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Original Research Article

Angiomyolipoma managed by partial nephrectomy: Outcomes and follow-up

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ABSTRACT

Introduction: Angiomyolipoma (AML) is a benign neoplasm and consists of thick-walled poorly organized blood vessels, smooth muscle, and varying levels of mature adipose tissue. We evaluated the impact of clinical characteristics, particularly tumor diameter, and surgical treatment in the form of partial nephrectomy on the outcome of sporadic renal AML.
Materials and Methods: Patients undergoing partial nephrectomy during the period Jan 2000 to Dec 2016 with a final diagnosis of angiomyolipoma formed the study group. Patient demographic data was collected, and data from during and after surgery was also reviewed.
Results: The median age of the patients was 51 (38-55) years. At presentation, most patients were asymptomatic (6/8, 75%) with the AML presenting as an incidental finding on imaging done for other reasons. There was classical triphasic AML, consisting of elements of adipose tissue, smooth muscle and abnormal blood vessels, in 5/10 tumours (50%). The more aggressive epitheliod variant AML was present in 2/10 (20%). The median follow-up of the patients was 38 (29-64) months. During the follow-up period one (12.5%) patient who had two lesions progressively showed evidence of rising creatinine and decreasing creatinine clearance.
Conclusions: AML is a benign renal neoplasm and should be treated initially conservatively. Surgical intervention when required should be nephron sparing so as to reduce the incidence of perioperative complications, loss of renal units, and development of CKD.

1. Introduction

Angiomyolipoma (AML) accounts for less than 10% of renal tumors, with autopsy series and ultrasound-screened populations showing incidences of 0.3% and 0.13%, respectively, in the general population.[1,2] It is a benign neoplasm and consists of thick-walled poorly organized blood vessels, smooth muscle, and varying levels of mature adipose tissue.[3,4] Initially it was considered to be a form of hamartoma however, recent evidence has suggested that it is neoplastic in origin with evidence of a monoclonal, rather than polyclonal, source.[1,5] Angiomyolipoma derives itself from perivascular epithelioid cells, belonging to a group of tumors referred to as PEComas (perivascular epithelioid cell tumors).[4,6] The tumor is predominantly found in females,[1] is rare before puberty, suggesting a potential hormonal influence and strongly expresses estrogen receptor β, progesterone receptor, and androgen receptor.[7]

The most common complication related to renal AML is retroperitoneal bleeding, which has been reported in 15%

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of patients[8] and may lead to shock in 20% to 30% of these patients. The primary indication for treatment of renal AML is the presence of symptoms or suspected malignancy as per the current guidelines of the European Association of Urology.[9] The treatment decisions for lesions with unusual growth and imaging characteristics could be guided by biopsy.[6] Large AMLs, women of childbearing age, and patients for whom follow-up or access to emergency care may be inadequate[9] may be included for prophylactic intervention as per level C recommendations. The treatment threshold for AML tumors till recently was a diameter of ≥4 cm, which has been disputed presently. Recent studies have shown that treating all AMLs of >4 cm may lead to an over-treatment rate of 65%.[10] The aim of this study was to evaluate the impact of clinical characteristics, particularly tumor diameter, and surgical treatment in the form of partial nephrectomy on the outcome of sporadic renal AML.

2. Materials and Methods

Patients undergoing partial nephrectomy during the period Jan 2000 to Dec 2016 at our institution formed the study group. After obtaining approval from the Institutional/University Ethical committee, we retrospectively reviewed the inpatient and outpatient case records using the hospital approved renal tumor departmental database. Of the patients undergoing partial nephrectomy, 8 had a final pathological diagnosis of AML.

Patient demographic data was collected, and data from during and after surgery was also reviewed. Preoperative imaging including renal ultrasonography (USG), contrast-enhanced Computed Tomography (CT) (Figure 1), or contrast-enhanced MRI done at our institution was also reviewed. Images were reviewed for evidence of the presence of fat- containing areas in the tumor. Pathological results were reviewed, and results were confirmed using light microscopy and immunohistochemistry as and when felt necessary.

The follow-up visits were at 3 months after surgery and then annually thereafter. Serial follow-up imaging was obtained using renal USG. Renal function was assessed with estimation of serum creatinine and creatinine clearance.

3. Results

Patient demographic data for the 8 patients undergoing partial nephrectomy was as shown in (Table 1). The median age of the patients was 51 (38-55) years. At presentation, most patients were asymptomatic (6/8, 75%) with the AML presenting as an incidental finding on imaging done for other reasons. Both (25%) the symptomatic patients had gross hematuria with ipsilateral flank pain. Four (50%) of the patients had a diagnosis of AML on preoperative imaging. In the remaining four patients a diagnosis of a heterogeneously enhancing mass with no fat noted was made on imaging. All the patients had a normal appearing and functioning contralateral kidney. Seven (87.5%) of the patients had a solitary lesion whereas one other patient had two lesions near to each other of similar size.

Pre-operative biopsy was not done in any of the patients given the strong suspicion of renal cell carcinoma/sarcoma and the notoriously inaccurate findings on needle biopsy with these fatty lesions. The variables during surgery were as listed in (Table 2). Open partial nephrectomy was performed in five patients (Figure 2), and laparoscopic partial nephrectomy in three others. The decision to perform open/laparoscopic was based on the surgeons choice.

None of the patients needed either intra-operative or post-operative blood transfusions. The median blood loss was 80.2±16.48 (50-100) cc, median operating time was 109.75±17.46 (90-150) mins. Two (25%) patients had minor post-operative complications including fever and upper respiratory tract infection. Serum creatinine was estimated at three months and at the end of 1 year after surgery. None of the patients had chronic kidney disease prior to surgery. At the end of one year, none of the operated patients had significant deterioration of estimated glomerular filtration rate (eGFR) and none of the patients progressed to chronic kidney disease (CKD). The median follow-up of the patients was 38 (29-64) months. During the follow-up period one (12.5%) of the two patients who had two lesions progressively showed evidence of rising creatinine and decreasing creatinine clearance. The patient progressed to CKD with eGFR of <60 ml/min.

The pathological findings were as listed in Table 4. In all, 10 tumors were removed from 8 patients. The median (range) histological size of the excised specimen was 5.84±0.99 (4.5 – 7.5) cm. There was classical triphasic AML, consisting of elements of adipose tissue, (Figure 3 a) smooth muscle and abnormal blood vessels (Figure 3b), in 5/10 tumours (50%). The more aggressive epitheloid variant (Figure 3 c) AML was present in 2/10 (20%).

4. Discussion

Angiomyolipoma is an uncommon benign renal tumor that accounts for <5% of enhancing renal masses.[11] The strategy for the treatment of renal AMLs was based mainly on evidence acquired during the 1980's.[12] As major retroperitoneal bleeding was known to be the most severe complication of AML, prophylactic treatment was indicated to avoid this hemorrhagic event. For many years, the threshold diameter for prophylactic treatment has been 4 cm.[12] The diagnostic methods for AMLs have improved significantly during recent years. In view of these improved diagnostic methods, it would be appropriate to re-evaluate the indications and efficacy of various invasive treatment strategies for AML.

Kuusk et al[13] performed a literature review covering the era of modern diagnostic modalities to obtain detailed

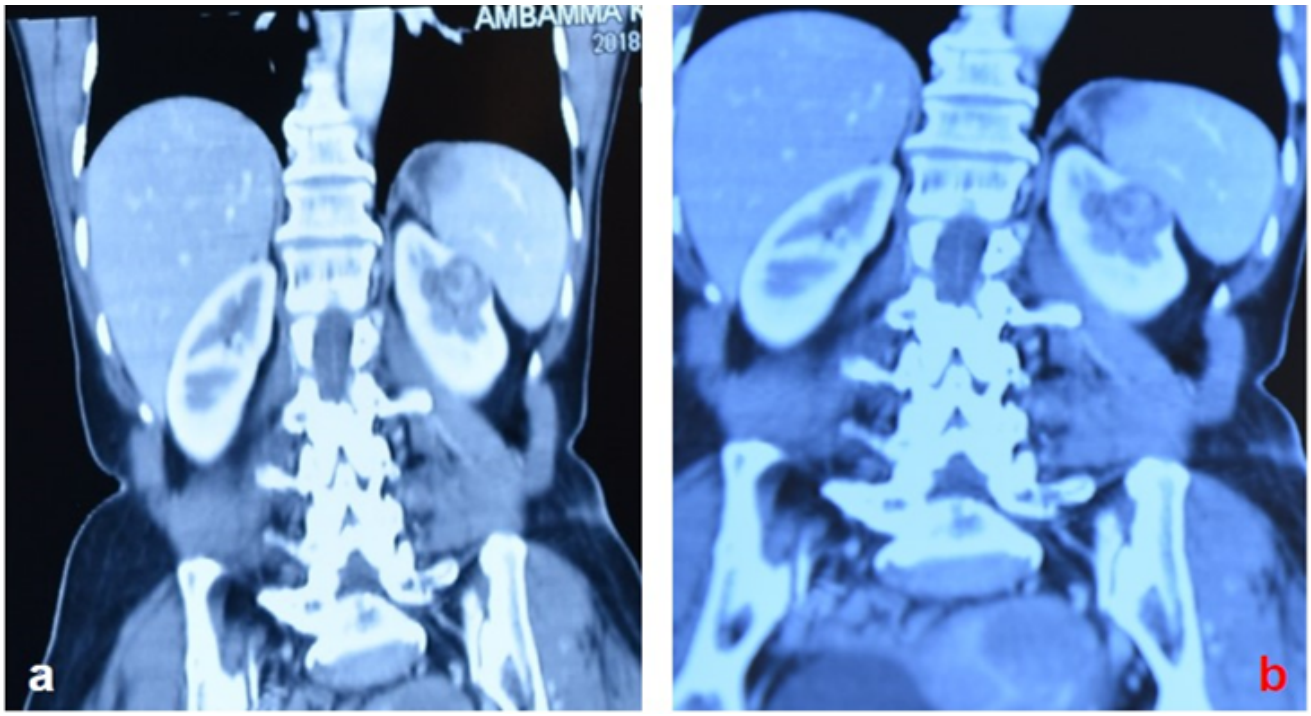

Fig. 1: a & b: Shows an ill-defined heterogeneously enhancing fat containing mass lesion involving upper inter-polar region of the left kidney measuring 6.1X1.7X2.3 cms. Medially it extends into right midpole calyx and renal pelvis.

Table 1: The demographics of the patients

No	Variable	Median (range) & n (%)
1	Gender	
	Female	7 (87.5%)
	Male	1 (12.5%)
2	Side	
	Left	5 (62.5%)
	Right	3 (37.5%)
3	Presentation	
	Incidental	6 (75%)
	Hematuria	2 (25%)
4	Size on imaging (cms)	5.84±0.91 (4.5-7.5)

Table 2: Operative variables

No	Variable	Median (range) & n (%)
1	Surgery performed – Open partial nephrectomy Laparoscopic partial nephrectomy	5 (62.75%) 3 (37.5%)
2	Warm ischemia time (mins)	21.18±2.85 (15-25)
3	Estimated blood loss (cc)	80.2±16.48 (50-100)
4	Blood transfusions	-
5	Length of post-operative hospital stay (days)	4.2±1.34 (3 – 7)
6	Operating time (mins)	109.75±17.46 (90-150)
7	Complications - minor	2 (25%)

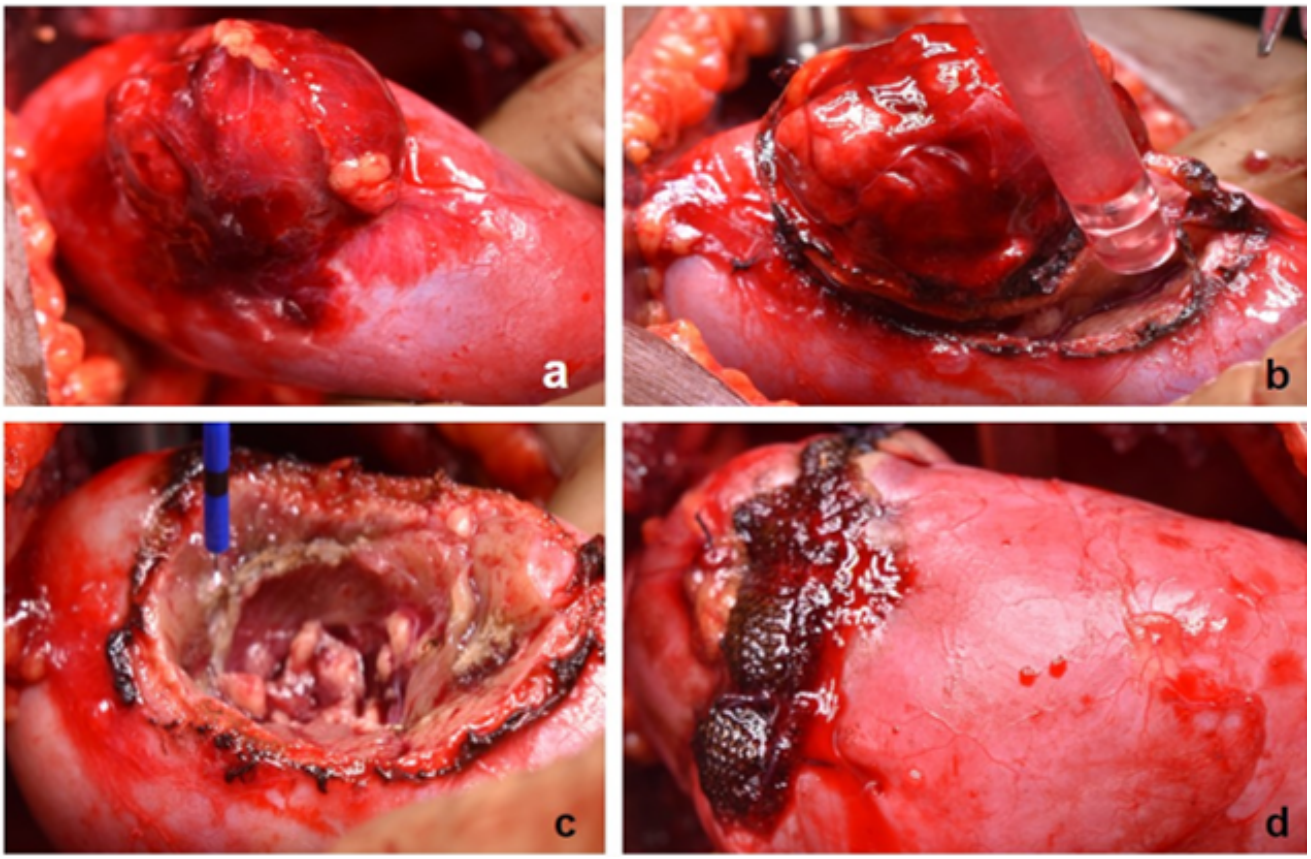

Fig. 2: a: The left kidney is exposed to reveal a red coloured mass lesion arising from the upper portion of left kidney;**b:** An incision is marked around the mass lesion; **c:** The mass lesion is excised, leaving a huge deficit; **d:** The kidney is sutured over surgicel

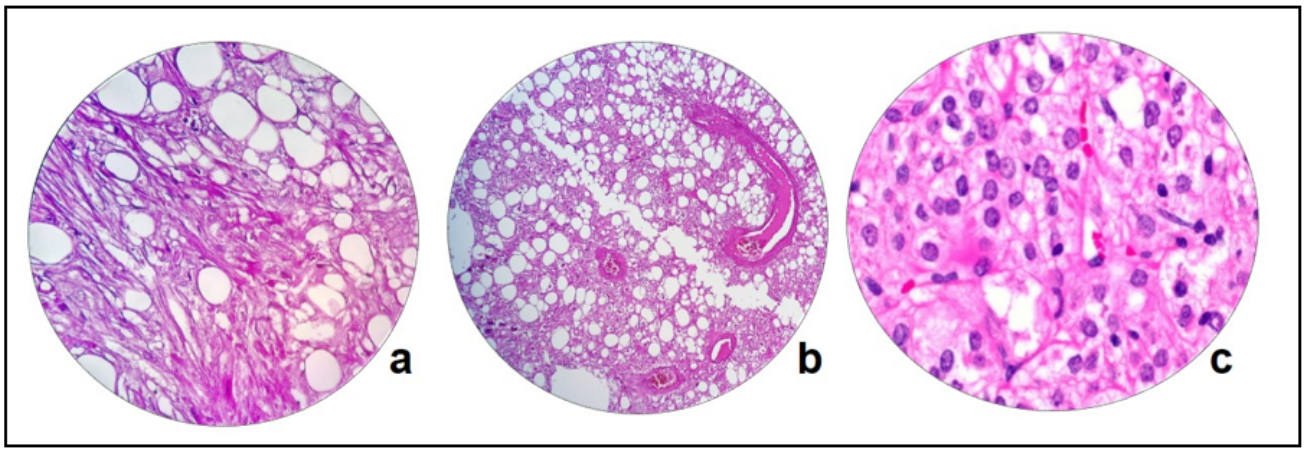

Fig. 3: a: Photomicrograph showing spindled myoid cells and adipose tissue (H & E stain, 400X); **b:** Photomicrograph showing distorted vessels with fat and angiomyolipoma. (H & E stain, 200 X); **c:** Photomicrograph showing clusters of epithelioid cells, separated by mature adipose tissue a feature of epithelioid variant of angiomyolipoma.

Table 3: Renal function of the patients

No	Variable	Pre-operative	3 months after surgery	1 year after surgery
1	Serum Creatinine mg% (range)	1.02±0.11 (0.9 – 1.2)	1.11±0.16 (0.9-1.3)	1.11±0.16 (0.9-1.3)
2	Estimated GFR ml/min (range)	90.5±13.86 (80-130)	80.2±27.06 (84-120)	88.4±18.78 (80-120)
3	Progression to new onset CKD at the end of 1 year		-	-

Table 4: Histopathology

No	Feature	N (%)
1	Histopathology	
	Triphasic (classic)	5 (50%)
	Epitheloid	3 (30%)
	Fat predominant	2 20%)
2	Surgical margins	
	Negative	9 (90%)
	Positive	1 (10%)
3	Median size (range) cm of the excised lesion	5.84±0.99 (4.5 – 7.5)

patient data on the efficacy of the current treatment strategies. They concluded that the prevalence of major bleeding was high in sporadic AMLs with a diameter of >6 cm. Among current treatment methods, embolization was associated with a significantly higher risk of re-intervention. They suggested a conservative treatment in AMLs of <6 cm in diameter. Kuusk et al[13] felt that there was a needto define the risk factors for bleeding and assess the relative benefits of different treatment modalities. The median size of the lesions in our series was 5.9 (4.5-7.5) on imaging and the excised lesion was 5.84±0.99 (4.5 – 7.5). Two (25%) patients in our series had gross hematuria.

Several minimally invasive techniques, including cryotherapy and arterial embolization (AE), have been successfully used to treat large symptomatic AMLs, including in the setting of acute haemorrhage. Ramon et al.[14] treated 48 kidneys with a mean tumour size of 10.3 cm with AE, with a 5-year freedom-from-surgery rate of 94%. Lane et al.[15] even treated patients with massive bilateral AMLs secondary to the tuberous sclerosis complex with AE, and was able to preserve renal function conservatively without intervention for prolonged periods (>20 years). Today surgical intervention for AML is only necessary in selected circumstances.

Nephron sparing-surgery for sporadic AMLs is known to offer preservation of renal function and is associated with acceptable complication and low local recurrence rates.[11] Boorjian et al.[16] in his series of 58 patients undergoing nephron-sparing surgery for AML, reported a 12% complication rate, including 5% of patients with sustained urine leaks. They reported that none of their patients developed de novo chronic renal insufficiency through a median follow-up of 8 years, based on only serum creatinine levels which is an inaccurate way to determine renal function.[17,18]

Berglund et al[11] in their series reported a 16% rate of loss of a renal unit and, 14% of patients had progressed to new-onset CKD at the last follow-up. Avoiding the development of CKD by avoiding unnecessary renal surgery is an important goal in diagnosing and treating AML renal masses. Though none of the patients in our series underwent nephrectomy, 12.5% of the patients progressed to CKD in the follow-up period. The limitations of our study were the small number of cases, the retrospective nature of our study and that we included patients undergoing partial nephrectomy only. A prospective study assessing all forms of intervention including surveillance would help us to elucidate that question of CKD. In conclusion, AML should be treated conservatively when diagnosed. Surgical intervention if necessary should be nephron sparing so as to reduce the incidence of perioperative complications, loss of renal units and the development of CKD.

5. Source of Funding

None.

6. Conflict of Interest

Nil.

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