CASE REPORT

Adrenal Myelolipoma: Profile of Six Patients With a Brief Review of Literature

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Six patients with adrenal myelolipoma (AML) are reported. They included 3 men and 3 women with mean age (+ SD) of 42.3 + 10.9 yrs ranging from 26 to 60 yrs. Four patients were symptomatic, while the other 2 had no symptoms. Detection of AML was 'incidental' in 4 patients while being investigated for non-adrenal symptoms (pain abdomen in 2 and work-up for renal disease in 2), while the remaining 2 patients, one (#5) with congenital adrenal hyperplasia due to 21 alpha-hydroxylase deficiency had myelolipomatous alterations in the adrenal gland and the other (#6) had detection of AML during work-up for hypertension. All patients were obese (BMI > 27), four were hypertensive and one had type 2 diabetes. Imaging was suggestive of AML in five of them. However, in one case radiological diagnosis of angiomyolipoma of the kidney was considered. Interestingly, the right adrenal was involved in five of them. Four patients underwent adrenalectomy in view of symptoms and size of the mass, while the other 2 are under follow-up. Cyto/histopathology was consistent with AML in all these patients. However, in one case myelolipomatous alterations were noted in the background of adreno-cortical tumor. No recurrence or alterations in tumor size was noted during the follow-up period ranging from 6 months to 4 years. A brief review of literature is also presented.

Key Words: Adipose tissue, Adrenal neoplasm, Hematopoiesis.

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Introduction

Adrenal myelolipoma (AML) is a rare, benign and invariably non-functioning tumor, composed of normal hematopoietic elements and mature adipose tissue.[1] Half of the patients with this disorder are asymptomatic with the tumor discovered 'incidentally' on imaging or at surgery/autopsy.[1] Until 2001, 158 cases of surgically documented AML have been reported in English literature.[1-6] Endocrine and/or metabolic disorders associated with AML include obesity,[1-6] type 2 diabetes,[1-6] congenital adrenal hyperplasia (CAH) due to 21 or 17 alpha-hydroxylase deficiency,[7,8] Cushing's disease,[9] Conn's syndrome,[10] pheochromocytoma[11] and polycystic ovarian disease.[12] We describe 6 patients with AML with varying associations in the existing repertoire of this rare entity and discuss their clinical presentations, adreno-cortical functions, imaging and cyto/histopathological observations together with a brief review of literature.

Materials and Methods

Case #1

A 42-year-old female presented with dull aching pain and a mass in the right lumbar

region for one and half years. She was detected to be hypertensive 3 months earlier. On examination, her body mass index (BMI) was 31.2 kg/m^2, BP 190/130 mmHg and had no cafe-au-lait macules. A firm, non-tender, bimanually palpable mass (15 ×15 cm) with well-defined margins was found in the right lumbar region. Examination of other systems was normal. On investigation, her serum cortisol profile, 17 alpha-hydroxy progesterone (17αOHP), plasma aldosterone (4 hour upright sample on salt adlib) and 24 hr urinary VMA were normal (Table 1). Contrast-enhanced computed tomography of (CECT) abdomen showed right adrenal heterogenous mass with areas of fat density (-30 to-50 HU) and hemorrhage (Fig. 1). Following her blood pressure control with amlodipine, she underwent exploratory laparotomy and the 25 × 15 × 8 cm (1700 gm) right adrenal mass was extirpated. Histopathology of the encapsulated lesion revealed mature adipose tissue and bone marrow elements (megakaryocytic, erythroid and granulocytic series) alongwith areas of hemorrhage (Fig. 2). She is still obese and remains hypertensive during follow up for the last 2 yrs.

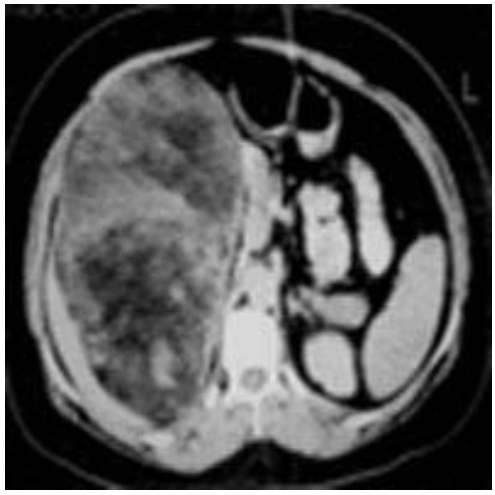

Fig. 1. CECT of abdomen showing large right adrenal mass with multiple hypodense areas (fat density) and hyperdense (soft tissue density) areas suggestive of AML.

Case #2

A 26-year-old male presented with right flank pain for 2 weeks. On examination, his BMI was 29.2 kg/m^2 and BP 110/70 mmHg. His serum cortisol profile, 17α OHP and 24 hr urinary VMA were normal (Table 1). On ultrasonography (US), a right adrenal mass was detected. CECT of abdomen showed an area of homogenous attenuation with fatty tissue component (CT value –34 to –54 HU)

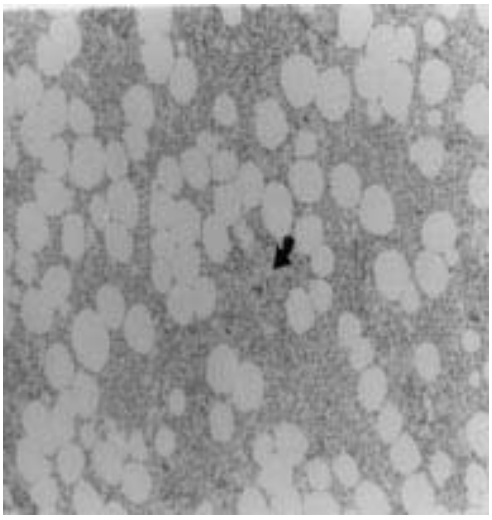

Fig. 2. Microphotograph showing myeloid and adipose tissues and many megakaryocytes (arrow). (H & E,× 280)

Table 1. Summary of the 6 cases

No.	Age & Sex	Presentation	Associated Disease(s)	Tumor site and size on imaging	Cortisol dynamics 17 OHP (ng/mL) VMA (mg/gm of creatinine)	Operative Procedure FNAC/ Histology
1.	42 F	Rt. flank pain	Obesity HTN	CECT Rt. adrenal mass 25 × 15 × 8 cm	Cortisol (nmol/L) AM 420 PM 360 Post Dx < 37 17αOHP 1.8 ng/mL VMA 6mg/gm Cr	Rt. Adrenalectomy Wt. 1700 gm H/P confirmation of AML
2.	26 M	Rt. flank pain	Obesity	CECT Rt. adrenal mass 10 × 8 × 6 cm	Cortisol (nmol/L) AM 560 PM 320 Post Dx < 37 17αOHP 2.0 VMA 4mg/gm Cr	Rt. Adrenalectomy Wt. 900 gm H/P confirmation of AML with adreno-cortical tumor
3.	60 M	Asymptoamtic	Obesity HTN Type 2 DM	MRI Rt. adrenal mass 7.8 × 4.1 × 4 cm	Cortisol (nmol/L) AM 430 PM 200 Post Dx < 37 17αOHP 1.4 ng/mL VMA 5mg/gm Cr	FNAC consistent with AML
4.	40 M	Oliguria Anasarca	Obesity HTN Crescentic glomerulo-nephritis	CECT Rt. adrenal mass 21 × 20 × 15	Not done (On steroid treatment)	Rt. adrenalectomy Wt. 1700 gm H/P confirmation of AML
5.	40 F	Asymptomatic	CAH 21 OHlase deficiency Obesity	CECT Lt. adrenal mass 5 × 4 × 4 cm	Cortisol (nmol/L) AM 260 PM 200 17αOHP 25 ng/mL ACTH 469 pg/mL	FNAC consistent with AML
6.	46 F	Headache sweating palpitation	Obesity HTN Gall stones	CECT Rt. adrenal mass 9 × 7 × 4 cm	Cortisol (nmol/L) AM 400 PM 300 Post Dx 76 17αOHP 1.3 ng/mL VMA 6mg/gm Cr	Rt. Adrenalectomy Wt. 135 gm H/P confirmation of AML

HTN: Hypertension, AML:Adrenal myelolipoma, Normal ranges for serum cortisol AM: 400-600 nmol/L, PM: 200-400 nmol/L. 17αOHP: 0.5-1.5 ng/mL, VMA: 3-7 mg/gm of creatinine

and a soft tissue component (CT value +38 to +44 HU) in right adrenal region. He underwent exploratory laparotomy and a mass of 10 × 8 × 6 cm (900 gm) was resected. Histopathology confirmed myelolipomatous alterations with areas of hemorrhage and necrosis in the background of primary adrenocortical tumor (Fig.3). He is asymptomatic during his 1-year. follow up.

Case #3

A 60-year-old male, with hypertension and type 2 diabetes mellitus, on insulin and

metformin therapy, was evaluated for diabetic renal disease. His BMI was 30.2 kg/m^2 and BP 140/90 mmHg on enalapril. His serum cortisol profile, 17αOHP and 24 hr urinary VMA were normal (Table 1). A right adrenal mass was discovered on ultrasound. MRI was descriptive of AML (Fig. 4). FNAC of the adrenal mass lesion was consistent with AML and he is under follow up for the last 4 years.

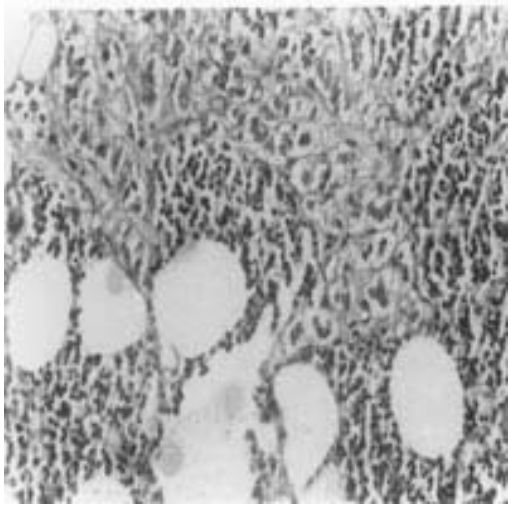

Fig. 3. Microphotograph showing an equal proportion of both myelolipomatous (left) and adrenocortical tumor cells (H& E, ×

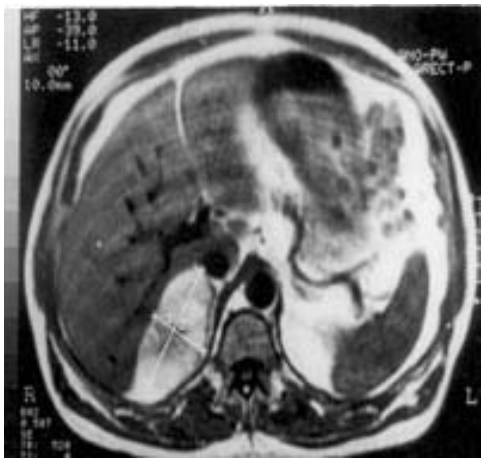

Fig. 4. MRI (T1W1) axial section showing an oval right suprarenal mass with peripheral hyperintense signal (fat tissue) and central hypointense signal (myeloid

Case #4

A 40-year-old man presented with oliguria, anasarca and breathlessness. On examination his BMI was 34.6 kg/m^2 and BP 160/110. A large abdominal mass was palpable in the right hypochondrium and lumbar region. On investigation, his urine showed proteins and red cell casts and blood urea and creatinine were elevated to 215 mg/dL and 11.8 mg/dL respectively. Renal biopsy confirmed the diagnosis of diffuse proliferative glomerulonephritis with crescent formation. He received supportive dialysis, prednisolone and antihypertensive medications (nifedepin and atenolol) and improved. Coincidentally, his abdominal ultrasonogram revealed a hyperechoic mass in relation to the upper pole of the right kidney. CECT showed a right adrenal heterogenous mass measuring 21 × 20 × 15 cm with predominantly low density (-63 to –83 HU) arising from the upper pole of the right kidney and a diagnosis of renal angiomyolipoma was thought of. On exploration, a right suprarenal mass was found and resected and the right kidney preserved. Histopathology showed fat spaces with interspersed haemopoietic component and areas of necrosis and hemorrhage consistent with myelolipoma. He has been asymptomatic during follow-up for the last 4 years.

Case #5

A 40-year-old unmarried woman, who was diagnosed as having congenital adrenal hyperplasia due to 21 alpha-hydroxylase deficiency at age 16, when she presented with primary amenorrhoea, mild hirsutism and clitoromegaly. She was put on prednisolone, which she took irregularly. On examination, her BMI was 32.1 kg/m^2 (height 139 cm, expected height 150 cm, weight 62 Kg), BP 110/70 mmHg, hirsute score 6/36 (Ferriman and Gallwey) and she had clitoromegaly. On investigation, her serum 17αOHP was 25ng/mL, androstenedione 6.1 ng/mL, ACTH 469 pg/mL with low normal cortisol profile (Table 1). CECT

abdomen showed bilateral adrenal hyperplasia with nodular transformation in left adrenal gland (Fig. 5a). MRI of head showed normal pituitary gland. Her repeat CECT of abdomen 3 years later showed myelolipomatous alterations (CT value – 35 HU) in the left adrenal gland (Fig. 5b). FNAC from the lesion confirmed the same.

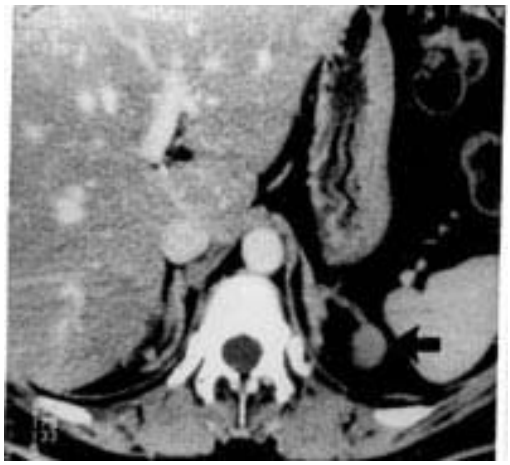

Fig. 5(a). CECT of abdomen showing bilateral adrenal hyperplasia with nodular transformation of left adrenal gland.

Fig. 5(b). CECT of abdomen 3 years later shows fat density in a nodule of the left adrenal gland.

Case #6

A 46 year female who was a known hypertensive for last 7 years presented with episodic headache, sweating and palpitation for last 2 years. On examination her BMI was 29.6 kg/m^2, pulse 100/min regular, BP 220/130 mm Hg. She had no café-au-lait macules and per abdominal examination was essentially normal. On investigation, her serum cortisol profile, 17αOHP, plasma aldosterone (4 hours upright sample on salt adlib) 24h urinary VMA and urinary norepinephrine and epinephrine (21 and 66 μg/gm creatinine respectively) were normal (Table 1). CECT abdomen showed right adrenal mass with hypodense area (CT value –30 to –50 HU) suggestive of fatty tissue and a rim of soft tissue (CT value +35 to +45 HU) (Fig. 6) and multiple stones in gall bladder. Her BP was controlled with amlodipine, α blocker, enalapril and atenolol. She underwent right adrenalectomy (9 x 7 x 4 cm, 135 gm) uneventfully and histopathology confirmed AML. There was no evidence of pheochromocytoma. She still remains hypertensive during follow-up for last 6 months.

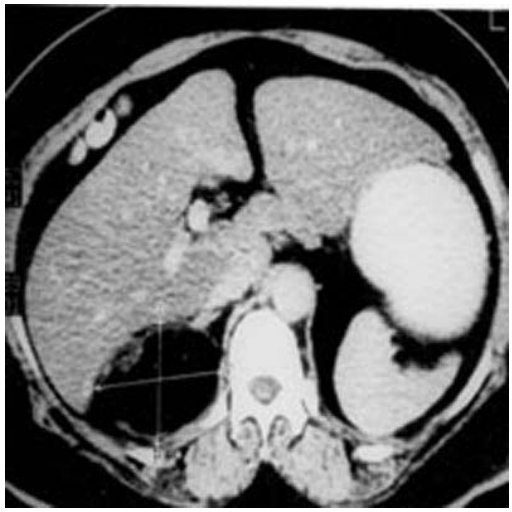

Fig. 6. CECT of abdomen showing right adrenal mass with hypodense area representing fat and hyperdense rim representing myeloid tissue, typical of

Table 2. Some important reviews and case reports on adrenal myelolipoma

No.	Author	Year	Cases	Age (Years)	Sex	Symptoms	Side	Remarks
1	Dieckmann et al [2]	1987	1	71	F	-	-	reviewed 59 surgically treated cases
2	Kanj et al [9]	1988	1	24	F	S	BL	associated with Cushing's syndrome
3	Albala et al[13]	1991	1	62	M	S	R	hemorrhage after trauma
4	Ayuso et al[14]	1991	2	30 50	M M	AS S	R L	incidentally associated with Hodgkin's disease
5	Belizini et al[15]	1992	1	50	F	S	R	associated with endometrioid carcinoma diagnosed by FNAC
6	Murakami et al [7]	1992	1	41	M	S	L	21 hydroxylase deficiency
7	Fuziwara et al [16]	1993	1	83	F	AS	R	associated with gastric cancer
8	Casey et al [17]	1994	2	47 28	F F	S S	R R	associated with cancer of the breast
9	Jenkins et al [18]	1994	1	44	F	S	R	associated with adrenal hyperplasia and Cushing's syndrome
10	Muraro et al [19]	1994	1	63	F	S	R	associated with dysplasia and epigastric pain
11	Hirakawa et al [20]	1994	1	-		S	-	giant myelolipoma
12	Hofmockel et al [3]	1995	20	12 - 73	M 12 F 8	S –16 AS - 4	R=18 L=1 BL=1	bilateral (1), renal cell carcinoma (2) bladder carcinoma (1)
13	Reynard et al [21]	1995	1	58	F	S	L	giant adrenal myelolipoma
14	Spinelli et al [22]	1995	4	43 48 57	F M M	S S S	L BL Not mentioned	laparotomy in 3 cases
15	Ukimura et al [11]	1995	1	44 39	M F	S S	R R	laparoscopic adrenalectomy associated with pheochromocytoma
16	Sander et al [1]	1995	7	40-65	M-5 F-2	S=5 AS=2	R=6 BL=1	-
17	Sharma et al [4]	1997	7	38-70	M-4 F-3	S=6 AS=1	R=7	associated with renal cell carcinoma and carcinoma cervix
18	Kenney et al [12]	1998	64	52.6	M-32 F-32	S- 17 AS-37 Not mentioned 10	R = 45 L = 11 B/L 8	adrenal myelolipoma (37) Myelolipoma with other adrenal disorders (18)
19	Kalafatis et al [12]	1999	1	34	F	S	R	bilateral giant AML and PCOD
20	Lam et al [6]	2001	20	18-81	M-12 F-8	S=16 AS=4	R=10 L=10	myelolipoma (11), lipoma, teratoma, angiomyolipomas

S: Symptomatic, AS: Asymptomatic, R-Right, L: Left, FNAC: Fine needle aspiration cytology, PCOD: Polycystic ovarian disease

Discussion

AML has been frequently reported in the 5th and 7th decades of life with no sex prediliction.[2-5] Involvement of the right adrenal is seen more often than the left (Right: Left ratio 3: 2.1) and bilateral involvement is rare.[2-5,9] The size of the affected adrenal is variable, 2 mm to 34 cm in diameter and its weight up to 5900 gm.[2-6]

AML is often quiescent with detection incidental to imaging being > 50%.[2-6] Its association with obesity (25%), hypertension (26%) and diabetes (26%) is also incidental. Frequency of AML in adrenal incidentalomas varies between 7-15%.[23] It may occasionally present with abdominal pain due to either being large in size or from spontaneous hemorrhage,[2-6] more likely when it is predominantly composed of myeloid tissue.[1]

Several malignant tumors like renal cell carcinoma and carcinoma of uterine cervix have been reported in a few patients.[2-6] Major observations made in important reviews and case studies on AML are shown in the Table 2. All six patients described by us are typical (Table 1), with equal sex distribution, in age group of 26 – 60 years. Five of them had right adrenal masses and only one had it on the left. AML was detected during imaging for non-adrenal etiologies in 4 instances, and in 2 presenting with abdominal pain when the mass was large and had intratumoral hemorrhage.

Instances of AML in association with CAH due to 21 alpha-hydroxylase or 17 alpha-hydroxylase deficiencies have been reported.[7,8] Excessive ACTH secretion over a long period may stimulate myelolipomatous alterations in the adrenal gland.[8] One of our patients with classical CAH due to 21 alpha-hydroxylase deficiency but taking steroid replacement intermittently, had nodular transformation and myelolipomatous alterations in the adrenal cortex. Co-existing myelolipoma with adrenocortical tumor, as was seen in patient #2 had been reported twice before, one with Cushing's syndrome and the other, with virilization.[24,25] Myelolipomatous tissue can replace either tumorous or hyperplastic adrenocortical cells or, simply represent secondary degenerative changes.[26]

The aetiopathogenesis of AML is not clear. Differential proliferation of the undifferentiated mesenchymal stem cells of the adrenal cortex into myeloid and adipose tissue in response to infection or stress or necrosis has been a projected view.[27]

The demonstration of fat density (hypodense) within an adrenal mass by CT is virtually diagnostic of AML.[5,28] The other differential diagnosis include renal angiomyolipoma, retroperitoneal lipoma and liposarcoma. Magnetic resonance imaging (MRI) is sometimes required to demonstrate origin of the tumor, to define the tissue planes when the tumor is large and heterogenous, and to distinguish benign from malignant lesions by comparing signal intensity ratios of adrenal to liver.[29] In five of our patients CECT could appreciably demonstrate the fat tissue component in the adrenal mass while, in one, MRI was informative.

Management of AML is individualized. Those with masses less than 4 cm in diameter and asymptomatic, diagnosed on imaging and/or in cytological studies, are best left to long term follow up.[30] Surgical resection is offered when it is large and symptomatic, exhibits areas of hemorrhage or necrosis, or malignancy is suspected.[2-6] Four of our patients were symptomatic and underwent surgical resection. The other two with no symptoms are being regularly followed up.

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