CASE REPORT

Virilization With Adrenal Myelolipoma, Adrenal Hyperplasia, and Fibroadenoma of Breast

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ABSTRACT

Adrenal myelolipoma is a rare, benign and usually hormonally inactive tumour. We report a case of a young female who presented with hormonally active tumour causing virilization and associated type-2 Diabetes mellitus. Laparoscopic adrenalectomy was done after CT finding of a large left adrenal mass that was producing large amounts of androgens. Adrenal myelolipoma with cortical hyperplasia was diagnosed on histopathological examination. Her diabetes progressively regressed after the removal of tumour and glucose tolerance remained normal up to 1 year of follow-up after surgery and there was no recurrence of tumour. She also had a lump in her breast which proved to be a fibroadenoma. We report this case due to its rarity, multiplicity of tumours and adrenal cortical hyperplasia-presenting as an unusual cause of severe virilization.

Key words: *Adrenal myelolipoma. Virilizing tumour. Diabetes. Fibroadenoma.*

INTRODUCTION

Adrenal myelolipoma (AML) is a rare benign usually non-functioning tumour, composed of variable mixture of mature adipose tissue and haematopoietic elements. The term "myelolipoma" was first described by Oberling in 1929. Autopsy studies have reported variable incidence 0.03-0.8%.[1] Among the primary adrenal tumours they account for 2.6% tumours.[2] Among incidentally discovered adrenal masses myelolipoma has a frequency of 7-15%.[3] Although asymptomatic these tumours are found to be associated with metabolic disorders like obesity, hypertension, diabetes and/or endocrine disorders of adrenal gland like congenital adrenal hyperplasia (CAH), Cushing's syndrome and Conn's syndrome. Large myelolipomas may also present with acute abdominal pain, fever and leucocytosis, as a result of necrosis or haemorrhage in the tumour.[4]

We report a case of AML being a rare cause of virilization in a young female.

CASE REPORT

A 25 years old female patient presented with amenorrhoea preceeded by oligomenorrhoea for 9 years, hirsutism for 5 years, deepening of voice, some weight loss and generalized weakness. On examination, her BMI was 25.2 kg/m^2. Eventhough BP was 140/100 mmHg at the initial visit, it remained normal throughout admission in the pre-operative period. She had temporal baldness, masculine body habitus with broad shoulders, acanthosis nigricans, clitoromegaly and severe hirsutism with a score of 48 (Modified Ferrimen Gallway). She had breast atrophy and a firm non-tender 2 x 2 cm nodule in left upper quadrant. Serum testosterone was markedly raised at > 1600 ng/ml and DHEA-SO4 at 1000 ng/dl whereas 170-H progesterone was slightly elevated at 5.9 ng/ml and FSH and LH were suppressed (Table I). Serum cortisol, urinary VMA, aldosterone and renin levels were not done due to cost constraints and the predominant clinical presentation of virilization.

Table I: Pre and postoperative hormone status.

Tests	Pre-operative hormone levels	Postoperative hormone levels	Normal range
Testosterone	> 1600 ng/dl (upto 20 ng/dl)	0.1 ng/ml	0.26-1.3 ng/ml
DHEA-SO4	1000 ug/dl	2.89 ug/dl	195-507 ug/dl
17OH progesterone	5.9 ng/ml	0.1 ng/ml	0.2-1.3 ng/ml
S. cortisol	-	1.30 ug/dl	1.7-16.6 ug/dl
C-peptide	-	3.70 ng/ml	1.1-5.0 ng/ml
FSH	0.23 mIU/ml	-	4-13 mIU/ml
LH	< 0.2 mIU/ml	-	1-18 mIU/ml

Her ultrasound showed a complex mass of 4.8 x 4.4 cm at the upper pole of left kidney, a bulky uterus and no evidence of polycystic ovaries.

She did not return for follow-up untill 2 years later, after having had an episode of severe pain at the left lumbar region. She had also developed Diabetes. CT scan abdomen showed a large soft tissue mass in the region of left adrenal gland. This mass was causing extrinsic compression on tail of the pancreas, was 6.0 x 5.0 cm in size, with smooth outline and some areas of necrosis. Tentative diagnosis of virilizing adrenal tumour was made. She was admitted and underwent laparoscopic left adrenalectomy while Diabetes was controlled with insulin.

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On gross examination, it was a brownish nodular mass measuring 5.5 x 4.5 cm with focal areas of haemorrhage (Figure 1 and 2). Histopathology revealed diffuse thickening of adrenal cortex with infiltration by fatty marrow spaces containing haematopoetic cells with trilineage haematopoiesis (Figure 3 and 4). Immunohistochemistry showed positive CD56 and synaptophysin in the adrenal cortex, cytokeratin was negative and features consistent with adrenal myelolipoma with cortical expansion and adrenal hyperplasia.

Postoperatively, she developed symptoms of adrenal insufficiency with hypotension and prostration. Spot serum cortisol was 1.30 ug/dl. Short synacthen test confirmed hypocortisolism. Poststimulation cortisol was 3.70 ug/dl with basal of 2.50 ug/dl. She was started on steroid replacement therapy. Her insulin requirement also decreased with time and she was later switched to oral hypoglycaemic agent (Gliclazide 80 mg/day). On follow-up 6 months later Gliclazide was stopped and Prednisolone (5 mg/day) was tapered off gradually over the next 6 months. At one year follow-up there was marked regression of virilization and she was off replacement steroid and doing well. She also underwent breast lumpectomy and it was found to be a fibroadenoma.

DISCUSSION

This patient presented with an endocrine disorder of severe virilization; the finding of an adrenal mass alongwith very high levels of androgens confirmed adrenal tumour, and a myelolipoma was not suspected pre-operatively. To the best of our knowledge only one case of myelolipoma with virilization has been described earlier.[5]

AML has been reported in both genders with an equal frequency in 5th to 7th decades of life. It usually arises in the adrenal gland, more commonly in the right adrenal gland (R:L=3:2) while bilateral involvement is rarely seen. Size of the tumour varies from few mm to 34 cm in diameter.[3]

Extra adrenal myelolipomas are also reported in the presacral retroperitoneal space, peri or infra-renal retroperitoneal space and low pelvic cavity. Synchronous

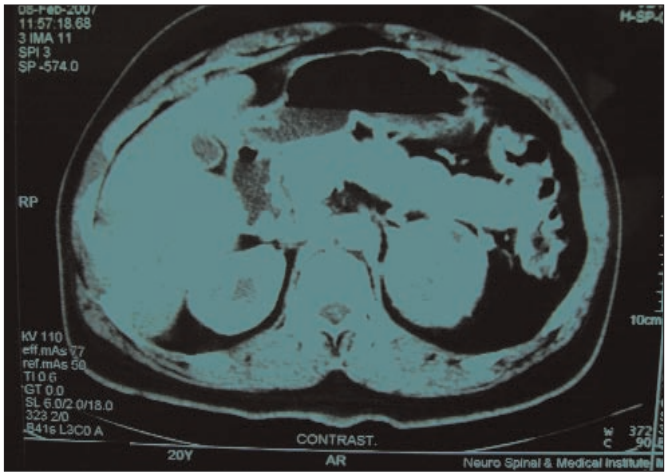

Figure 1: Transverse section of CT scan abdomen showing large soft tissue mass (6.0 x 5.0 cm) in left adrenal region causing compression of the tail of the pancreas.

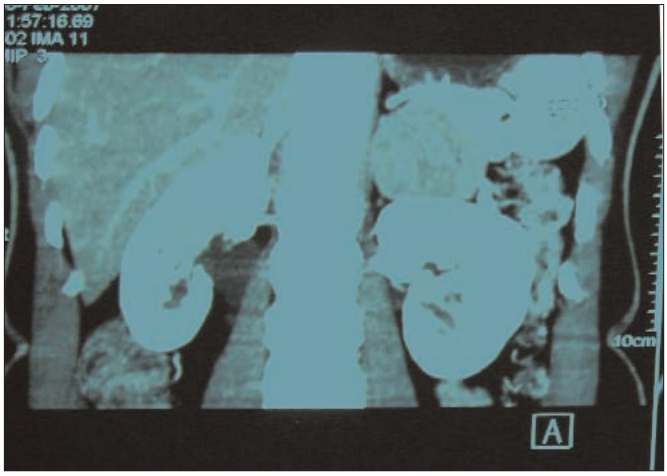

Figure 2: Coronal section of CT scan abdomen showing large soft tissue mass in left adrenal region causing compression of the left kidney.

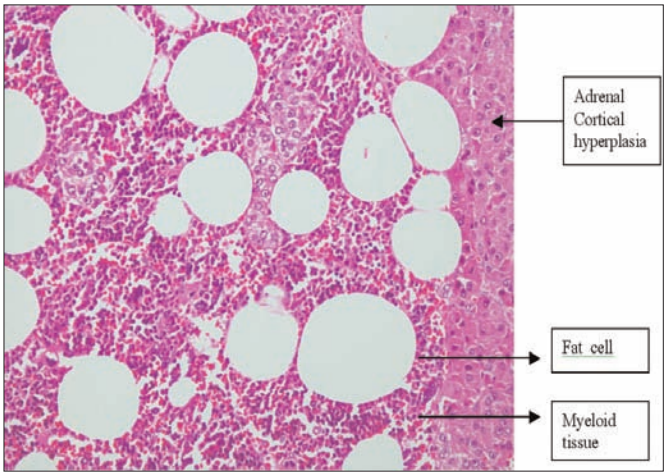

Figure 3: AML composed of bone marrow elements and mature fat (H&E stain 20X magnification).

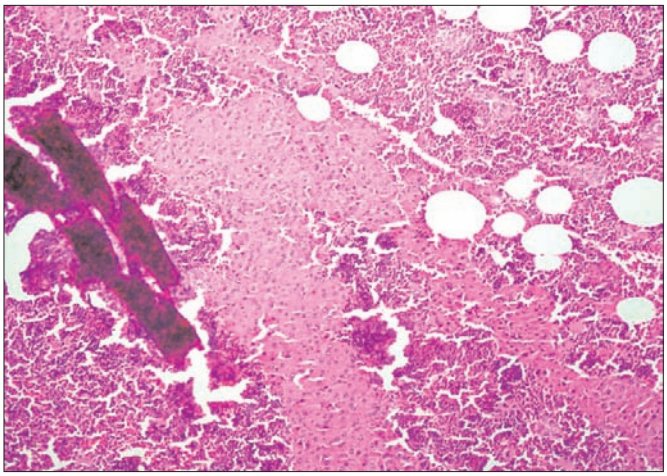

Figure 4: Histological features of adrenal myelolipoma low power micrograph. Showing an intimate admixture of adipose tissue and bone marrow elements with hyperplastic adrenal cortical cells (H & E Stain: 10X).

occurrence of 2 adrenal tumours i.e. adrenal myelolipoma and adrenal adenoma/hyperplasia within the same adrenal is an unusual occurrence. Cases of myelolipoma with functional and non-functional adenoma have been reported.[6,7] In addition myelolipomatous foci can be found within adrenal hyperplasia or adenoma. Bilateral myelolipomas have been described with Cushing's disease and CAH.[8]

In this patient, marked elevation of androgenic hormones was suggestive of a tumour source, however, the mass removed contained no adrenal tumour but cortical adrenal hyperplasia. Postoperative hypotension and hypocortisolism was probably due to the suppression of normal adrenal gland by the hyperplastic gland.

Most myelolipomas are asymptomatic, found incidentally on imaging in > 50% cases.[3] Others may present with abdominal pain due to huge size or haemorrhage or necrosis within tumour. Adrenal myelolipomas are also associated with endocrine dysfunction.[9] Cases with Conn's syndrome, Cushing's syndrome and congenital adrenal hyperplasia due to 21-hydroxylase deficiency and pheochromocytoma have been reported.

The aetiology is still unclear. Most widely accepted theory is metaplasia of mesenchymal cells of adrenal cortex as a result of stress, infection, or necrosis.[1] In patients with endocrine dysfunction such as Cushing's disease and CAH, excessive long-term ACTH stimulation has been incriminated. Myelolipomatous tissue can replace either hyper plastic or tumourous adrenal tissue explaining the endocrine presentation of these tumours. CT scan is the best diagnostic modality showing fat density (hypodense) in the adrenal gland. Other differential diagnoses include angiomyolipoma, liposarcoma and retroperitoneal lipoma. MRI is sometimes required to demonstrate the origin of tumour, to define tissue planes when it is large and heterogenous. Percutaneous biopsy is at times required when tumour contains large amount of myeloid tissue and no recognizable fat, making recognition difficult on imaging studies.

The management of adrenal myelolipoma is individualized. Usually small sized tumours (< 4 cm) and asymptomatic ones are managed conservatively. Those with larger size, symptomatic or suspicious of being malignant are best treated by surgical removal. This patient was symptomatic with large size tumour so she underwent adrenalectomy.

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