CASE REPORT

Rare cause of adrenal insufficiency

Justin WS Hii,^{1,2} Michael M Page,³ Andrew Wesseldine¹

¹Department of Geriatrics and General Medicine, St John of God Hospital, Subiaco, Western Australia, Australia

²Department of Anaesthesia and Pain Medicine, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

³Department of Clinical Biochemistry, PathWest, Fiona Stanley Hospital, Murdoch, Western Australia, Australia

Correspondence to

Dr Justin WS Hii,
justinwhii@gmail.com

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SUMMARY

A 72-year-old man presented with weight loss, night sweats and haemoptysis and was hypotensive. CT imaging showed rapidly enlarging bilateral adrenal masses, and he was found to have primary adrenal insufficiency. An adrenal gland biopsy revealed the rare diagnosis of primary adrenal lymphoma. This unique case highlights possible rare causes of adrenal masses and adrenal insufficiency, their investigation and management principles.

BACKGROUND

An adrenal incidentaloma is an adrenal mass discovered during a radiological examination performed for an indication other than adrenal pathology.¹ Most are non-functioning and fewer than 5% are malignant, although larger lesions are more likely to be.^{1,2} Adrenal insufficiency occurs where more than 90% of tissue has been destroyed.

CASE PRESENTATION

A 72-year-old man presented to his general practitioner with night sweats, 8 kg weight loss in 6 months and 2 months of haemoptysis. The patient had a history of tuberculosis treated in early adulthood with no other significant medical history.

Initial CT imaging of the chest showed mild scarring of the left lung apex. There was no lymphadenopathy. It also incidentally noted bilateral adrenal masses (maximum diameter of 5.1 cm on the right and 3.9 cm on the left, [figure 1](#)). Once a pheochromocytoma was excluded, due to the clinical picture and normal urine and plasma metanephrines ([table 1](#)), a diagnostic adrenal gland biopsy was planned.

While awaiting the biopsy, the patient became increasingly unwell with nausea and a productive cough, and was admitted to hospital. On admission,

Figure 2 Coronal CT image demonstrating rapid increase in size of left and right adrenal masses.

he was febrile (38.1°C), hypotensive (94/60 mm Hg) with no postural drop and not tachycardic. There were no other remarkable examination findings, specifically no palpable lymphadenopathy, and skin hyperpigmentation was not evident. There were no noted abdominal masses.

INVESTIGATIONS

Investigations revealed mild hyponatraemia ([table 1](#)). Although the morning serum cortisol level was within the reference interval (RI) at 283 nmol/L (RI, 140–600), suspicion of primary adrenal insufficiency was raised by a concurrently raised adrenocorticotrophic hormone level of 15.3 pmol/L (RI, 2–10). This suspicion was confirmed with a tetracosactrin (short Synacthen stimulation) test ([table 1](#)). Inflammatory markers were raised. Lactate dehydrogenase (LDH) was twice the upper reference limit (377 U/L (RI, <190)). Three sputum samples were negative for acid fast bacilli on microscopy and culture. Blood cultures were negative. Serology for HIV, hepatitis, cryptococcus and histoplasma was negative. Repeat CT 6 weeks after the original scan showed an increase in size of the adrenal masses to 8.8 cm on the right and 6.0 cm on the left ([figure 2](#)). There was no corresponding lymphadenopathy. Positron emission tomography imaging showed intense fluorodeoxyglucose uptake in both adrenal glands with moderate uptake in upper abdominal retroperitoneal para-aortic lymph nodes ([figure 3](#)). The latter had not been appreciated on earlier CT imaging. An ultrasound-guided adrenal biopsy was performed, and demonstrated extensive replacement of adrenal tissue with high-grade tumour. Immunohistochemistry was consistent with high-grade diffuse large B cell lymphoma.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses in this case included metastases, secondary lymphoma, pheochromocytoma, adrenocortical adenoma or carcinoma, hyperplasia,

Figure 1 Coronal CT images demonstrating left and right adrenal masses at initial presentation.

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Table 1 Initial inpatient investigation results

Analyte	Result	Reference interval
Haemoglobin (g/L)	124	130–180
White cells ($\times 10^9$ /L)	6.4	4.0–11.0
Platelets ($\times 10^9$)	123	150–400
Sodium (mmol/L)	128	136–145
Potassium (mmol/L)	4.3	3.5–5.3
Bicarbonate (mmol/L)	25	22–32
Urea (mmol/L)	3.9	2.9–8.2
Creatinine (μ mol/L)	92	55–115
eGFR (mL/min/1.73 m^2)	71	90–120
Osmolality (plasma) (mmol/kg)	270	275–295
Osmolality (urine) (mmol/kg)	473	50–1200
LDH (U/L)	377	(<190)
CRP (mg/L)	127	<8
ESR (mm/hour)	52	2–30
Cortisol, early morning (nmol/L)	283	140–600
Tetracosactrin (Synacthen) stimulation test (nmol/L), serum cortisol	96 (preinjection) 105 (30 min) 101 (60 min)	>430 at 30 min
ACTH (pmol/L)	15.3	2–10
Aldosterone (pmol/L)	<50	60–980
Renin (mU/L)	41	4–46
Normetanephrine (plasma) (pmol/L)	470	<1050
Metanephrine (plasma) (pmol/L)	<70	<300
Normetanephrine (urine) (μ mol/day)	2.75	<3.00
Metanephrine (urine) (μ mol/day)	<0.09	<1.30
3-Methoxytyramine (urine) (μ mol/day)	1.20	<2.70

All results are for serum or plasma, unless otherwise indicated.

ACTH, adrenocorticotrophic hormone; ALP, alkaline phosphatase; ALT, alanine aminotransferase; CRP, C reactive protein; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase.

adrenal haemorrhage and infection.¹ Tuberculosis was particularly considered in this patient owing to his history.

TREATMENT

Initial management included steroid replacement for adrenal insufficiency, and empirical antituberculosis therapy. There was rapid improvement in clinical status, thought to be due to adrenal hormone replacement therapy. After the adrenal biopsy results became available, antituberculosis therapy was ceased, the patient was referred to the haematology service and commenced on a cyclophosphamide, hydroxyl doxorubicin, Oncovin and prednisolone (CHOP)-based chemotherapy regimen with methotrexate central nervous system prophylaxis.

OUTCOME AND FOLLOW-UP

After seven cycles of chemotherapy, the patient developed septicaemia and died shortly thereafter.

DISCUSSION

Despite secondary adrenal involvement by lymphoma being not uncommon, primary adrenal lymphoma (PAL) is extremely rare, with fewer than 200 cases published worldwide.^{2–5} It is defined as lymphoma in one or both adrenal glands occurring in patients without prior lymphoma elsewhere. If extra adrenal sites are involved, adrenal lesions must be dominant.⁴ The aetiology of PAL is unclear, and may be related to haematopoietic tissue similar to adrenal myelolipoma, previous autoimmune

Figure 3 FDG-PET scan indicating intensely avid uptake by both adrenal glands. FDG, fluorodeoxyglucose; PET, positron emission tomography.

adrenalitis, Epstein-Barr virus and mutations of p53 and c-Kit.⁶ PAL is more common in older men (median age 68 years and 2–3:1 male:female ratio).³ The presentation is most often with bulky, bilateral disease.⁷ Most patients have B symptoms and elevated LDH.⁴ Particularly if there is an extensive adrenal involvement, adrenal insufficiency symptoms such as fatigue, vomiting, hyperpigmentation and hypotension are prominent.⁸ Around 90% of PAL cases are with diffuse large B cell lymphomas.^{9,10} Overall survival is 13–15 months and although CHOP and CHOP-like regimens that incorporate rituximab have revolutionised the treatment of aggressive non-Hodgkins lymphomas more generally, durable remission for PAL is not common with only one-third of patients achieving this following chemotherapy treatment.^{3,4,6,9,10} Nonetheless, the PAL treatment remains multiagent chemotherapy with central nervous system prophylaxis.⁹ Adjunctive adrenal resection and radiotherapy may be considered for debulking.

In conclusion, we report a rare but important cause of bilateral adrenal masses with adrenal insufficiency. An isolated morning serum cortisol level within the reference interval does not necessarily rule out adrenal insufficiency, and further testing with tetracosactrin stimulation is indicated where clinical suspicion is high.⁴

Learning points

- ▶ There is a broad differential for adrenal gland masses, with biopsy sometimes necessary to establish the diagnosis.
- ▶ Pheochromocytoma should be excluded by measuring serum or urine metanephrines before the adrenal gland biopsy, owing to the risk of haemorrhage and hypertensive crisis.
- ▶ An apparently normal serum cortisol level does not exclude adrenal insufficiency.
- ▶ Primary adrenal lymphoma is a rare and generally an aggressive disease with a poor prognosis but early recognition and subsequent treatment will improve mortality.

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