital under the care of his general practitioner after collapsing at home. He described a six month history of declining health with lethargy, poor appetite, sweats and weight loss. He had been previously healthy and still playing hockey. His past medical history included:

- epilepsy
- TURP
- reflux oesophagitis and hiatus hernia (endoscopy 1999)
- diverticulosis (colonoscopy 2000), and
- hypertension.

Medications at the time of admission included pantoprazole, bendrofluazide and phenobarbitone.

On examination he was mildly dehydrated and had postural hypotension (BP 120/60 supine, 80/- erect). There were no other abnormal neurological or cardiac findings to suggest on aetiology for his collapse and ailing health.

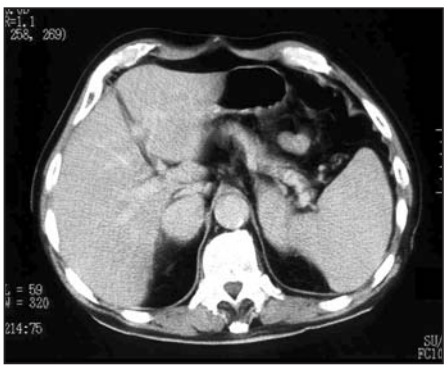

Figure 1. CT scan of abdomen showing bilateral adrenal mass lesions

Initial assessment

Serum electrolytes on admission revealed sodium 131 mmol/L, potassium 3.6 mmol/L, urea 10.9 mmol/L, creatinine 112 mmol/L. His bendrofluazide was ceased and he was given intravenous fluids. Despite this he remained hypotensive and his hyponatraemia persisted, although the minor renal impairment improved. The causes of hyponatremia were reviewed (Table 1). His lethargy, hypotension and hyponatremia were all in keeping with glucocorticoid deficiency.

Glucocorticoid deficiency

Advice was sought from the endocrinology department of the Fremantle Hospital (a tertiary referral centre) with regards to the appropriate investigations. A short synacthen test revealed adrenal insufficiency with a baseline cortisol concentration of 170 nmol/L and a 30 minute level of 340 (normal response cortisol >550 nmol/L after ACTH 250 ug IMI). An ACTH level was elevated at 15.3 pmol/L, consistent with primary adrenal failure. Other anterior pituitary hormones were checked and were normal. A CT scan of his chest and abdomen revealed bilateral adrenal masses (42x31 mm on the right, and 57x39 mm on the left), but no other mass lesions, lymphadenopathy or organ enlargement (Figure 1).

Mr R L was commenced on cortisone acetate and fludrocortisone with rapid improvement in his clinical state and normalisation of his blood pressure. He was discharged from hospital and arrangements were made for him to be seen in the endocrinology outpatient clinic of the hospital. At review he was well, with a blood pressure of 120/80 without postural changes, and he reported an improved appetite. Of note he had persistent sweats particularly at night.

What is the underlying cause?

Although primary adrenal insufficiency had been diagnosed on biochemical grounds the underlying aetiology had not

Table 1. Causes of hyponatraemia

Pseudohyponatraemia

- Normal plasma osmolality
  - hyperlipidaemia
  - hyperproteinaemia
- Increased plasma osmolality
  - hyperglycaemia
  - mannitol

Hypoosmolar hyponatraemia

- Primary sodium loss (secondary water gain)
  - integumentary sodium loss: sweating, burns
  - gastrointestinal loss: vomiting, fistula, obstruction, diarrhoea
  - renal loss: diuretics, hypoaldosteronism, salt wasting nephropathy, postobstructive diuresis
- primary water gain (secondary sodium loss)
  - primary polydipsia
  - decreased solute intake (beer potomania)
  - ADH release due to pain, nausea, drugs
  - syndrome of inappropriate ADH secretion
  - glucocorticoid deficiency
  - hypothyroidism
  - chronic renal insufficiency
- primary sodium gain (exceeded by secondary water gain)
  - heart failure
  - hepatic cirrhosis
  - nephrotic syndrome

Table 2. Causes of primary adrenal failure

Autoimmune adrenalitis	70-90%
	Anti-adrenal antibodies (including 21-hydroxylase)
	Isolated or part of polyglandular autoimmune syndromes
APS 1	Hypoparathyroidism, mucocutaneous candidiasis, adrenal insufficiency, primary hypogonadism
APS 2 (more common)	Primary adrenal insufficiency, thyroid disease, type 1 diabetes, primary hypogonadism, hypopituitarism, non-endocrine autoimmune disorders (vitiligo, lupus)
Infectious adrenalitis	Tuberculosis 7-20%
	Disseminated fungal infection, HIV
Haemorrhagic infarction	Meningococcus, pseudomonas, adrenal vein thrombosis, antiphospholipid syndrome, anticoagulants
Metastases	Lung, breast, melanoma, GIT, lymphoma
Drugs	Ketoconazole, metyrapone, aminoglutethemide, mitotane
Adrenoleukodystrophy	Young men, associated neurological symptoms

been clarified. The causes of primary adrenal failure are listed in Table 2. The most common cause is isolated adrenalitis, which would not be associated with mass lesions. Tumour was of concern given the size of the bilateral masses but there was no evidence of a primary lesion (otherwise normal chest and abdominal CT scan and normal colonoscopy two years ago). Mr R L had spent many years in the army in India and thus tuberculosis was a possibility, but he had no clear past history of exposure and a normal chest CT. Bilateral haemorrhage could give rise to mass lesions but would give sudden onset of symptoms and the radiological appearance was not in keeping with haemorrhage. Advice was sought from the radiology department who felt biopsy of one of the lesions could be possible.

Bilateral adrenal lymphoma

Mr R L consented to undergo CT guided biopsy of the adrenal gland. Histological examination of the specimen revealed a large cell B-cell non-Hodgkin's lymphoma. A bone marrow biopsy was performed and immunophenotyping was consistent with lymphomatous infiltrate. The diagnosis of lymphoma was a little unexpected but in retrospect he had significant night sweats, a 'B symptom' of lymphoma (weight loss, night sweats and fever). B symptoms (Ann Arbor classification) are less common in non-Hodgkin's lymphoma (approximately 20%) than Hodgkin's lymphoma.

He commenced treatment with a combination of cyclophosphamide, epirubicin, vincristine and prednisolone (CEOP) with G-CSF cover. To date (10 months since diagnosis) he has successfully completed six cycles of chemotherapy and is doing well. His night sweats and lethargy have resolved, and repeat CT scanning of the adrenals shows no residual masses (Figure 2), although he remains on glucocorticoid and mineralocorticoid replacement.

Non-Hodgkin's lymphoma affecting the adrenal glands is usually associated with widespread disease. Disease arising in the adrenal glands is termed primary adrenal lymphoma. Only five cases of bilateral adrenal lymphoma presenting with adrenal insufficiency have been reported in the English literature.[1–5] The case presented did have evidence of bone marrow infiltration on immunophenotyping by flow cytometry at the time of diagnosis. However, previous case reports have either not performed a bone marrow aspirate[1] or have not performed immunophenotyping to exclude bone marrow involvement.[2–5]

No doubt because of the rarity of this syndrome there is limited experience with treatment. Of the five cases reported three underwent various regimens of combination chemotherapy. Only one patient had a significant response to treatment and survived nine months[4]; the others all died within two months of diagnosis. It is there-

fore, a potentially treatable malignancy of the adrenal glands that has been described as having a poor prognosis.[5] Despite his age our patient has responded well to therapy. We follow with interest to see if there will be recovery of endogenous steroid production.

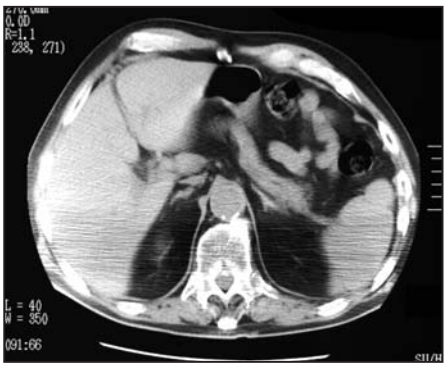

Figure 2. Resolution of mass lesions

Conclusion

We present this case, despite its rarity, because it highlights the successful communication between a primary care giving GP and a tertiary hospital with regards to a complex case. Although definitive tests and management were initiated in a tertiary hospital it was the patient's GP who astutely suspected the biochemical problem of glucocorticoid deficiency. Falls are common in the elderly, and the patient's other symptoms of lethargy and weight loss could easily have been ignored, or simply been explained as 'just getting old'. Although we aren't advocating extensive investigation in all cases, this was an instance were it has improved quality and probably duration of life.

Conflict of interest: none declared.

References

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