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CLINICAL GUIDELINES

Variants of Leiomyoma: Histomorphological Study of Tumors of Myometrium

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ABSTRACT

Objectives: To study the histomorphological features of variants of leiomyomas of myometrium in our institution from hysterectomy and myomectomy specimens.

Methods: In this prospective study, 1,845 hysterectomy and myomectomy specimens collected over a period of two years were studied. A detailed gross and microscopic examination of tumors of myometrium were made after fixing and staining the specimen with routine H&E.

Results: Neoplastic lesions of the myometrium were diagnosed in 441 (23.90%) of the total 1,845 specimens. Benign tumors were diagnosed in 440 cases, and all the benign tumors were leiomyomas except one case of adenomyoma. Leiomyoma was the most common tumor of the myometrium constituting 99.54%. Usual leiomyoma constituted for 95.45% and variants of leiomyomas were 4.55%. Malignant tumor of the myometrium was diagnosed in one hysterectomy specimen out of 1,845 specimens.

Conclusion: Variants of leiomyomas were relatively less, but it is important to differentiate them from malignant neoplasms of the myometrium, as they have good prognosis. Tumor size, nature of margin, presence or absence of vascular invasion, coagulative necrosis and cytological atypia are the most important histological features for differentiation.

Keywords: Myometrium, Leiomyoma variants, Smooth muscle tumor, Hysterectomy.

INTRODUCTION

Smooth muscle tumors (SMTs) are the most frequent mesenchymal tumors of the uterus. The majority of the uterine SMTs are readily classifiable as benign or malignant based on their gross and microscopic appearances. However, when unusual features are seen in some leiomyoma variants, the differential diagnosis with leiomyosarcoma and also with non-smooth muscle tumors may become challenging. Patterns of growth, histological appearance, associations with vessels and degenerative changes provide the basis for the classification of most benign smooth muscle tumors of uterus.[1]

The present study is proposed to be undertaken, because myometrial tumors continue to be a major cause of morbidity and leading indication for hysterectomy in premenopausal women. And some of the leiomyoma variants, such as mitotically active leiomyoma, bizarre leiomyoma, may simulate leiomyosarcoma or other malignant tumors as these tumors carry better prognosis and require detailed morphological study.

METHODS

This prospective study consists of 1,845 hysterectomy and myomectomy specimens collected over a period of two years. Brief essential clinical history and finding were recorded.

A detailed gross examination, including size, appearance and external surface, were noted. The specimens were allowed to fix in 10% formalin for 24 to 48 hours. Multiple parallel sections were made and each surface was examined. The tissue bits from representative areas were taken for histopathological examination. Multiple sections of five microns thickness were cut and routinely stained with hematoxylin and eosin stain. The following histological features were studied and recorded: The degree of cellularity, presence or absence of degeneration, type of degeneration, mitotic index, the degree of cytological atypia, if any, the presence or absence of necrosis and type of necrosis, the status of the margins of the tumor with the surrounding myometrium and presence of intravascular invasion by tumor.

RESULTS

This prospective study on histomorphological study of variants of leiomyoma of myometrium was undertaken in the Department of Pathology, JJM Medical College, over a period of two years.

CLINICAL FEATURES OF LEIOMYOMA

Menorrhagia was the commonest symptom constituting 35.14%, followed by mass per abdomen (13.24%), white discharge per vagina (12.98%) and mass/vagina (12.53%). Remaining features are as shown in Table 1.

Of the total 12,285 surgical specimens received for histopathological examination in the department during the study period, 1,832 were hysterectomies and 13 were myomectomy specimens. The neoplastic lesions of myometrium were diagnosed in 441 (23.90%) of the total 1,845 specimens. Benign tumors were diagnosed in 440 cases, and all the benign tumors were leiomyomas except one case of adenomyoma.

Table 1 Symptoms of leiomyoma

Symptoms	*No. of cases*	*Percentage*
Menorrhagia	155	35.14
Mass/abdomen	58	13.24
White discharge /vagina	57	12.98
Mass/vagina	55	12.53
Pain abdomen	48	10.93
Dysmenorrhea	25	5.69
Primary infertility	18	4.11
Intermenstrual bleeding	13	3.12
Bladder disturbances	5	1.13
Backache	5	1.13
Total	439	100.00

419 cases (95.45%) showed features of usual leiomyoma, malignant tumor of the myometrium was diagnosed in one hysterectomy specimen out of 1,845 specimens studied (0.054%).

Variants of leiomyomas were seen in 20 cases constituting 4.55% (Table 2).

Table 2 Variants of leiomyoma

Leiomyoma variants	*No. of cases*	*Percentage*
Lipoleiomyoma	9	2.05
Myxoid leiomyoma	4	0.91
Hemorrhagic cellular	2	0.45
Cellular leiomyoma	1	0.22
Epitheloid leiomyoma	1	0.22
Bizarre leiomyoma	1	0.22
Neurilemoma type	1	0.22
Leiomyoma with lymphocyte infiltrations	1	0.22
Total	20	4.55

DISCUSSION

Several histopathological variants of leiomyomas have been described in the literature. Variants of leiomyomas were seen in 20 cases constituting 4.55%, which included four myxoid, nine lipoleiomyomas, two hemorrhagic cellular, one case each of cellular, epitheloid, bizarre, neurilemoma type and leiomyomas with lymphocytic infiltration. No case of growth pattern variants was seen.

Myxoid leiomyomas were diagnosed in 25 to 45-year-old females (Figs 1 and 2). The histological features of elongated uniform spindle cells suspended in amorphous myxoid material in the present study were similar to features mentioned by various authors (Fig. 3).[3-5] Useful features in differentiating malignant from benign myxoid tumors are, tumor size, the nature of the margin, presence or absence of vascular invasion. Grossly, both myxiod leiomyoma and leiomyosarcoma show soft, gray gelatinous cut surface and often a well-circumscribed border. On microscopic examination, it is important to relay on the low-power scrutiny to identify the real margin of the tumor. It is even more important to sample the tumor very extensively in order to find areas with more pronounced atypia or mitotic activity.

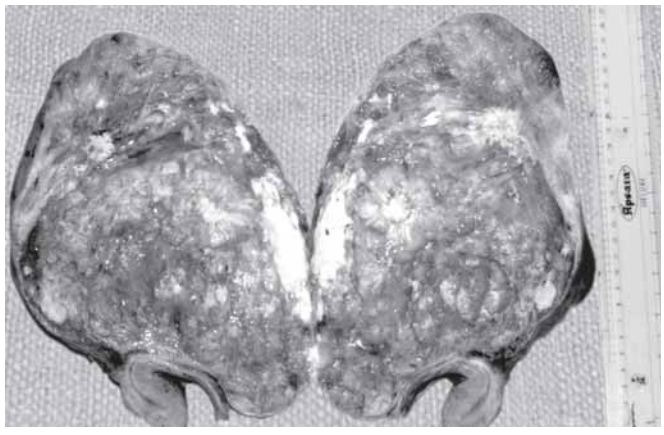

Fig. 1: Leiomyoma with myxoid degeneration

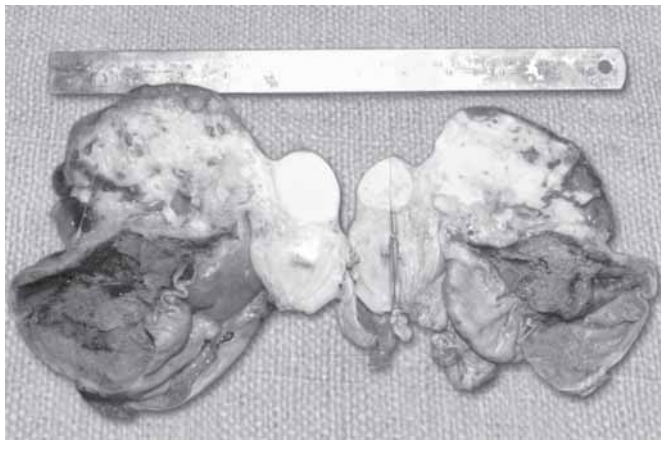

Fig. 2: Leiomyoma with myxoid and cystic change

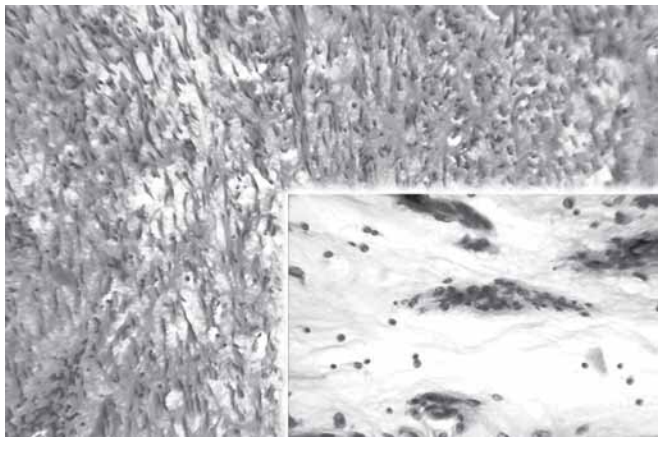

Fig. 3: Myxoid leiomyoma (H&E; LP; inset HP)

Nine cases of lipoleiomyomas were diagnosed in 38 to 46-year-old patients. The histological features of admixture of varying amounts of mature adipose tissue with smooth muscle cells in the present were similar to features mentioned by various authors (Fig. 4).[2-5]

Patients with hemorrhagic cellular leiomyomas were 25 and 31-year-old females showed histological features of smooth muscle cells with areas of hemorrhage. Cellularity was more around areas of hemorrhage (Fig. 5).

Cellular leiomyoma was diagnosed in a 38-year-old female. The clinical features, size, location and microscopic features were similar to the study made by Oliva,[7] who studied 33 cases. Epitheloid leiomyoma was diagnosed in 30-year-old female. The tumor measured 4 cm and showed classical microscopic features of epitheloid cells. Cells were round to polygonal with clear to acidophilic cytoplasm with round, centrally placed nuclei (Fig. 6). Similar features were described by various authors.[4,8,9] The behavior of epitheloid leiomyomas with two or more of the following features are not well-established:

1. Large size (greater than 6 cm)
2. Moderate mitotic activity
3. Moderate to severe cytologic atypia
4. Necrosis.[10]

One case of bizarre leiomyoma was diagnosed in a 35-year-old female, showed pleomorphic cells bordered by spindle-shaped cells and was admixed with multinucleated giant cells (Fig. 7). Around 24 cases of bizarre leiomyomas studied by Down and Hart,[6] also showed similar age group, location and other features of bizarre leiomyomas.

Most important clue in differentiating bizarre leiomyoma from malignant tumor is the patchy or multifocal distribution of bizarre cells in the tumor. Other helpful features are low mitotic activity, absence of tumor cell necrosis. Ancillary techniques, such as ploidy, MIB-1 and p53 expression, also can be used.

Leiomyoma with lymphoid infiltration was diagnosed in 38-year-old patient who presented with pain in abdomen. The subserosal tumor measured 45 cm in diameter and well circumscribed. Microscopically, the tumor was composed of scattered to diffuse infiltrate of small lymphocytes within smooth muscle cells (Fig. 8). Few eosinophils and hyaline degeneration were also seen. The main differential diagnosis is from a malignant lymphoma and inflammatory pseudotumor.[2,3]

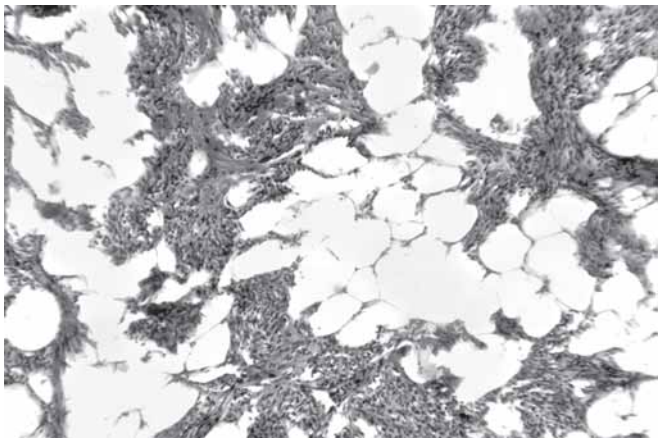

Fig. 4: Lipoleiomyoma (H&E; LP)

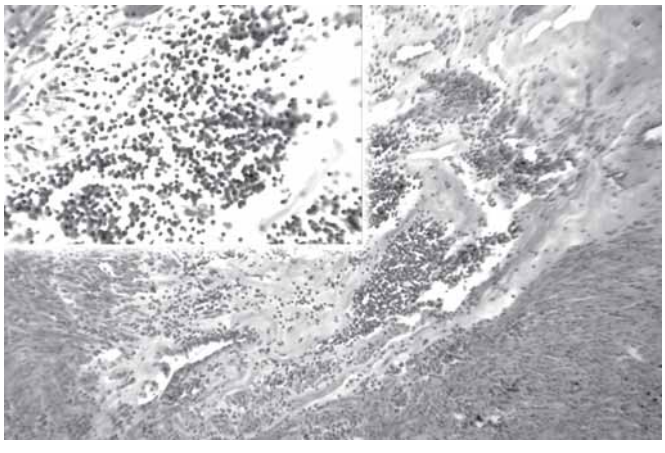

Fig. 5: Hemorrhagic cellular leiomyoma (H&E; LP)

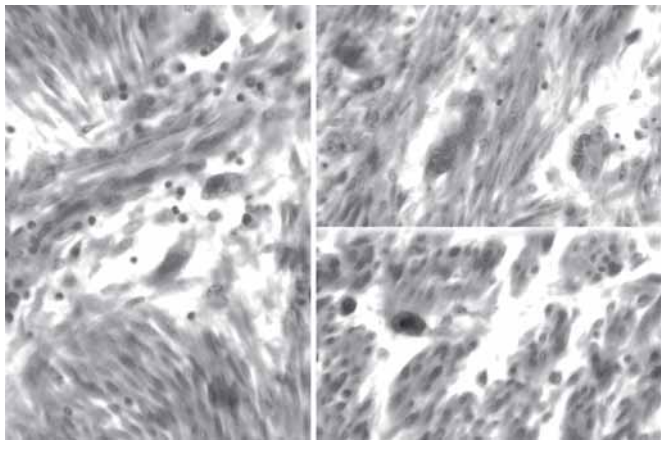

Fig. 7: Bizarre leiomyoma with multinucleated giant cells (H&E; LP; inset HP)

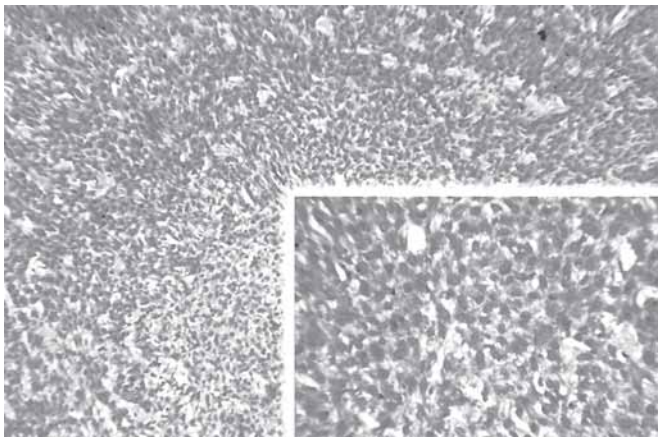

Fig. 6: Epitheloid leiomyoma (H&E; LP; inset HP)

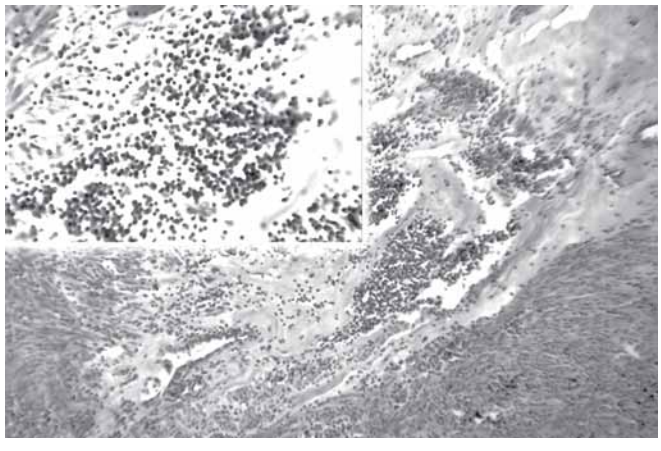

Fig. 8: Leiomyoma with lymphocytic infiltration (H&E; LP; inset HP)

Leiomyoma with lymphoid infiltration, on gross examination, resembles typical leiomyomas. Malignant lymphomas, in contrast, have a softer, fleshy, poorly circumscribed appearance. The lymphocytes in leiomyomas with lymphoid infiltration tend to be small and admixed with plasma cells and eosinophils, with the lymphoid infiltrate almost clearly confined to the leiomyomas.[2,3]

A case of neurilemmoma type leiomyoma was diagnosed in 40-year-old female, who presented with excessive bleeding. The tumor was intramural in location, measured 4.5 cm in diameter. Histological examination showed typical fascicular pattern of a leiomyoma. The tumor also showed areas with nucleus palisading mimicking a schwannoma, and was associated with hyaline degeneration.

CONCLUSION

Variants of leiomyomas were relatively less, but it is important to differentiate them from malignant neoplasms of the myometrium, as they have good prognosis. Tumor size, nature of margin, presence or absence of vascular invasion, coagulative necrosis, cytological atypia are most important histological features for differentiation.

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