

## Histomorphological study of uterine leiomyomas and its variants with brief review of literature

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DOI: <https://doi.org/10.17511/jopm.2019.i07.09>


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**Background:** Uterine mesenchymal tumours are a heterogeneous group of neoplasms that can frequently be diagnostically challenging. Most subtypes of leiomyoma are chiefly of interest in that they mimic malignancy in one or more respects. **Objective:** To evaluate the histomorphological features of uterine leiomyomas and its variants. **Materials and methods:** Total of 477 cases of uterine leiomyomas and its variants were analysed prospectively in a period of 2 years during July 2010 to June 2012 to assess the various pattern of leiomyomas. Cases were studied in detail about complete history, clinical examination and other findings. **Results:** In the study 468 (98.11%) cases showed features of conventional leiomyoma and 8 cases showed variants of leiomyomas (1.68%). **Conclusion:** Although their diagnosis is straight forward in most cases, difficulties arise with particular leiomyoma variants, especially highly cellular leiomyoma (often confused with an endometrial stromal tumour) and leiomyoma with bizarre nuclei, mitotically active leiomyoma which may cause concern for leiomyosarcoma.

**Keywords:** Apoplectic, Cellular, Leiomyoma, Lipoleiomyoma, Uterus, Variants

Corresponding Author	How to Cite this Article	To Browse
Manasa G. C., Associate Professor, JJM Medical College, Davangere, Karnataka, India. Email: <a href="mailto:manasachandru@gmail.com">manasachandru@gmail.com</a>	Budihal N, Pawar JG, Manasa GC. Histomorphological study of uterine leiomyomas and its variants with brief review of literature. Trop J Pathol Microbiol. 2019;5(7):466-472. Available From <a href="https://pathology.medresearch.in/index.php/jopm/article/view/289">https://pathology.medresearch.in/index.php/jopm/article/view/289</a>	

Manuscript Received  
2019-05-30

Review Round 1  
2019-05-08

Review Round 2  
2019-05-16

Review Round 3

Accepted  
2019-06-22

Conflict of Interest  
No

Funding  
Nil

Ethical Approval  
Yes

Plagiarism X-checker  
8%

Note



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## Introduction

Uterine mesenchymal tumours are a heterogeneous group of neoplasms that can frequently be diagnostically challenging [1]. The most common benign and malignant tumours are leiomyoma and leiomyosarcoma respectively [2]. Leiomyoma is a benign neoplasm composed of smooth muscle cells with a variable amount of fibrous stroma, most commonly affects the body of the uterus [3,4].

It is present in 20-30% of women over 30 years of age rising to more than 40% in those over 40 years old [4,5,6]. Prevalence of fibroids increases to more than 70% with pathological examination of the uterus, indicating that many women who have fibroids are asymptomatic [7].

Most subtypes of leiomyoma are chiefly of interest in that they mimic malignancy in one or more respects [3]. Diverse histological features of uterine leiomyomas are responsible for an erroneous diagnosis of malignancy [8]. Difference between the benign and malignant counterparts of mesenchymal tumours is significant due to the differences in the clinical outcome and the role of the surgical pathologist in making this distinction (especially in difficult cases) cannot be underestimated [1].

## Materials and Methods

**Setting and type of study:** This study was undertaken in the Department of Pathology, JJM Medical College, Davangere. It was prospective study. The study period of two years from July 2010- June 2012.

**Sampling method:** Material for the study consisted of hysterectomy specimens & myomectomy specimens which were sent for histopathological examination to the Department of Pathology, JJM Medical College from Bapuji Hospital, Chigateri General Hospital and also from private hospitals in and around Davangere. Relevant clinical data was collected from the hospital and laboratory records.

The specimens were received in 10% formalin; after adequate fixation were subjected to thorough gross examination and appropriate sections were taken. After tissue processing, multiple 4-6µ thick paraffin sections were stained with hematoxylin and eosin.

**Sample size:** Among 12,285 surgical specimens received for histopathological examination in the Department during the study period.

1914 were hysterectomies, 25 were myomectomies, 3 were debulking specimens and one was polypectomy specimen.

Of the total 1943 specimens, 492 cases were mesenchymal tumours (including 8 cases of mixed epithelial and mesenchymal tumours).

**Inclusion criteria:** Histologically proven mesenchymal tumours and mixed epithelial and mesenchymal tumours like carcinosarcoma, carcinofibroma, adeno-fibroma and adenomyoma of the uterine corpus were included in the present study.

**Exclusion criteria:** Epithelial tumours and related lesions, gestational trophoblastic disease, lymphoid and hematopoietic tumours and metastatic tumours of the uterine corpus were excluded from the present study.

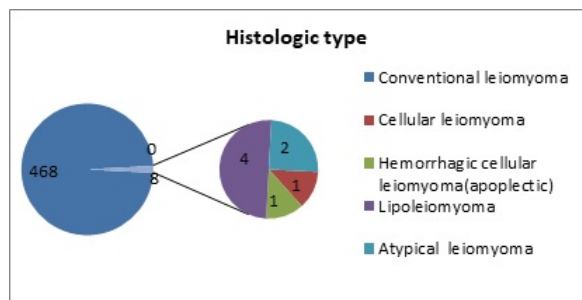
**Ethical considerations and permissions:** The study was started after due approval from institutional ethical committee.

**Data analysis:** The data was entered in MS excel and descriptive statistics were applied

## Results

Hysterectomy is the most common surgical operative procedure encountered in gynecological practice.

Among 12,285 surgical specimens received for histopathological examination in the Department during the study period. 1914 were hysterectomies and 25 were myomectomies.



**Figure 1: Histologic types of leiomyomas**

Of the total 1939 specimens, Leiomyoma was diagnosed in 477 cases, of which 24 were myomectomy specimens. Thus, the incidence of leiomyoma was 24.92% of total 1914 hysterectomy specimens. Thus, leiomyoma was the most common tumour 96.95% of all the tumours.

**Variants of leiomyoma:** Variants of leiomyomas were seen in 8 cases constituting 1.68% of all leiomyomas. Of these, 4 cases were lipoleiomyoma, 2 atypical leiomyoma, one cellular leiomyoma and one apoplectic leiomyoma.

**01. Lipoleiomyoma:** 4 cases of lipoleiomyomas were seen between 5th & 6th decades of life. 3 patients presented with mass per abdomen and one with menstrual disturbance (table I). These tumours measured 3-6cm in their greatest dimensions and were intramural and subserosal in location. One of the tumours showed gross evidence of lipoleiomyoma (Figure 2).

**Table-1: Details of cases of lipoleiomyoma.**

Cases	Age	Presenting complaint	Location of leiomyoma	Additional features
Case 1	45	Menstrual disturbance	Intramural	-
Case 2	47	Mass per abdomen	Intramural	Cystic change
Case 3	49	Mass per abdomen	Intramural	-
Case 4	51	Mass per abdomen	Subserosal	Myxoid change



**Figure 2: Sectioned surface of uterine lipoleiomyoma showing distinct pale yellow appearance one side and a subserosal leiomyoma on the other side**

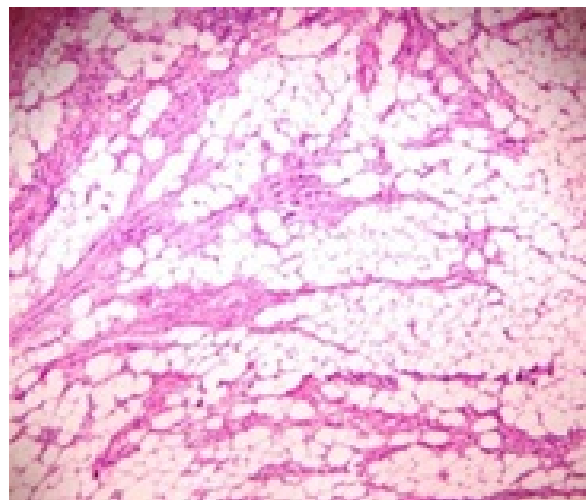
Microscopically, the tumours were composed of admixture of varying amounts of mature adipose tissue with smooth muscle cells (Figure 3). The adipose tissue was scattered and at places diffusely distributed within leiomyomas.

**02. Atypical leiomyoma:** Was diagnosed in two cases, (table II) Cut section of tumour in both the cases was grey white with whorled appearance.

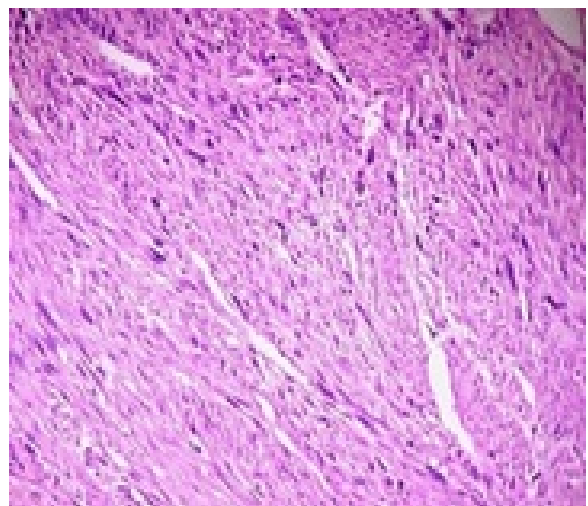
**Table 2: Details of cases of atypical leiomyoma.**

Feature	Case 1	Case 2
Age	32years	36years
Presenting complaint	Mass per abdomen	Mass per abdomen
Type of specimen received	Myomectomy	Hysterectomy
Measurement of leiomyoma	13x8x7cm*	Subserosal -7x6cm, intramural -2x1cm
Additional features	-	Mucoid and cystic change

\*Location could be identified in myomectomy specimen



**Figure 3: Lipoleiomyomashowing mature adipocytes intermingled with smooth muscle cells**



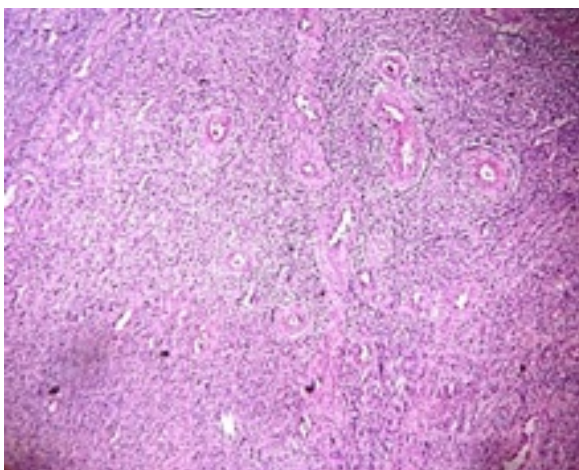
**Figure 4: Diffusely distributed atypical cells throughout the leiomyoma**

Microscopic sections from both the cases showed smooth muscles with moderate to severe cellular atypia arranged in fascicles with areas of smooth muscles with markedly pleomorphic and enlarged nuclei (nuclear atypia appreciated at lower magnification) (Figure 4). Clusters of bizarre hyperchromatic and multinucleated smooth muscle cells were seen. Also noted degenerative cells, smudged chromatin and intranuclear vacuolation. Occasional mitoses (2-3/10 HPFs) were noted. Necrosis was absent.

### 03. Haemorrhagic cellular (apoplectic)

**leiomyoma:** A case of haemorrhagic cellular leiomyoma was diagnosed in a 43yr old female who presented with mass per vaginum. On gross examination, tumour showed a polypoidal mass in the endometrial cavity measuring 5x3cm with foci of hemorrhage. Microscopically, the tumour was cellular, with closely packed round to spindle cells with scanty cytoplasm. There was no cytologic atypia. Blood vessels were large with thick muscular wall and cleft like spaces seen. Patchy areas of haemorrhage and oedema were made out. Also noted scattered lymphocytes and hemosiderin macrophages. Occasional MFs (<2/10 HPFs) were seen. The tumour appeared to merge with the surrounding myometrium.

Cellular leiomyoma: A case of cellular leiomyoma was diagnosed in a 40yr old female who presented as mass per abdomen. Two intramural leiomyomas were made out on gross examination, larger measuring 4cm in diameter which was soft in consistency and showed areas of mucoid change on cut section and the smaller one measured 3cm in diameter which showed regular whorled appearance on cut section.



**Figure 5: Microphotograph showing markedly cellular tumour and the cells are small and round to spindle shaped giving a basophilic hue with more blood vessels**

Microscopy of both the tumours showed densely cellular benign looking smooth muscle cells arranged in whorled pattern at places. In few areas these smooth muscle cells were small and rounded. Palisading of nuclei was present in some areas. Many large blood vessels with thick muscular wall and cleft like spaces were noted within these tumour cells (Figure 5). 5-6 MFs/10 HPFs were noted but there was no atypia. Hydropic, fatty, hyaline and myxoid changes were noted within the tumour.

## Discussion

The most common pelvic tumour in the reproductive age group is leiomyoma, occurring in 20–40% of females. Leiomyomas may have a diverse clinical, radiological and morphological pattern and are hormone responsive. Clinically they may be sporadic or syndromic and may present with abdominal pain, menorrhagia and pelvic mass[9].

The World Health Organization has recently (2014) updated its criteria for mesenchymal tumours of the female reproductive tract [10], and variants of benign smooth muscle tumors are diagnosed according to their unusual histologic features. Mitotically active leiomyomas are defined by the presence of 10–15 mitoses/10 high-power fields (hpf) [11,12] and may be seen in patients with enhanced hormonal states (pregnancy or taking exogenous hormones).

Increased cellularity, higher than that of nearby myometrium, is seen in a cellular leiomyoma, and at times, a cellular leiomyoma may have short spindle cells resembling an endometrial stromal tumor. Leiomyoma with bizarre nuclei (also called atypical, symplastic and pleomorphic) show the presence of scattered large atypical cells.

These atypical smooth muscle cells have abundant eosinophilic cytoplasm, irregular nuclear shapes, and multinucleation. The nuclei are hyperchromatic, often with intranuclear inclusions. Occasionally, cells have further chromatin-condensation and fragmentation, resembling atypical mitotic figures.

A proper pathological study of mesenchymal tumours of the uterus is predicated, on careful gross examination and adequate sectioning.

The tumour should be examined thoroughly, and one block of tissue should be taken for each centimeter of tumour diameter, except from grossly typical leiomyomas; even the latter may have to be examined extensively if the microscopic appearance is unusual [5]. Variants of leiomyomas were seen in eight cases constituting 1.68% of all leiomyomas. Of these, four cases were lipoleiomyomas, two atypical leiomyoma, one cellular leiomyoma and one apoplectic leiomyoma.

**01. Lipoleiomyoma:** Lipoleiomyoma is a rare entity which should be differentiated from liposarcoma. Four cases of lipoleiomyoma were diagnosed constituting to 0.84% of all leiomyomas (table III). On gross examination in addition to white whorled appearance yellowish discoloration was seen. On microscopy interlacing bundles of smooth muscles were mixed with mature adipocytes.

**Table-III: Comparison of incidence of lipoleiomyoma in various studies.**

Author	Year	Incidence
Ueda H et al [16]	1999	0.8%
Avritscher [17]	2001	0.03-0.2%
Wang X et al[11]	2006	2.1%
Present study	2012	0.84%

**Table-IV: Comparison of age incidence of lipoleiomyoma in various studies.**

Author	Year	Average age in years
Bajaj P [13]	2000	43
Avritscher [11]	2001	48
Wang X et al[17]	2006	53.9
Manjunath HK[12]	2010	50
Present study	2012	47

The mean age of occurrence of lipoleiomyoma in the present study was found to be in 5th decade (table IV)

**02. Atypical leiomyoma:** Important entity as it can be misdiagnosed as leiomyosarcoma (Figure-3). It is characterized by spindle cells along with scattered multinucleated bizarre cells with prominent nucleoli that may mimic atypical cells [13]. A study by Philip PC et al stated that the term atypical leiomyoma is considered if the tumour showed focal or multifocal moderate to severe atypia, and no tumour cell necrosis [14]. Similar features were seen in the present study.

Average rate of mitoses of 2-3/10HPFs noted in the present study also correlated with the study by Oliva E et al [15].

Final diagnosis of atypical leiomyoma with low risk of recurrence was offered according to the study by Philip PC et al [14].

**01. Cellular leiomyoma:** A case of cellular leiomyoma was diagnosed in a 40 year old female. In the study done by Oliva E et al in 33 cases of cellular leiomyoma the age ranged from 29-65 years [15]. By definition cellular leiomyoma is a smooth muscle tumour with increased cellularity when compared to surrounding myometrium.

The histological features of dense cellularity of cellular leiomyoma in the present study were similar to the features mentioned by various authors [5, 15, 16, 17, 18].

The most important differential of cellular leiomyoma is endometrial stromal sarcoma. In most of the cases routine histopathology is sufficient to differentiate these lesions. However, in few cases with extremely cellular leiomyomas immunohistochemistry is used to resolve this dilemma [19].

## Conclusion

Smooth muscle tumours and endometrial stromal tumours represent the two main categories of mesenchymal tumours of the uterus. Although their diagnosis is straight forward in most cases, difficulties arise with particular leiomyoma variants, especially highly cellular leiomyoma (often confused with an endometrial stromal tumour) and leiomyoma with bizarre nuclei, mitotically active leiomyoma which may cause concern for leiomyosarcoma.

Differentiation between the benign and malignant counterparts of mesenchymal tumours is through the use of multivariate criteria; that is, criteria that involves several microscopic features such as differentiated cell type, presence and type of tumor necrosis, the degree of cytologic atypia, the mitotic index, and the relationship to surrounding normal structures, including extra uterine sites.

## What this study adds to the existing knowledge?

This study contributes to the data regarding histological variants of leiomyoma. Much remains to be learned clinically, particularly regarding those histologic entities that lie between, called leiomyoma variants.

Nonetheless, the bottom line is that, at the present time, the diagnosis of a leiomyoma variant cannot be made with certainty until a pathologist, guided by recently updated 2014 World Health Organization criteria [10], thoroughly examines the specimen.

## Author's Contribution

**Nischita Budihal:** Data collection, analysis Conceptualization, literature search & writeup.  
**Jayashree G Pawar:** Designing the study and supervised the study.  
**Manasa G C:** Manuscript preparation and proof reading.

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