

**Original Research Article****Clinicopathological Evaluation of Uterine Sarcomas: An Institutional Experience****Tarannum Fathima<sup>1</sup>, Rau Aarathi Rangan<sup>2</sup>**<sup>1</sup>Post Graduate <sup>2</sup>Professor, Department of Pathology M.S. Ramaiah Medical College, Bengaluru, Karnataka 560054, India.**Abstract**

**Introduction:** Uterine sarcomas are highly malignant tumors accounting for 3-7% of all uterine malignancies. According to the World Health Organization, uterine sarcomas consist of two main categories: mesenchymal tumours and mixed tumours.

**Aims:** To study the clinical presentation and analyze the spectrum of gross and microscopic features of uterine sarcomas.

**Methods:** The present retrospective study was conducted in the department of pathology of a medical college teaching hospital from 2011 to 2016. Total number of hysterectomies were 1837, of which leiomyomas accounted for 70% and uterine sarcomas accounted for 0.6% (11 cases). Haematoxylin and Eosin stained slides of 11 cases of all uterine sarcomas were retrieved from the histopathology archives. Clinical features were taken from medical records and all H and E stained slides studied.

**Statistical Analysis:** Continuous data was summarised using descriptive statistics. Qualitative variables were summarized using frequency and percentage

**Results:** We report a series of 11 cases with mean age of presentation being 44.8 years. In majority of cases the clinical presentation was abdominal pain and vaginal bleeding and the commonest clinical diagnosis was fibroid uterus followed by endometrial carcinoma. Out of 11 cases, 6 cases were of endometrial stromal sarcoma, 2 carcinosarcoma and one case each of leiomyosarcoma, adenosarcoma and undifferentiated sarcoma. The stage of the tumors was predominantly stage I (72.7%) followed by stage IV (18.1%) and stage II (9%).

**Conclusion:** Uterine sarcomas are rare malignant tumor. The diagnosis is difficult due to varied pathological differentiation and can be aided by immunohistochemistry.

**Keywords:** Endometrial Stromal Sarcoma; Carcinosarcoma; Leiomyosarcoma.

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**Introduction**

Uterine Sarcomas are rare tumours of mesenchymal origin which account for less than 1% of female genital tract malignancies and 3% to 7% of uterine malignancies [1]. According to the World Health Organization, uterine sarcomas consist of two main categories: mesenchymal tumours and mixed tumours [2]. Pure mesenchymal

tumors can be classified into endometrial stromal sarcoma (ESS), leiomyosarcoma and undifferentiated uterine sarcoma. Mixed tumors include carcinosarcoma and adenosarcoma. Uterine sarcomas occur primarily in peri and post menopausal women. The most common symptoms of patients being abnormal uterine bleeding, abdominal or pelvic mass and pain [3]. However, these symptoms are not specific for uterine sarcomas.

Uterine sarcomas are characterized by aggressive behaviour, high rates of local recurrence, distant metastasis, and poor prognosis, with an overall two-year survival rate less than 50% [4]. The contribution of both radio imaging and endometrial biopsy, in the preoperative diagnosis is mostly unsatisfactory and may pose a diagnostic challenge. The diagnosis is therefore based on histopathological examination of hysterectomy specimens.

Prognostic predictors and guide to treatment in uterine sarcomas are the tumour stage, histological sub type, grade, lymphovascular invasion and menopausal status [5].

#### *Aims and Objectives*

1. To study the clinical presentation of uterine sarcomas.
2. To analyze the spectrum of gross and microscopic features of uterine sarcomas with emphasis on tumour stage.

#### **Materials and Methods**

This was a retrospective study undertaken in the department of pathology of a medical college hospital, after obtaining the permission of institutional ethical committee. All 11 cases of uterine sarcomas were included in these study. Haematoxylin and eosin stained slides were retrieved from the histopathology archives. Clinical records of the patients were retrieved from medical record department. Clinicopathological variables were analysed. Surgical staging was done according to International Federation of Gynecology and Obstetrics (FIGO).

#### *Statistical Analysis*

Continuous data was summarised using descriptive statistics. Qualitative variables were summarized using frequency and percentage.

#### **Results**

A total of 11 cases of uterine sarcomas were diagnosed. Mean age of patients was 44.8 years (range 29–60 years) with the majority of patients (63.6%) belonging to perimenopausal age group. The main presenting symptoms in most of the cases were abdominal pain (100%), abnormal vaginal bleeding (90.9%), mass per abdomen (45.4%) and 1 case (9%) presented as recurrent cervical polyp. The clinical diagnosis in the majority of cases were fibroid uterus, followed by endometrial carcinoma.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy specimens were evaluated in all cases

and diagnosed in 6 cases as Endometrial stromal sarcoma (46%), 2 as carcinosarcoma (27%), one each of adenosarcoma (9%), leiomyosarcoma (9%) and undifferentiated sarcoma (9%). In all cases the endometrial curettings was normal.

Out of six cases of ESS, five cases had gross appearance of grey white fleshy mass in endometrial cavity with infiltration into myometrium and one case presented as cervical polypoidal mass. Leiomyosarcoma and undifferentiated uterine sarcoma on gross examination showed large intramural fleshy mass with variegated appearance. Two cases of carcinosarcoma had gross appearance of grey white fleshy mass in endometrial cavity with one infiltrating and forming right parametrial mass and involving the small intestine and the other case showing involvement of ureter and aorta.

Out of 6 cases of ESS, 3 cases were diagnosed as low grade ESS composed of uniform, oval to spindle-shaped cells of endometrial stromal-type present around network of delicate small arterioles with absence of significant atypia, pleomorphism and mitotic count of 3-4/10HPF. One case presented as ovarian mass and diagnosed as spindle cell tumour on frozen section of ovary, but permanent sections revealed a primary ESS of the uterus and ovarian metastasis.

Two cases were diagnosed as undifferentiated endometrial sarcoma with presence of cellular atypia, pleomorphism and increased mitotic count. One case presenting as recurrent cervical polyp was diagnosed as smooth muscle tumour of unknown malignant potential on histology but subsequent immunohistochemistry showed CD10 to be strongly positive, WT1 weakly positive, focal positivity of h-caldesmon,  $\beta$ -catenin, smooth muscle actin and scattered desmin positivity. Cytokeratin (CK) and epithelial membrane antigen (EMA) were negative. A final diagnosis of low grade ESS was given.

Both cases of carcinosarcoma had endometroid type of glandular element and sarcomatous elements exhibited heterologous differentiation, one with rhabdomyoblastic and other with chondrosarcomatous differentiation. Adenosarcoma had benign glandular element and low grade stromal component with characteristic periglandular stromal cuffing.

A case of leiomyosarcoma showed fascicular growth pattern with infiltrative borders of spindle cells resembling smooth muscle with cigar shaped nuclei and fibrillary eosinophilic cytoplasm, moderate to severe pleomorphism, > 10 mitotic figures/10 HPF and large areas of necrosis. A case of undifferentiated sarcoma showed highly pleomorphic tumour cells with numerous tumour giant cells, atypical mitotic figures, large areas of necrosis, extensive myometrial invasion and vascular tumour emboli.

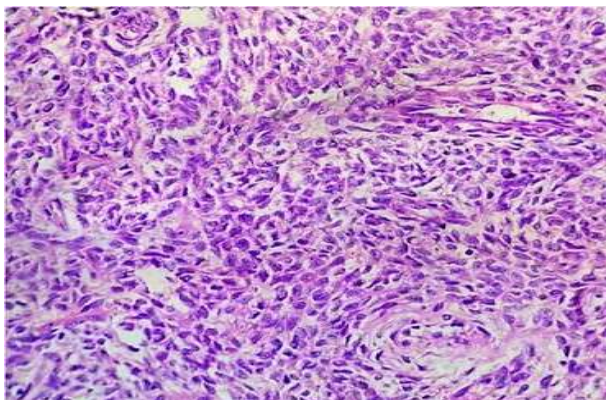
The stage of the tumors was mostly stage I in 8 cases (72.7%) followed by stage IV in 2 cases (18.1%) and stage II in 1 case (9%). Both cases of carcinosarcoma presented in stage IV with extensive local spread one involving small bowel and one involving the aorta and the ureter. The metastatic deposit in the small bowel, aorta and ureter showed both carcinomatous and sarcomatous elements. No distant metastasis was documented.



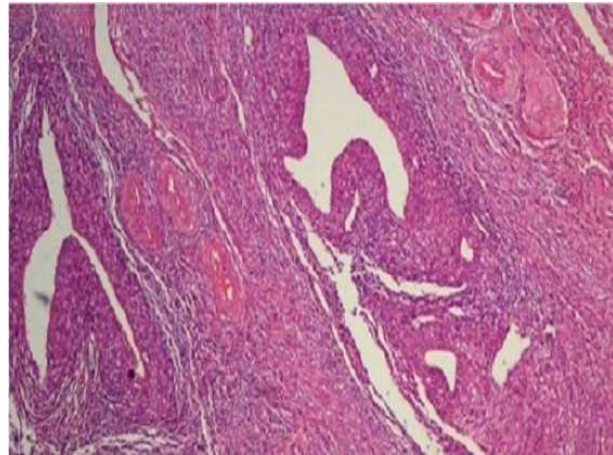
**Fig. 1:** Gross specimen of uterus with cervix shows endometrial cavity obliterated and distorted and replaced by a large, ragged, ill circumscribed grey white mass



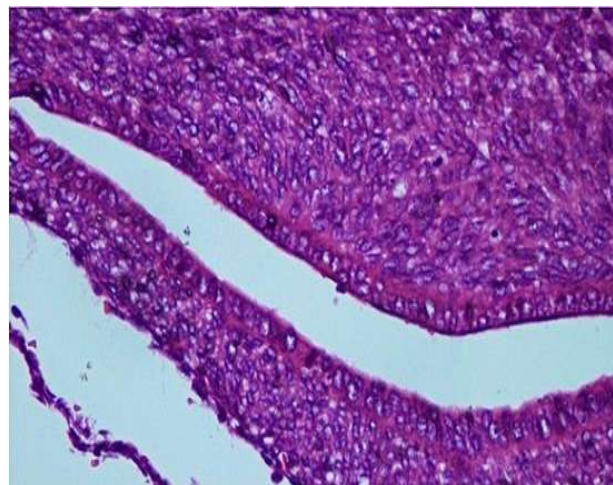
**Fig. 2:** Gross specimen showing uterus (U) with grey white fleshy tumour (UT) infiltrating and forming right parametrial mass (RPT). Adherent small intestinal coils with mucosa (IM) showing tumour (IT)



**Fig. 3:** Photomicrograph showing Endometrial stromal sarcoma composed of thin walled blood vessels and monotonous ovoid to spindle cells with minimal cytoplasm (H&E; 40x)



**Fig. 4:** Photomicrograph showing adenosarcoma composed of benign epithelial and stromal component. The glands are large and dilated with periglandular stromal cuffing. (H&E; 10x)



**Fig. 5:** Photo micrograph showing adenosarcoma composed of uniform single layered lining epithelium of benign glands with sarcomatous overgrowth (H&E; 40x)

## Discussion

Uterine sarcomas are rare malignant tumours. The mean age of presentation in this study was 44.8 years which was almost similar to study by other Indian authors in which the mean age was 42.6 yrs [6]. One case of ESS in this study was 29 yr old, however, a case of ESS in 17 yr old has been previously reported [7].

The common presentation of uterine sarcomas were pain abdomen and bleeding per vaginum which correlated with other studies [6]. One case of ESS had a unusual presentation of recurrent cervical polyp. There are few reported cases in the literature of ESS in the cervix. A case of ESS of cervix presenting as haemorrhagic mass in the endocervix in 44 yr old has been reported [8].

A case of ESS Presented as ovarian mass, and histopathology revealed a primary ESS in the uterus with ovarian metastasis. Rarely ESS initially present at

an extrauterine site, most commonly the ovary [9]. It can be a primary or metastatic lesion from endometrium, but primary ovarian sarcoma is very rare, hence a meticulous examination of hysterectomy specimen is important to look for primary uterine sarcomas as was done by us.

In our study ESS was the commonest (46%) followed by carcinosarcoma (27%) with equal incidence of leiomyosarcoma, adenosarcoma and undifferentiated sarcoma (9% each). A similar distribution was described by another Indian study [6]. This is in contrast to a study in Western literature which described leiomyosarcomas as the commonest (55%) followed by 30% of carcinosarcoma and 15% of ESS [3]. Whether this is a real difference in the distribution requires larger number of cases to be included. The use of tamoxifen therapy for breast cancer is associated with higher incidence of Carcinosarcoma and leiomyosarcoma and none of our patients gave this history.

In our study of ESS, 66.7% cases belonged to low grade ESS and 33.3% belonged to undifferentiated endometrial sarcoma, similar to a study by Leath et al. [10] who recorded a higher percentage of low grade ESS. Based on tumor margin status and cytological features, the WHO has classified endometrial stromal tumor into benign endometrial stromal nodule (ESN) and endometrial stromal sarcoma [2]. The microscopic appearance of ESS and ESN are identical with well demarcated margins in ESN and infiltrative margins and distinctive growth as worm-like cords in low-grade ESS. Hence, extensive sampling of tumor margins and detecting vascular invasion are extremely important in distinguishing between the two. ESSs are divided into low-grade and Undifferentiated endometrial or uterine sarcoma (UES) based on nuclear pleomorphism and necrosis not taking into account the mitotic count [2].

One case of ESS presenting as recurrent cervical polyp showed features of smooth muscle differentiation on histology. The main differential diagnosis of low-grade ESS includes ESN and cellular leiomyoma. ESS should be differentiated from smooth muscle tumours because the criteria for malignancy differ for the two tumor types. The vessels in endometrial stromal tumors are mainly thin-walled arching capillaries, in contrast smooth muscle tumours show the presence of thick-walled vessels within the lesion. A fascicular arrangement of the constituent cells also favors a smooth muscle tumor [11]. IHC plays a role in distinguishing this two entities with endometrial stromal cells showing CD10 positivity, but so are the cells in one third to one half of smooth muscle neoplasms. Caldesmon appears to be specific marker for smooth muscle cells and is useful in distinguishing cellular leiomyoma from endometrial stromal neoplasms. Hence

a panel of desmin, h-caldesmon, and CD10 are found to be helpful. Strong CD10 staining and weak or absent desmin and caldesmon staining provides support for endometrial stromal differentiation, strong desmin or caldesmon staining with weak or absent CD10 favors a smooth muscle tumor [11]. Recently, a fusion of two zinc finger genes JAZF1 and JJAZ1 has been reported to be useful in differential diagnosis of leiomyoma and ESS [12].

Both cases of carcinosarcoma in our study showed heterologous sarcomatous differentiation comprising of chondrosarcoma and rhabdomyosarcoma components respectively. Heterologous differentiation is encountered in 50% of cases, the commonest being rhabdomyosarcomatous and chondrosarcomatous differentiation [13]. Patients of carcinosarcoma with heterologous differentiation have survivals that are significantly worse and hence its documentation has prognostic significance [13].

Adenosarcoma should be distinguished from adenofibroma both of which show uniformly distributed, often dilated glandular elements. Adenosarcoma shows hypercellular stroma, including the distinctive hypercellular cambium layer around the glands showing characteristic appearance of periglandular stromal cuffing with the presence of intraglandular papillae, and the mitotic index of 4/10 HPF [11].

Leiomyosarcoma should be differentiated from atypical leiomyoma which exhibits moderate to severe atypia similar to leiomyosarcoma. Generally leiomyosarcoma are hypercellular with moderate to severe cytologic atypia, coagulative tumor cell necrosis and elevated mitotic index of >10/10 HPF, on the other hand atypical leiomyoma shows either focal or diffuse moderate to severe cytological atypia without coagulative tumor cell necrosis and mitotic index of <10/10 HPF [11].

5 cases of ESS and 1 case each of leiomyosarcoma, adenosarcoma and undifferentiated sarcoma were stage I, which is similar to study on ESS by Haberal et al. [14] who recorded higher percentage of ESS of stage I. One case of ESS with ovarian metastasis was stage II. No stage III was noted in our study. Both cases of carcinosarcoma were stage IV. This is in contrast to Rajshekhar et al. [15] who reported most of the carcinosarcoma of stage III. Depth of myometrial invasion, serous or clear cell carcinoma element and heterologous elements of carcinosarcoma are associated with adverse prognosis as in our cases had heterologous elements.

Both cases of carcinosarcoma showed both carcinomatous and sarcomatous component in the local metastatic deposit. No distant metastasis was documented. Other studies recorded that the metastatic lesions of carcinosarcoma almost always contain elements of carcinoma with or without a co-existing



sarcoma, and solitary sarcomatous metastasis was uncommon [16]. Hence, grade of the carcinoma component is important to predict prognosis.

### Conclusion

Uterine sarcomas have variable clinical presentation. Meticulous examination of the tumours to identify the presence of glandular elements, whether benign or malignant and evaluation of the stroma is important for the diagnosis and can be aided by immunohistochemistry.

### Acknowledgement

Nil

### Conflict of Interest

Nil

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