

## Review Article

**Adrenal Myelolipoma**Ashmeet Kaur<sup>1\*</sup>, Mansi Faujdar<sup>2</sup>, Shubha Gupta<sup>2</sup>, Alekh Saxena<sup>3</sup><sup>1</sup>Senior Resident, Department of Pathology, Santokba Durlabhji Memorial Hospital, Bhawani Singh Road, Near<sup>2</sup>Honorary Consultant, Rambagh Circle, Jaipur, Rajasthan 302015, India<sup>3</sup>DNB Resident, Department of Pathology, Santokba Durlabhji Memorial Hospital, Bhawani Singh Road, Near Rambagh Circle, Jaipur, Rajasthan 302015, India**\*Corresponding author**

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**Abstract:** Adrenal myelolipoma (AML) is a rare, benign neoplasm composed of mature adipose tissue with variable amount of hematopoietic element mostly occurring as unilateral adrenal masses. They are usually hormonally inactive and asymptomatic until they reach large sizes. With the routine use of cross sectional imaging, these lesions are now being discovered with increasing frequency. We hereby present 4 cases of myelolipoma involving adrenal cortex. These include cases of, 2 men and 2 women with mean age of 39.5 yrs ranging from 28 to 55 yrs. Detection of AML was 'incidental' in 3 patients while being investigated for non-adrenal symptoms (pain abdomen in 2 and work-up for gall stone disease in 1) and the other one was detected with AML during work-up for hypertension. All patients were obese (BMI > 27), two of which were hypertensive and one had type 2 diabetes. Imaging was suggestive of AML in all of them. After performing a comprehensive review of literature using the PubMed database containing the keyword adrenal myelolipoma. We identified 792 articles written from 1947 to 2016, most of which were reviewed in detail including the author's own experience, whereafter we are highlighting the clinical features, salient diagnostic features and differential diagnosis of this neoplasm. Adrenal myelolipoma is not a common neoplasm and osteoid metaplasia in an adrenal myelolipoma is a rare incident. Adrenal myelolipoma may grow over time. Symptomatic tumors or more than 7cms should be removed due to increased risk of spontaneous rupture with retroperitoneal hemorrhage.

**Keywords:** Adrenal myelolipoma, Adrenal gland, Incidental, Diagnosis, Laparoscopy.

**INTRODUCTION**

Myelolipomas are rare, benign tumors of adrenal gland. Myelolipomatous foci can be concomitant with other suprarenal diseases or in extra-adrenal locations [1, 2]. Gierke first described the occurrence of myeloid and erythroid cells admixed with mature fat in 1905 [1, 3]. It was later termed myelolipomatosis by Oberling in 1929 [3, 4]. Its incidence is reported to be 0.08 to 0.4% at autopsy [5, 6]. Adrenal myelolipomas account for approximately 3 to 5% of all the primary adrenal tumors [3]. Although the true incidence of these tumors is unknown, less than 200 cases have been described in the literature so far [3, 7-13]. We present 4 cases of adrenal myelolipoma in the light of recent literature.

**MATERIALS AND METHODS****Case #1**

A 28 year old female was detected a stone in gall bladder on ultrasonography. On Computerized

Tomography(CT), she was incidentally found to have a well-defined, heterogeneous enhancing soft tissue density lesion in the right retroperitoneum while undergoing evaluation for gall stone. The maximum diameter of the mass lesion was 6.0 cm. She had no specific symptoms and her physical examination were also unremarkable. In the abdominal MRI, the right tumor measured 6.0 cm in maximum diameter, had high signal intensity on both T1- and T2-weighted images, and low signal intensity on T1 fat-suppressed images. The biochemistry profile showed plasma epinephrine, norepinephrine, cortisol, renin, aldosterone, and 24-hour urinary cortisol, metanephrine, vanillylmandelic acid, and homovanillic acid were all within normal limits. This suggested the diagnosis of incidental retroperitoneal masses, probably a myelolipoma. A differential diagnosis for malignant tumors was necessary, so the patient was subjected to transperitoneal laparoscopic right adrenalectomy. On macroscopic examination of the surgically removed

specimen, the tumor was yellowish-brown in color, measuring 6x4 cm, and weighing 90 g. Microscopic examination revealed that the tumor was composed of mature fat with admixed hematopoietic elements including megakaryocytes. Finally, histopathology ruled out malignancy and the diagnosis of AML was made. The diagnosis of adrenal myelolipoma was given. On follow up, the patient recovered well without any complications.

#### Case #2

A 42 year old female presented with dull aching pain and a mass in the right lumbar region for 1 year. She was on antihypertensive drugs since 6 months and had type 2 diabetes since 3 years. On examination BMI was 30kg/m<sup>2</sup>, BP 170/110 with no macules on skin. A bimanually palpable firm, non tender mass which was felt measuring 1x1 cm in right lumbar region. Other systemic examination was normal. Serum Cortisol, 17alpha OH prednisolone, plasma aldosterone and 24 hr Urinary VMA were within normal limits. CECT abdomen showed a large well defined lesion of 18 x 14.6 x 12.6 cm in right suprarenal region showing areas of calcification, necrosis and producing mass effect over adjacent abdominal viscera. No infiltration was noted-suggestive of adrenal myelolipoma. Following BP control, trucut biopsy was done. Microscopic examination showed mature adipose tissue, bone marrow elements (granulocytes, eosinophils and megakaryocytes)and osteoid metaplasia which confirmed the diagnosis.

#### Case #3

A 33 year old male presented with right flank pain for last 2 weeks. On examination his BMI was 31.5kg/m<sup>2</sup>. On ultrasonography, right adrenal mass was detected. Serum Cortisol, 17alpha OH prednisolone,

Plasma aldosterone, 24 hr Urinary VMA, urinary norepinephrine and epinephrine were normal. On CT, right adrenal mass measuring 18x16x7cm with hypodense areas suggestive of fatty tissue and a rim of soft tissue was detected. His BP was controlled and he underwent right adrenalectomy uneventfully. Histological examination confirmed the diagnosis of myelolipoma.

#### Case #4

A 55-year-old male, known to have hypertension, presented with pain in right loin, occasional palpitations and increased flushing, for the last 6 months. His BMI was 30kg/m<sup>2</sup>, pulse 100/min regular and BP was 200/120mm Hg. The physical examination was unremarkable and an ultrasound (US) of the abdomen revealed a left adrenal mass lesion. Laboratory investigations revealed the non-functioning nature of the mass, such as, adrenaline 20 ng/L, noradrenaline 217 ng/L and plasma cortisol 48 nmol/l. Free cortisol in 24 hours collected urine (total volume 1500 ml) was 80 nmol/L. Urinary levels of adrenaline were 10.86 ug/24 hours (ref: 4-20ug/24 hours), noradrenaline 57 ug/24 hours (ref: 23-105ug/24 hours), Dopamine 394 ug/24 hours (ref: 62-446 ug/24 hours) and urinary VMA was 11.61 mg/24 hours (ref: 0-13.6 mg/24 hours). A contrast CT revealed a non-enhancing mass lesion, arising from the laterally from the left adrenal gland, measuring 7x 5.4 cm. As there was no evidence of functioning pheochromocytoma, she was diagnosed with essential hypertension and managed with medications. Keeping in view the large size of the mass lesion and duration of symptoms, she underwent laparoscopic right adrenalectomy. The postoperative course was uneventful. Histopathology revealed myelolipoma with extramedullary haematopoiesis.

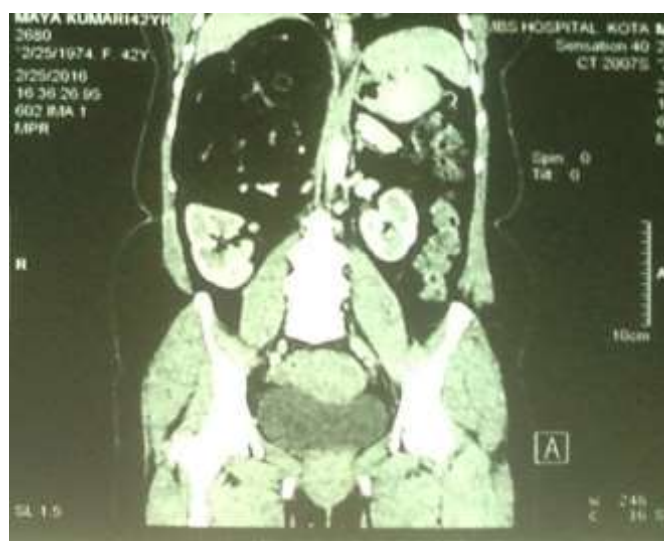
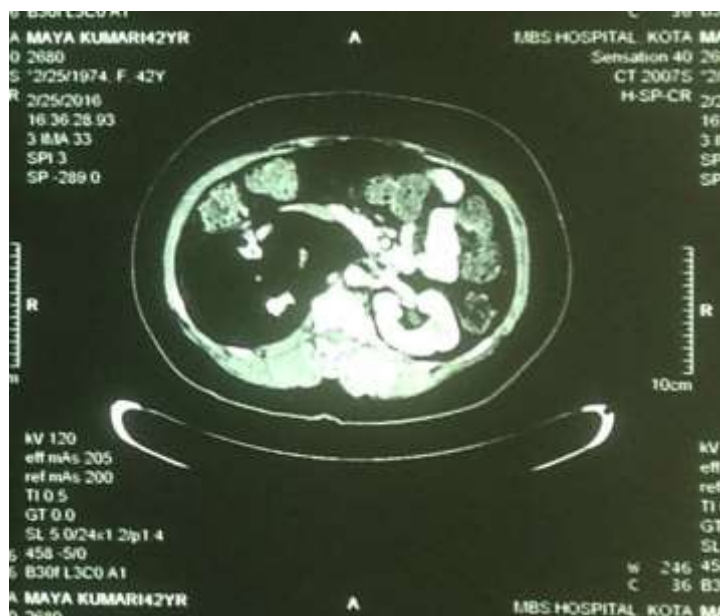
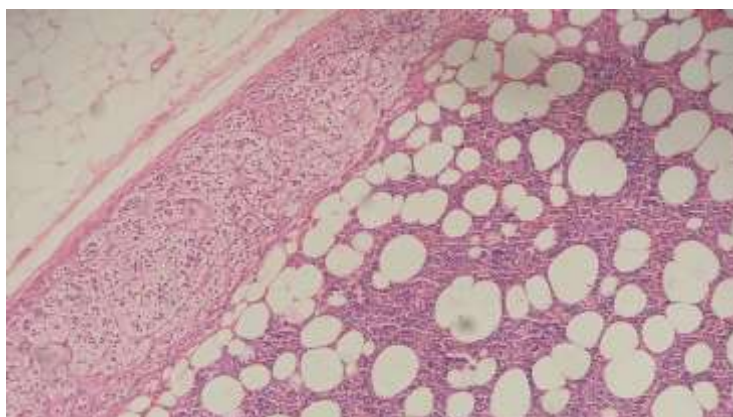


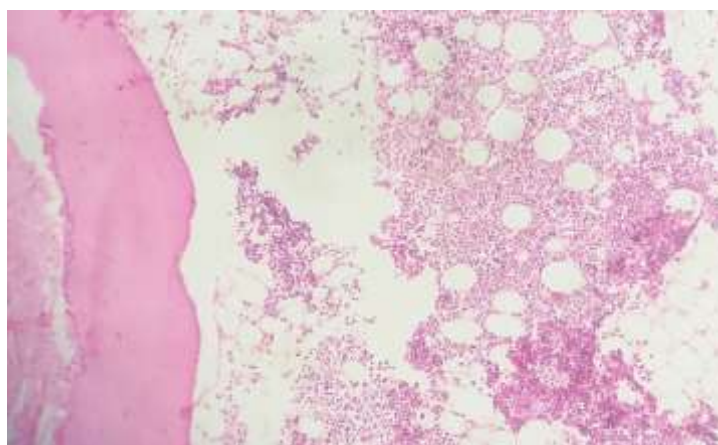
Fig-1: Coronal CECT of a 42 year old woman showing large fat density mass lesion with calcification was seen in the right suprarenal region



**Fig-2: Abdominal Axial CECT scan in a 42-year-old woman who presented to our department with vague right abdominal discomfort of 4 weeks' duration. CECT abdomen showed large well defined lesion of 126x146x180 mm in right suprarenal region showing areas of calcification, necrosis and producing mass effect over adjacent abdominal viscera, No infiltration was noted-suggestive of adrenal myelolipoma**



**Fig-3: Histopathological picture showing fat lobules in the background of the stromal element. normal adrenal tissue seen at periphery. (H&E, x10)**



**Fig-4: Histopathological picture showing myeloid cells intermixed with fat lobules area of osteoid metaplasia is seen at left. (H&E, x10)**

**RESULTS**

A total of four patients were diagnosed in SDMH during the last one year. Complete endocrine evaluation was performed to rule out a functional

tumor. Most tumors were incidentally diagnosed and surgery was indicated. Mean size was 12 cm(6cm-18 cm). Final on histopathology, all the cases were confirmed as myelolipoma.

**Table 1: Table showing some important reviews and case reports on adrenal myelolipoma**

No.	Author	Year	Cases	Age (Years)	Sex	Symptoms	Side	Remarks
1	Dieckmann <i>et al</i> [8,13]	1987	1	71	F	-	-	reviewed 59 surgically treated cases
2.	Kanj <i>et al</i> [13,14]	1988	1	24	F	S		Bilateral associated with Cushing's syndrome
3.	Murakami <i>et al</i> [15]	1922	1	41	M	S	L	21 hydroxylase deficiency
4.	Jenkins <i>et al</i> [16]	1994	1	44	F	S	R	associated with adrenal hyperplasia and Cushing's syndrome
5.	Reynard <i>et al</i> [17]	1995	1	58 43 48	F F M	S S S	L L BL	giant adrenal myelolipoma laparotomy in 3 cases
6.	Kenney <i>et al</i> [11]	1998	64	52(mean)	M-32 F-32	S-17 AS-37 Not mentioned 10	R = 45 L = 11 BL = 8	adrenal myelolipoma (37) Myelolipoma with other adrenal disorders (17)
7.	Lam <i>et al</i> [12]	2001	20	18-81	M-12 F-8	S-16 AS-4	R-10 L-10	myelolipoma (11), lipoma, teratoma, angiomyolipomas
8.	Bhansali A <i>et al</i> [13]	2003	6	26-60	M-03 F-03	S-4 AS-2	R-05 L-01	Associated with CAH ,21 OHLase Deficiency
9.	Francesca Manassero <i>et al</i> [18,19]	2004	1	64	F	AS	L	associated with non functioning adenoma
10.	Manabu Sakaki <i>et al</i> [20]	2006	1	69	F	S	BL	Associated with adrenogenital syndrome
11.	Octavio A. Castillo [21]	2007	18	35-75	M-12 F-06	S-03 AS-15	R-16 L-03	Laparoscopic Adrenalectomy
12.	Ingrid Nermoen [22]	2009	2	50,68	M	S	R	21-Hydroxylase Deficiency
13.	Blake B Anderson [23]	2010	1	35	M	S	R	Symptomatic giant Adrenal Myelolipoma
14.	Grażyna Orlicz-Szczęsna [24]	2011	1	53	M	AS	R	Large adrenal myelolipoma – case report
15.	Mustafa Ates [25]	2012	2	28,35	M	AS	R	Laprosopic surgery for adrenal myelolipoma
17.	Gunter Gerson [26]	2015	1	60	F	AS	R	Giant retroperitoneal myelolipoma

M-male, F-female, S-symptomatic , AS-asymptomatic, R-right, L-left, BL-bilateral

**DISCUSSION**

AML is frequently reported in the 5<sup>th</sup> and 7<sup>th</sup> decades of life with no sex predilection [13, 14, 27, 28]. Usually, the male-to-female ratio is 1:1, however, few studies have reported a male-to-female ratio of 2:3 [6, 29] Adrenal myelolipoma present as a site of extramedullary haematopoiesis [6]. These lesions are usually unilateral and asymptomatic, although a number of bilateral tumors have been described in the literature [3]. With the vast use of non-invasive imaging, its incidental detection of adrenal myelolipoma has become more common, reaching up to 7% of the adrenal masses [6, 30]. Myelolipomas are usually less

than 4 cm in diameter when discovered; however, they can attain very large sizes [3, 31, 32]. The largest adrenal myelolipoma reported in the literature weighed 5900 g [3, 33]. After excision, they generally do not recur, with recurrence-free survival rates of up to 12 years being reported [3, 12].

Major observations made in important reviews and case studies on AML are shown in the Table 1. All four patients described in our case reports are typical , with equal sex distribution, in age group of 28 – 55 years. Three of these patients, had right adrenal masses and only one had adrenal mass on the left. Adrenal

myelolipoma are generally hormonally inactive, although they have been seen in association with adrenal cortical tumors accompanied by Cushing syndrome, [34] with congenital adrenal hyperplasia [35] and adrenal ganglioneuroma [36].

The pathogenesis of myelolipomas remains equivocal with the most widely accepted theory being the existence of metaplasia of reticuloendothelial cells of blood capillaries in the adrenal glands, in response to stimuli, such as, necrosis, infection or stress [6, 37]. Bishop *et al* demonstrated non random X chromosome inactivation in the hematopoietic elements and fat in 8 of 11 myelolipomas from female patients in support of a clonal origin of these tumors [38].

These lesions are typically asymptomatic, however, they can present with abdominal or flank pain as a result of haemorrhage, necrosis or pressure effect on surrounding organs [39]. Ultrasonography, CT, and MRI are effective in diagnosing adrenal myelolipomas in more than 90% of cases [3, 40, 41]. The sonographic appearance varies with the composition of the individual tumor. If the tumor contains mostly fat, a uniformly hyperechoic suprarenal mass will be seen. Adrenal myelolipoma has mixed hyperechoic and hypoechoic areas, reflecting varying amounts of fatty and myeloid elements. The tumor may be completely hypoechoic if composed primarily of myeloid cells [41, 42]. However, hemorrhage may produce hypoechoic areas and calcification obscures the internal sonographic characteristics. Although, a predominantly hyperechoic adrenal mass should suggest myelolipoma, sonography is not as specific as CT. CT is the most sensitive diagnostic imaging modality [42]. The appearance of myelolipomas on CT also depends on their histologic composition, with some tumors showing only small regions of fatty tissue in a predominantly soft-tissue mass, whereas others are predominantly composed of fat. These masses are seldom calcified and often have a recognizable capsule. Although an adrenal adenoma may have low attenuation values due to a large amount of intracellular lipid, the density of an adenoma is usually not less than -20 H [42, 43]. In nearly all myelolipomas, some regions with density less than -30 H (often as low as -100 H) can be identified. Fat has high signal intensity on both T1 - and T2-weighted MR images; hematopoietic marrow elements have low signal intensity on T1 -weighted images and moderate signal intensity on T2-weighted images; signal intensity of hemorrhage varies depending on the age of the blood [42]. As with CT and sonography, the MR appearance of a myelolipoma reflects the relative predominance of fatty and myeloid elements. A predominantly fatty mass has a uniformly high signal intensity on both T1 - and T2-weighted images. A mass with little fat and a great deal of myeloid tissue has mixed signal intensity on T1 -weighted images and

moderate-to-high signal intensity on T2-weighted image [42, 44].

Differential diagnosis of myelolipoma are: retroperitoneal lipoma, liposarcoma, exophytic renal angiomyolipoma, adrenal adenoma, adrenal metastasis and primary adrenal malignancy [21]. Retroperitoneal liposarcomas usually can be excluded as they are nonhomogeneous on CT and are infiltrative in nature.

Grossly, AML typically shows sharply defined yellow adipose tissue with varying amounts of red-brown hematopoietic elements. Microscopic examination shows scattered islands of fat cells intermixed with hematopoietic stem cells. Although rare, areas of hemorrhage, calcification and necrosis may be observed.

Incidentally discovered adrenal myelolipomas requires appropriate treatment modalities which include observation and surgical removal. Small asymptomatic tumors less than 4cm are monitored clinically and advised follow up. Symptomatic tumors or myelolipomas larger than 7 cm should be removed since the risk of spontaneous rupture with retroperitoneal hemorrhage is imminent.

## CONCLUSION

Adrenal myelolipoma is not a common neoplasm and osteoid metaplasia in an adrenal myelolipoma is a rare incident. These tumors may grow over time. Patients with small, asymptomatic myelolipomas must be monitored clinically and routine follow-up imaging studies may be done, but surgical treatment must be reserved for selected patients with large and symptomatic lesions. Occasionally large silent tumours are excised, to prevent the occurrence of a rupture or intra-tumoral haemorrhage.

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