Rare disease

A giant myelolipoma discovered as an adrenal incidentaloma: radiological, endocrine and pathological evaluation

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Summary

A 51-year-old Filipino woman presenting with hypertension was unexpectedly found to have a large right adrenal mass by ultrasound. As she did not have symptoms of adrenal disease, this was labelled an adrenal incidentaloma. Ultrasound and CT imaging demonstrated a large adrenal mass on the right measuring 15 cm at its greatest diameter, with both benign and malignant features. Tests for endocrine hyperfunction (excess of cortisol, catecholamines and aldosterone) concluded that the mass was hormonally non-functioning. The patient eventually underwent open adrenalectomy. Histopathological examination revealed myelolipoma.

BACKGROUND

Adrenal incidentalomas are increasing in frequency due to the widespread use of imaging procedures. In presenting this case, we describe the radiological and hormonal diagnostic evaluation and management of such masses. This case turned out to be a giant myelolipoma, an uncommon cause of adrenal incidentaloma.

CASE PRESENTATION

History

The patient was a 51-year-old Filipino woman who had had hypertension since the age of 47, with a highest blood pressure of 180/130 mm Hg, with no regular blood pressure monitoring. She did not have angina, dyspnoea on exertion, orthopnoea or bipedal oedema. She also had no palpitations, tremors or unexplained weight loss. She denied having frothy urine, facial oedema, haematuria or decreasing urine output. She was not aware of any heart disease, kidney disease or diabetes. Both of her parents had hypertension. She did not smoke or drink. She also denied illicit drug use. She was gravida 4 para 4 (3013) and had been menopausal since the age of 47.

Physical examination

Physical examination revealed an obese woman, with height of 150 cm, weight of 57 kg and a body mass index of 25.3 kg/m². Her blood pressure was 110/60 mm Hg with a normal heart rate of 80/min. The patient was taking verapamil 180 mg per day on the advice of her initial physician. She was not pale and did not have acne, moon facies, buffalo hump, facial hirsutism or anterior neck mass. She had regular a cardiac rhythm and the apex beat was not displaced. The abdomen was round and soft, with no palpable masses, tenderness or violaceous striae. She had no oedema, tremors or ecchymoses, and had equal peripheral pulses. There were no signs of virilisation.

INVESTIGATIONS

Laboratory evaluation

Diagnostic work-up was performed to determine secondary causes of hypertension, and to assess target organ damage. Complete blood count was normal. Urinalysis did not reveal proteinuria or haematuria. She had a normal creatinine of 55.6 µmol/l, while potassium was 3.77 mmol/l. She had impaired fasting glucose (5.67 mmol/l). She was also dyslipidaemic, with elevated low-density lipoprotein (5.66 mmol/l), low high-density lipoprotein (1.11 mmol/l) and high triglycerides (5.00 mmol/l). Chest x-ray showed normal lung fields and no cardiomegaly. Her two-dimensional echocardiogram showed a normal-sized heart with good wall motion and contractility.

Radiological imaging

Abdominal ultrasound showed normal-sized kidneys with distinct cortico-medullary junctions. There was increased liver parenchymal echogenicity, which was interpreted as fatty liver. There was an incidental finding of a large mass measuring 15.0×12.7×10.97 cm in the right upper abdominal quadrant displacing the right kidney inferomedially and anteriorly. It was reasonably delineated, rounded with an irregular outline, and solid in consistency with a heterogeneous echotexture, mostly hyperechoic in appearance.

Abdominal CT to better characterise the mass seen on ultrasound, revealed a large, well-defined, complex, predominantly fatty, heterogeneously enhancing mass with calcifications in the right retroperitoneal region measuring approximately 13.0×13.0×12.5 cm (figure 1). It displaced the right kidney inferiorly. The aorta was atherosclerotic. There were no enlarged paracaval or paraaortic lymph nodes. The CT image showed a large complex, heterogeneously enhancing retroperitoneal mass, most likely adrenal in origin, for which histopathological investigation was suggested.

Figure 1 A large heterogeneous right adrenal mass seen on CT scan. Note the calcification on the right edge of the mass, seen on the upper CT images.

The impression at this stage was of a large adrenal mass on the right, with the following aetiologies being considered: (1) adreno-cortical carcinoma, (2) aldosterone-producing adenoma, (3) pheochromocytoma and (4) cortisol-producing adenoma. Other medical diagnoses were hypertension, impaired fasting glucose, dyslipidaemia and obesity (all components of the metabolic syndrome).

Hormonal evaluation

Hormonal evaluation was carried out (see table 1).

Test for glucocorticoid excess/Cushing's syndrome

To screen for Cushing's syndrome, 24 h urine free cortisol was measured together with urine creatinine. Urine collection was adequate as evidenced by a urine creatinine of 7068 $\mu\text{mol/day}$ (normal: 3812–11 437 $\mu\text{mol/day}$). Cushing's syndrome was ruled out based on a urine free cortisol of 36.4 nmol/day (normal: 55–248 nmol/day).

Test for catecholamine excess/pheochromocytoma

Two 24-h urine metanephrine values were measured (2 days apart), and neither were high enough to make the diagnosis of pheochromocytoma (10.8 $\mu\text{mol/day}$ and 5.5 $\mu\text{mol/day}$) (normal: <5.458 $\mu\text{mol/day}$).

Table 1 Summary of hormonal diagnostic evaluation

Endocrine condition being screened	Test done	Result	Normal value	Interpretation
Cortisol excess/Cushing's syndrome	24-h Urine free cortisol	13.2 ng/24 h	20–90 ng/24 h	Negative screening test
Catecholamine excess/ pheochromocytoma	24-h Urine metanephrine	1.98 ng/24 h	<1 ng/24 h	Negative screening test
1.01 ng/24 h	>2–4 ng/24 h for diagnosis of pheochromocytoma			
Aldosterone excess/primary aldosteronism	PAC	3.77 ng/dl	0.80–17.2 ng/dl (supine)	
PRA	0.10 ng/ml/h	0.5–1.9 ng/ml/h (supine)		
PAC/PRA ratio	37.7	<20	Positive screening test	
PAC after acute saline suppression test	0.37 ng/dl	<5 ng/dl	Negative confirmatory test	

PAC, plasma aldosterone concentration; PRA, plasma renin activity.

Figure 2 A mixture of mature fat and myeloid elements comprise the tumour (left). To the right is normal adrenal cortical tissue enclosed by the capsule ($\times 100$ magnification).

Figure 3 High power ($\times 400$) magnification showing mature fat cells and haematopoietic tissue on the left, and normal adrenal cortical tissue on the right.

Test for aldosterone excess/primary aldosteronism

To screen for primary aldosteronism, the plasma aldosterone concentration/plasma renin activity (PAC/PRA) ratio was determined. PAC was 105 pmol/l (3.77 ng/dl) (normal: 22–477 pmol/l; 0.80–17.2 mg/dl), while the PRA was 0.03 ng/(l*s) (0.10 ng/ml/h) (normal: 0.14–0.53 ng/(l*s); 0.5–1.9 ng/ml/h), resulting to a PAC/PRA ratio of 37.7 ng/dl per ng/ml/h. The patient was in a supine position for 30 min prior to blood extraction for these tests. Thus, this was a positive screening test for primary aldosteronism.

Confirmatory dynamic testing was carried out with the saline loading test (acute saline suppression test) where 2 l of 0.9% NaCl solution was infused intravenously over 4 h. The postinfusion PAC was 10 pmol/l (0.37 ng/dl), ruling out primary aldosteronism. A postinfusion PAC of <139 pmol/l (<5 ng/dl) suggested adequate aldosterone suppression and excluded primary aldosteronism.

Based on the hormonal evaluation described above, it appeared that the adrenal mass was not producing cortisol, aldosterone or catecholamines, and, therefore, was hormonally non-functioning.

DIFFERENTIAL DIAGNOSIS

Clinical diagnosis

- ▶ Large right adrenal mass, hormonally non-functioning (ruling out adreno-cortical carcinoma).
- ▶ Metabolic syndrome: obesity, impaired fasting glucose, hypertension and dyslipidaemia.

TREATMENT

Surgical management

The patient underwent open adrenalectomy on the right. Intraoperative findings revealed a 15×7 cm lipomatous mass. The mass was displacing the right kidney and duodenum.

Anatomic diagnosis

Histological examination of the right adrenal gland showed a mass composed of mature adipose and bone marrow tissue. This mass was compressing the normal adrenal cortex (figures 2, 3). The mass was interpreted as a myelolipoma.

OUTCOME AND FOLLOW-UP

Postoperative course

The patient was able to tolerate the open adrenalectomy and was sent home 2 days after surgery with no glucocorticoids.

Her blood pressure was maintained between 110 and 120/80 mm Hg without the need for any antihypertensive medication. Her fasting blood sugar also slightly improved to 5.51 mmol/l (from 5.67 mmol/l) and serum potassium to 4.65 mmol/l (from 3.77 mmol/l). These improvements in blood pressure, fasting blood sugar and serum potassium after the adrenalectomy are interesting since the mass was hormonally non-functioning during preoperative evaluation. This would not have been surprising if the mass had been secreting excess glucocorticoids, aldosterone or catecholamines.

Serum cortisol taken at 08:00 h at 12 weeks postoperatively was normal at 388.1 nmol/l. This suggests that the

patient had no adrenal insufficiency despite having only one adrenal gland.

DISCUSSION

Adrenal incidentalomas

Adrenal incidentalomas are adrenal masses that are unexpectedly discovered during imaging procedures performed as a result of signs or symptoms unrelated to adrenal disease.^{1–3} For this patient, the mass met the definition of an incidentaloma since the reason for the abdominal ultrasound (the first imaging test done) was to search for renal parenchymal disease or renovascular disease which are common secondary causes of hypertension.

Adrenal incidentalomas have been called the ‘epidemic of modern technology’ because the incidence has risen due to the widespread use of modern imaging procedures.^{4 5}

In the evaluation of adrenal masses, two important questions must be answered: (1) Is the mass hormonally functioning? and (2) Is the mass benign or malignant?

Hormonal evaluation

For this patient, diagnostic work-up for hormonal function was carried out to screen for Cushing's syndrome, pheochromocytoma and primary aldosteronism. Screening for cortisol, catecholamine and aldosterone excess, as in this patient, must be done since all three conditions may cause elevated blood pressure.

Determination of 24-h urine free cortisol levels eventually showed normal results, making Cushing's syndrome unlikely.

Two measurements of 24-h urine metanephrine were carried out and both were no more than two to four times the upper limit of normal. Thus, the mass was unlikely to be a catecholamine-secreting tumour.

Initial screening for primary aldosteronism was performed using the PAC (in ng/dl)/PRA (in mg/ml/h) ratio. The PAC/PRA ratio for this patient was 37.7, which suggested primary aldosteronism.^{1 2} Confirmatory dynamic testing for primary aldosteronism was done using the acute saline suppression test. A PAC of <139 pmol/l (<5 ng/dl) after the 4 h infusion suggested adequate aldosterone suppression, ruling out primary aldosteronism. For this patient, the plasma aldosterone level was suppressed at 10 pmol/l (0.37 ng/dl).

Dehydro-epiandrosterone sulfate (DHEA-S), a marker for adrenal androgen excess, was not determined as the patient did not have virilising features on physical examination.

Radiological evaluation

The second important question to be answered is whether the mass is benign or malignant. Size and appearance on imaging procedures are important in this respect. The risk of adrenal carcinoma increases as the tumour size increases.⁶ Based on the CT scan, the mass in this patient had a maximum diameter of 13.0 cm, thus suggesting malignancy on size alone.

Appearance on CT is also used to differentiate benign from malignant adrenal masses. Benign masses usually have a smooth border, conform to the shape of the adrenal gland, have no calcifications, are homogenous and do not enhance after contrast administration. Malignant masses, on the other hand, are poorly delineated, have stippled

Figure 4 A megakaryocyte (centre) among the haematopoietic tissue component, with an adipocyte seen at the top and upper left corner ($\times 1000$ magnification). This provides a specific diagnosis of myelolipoma.

Figure 5 Basophilic-staining crystal-like areas indicative of calcification are seen at the periphery of the tumour ($\times 100$ magnification)

calcification, have areas of necrosis, show local invasion and may have associated enlarged lymph nodes.^{7 8}

The mass of this patient had both benign and malignant features: it was well delineated and had a smooth border, but it contained calcification and was heterogeneously enhancing.

Because there were radiological features suspicious for adrenal carcinoma, the patient was advised to undergo open adrenalectomy.

Adrenal myelolipoma

During open adrenalectomy, a 15×7 cm lipomatous mass was seen, displacing the right kidney and duodenum.

Based on a series in Italy, myelolipoma is an uncommon cause of adrenal incidentaloma.^{4 9} Myelolipomas only comprised 8% in that series, in contrast to the more frequently occurring adenoma (52%), adrenal carcinoma (12%) and pheochromocytoma (11%). This benign fatty tumour usually affects older patients (41–84 years, mean 62).

There have been no published reports of adrenal myelolipoma here in the Philippines.

A myelolipoma is a benign, hormonally non-functioning tumour that histologically has mature fat cells interspersed with haematopoietic elements resembling bone marrow.¹⁰ The presence of myeloid precursors, specifically megakaryocytes, in a fat-containing mass confirms the diagnosis of myelolipoma (figure 4).^{11 12} In an isolated adrenal myelolipoma, normal-appearing adrenal cortical tissue can be seen separate from the mass, as in this patient.

Adrenal myelolipomas are hormonally non-functioning, as demonstrated in this case. However, there are reports that they can be associated with Cushing's syndrome and Conn's syndrome.^{10 13–16} Adrenal myelolipomas do not cause adrenal insufficiency.¹⁰

The mixture of fat and haematopoietic elements explains the heterogeneous appearance of myelolipomas on imaging. In addition, the ratio of adipose tissue to haematopoietic tissue varies, so that myelolipomas appear different with different imaging procedures.

Ultrasonographically, the fatty areas are hyperechoic while the haematopoietic areas are hypoechoic.¹⁰ In our patient, the mass had a heterogeneous echotexture but was mostly hyperechoic, suggesting it was predominantly composed of fat.

On CT, fatty areas have lower attenuation (appearing more radiolucent), while the haematopoietic elements have higher attenuation (appearing more radioopaque). Some reports have demonstrated that calcification may be seen up to 24–27% of isolated adrenal myelolipomas.^{10 17} Thus, the finding of calcification in this case (demonstrated by both CT scan and histopathological analysis) is compatible with a myelolipoma (figure 5). Therefore, the presence of calcification does not always equate with adrenal carcinoma.

This patient was fortunate that haemorrhage did not occur, as there is a greater chance of this happening in larger tumours.

If imaging procedures demonstrate that an adrenal mass has a high fat content, fine needle aspiration biopsy can be performed. If mature adipose tissue is seen with bone marrow elements, myelolipoma is then diagnosed and surgical excision may not be necessary as the mass can be just

observed. However, the risk of haemorrhage in large tumours should also be considered.¹⁷

Treatment for adrenal myelolipoma is surgical excision. No long-term follow-up is needed.

In this patient's case, prior to histological diagnosis that this mass was a myelolipoma, the decision to perform excision was based on the need to exclude adrenal carcinoma because of its large size and equivocal imaging features. After the diagnosis of myelolipoma had been made, it seemed wise to excise the mass since due to its large size it was at a high risk of haemorrhage and because some carcinomas may mimic myelolipomas on CT showing high fat content.^{15 18 19}

Learning points

- Adrenal incidentalomas are increasingly frequent due to widespread use of imaging procedures.
- It is important to determine whether these masses are benign or malignant, and whether they are hormonally hyperfunctioning.
- This case describes the radiological and hormonal diagnostic evaluation and management for such masses.
- This case turned out to be a giant myelolipoma, an uncommon cause of adrenal incidentaloma.

Competing interests None.

Patient consent Obtained.

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