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## Clinicopathological Evaluation of Leiomyosarcomas: A Study of Ten Cases

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#### Abstract

Leiomyosarcoma is a rare aggressive soft tissue tumor derived from smooth muscle cells usually of uterine, gastrointestinal or soft tissue origin. Ten cases of leiomyosarcomas presenting at various sites were retrospectively reviewed. Four were of uterine origin, three were located in the extremeties involving the thigh, gluteal and perianal region respectively and single case of retroperitoneal origin was found. Two rare cases of scrotal and colonic leiomyosarcoma were also included. Age of the patients ranged from 40-68 years with a male: female ratio of 3:7 respectively. Uterine and retroperitoneal leiomyosarcomas were larger, higher grade, and more commonly associated with synchronous metastases. Although larger and higher grade, retroperitoneal and uterine LMS share similar survival and recurrence patterns with their trunk and extremity counterparts. Presence of metastatic disease remained the most important prognostic factor. Extensive studies including large number of cases need to be done for setting definitive treatment protocols for these aggressive neoplasms

Keywords: Leiomyosarcoma, aggressive, neoplasms, prognosis.

### Introduction

Leiomyosarcoma is a rare aggressive soft tissue sarcoma derived from smooth muscle cells typically of uterine, gastrointestinal or soft tissue origin. Women are affected more than men (2:1). Disease typically occurs in the 5th and 6th decades of life. Accurate diagnosis, classification, and multimodality treatment are utmost important. Rarity of these tumors makes definitive treatment protocols difficult to be set. Prognosis is poor, with survival rates among the lowest of all soft tissue sarcomas.

#### **Material and Method**

The study was conducted in the Department of Radiation Oncology, Regional Cancer Centre in Pt.B. D. Sharma UHS, Rohtak. Ten cases of leiomyosarcomas presenting at various sites were treated and followed to find the clinical characteristics and outcome in these patients.

### Results

Out of ten cases, four were of uterine leiomyosarcomas, three were located in the

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extremeties involving the thigh, gluteal and perianal region respectively and single case of retroperitoneal origin was found. Two rare cases of scrotal and colonic leiomyosarcoma were also included. Age of the patients ranged from 40-68 years with a male: female ratio of 3:7 respectively. Diagnosis was made on the basis of histopathology and immunohistochemical positivity of the tumor cells for smooth muscle actin and desmin. Standard treatment including surgery with adjuvant chemotherapy and/or radiotherapy was given depending upon the location, stage of tumor, age and general condition of the patient. Cases of uterine leiomyosarcomas presented with variable complaints like bleeding per vaginum and lower abdominal heaviness and pain. Out of four, one case presented with multifocal lesions in the

myometrium. Disease free survival period ranged from 4 months- 2.8 years. Recurrence at local site and distant metastasis to lung and brain was noted in these cases.

Extremity leiomyosarcoma were found to be associated with features like multifocality, larger size of upto 17cms, early recurrence and had dismal prognosis. One out of three cases, had paraaortic lymphnode involvement, liver and bilateral lung metastasis at the time of initial presentation. Scrotal leiomyosarcoma, clinically misdiagnosed as sebaceous cyst presented as a small nodule of 2 cm size, was treated with wide surgical alongwith adjuvant radiotherapy and patient has been kept on follow up. [Table 1]

S.No	Age	Clinical	Radiological findings	Surgery		Diagnosis	Follow up	Prognosis
		complaints					period	
1	40 F	Bleeding per vagina, Pain abdomen, Loss of appetite	-	• 60Gy/30Fr Wks	TAH+ BSO f/b adjuvant CT: Ifosamide, adriamycin, dacarbazine F/B RT //6	Uterine leiomyosarcoma	30-months	Bilateral lung metastasis
2	42 F	Difficulty in urination	CT revealed- subserosal fibroid in the cervical region obliterating thePouch of douglas	•	TAH+ BSO Radical RT 50 Gy/25 Fr/ 5 wks Vaginal Cuff brachytherapy (3 cycles)	Uterine leiomyosarcoma	24-months	On regular follow up
3	42 F	Bleeding	-	•	TAH+BSO f/b CT Ifosamide Vincristine Cisplatin	Uterine leiomyosarcoma	6-months	Brain Metastasis
4	60 F	Mass protruding from vagina ( K/C/O uterine LMS)	-	•	RT 20 Gy/5Fr/5 wks f/b CT Adriamycin, ifosamide	Recurrent uterine leiomyosarcoma	-	Lost to follow up
5	65 F	Swelling Perianal	-	•	Surgical resection f/b RT ( 60 Gy/30Fr/6 wks)	Perianal Leiomyosarcoma	8-months	Recurrence beneath Scar
6	40 F	Swelling Gluteal region	Ultra-sonography revealed- Paraaortic, liver, lung metastasis MRI- mass arising from gluteus maximus	•	Wide excision f/b CT- single course VAC regimen	Gluteal Leiomyosarcoma	-	Death
7	51 F	Thigh Swelling	MRI revealed- 3.6x3x2 cm inhomogenous mass touching adductor fascia	•	Resection with negative margins Adjuvant RT 66 Gy/33 Fr f/b Single agent doxorubicin	Leiomyosarcoma left thigh	12 months	Liver and ascending colonic mets
8	50 M	Abdominal discomfort	CT revealed- 28 x21x15 cm tumor in right retroperitoneum compressing IVC	•	Surgical resection- recurrence within 32 days f/b Adjuvant CT- doxorubicin Ifosamide 6 cycles, 3 wkly f/b EBRT 50 Gy/25 Fr	Retroperitoneal Leiomyosarcoma	17-months	Right lung
9	68 F	Diffuse pain abdomen	Computed tomography revealed Exophytic mass arising from descending colon (splenic flexure to sigmoid colon)	•	Left hemicolectomy f/b Adjuvant CT- adriamycin, carboplatin	Colonic Leiomyosarcoma	4-months	Follow up
10	64 M	Painless Scrotal swelling	-	•	Wide Excision With negative margins	Scrotal Leiomyosarcoma	36- months	Follow up

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## Discussion

The term leiomyosarcoma encompasses a spectrum of disease ranging from low grade cutaneous lesions with relatively benign behavior to aggressive deep lesions of the abdomen or extremity with significant metastatic potential.<sup>1</sup> Owing to the rarity of these tumors, there is paucity of literature regarding their biological behaviour and definitive treatment protocols. These tumors present non specifically as an enlarging mass causing vague discomfort, compression symptoms, pain with few constitutional signs like nausea, vomiting and weight loss. Preoperative diagnosis of LMS is very difficult inspite of the use of modern imaging and definitive diagnosis is possible only on postsurgical histomorphological examination of the tumor aided with immunohistochemical marker application. Microscopy of the tumor reveals interlacing fascicles of atypical spindle cells which reveal positivity for smooth muscle actin and desmin. Atypical mitotic figures, necrosis and cellular pleomorphim are the indictors of high grade malignancy. In our study, we evaluated ten cases of leiomyosarcomas of various sites including uterus, retroperitoneum, colon, scrotum and extremeties. Overall status of patients was poor. Patients presented with non specific complaints leading to diagnosis at late stages. Features like recurrence, wide spread distant metastasis to lung, liver, ascending colon and paraaortic lymph nodes were with uterine and noted. retroperitoneal leiomyosarcomas having common association with synchronous metastases. Disease free survival ranged from 4- 32 months and metastasis and recurrence at local site occurred despite standard treatment protocols.

Aggressive biological behaviour of these tumors warrants discussion. In a previous study it has been documented that the majority (63%) of leiomyosarcoma patients present with metastasis and/or local recurrence<sup>2</sup> Recent study by Gladdy et al stated that recurrence occurred in 139 of the 353 patients (39%) included. The rate of first recurrence varied by site: 51% of abdominal/retroperitoneal, 33% of extremity, and 26% of truncal patients.<sup>3</sup> In cases

of uterine leiomyosarcomas, recurrent disease rate is up to 70% in stage 1 and 2 even after surgical treatment. Commonly, place of recurrence are lungs or upper abdomen: liver, abdomen, pelvis and pelvic or paraaortic lymph nodes are other site of metastases.<sup>4</sup> In our study, one case of brain metastasis was also evident. Previous studies on extremity sarcomas have shown that deep location and larger tumor size were associated with increased risk of metastasis and poorer patient survival.<sup>5</sup> It has been seen that metastasis occurs within first years of diagnosis or after surgical resection. Metastases of nonretroperitoneal leiomyosarcomas typically arise in the lungs as a result of hematogenous spread.<sup>6</sup> Our study also documents features like larger size, multifocality, early reccurence beneath scar within 4 months after surgery and distant metastasis at the time of initial presentation in the cases of extremity leiomyosarcomas reflecting their poor prognosis. Leiomyosarcomas encountered at rare sites like scrotum may be clinically present as benign cysts and correct diagnosis mandates high index of suspicion. The recommended treatment of localized leiomyosarcoma of the scrotum is wide excision. Surgical margin of at least 10 mm is required to reduce the risk of local tumour recurrence. <sup>7</sup> Long term follow up is must for all the patients presenting with leiomyosarcomas as late recurrences have also been noted in a number of cases.

Local control of leiomyosarcomas is usually achieved with wide surgical resection. Radiation therapy plays an important role in tumors with close proximity to vital structures and as a palliative local control in cases with extensive metastasis. Chemotherapy drugs like vincristine, doxorubicin, ifosfamide, dacarbazine, gemcitabine, docetaxel play a primary role in treating metastatic cases with a objective response rate of 30% for both combination chemotherapy regimens; doxorubicin + dacarbazine and ifosfamide + dacarbazine and response rate of 27% for combination chemotherapy of gemcitabine + docetaxel.<sup>8</sup> These drugs also help in local control by causing shrinkage of tumor mass thus making surgical resection easy. Despite using

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the chemotherapeutics, results are unsatisfactory. Extensive studies including large number of cases of leimyosarcomas need to be performed for setting definitive treatment protocol.

### Conclusion

Uterine and retroperitoneal leiomyosarcomas are larger, higher grade, and more commonly associated with synchronous metastases. Although larger and higher grade, retroperitoneal and uterine LMS share similar survival and recurrence patterns with their trunk and extremity counterparts The presence of metastatic disease remains the most important prognostic factor for LMS. Extensive studies including large number of cases of leimyosarcomas need to be performed for setting definitive treatment protocols for these aggressive neoplasms.

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