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GIANT RENAL ANGIOMYOLIPOMA: CASE SERIES AND REVIEW OF THE LITERATURE

Pathology

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ABSTRACT

Angiomyolipoma belongs to a family of neoplasms called perivascular epithelioid cell tumours (PEComas). (1) The World Health Organization (WHO) defines PEComas as "mesenchymal tumours composed of histologically, ultra-structurally, and immunohistochemically distinctive perivascular epithelioid cells. (2) Angiomyolipoma is rare benign tumour which is composed of an intimate admixture of blood vessels, smooth muscle cells and fat hence this name is given. They occur at many sites, more commonly in kidney. It is also referred to as renal hamartoma and is rare solid tumour without malignant characteristics. The inheritance pattern of renal AML is autosomal dominant. They are seen in 25-50% of patients with tuberous sclerosis. Unilateral presentation is uncommon. (3) If the lesion grows to a large size, a series of clinical manifestations and serious complications may occur. Due to the haemorrhagic aneurysms that develop with the enlarging AML, the incidence of compression symptoms and the risk of bleeding from rupture increase. (4) Angiomyolipoma presenting as enlarged lump may mimic renal cell carcinoma, yet malignancy has to be ruled out. Excision is recommended for definite histological diagnosis in symptomatic patients and to prevent risk of haemorrhage and malignancy. We herein present a case series of three cases received in the duration of 5 years (2018-2022), all three patients were females presented with complaint of unilateral flank pain and one of them presented with symptoms of haematuria.

KEYWORDS

Angiomyolipoma, PEComas, mesenchymal tumours

INTRODUCTION

Renal angiomyolipoma (AML) was first defined in 1951 by Morgan et al.[5] They are mesenchymal kidney tumors containing smooth muscle cells, dysmorphic blood vessels, and adipocytes (triphasic histology).[6] The associated tortuous thick-walled blood vessels lacking elastic tissue lamina often have bundles of tumour cells that seem to emanate from the vessel walls.

AMLs are rare kidney tumors and constitute 2%-6.4% of all renal tumors.[7] The prevalence of renal AML in the adults is more and female individuals are four times at risk than their male counterparts.[8]

The tumour may be found incidentally or result in retroperitoneal haemorrhage, which can be massive and even fatal. When renal AMLs grow to a size of >10 cm, they are referred to as 'giant' AMLs. Giant renal AML is uncommonly reported in the literature.[9]

Most small angiomyolipoma are asymptomatic and found incidentally on imaging studies, usually incidental from USG or CT scans performed for unrelated clinical indications. In minority cases, they classically present with flank pain (53%), a palpable tender mass (47%) and gross hematuria (23%); this is known as 'Lenk's triad'.[10]

Case Reoprt -1

In July 2022, a 29-year-old female patient was admitted to the Department of Urology, SMS Medical College, Jaipur with chief complaints of hematuria and pain in right flank of her abdomen for 12 days. Patient had similar episode around 15 years back-managed conservatively. History of hypothyroidism for one year. Patient's vitals were pulse rate- 128/minute, blood pressure- 96/68 mmHg, respiratory rate- 21/minute and afebrile.

On physical examination, A large (>15cm) mass was palpable in her right upper quadrant, margins ill defined, tender, mobile, ballotable.

Laboratory results demonstrated normal hemoglobin 4.5 mg% and creatinine 1.09mg%, as well as urine analysis indicate presence red blood cells.

X- ray chest shows raised right dome of diaphragm. Ultrasound of abdomen reports SOL of size 15x12 cm arising from right middle-lower pole in Right kidney.

CT scan whole abdomen with urography shows large heterogeneous mass of size 18x13x13 cm with confluent areas of internal fatty attenuation seen arising from lower half of right kidney-suggestive of angiomyolipoma. Multiple sub-centimetric varying size fatty nodules also seen bilateral kidneys- likely multiple angiomyolipoma.

In view of above findings and pain, malignancy has to be ruled out. She was scheduled for angioembolization followed by wide excision under GA with consent and possibility for right radical nephrectomy and adrenalectomy. Intraoperatively mass was seen grossly encasing right kidney. Right nephrectomy was done, right adrenal glands was normal and not removed. She made an uneventful recovery and was discharged on POD 8.

In Histopathological examination, macroscopically the mass was solid measured 18×14×12cm with weight of 850 grams.

Grossly outer surface is capsulated and fibrofatty. On cutting kidney is replaced by fat. No corticomedullary differentiation seen. A tan brown area identified measuring 9x8x6cm. Normal renal parenchyma identified at lower pole.

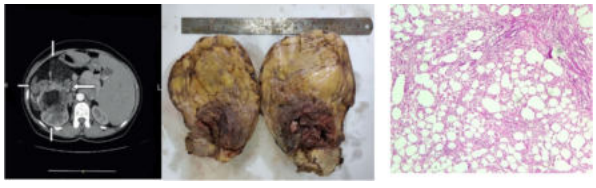


Figure1: CT scan Heterogenous mass in right kidney.
Figure 2: Right nephrectomy specimen is replaced by fat and tan brown area seen.
Figure 3: Tumour consist of mature adipose tissue, thick-walled blood vessels and smooth muscle(40x)

Microscopically, peculiar growth pattern identified mature adipose tissue intermixed with smooth muscle component of varying degree with few thick-walled blood vessels. There are numerous polygonal cells having dense eosinophilic cytoplasm, multilobation of nucleus as well as multinucleation. There are vast areas of necrosis and foci of hemorrhage seen along with presence of foreign body giant cell reaction. Final histopathological diagnosis was giant renal

angiomyolipoma.

Case Report-2
A 49-year-old female presented to outpatient department, with fever since last one month, left flank pain and lump in left half of abdomen.

Examination revealed a stable patient with a 18x15 cm. lump in left hypochondrium and lumber region.

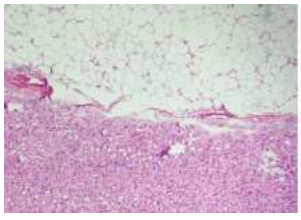
Blood investigations revealed a hemoglobin of 11.9 g/dL, a total leukocyte count of 9000/mm3, and a platelet count of 150 x 10 3 /mm, creatinine of 1.7 mg/dL and a blood urea nitrogen (BUN) of 58 mg/dL.

Chest X-ray, urine analysis and blood culture were negative.

An ultrasound scan of the abdomen revealed a mass of heterogenous echogenicity involving and expanding the upper pole of the left kidney.

CECT revealed a 18x16x12 cm heterogeneous mass containing fat density 13 Hounsfield units with hypervascularity arising from middle pole of left kidney confirming it to be a giant angiomyolipoma. As the patient was diabetic with borderline renal function, angioembolization followed by left partial nephrectomy was done.

Grossly kidney ms. 10x7x6 cm., large mass ms. 18x15x11cm. External surface of tumor is capsulated, globular smooth with predominant vascular markings. On serial sectioning the mass is soft predominantly homogenous, fibrofatty with few cystic and hemorrhagic areas. It seems to be arising from renal pelvis and is sharing same capsule as kidney. Adjacent kidney normal corticomedullary differentiation seen and is unremarkable.



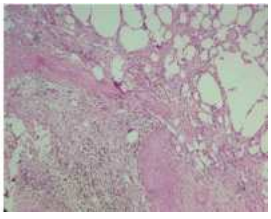


Figure 4: Normal renal parenchyma with adipose tissue component of tumor (10x)
Figure 5: Thick-walled congested blood vessel with mature adipose tissue (40x)

Histopathological analysis revealed a tumor continuous with renal hilum composed of mature adipocytes with interspersed, scattered abnormal blood vessels with thick walls. At places the vessels are rimmed by radially oriented smooth muscle. Attached kidney is unremarkable. No evidence of atypia or mitosis noted.

Histomorphological features are consistent with renal angiomyolipoma.

Case Report -3
A 28-year-old female patient presented to out patent department of SMS Medical College and hospital, Jaipur with chief complaint of fever and right flank pain for one month.

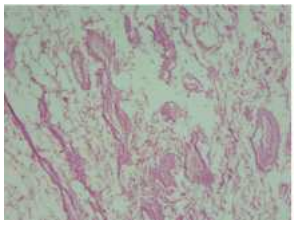
On physical examination, A mass palpable in right hypochondrium approximate size 12x10cm.

Laboratory investigation demonstrate Hb 10.5mg%, creatinine 1mg% and urine analysis and blood culture are negative.

Ultrasound whole abdomen reveals mass of size 11x4cm. in middle pole of right kidney pushing pelvicalyceal system medially.

Computed tomography demonstrates a 11x4x3.5cm. sized heterogenous mass with confluent areas of internal fatty attenuation seen in middle pole of right kidney, renal parenchyma is compressed and pelvicalyceal system is pushed medially.

Grossly, kidney is replaced almost completely by yellowish white areas which are firm to soft in consistency ms. 11x4x3cm. At periphery compressed renal parenchyma seen. Corticomedullary differentiation is completely lost. At lower end of ureter tiny calculi are seen impacted in the lumen.



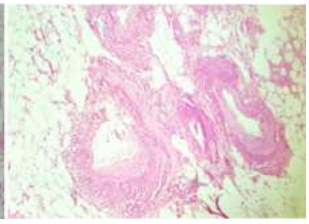


Figure 6,7: Microphotograph- Renal AML tumour showing thickened vessels, adipocytes, proliferating spindle cells (40X).

Histopathology reveals features of angiomyolipoma in specimen of radical right nephrectomy. Mitotic rate-0-2/hpf, Necrosis-not identified. All margins were free from tumor pathology. Adjacent renal parenchyma shows sclerosed renal glomeruli with hyaline tubular cast-showing chronic pyelonephritis.

DICUSSION
Renal angiomyolipoma (AML) is a triphasic benign mesenchymal tumor consist of smooth muscle, dysmorphic vessels and adipocytes. These are of two types sporadic and inherited.

The first type, sporadic (80%), shows a strong female predilection (F:M of 4:1), are unilateral and typically identified in adults (mean age 45 years). Nearly all patients i.e. about 77% of tumours that are less than 4 cm in size are asymptomatic, however 82% of AMLs that are bigger than 4 cm exhibit symptoms that include fever, nausea, vomiting, pain, palpable mass, haematuria, hypertension, anaemia, and shock. Retroperitoneal haemorrhage (Wunderlich syndrome) usually seen in up to 50% of cases with large tumours.[11]

The second type is inherited AML (10-20%) are seen in association with phakomatoses, the vast majority in the setting of tuberous sclerosis, although they have also been described in setting of von Hippel Lindau syndrome (VHL) and neurofibromatosis type 1 (NF1). In these cases, they present earlier (usually identified by the age of 10 years), much larger, far more numerous and seen in both sexes. They are more likely to be fat-poor, which accounts for their earlier presentation. The clinical presentations of inherited AML are similar to that of sporadic AML, but also include neurological & cutaneous symptoms of tuberous sclerosis as mental retardation, seizure and adenoma sebaceum.[12]

AMLs were histologically classified as Classical AML(CAML) and Epithelioid AML(EAML) according to the 2016 WHO Classification of Tumors of the Urinary System and Male Genital Organs. CAMLs were diagnosed when the tumour is composed of a variable proportion of adipose tissue, smooth muscle cells and abnormal thick-walled blood cells. When the tumour shows proliferation of predominantly epithelioid cells, the diagnosis was EAML.[13]

Differential diagnosis of AML, renal cell carcinoma (RCC), oncocytoma, liposarcoma, leiomyosarcoma and metastasis of any other primary tumours are present. Epithelioid AML is a monotypic type of AML that can mimic RCC. Fat-predominant and muscle-predominant AMLs may mimic liposarcoma and leiomyosarcoma, respectively, which are the most common types of retroperitoneal sarcomas.[14]

A previous study examined > 60,000 patients by sonography abdomen, reported prevalence of renal angiomyolipoma vary from 0.2% to 0.6% with 0.28% in male and 0.6% in female population. In the same study found 57% of the patients had right kidney and 43% had left kidney involvement.[15] One another study examined approx. 2000 patients by abdominal computed tomography and reported AML prevalence of 2.2% and mean tumor size of 5mm.[16] On comparing both the studies CT scan examination can detect smaller tumors, hence high incidence of AML was the result of advanced imaging technique of CT.

A large number of AML cases were detected incidentally on imaging and were asymptomatic. Management of tumor size <4 cm was usually conservative with periodic follow-up, while tumor of size 4-9 cm was managed with close monitoring of symptoms and intervention was done when there is suspicion for progression and malignancy.[17]

Indication for intervention-tumor size >8 cm., increase in size of

previous tumor(>4cm.), symptomatic cases, hemorrhage and associated renal function.[18]

In our study, all patients are female with mean age of 35.33 years, which ranges from 28 to 49 years. Tumor location of was in right kidney in two cases and in left kidney in one case. Among three cases two were unifocal, unilateral and one was multifocal, bilateral. The tumor ranged from 9 to 18 cm. in greatest dimension, mean greatest dimension 12.66 cm. Cut surface of the tumors varied from yellow to tan brown depending on the percentage of the components they contained.

On the basis of an extensive literature review, Oesterling et al., reported that 82% of patients with AMLs larger than 4 cm in diameter were symptomatic, with 9% in haemorrhagic shock at the time of presentation; in contrast, patients with smaller tumours were symptomatic 23% of the time.[19]

The treatment approach is consisting of two main strategies to manage this tumor are renal angioembolization (RAE) and surgery. A randomized control study was conducted in year 2011 on 59 patients with renal angiomyolipoma, out of which 17 patients underwent RAE alone. As a result, tumor size decreased by 50% to 60% only on follow up and 14% of these required repeated RAE sessions. It was observed that RAE was effective in tumor with single feeding vessel and in condition of acute hemorrhage.[18]

Most patients with acute or potentially life-threatening haemorrhage require total nephrectomy if it is explored; in such circumstances, selective embolization can temporize and, in many cases, prove definitive. Partial or total nephrectomy if planned should be done within few days of angioembolisation to avoid extensive adhesion. [17,20] The anatomical course of the vascular supply and the extent of involvement of renal parenchyma seen intraoperatively was vital in deciding on preservation of the involved kidney. If surgical option is not present then everlimus may be considered as alternative therapeutic options.

CONCLUSION

Angiomyolipoma is a rare benign tumor. In our study all three patients were middle aged female presented with complaint of unilateral flank pain and one of them had hematuria.

CT Scan and USG help in diagnosis. The mass appears to be echogenic on ultrasound and has the density of fat on CT scanning.

Grossly, all three cases were of giant renal angiomyolipoma. Cut surface varied from yellow to tan brown.

On histopathological examination, Presence of admixture of all these components (mature adipose tissue, spindle cells and thick-walled vasculature with presence of perivascular epithelioid cells) makes the diagnosis of angiomyolipoma easy.

Patients with lesion greater than 4cm with moderate or severe symptoms (bleeding or pain) should undergo surgical intervention either in form of tumour excision with or without nephrectomy, renal sparing surgery or renal arterial embolization. Embolization is the treatment of choice for acutely bleeding AML. [21]

Hence, our experience conclude that giant renal AML may be diagnosed with the help of imaging and is confirmed by histology and immunohistochemistry. As this tumour is associated with risk of hemorrhage, patient require surgical excision.

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