

## Original Research Article

# Primary renal leiomyosarcoma: a rare entity

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### ABSTRACT

**Background:** Primary leiomyosarcoma of the kidney is an exceptionally rare tumor with an aggressive behavior. However, reported literature is very limited. Since the prognosis for a renal sarcoma is extremely poor, differentiation from sarcomatoid renal cell carcinoma (RCC) is necessary. Histopathology and immunohistochemistry are the only modes of diagnosing these sarcomas as they have no specific diagnostic features clinically and radiologically. Objectives was to evaluate the clinicopathological pattern of leiomyosarcomas arising from kidney.

**Methods:** This study was conducted in the Department of Pathology, Government Medical College, Srinagar. It was a retrospective study done over a period of 3 years, July 2014 to June 2017. A total of 4 patients, who underwent surgery and were diagnosed with primary LMS of the kidney, were included in the present study.

**Results:** The study was done to evaluate the clinicopathological pattern of 4 cases of primary renal LMS diagnosed at a tertiary care hospital. Age of the patients ranged from 35-64 years with a mean age of 53.5 years. Sex ratio of 1:1 was observed. Major presenting symptom was flank pain (75%) followed by mass abdomen (50%). Also, one of the patients presented with spontaneous rupture of kidney. Radical nephrectomy was done in all patients. On gross examination tumor had originated from renal pelvis (50%) in 2 patients, renal vein (25%) in one patient whereas, renal capsule (25%) appeared to be the site of origin in other patient. Histopathological examination and immunohistochemistry proved the lesion as primary leiomyosarcoma of kidney.

**Conclusions:** Being a rare tumour, renal leiomyosarcoma needs to be considered in the differential diagnosis of renal masses even in patients younger than 40 years.

**Keywords:** Immunohistochemistry, Leiomyosarcoma, Tumour, Sarcomatoid

### INTRODUCTION

Primary renal sarcomas are exceptionally rare, constituting 1-2% of adult renal tumours.<sup>1,2</sup> Leiomyosarcoma is the most common histological subtype accounting for 50-60% of the primary renal sarcomas, followed by liposarcoma, haemangiopericytoma, fibrosarcoma, malignant fibrous histiocytoma and rhabdomyosarcoma.<sup>3</sup> Leiomyosarcomas (LMS) originate from the smooth muscles of the renal capsule, renal pelvis, calyces, and blood vessels, last one is the most frequent.<sup>4,5</sup>

Overall, primary renal sarcomas show a female predilection and present in the age ranging from 28 to 70 years, with a median age of 49 years.

These tumors usually have an insidious presentation, with signs and symptoms occurring at late stages of the disease: abdominal pain, palpable mass, vomiting, hematuria and weight loss.<sup>6</sup> Few cases present with spontaneous rupture.<sup>7</sup> It is extremely challenging, on the basis of radiological and pathological features, to differentiate LMS of the kidney from renal cell cancer which have undergone sarcomatoid differentiation.<sup>8</sup>

Renal LMS usually have an aggressive biological behavior with poor prognosis. 90% of patients present with distant metastasis, pulmonary metastasis being the most common followed by liver and bone. Radical nephrectomy is the treatment of choice.<sup>4,10</sup> The major prognostic factor is total surgical resection, when it is completed the 5 year disease free survival could be of 60%.<sup>10</sup> Other than the complete surgical resection, tumor grade and diameter are the important prognostic factors in primary LMS of the kidney.

Renal sarcomas have a lower life expectancy as compared to the other sarcomas of the urinary tract. The 5-year survival is 82% in patients with retroperitoneal sarcoma, 73% in patients with the sarcomas of the bladder, 44% in patients with prostate sarcoma, and 39% in patients with the sarcomas of the kidney.<sup>11</sup> The ominous nature of these lesions necessitates timely diagnosis and treatment.

**METHODS**

This study was conducted in the Department of Pathology, Government Medical College, Srinagar. It was a retrospective study done over a period of 3 years from July 2014 to June 2017. A total of 4 patients, who underwent surgery due to renal mass during this period and who were diagnosed with primary LMS of the kidney, were included in the present study.

During this period, radical nephrectomy was applied to 107 patients. 4 (3.73%) of these patients were diagnosed with leiomyosarcoma. All the cases were retrieved with the help of medical records. All clinically relevant data such as age, sex, clinical and radiological findings was collected from the records.

In order to make a diagnosis of a primary renal sarcoma the following criteria as laid down by Grignon et al in their study were followed<sup>3</sup>

- The patients included in this study were not having a sarcoma elsewhere to rule out metastasis.

- Gross was compatible with origin in the kidney rather than involvement due to retroperitoneal sarcoma.
- Sarcomatoid renal cell carcinomas were excluded from this study with the help of immunohistochemistry.

The pathological diagnosis and grade of the tumor were evaluated according to the classification of French Federation of Cancer Centers Sarcoma Group (FNCLCC). The histological grade was scored based on the level of differentiation, presence of mitosis, and necrosis in each high power field. Markers used for immunohistochemical analysis, were used to distinguish renal LMS from sarcomatoid variant of renal carcinoma, atypical Angiomyolipoma, Genitourinary pacemaker cell tumors and other sarcomas.

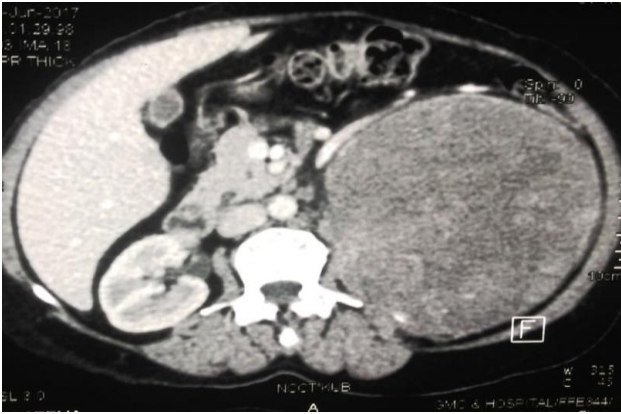
Immunohistochemically, the tumor cells of leiomyosarcoma were positive for SMA, desmin, and negative for antibodies to CK, S-100 protein, HMB-45 and CD117 (C-kit). The angiomyolipomas will show HMB-45 positivity while the sarcomatoid variant of renal cell carcinoma will be CK positive. CD 117 and CD 34 positivity will be seen in the genitourinary pacemaker cell tumors. The staging of the tumor was done as per staging system developed by the American Joint Cancer Committee (AJCC-2013) for the staging of soft tissue sarcomas.

**RESULTS**

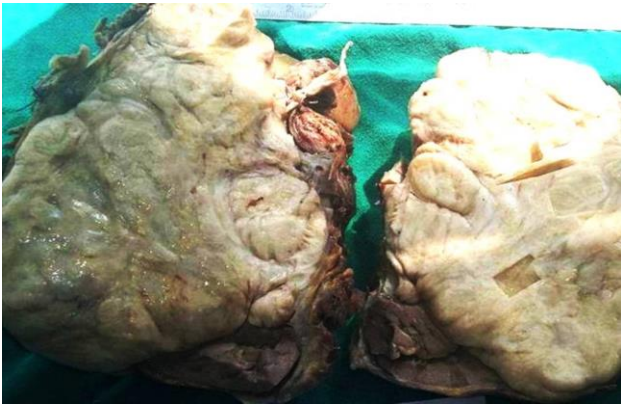
Our study period of 3 years included four cases of primary renal leiomyosarcoma. Age of the patients ranged from 35-64 years with a mean age of 53.5 years. Male to female ratio of 1:1 was seen. The most common presenting symptom was flank pain occurring in three (75%) patients, followed by renal mass (50%) (Table 1). Spontaneous rupture of kidney was present in a 35-year-old male (Figure 6). All the four patients were subjected to ultrasonography (USG) and CECT abdomen (Figure 1). 3 (75%) patients had left sided renal mass and only one patient has right sided renal mass.

**Table 1: Distribution of cases according to age, sex, site, clinical appearance and treatment of lesion.**

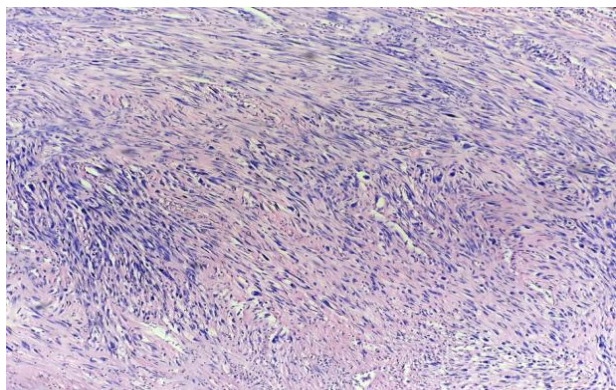
Age (yrs)	Gender	Laterality	C/F	Tumor size (cm)	Stage	Treatment
35	M	Right	Flank pain	12x5.5x4	pT <sub>2b</sub> N <sub>0</sub> M <sub>0</sub>	Radical nephrectomy
65	F	Left	Renal mass, hematuria	5.5x4x2.5	pT <sub>2b</sub> N <sub>0</sub> M <sub>0</sub>	Radical nephrectomy
55	F	Left	Flank pain, anorexia, Fever	7x4x2.4	pT <sub>2b</sub> N <sub>1</sub> M <sub>0</sub>	Radical nephrectomy
64	M	Left	Flank pain, renal mass, weight loss	4x3x1.5	pT <sub>1b</sub> N <sub>0</sub> M <sub>0</sub>	Radical nephrectomy



**Figure 1: Computed tomography of abdomen showing a large hypodense lesion arising from inferior cortex of upper/ midpole of left kidney.**



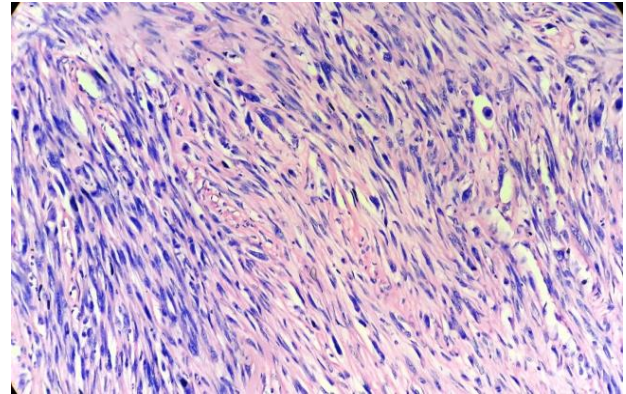
**Figure 2: Cut section showing a greyish white lobulated tumour with a peripheral rim of normal kidney towards upper pole.**



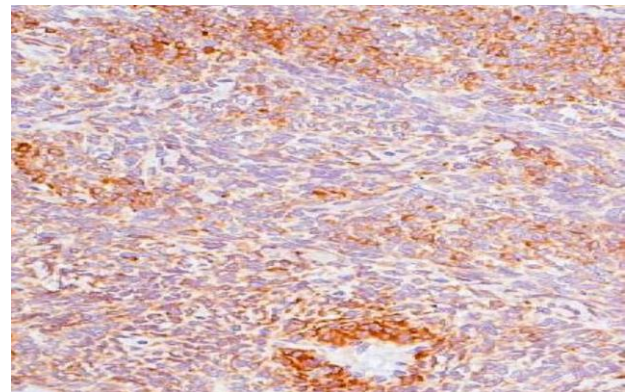
**Figure 3: Hematoxylin and eosin staining demonstrating spindle cell neoplasm arranged in alternating fascicles with cells having eosinophilic cytoplasm and marked nuclear pleomorphism (10X).**

Radical nephrectomy was done in all patients. On gross examination tumor had originated from renal pelvis in 2 patients, renal vein in one patient whereas renal capsule appeared to be the site of origin in other patient. On cut section tumours had a grey white, lobulated appearance

resembling smooth muscle tumours (Figure 2). On histopathological examination, hematoxylin and eosin stained sections of all the cases revealed malignant tumor composed of spindle cells with oval tapering nuclei arranged in fascicles (Figure 3, 4).



**Figure 4: Hematoxylin and eosin staining demonstrating spindle cell neoplasm arranged in alternating fascicles with cells having eosinophilic cytoplasm and marked nuclear pleomorphism (40X).**

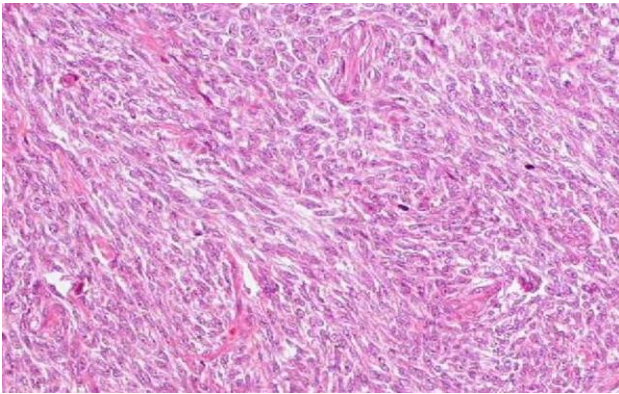


**Figure 5: Immunohistochemical stain showing diffuse positivity for smooth muscle actin.**



**Figure 6: Gross showing a nephrectomy specimen with ruptured area in the lower pole and separate tumour fragments.**

Marked nuclear pleomorphism was seen. Increased mitotic activity including typical and atypical mitosis was seen (Figure 7). Focal myxoid change and areas of necrosis were also noted microscopically. A diagnosis of renal leiomyosarcoma was made which was confirmed with positive immunostaining for smooth muscle actin (Figure 5) and desmin. All patients exhibited negative staining for cytokeratin, CD 34 and CD 117.



**Figure 7: Hematoxylin and eosin staining demonstrating high-grade sarcomatoid cells with numerous mitotic figures (40x).**

## DISCUSSION

Leiomyosarcomas are malignant neoplasms of smooth muscle origin. They are most commonly found in the uterus, stomach, small intestine, and retroperitoneum.<sup>12</sup> Primary renal leiomyosarcomas are rare and constitute 1-2% of all malignant renal tumors.<sup>1,2</sup> but are the commonest renal sarcoma. However, only 27 cases were identified during a 23-year period at 3 large institutions depicting its exceeding rarity.<sup>13</sup> Similar to this we also observed 4 cases of primary renal LMS in a study period of 3 years. Renal leiomyosarcomas may arise from renal vein and artery as well as from the smooth muscle cells of renal capsule or muscular wall of renal pelvis. Primary leiomyosarcoma of the kidney has preponderance in women and is more frequent in fourth decade of life but can be found in almost any age group, with a gradually increasing incidence in the later period of life.<sup>5</sup> In this study, we observed equal sex incidence. Our patients were in the age range of 35-64 years with mean age of 53.5 years. This was in accordance to the studies which have reported renal LMS to be more common in patients aged 50-60 years although one of our patients was aged below 40 years.<sup>14</sup>

This neoplasm most commonly presents with flank pain, hematuria, and abdominal mass mimicking the presentation of RCC. The symptoms increase with the advancing stage of disease. It is extremely difficult to differentiate LMS of the kidney from renal cell cancer having sarcomatoid differentiation as both of them exhibit similar clinical, radiological, and pathological features. Microscopically, the tumor shows alternating

fascicles of spindle shaped cells with marked nuclear atypia and prominent mitotic figures. The absence of epithelial elements on extensive sampling and IHC clearly ruled out sarcomatoid RCC in the present study. Bulky tumour instead of small intraparenchymal lesions ruled out the possibility of metastasis.<sup>13</sup> On immunohistochemistry, they show a positive reaction to smooth muscle markers like smooth muscle actin and desmin with negative cytokine markers.

Leiomyosarcomas usually show infiltration into perirenal adipose tissue. Local recurrence is reported in 40% of the cases and distant metastases are primarily to the lungs, followed by liver and bones.<sup>15-18</sup> Metastatic tumors are frequently high grade tumors. No metastases were reported in any of our cases.

Renal LMS usually have an aggressive biological behavior with poor prognosis owing to its rapid growth. Small size (<5cm), low histologic grade, and renal limited disease are associated with the most favorable outcome.<sup>19</sup> Radical nephrectomy is the treatment of choice.<sup>10</sup> The major prognostic factor is total surgical resection, when it is completed, 5 years disease free survival could be of 60%.<sup>10</sup> The role of adjuvant chemotherapy/radiotherapy remains obscure due to paucity of data on treatment of this rare renal neoplasm and the majority of patients develop metastatic disease regardless of treatment.

## CONCLUSION

From our study, we conclude that renal sarcomas need to be considered in the differential diagnosis of all renal masses even in patients younger than 40 years. An early and accurate diagnosis followed by aggressive surgery are the keys to long-term survival of patients. The prognosis of advanced renal leiomyosarcomas is poor and the appropriate treatment is yet to be determined.

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