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Research Article

Clinicopathological spectrum of uterine leiomyomas in a state of Northern India: a hospital based study

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ABSTRACT

Background: Myometrial lesions form a diverse group amongst which leiomyoma is the commonest visceral neoplasm affecting females in the reproductive age group. They are noted clinically in 20-30% of women over 30 years of age; are rare prior to the menarche, common in reproductive life and have a tendency to regress after the menopause. Their gross appearances are often altered by various secondary changes. Subtypes of leiomyoma are chiefly of interest as they may mimic malignancy in some cases.
Methods: All the hysterectomy and myomectomy specimens which were received in the department of pathology, ASCOMS hospital Jammu, Jammu and Kashmir over a period of one year, out of which 79 cases with leiomyomas were included in the study. The specimens were properly labeled, fixed (in NBF), examined grossly, processed, stained and examined microscopically.
Results: Age range of the patients with leiomyoma was18-62 years. Majority of the patients were between 41-50 years (46.84% cases). Menorrhagia was the commonest symptom constituting 37.97% cases and fibroid uterus was the most common clinical diagnosis provided (44%). Most common location of leiomyoma's was intramural (57.43%) followed by subserosal (30.69%). 56.96% leiomyoma's were single and 43.04% were multiple. Degenerative changes were observed in 16.46% cases, amongst which hyaline change was the most common (6.33%). 9 types of leiomyoma variants were seen, amongst which cellular leiomyoma (6.33%) was the commonest. Adenomyosis was associated with leiomyoma in 19.23% cases.
Conclusions: This study was conducted to analyze the clinic pathologic spectrum of uterine leiomyoma's in northern India with regards to their clinical presentation, associated changes and variants, and to compare our findings with similar studies from different parts of the world.

Keywords: Leiomyoma, Myometrium, Hysterectomy, Myomectomy

INTRODUCTION

Myometrium (Latin myo-muscle + Greek metra-womb) is the thick, smooth muscle coat of the uterus which encases the endometrium and is lined by the peritoneum derived serosa.[1] Myometrial lesions form a diverse group amongst which leiomyoma (benign smooth muscle tumor) is the commonest; followed by adenomyosis, leiomyosarcoma, endometrial stromal tumors, secondary tumors, vascular lesions, etc.

Leiomyoma is the commonest visceral neoplasm affecting females in reproductive age group.[2] Fibroid, fibromyoma and myoma are the terms synonymously used with this benign neoplasm. Originally believed to be fibromas, the misnomer "fibroid" has come to be so widely employed that it is generally considered synonymous with leiomyoma. They are noted clinically in 20-30% of women over 30 years of age, and are found in as many as 75% of uteri when a systematic search is conducted.[3] They are rare prior to the menarche, common in reproductive life, have a tendency to regress after the

menopause and are associated with endometrial hyperplasia, all of which suggest their estrogen dependence. Also, the myometrium of leiomyoma's expresses higher levels of estrogen receptors.[4] The importance of leiomyoma's lies in the symptoms they cause-pain, abnormal uterine bleeding and a sensation of pressure. Large tumors produce diffuse uterine enlargement or an irregular uterine contour, which may be associated with infertility. Some leiomyoma's are pedunculated and protrude through the cervical os.[4]

Grossly, they are well-circumscribed, firm, gray-white bulging masses (varying in size from barely visible nodules to large tumors that fill the pelvis) that can be easily shelled out from the myometrium and have a whorled appearance on cut surface with cells arranged in crisscrossing fascicles on microscopy. They are difficult to diagnose on curettage material, since they resemble superficial myometrium. The gross appearances are often altered by secondary or degenerative changes, which are commonly seen.[5,6] Hyaline degeneration/necrosis is present in more than 60%, particularly in postmenopausal women, and cystic degeneration, myxoid change, fatty degeneration and calcification each occur in about 4%. After menopause or delivery, leiomyomas can undergo atrophy with significant shrinkage and fibrosis. Red degeneration is associated with pregnancy and contraceptive use, and is due to tumor vessel thrombosis.[4,5]

Most subtypes of leiomyoma are chiefly of interest in that they mimic malignancy in one or more respects.[4] These subtypes are mitotically active leiomyoma, cellular leiomyoma, haemorrhagic cellular leiomyoma, leiomyoma with bizarre nuclei, epithelioid leiomyoma, and myxoid leiomyoma. Smooth muscle proliferations with unusual growth patterns may be in the form of diffuse leiomyomatosis, dissecting leiomyoma, parasitic leiomyoma, disseminated peritoneal leiomyomatosis, intravascular leiomyoma and benign metastasizing leiomyoma.[7-9]

Only a few studies have elaborated on the clinic-pathological changes seen in uterine leiomyoma's, hence in this context the present study was taken up. This is also the first comprehensive study on uterine leiomyoma pathology from Northern India.

METHODS

The material consists of all the hysterectomy and myomectomy specimens who were received in the department of pathology, Acharya Shri Chander College of medical sciences hospital Jammu, Jammu and Kashmir over a period of 1 November 2014 to 31 October 2015. A total of 165 specimens were received for histopathological examination in the department of pathology, out of which 79 cases diagnosed with leiomyoma's were included in the study. The clinical information and the relevant investigations of the patients were obtained from the histopathological requisition forms and clinical record files. The specimens received in the department of pathology were properly labeled, numbered and fixed in 10% buffered formalin. After a detailed gross examination of the specimens, multiple sections were taken from representative sites, processed and paraffin blocks were made. The blocks were sectioned and stained routinely with hematoxylin and eosin. Special stains were used wherever required.

RESULTS

Age of the patients with leiomyoma ranged from18-62 years. Majority of the patients were between 41-50 years accounting for 46.84% cases (Table 1).

Table 1: Age wise distribution of patients with leiomyoma.

Age range (in years)	No. of cases	Percentage
Below 20	01	1.27%
21-30	40	5.06%
31-40	16	20.25%
41-50	37	46.84%
51-60	19	24.05%
Above 60	02	2.53%
Total	**79**	**100%**

Clinical presentation

Menorrhagia was the commonest symptom constituting 37.97% cases, followed by pain in abdomen in 18.99% cases and dysmenorrhea in 17.72 cases (Table 2). Clinical diagnosis by the concerned physician was fibroid uterus in 44% cases, utero-vaginal prolapse in 20% cases, dysfunctional uterine bleeding in 19% cases and pelvic inflammatory disease in 17% cases.

Table 2: Chief complaints in patients with uterine leiomyoma.

Chief complaint	No. of cases	Percentage
Menorrhagia	30	37.97%
Pain in abdomen	15	18.99%
Dysmenorrhea	14	17.72%
Mass per vaginum	13	16.46%
Post-menopausal bleeding	04	5.06%
Leucorrhoea	02	2.53%
Infertility	01	1.27%
Total	**79**	**100%**

Most common site of leiomyomas was intramural (57.43%) followed by subserosal leiomyomas (30.69%), submucosal leiomyomas constituted 8.91% cases while broad ligament leiomyomas constituted 2.97% cases.

In the present study, out of 79 cases of leiomyomas, 45(56.96%) were single and 34 (43.04%) were multiple

(Table 3). Number of leiomyomas observed in the present study varied from 1 to 10.

Table 3: Location and number of leiomyoma's in uterus.

Location of leiomyoma	Single location	Multiple location	Total number	Percentage
Intramural	36	22	58	56.86%
Subserosal	21	11	32	31.37%
Submucous	06	03	09	08.83%
Broad ligament	03	0	03	02.94%
Total	**66**	**36**	**102**	**100%**

Size of leiomyomas

Sub-serosal leiomyomas varied from few mm to 6 x 5 x 4 cm in size. Intramural leiomyomas varied from few mm to 12 x 10 x 8 in diameter. Sub-mucosal leiomyomas varied from few mm to 3.5 cm in diameter.

In this study, majority of leiomyomas were diagnosed in multiparous women. Out of 79 patients with leiomyomas, 78 (98.73%) were parous, which includes 10 cases of uniparous patients and only 1 was nulliparous (1.28%).

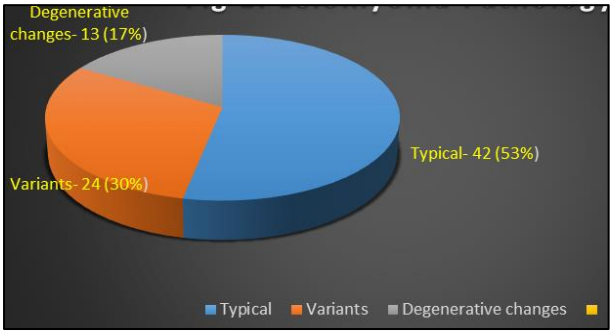

Figure 1: Various pathological changes seen in uterine leiomyomas.

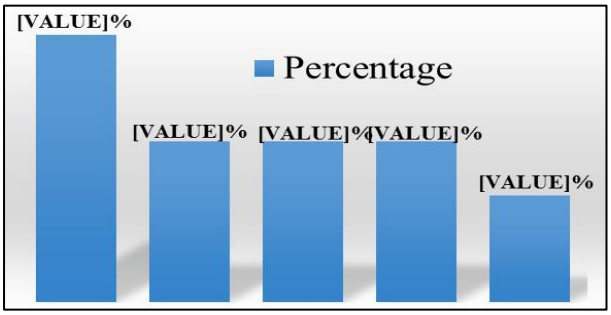

Figure 2: Various degenerative changes seen in uterine leiomyomas.

Types of leiomyomas: in our study, we observed 42 cases of typical leiomyomas (53.16%), followed by leiomyoma variants in 24 cases (30.38%) and degenerative changes in 13 cases (16.46%) (Figure 1).

Degenerative changes were observed in 13 leiomyomas (16.46%) (Figure 2). Among these, 05 leiomyomas (6.33%) showed hyaline change which constituted the most common degenerative change observed in this study, 03 leiomyomas (3.8%) showed myxoid change, 03 cases (3.8%) showed calcification, 03 cases (3.8%) showed cystic and 02 cases (2.53%) demonstrated carneous (red) degeneration [Figure 3(c)].

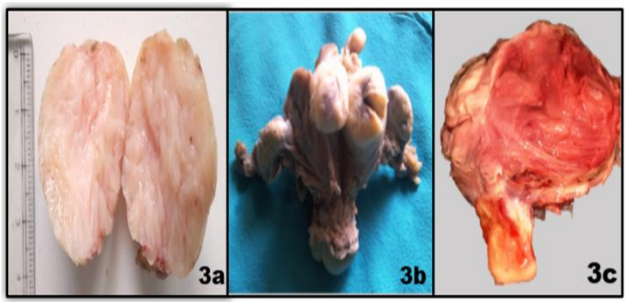

Figure 3(a): Cut section of a myomectomy specimen of whorled, raw-silk appearance typical of a fibroid; (b) gross section of uterus of diffuse leiomyomatosis; (c) cut section of uterine leiomyoma of red degeneration.

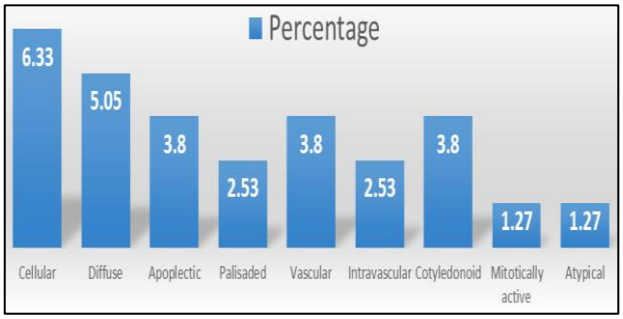

Figure 4: Variants of uterine leiomyoma's observed in the present study.

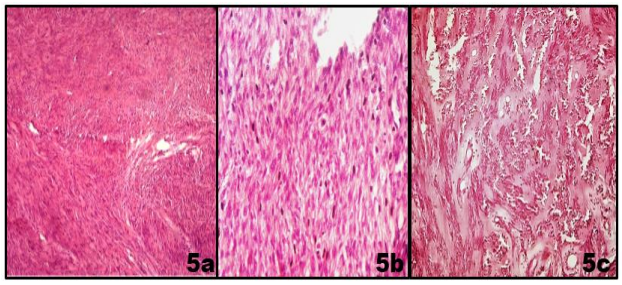

Figure 5(a): Photomicrograph of a cellular leiomyoma of dense crisscrossing trabeculae; (b) photomicrograph of mitotically active leiomyoma demonstrating increased mitotic activity in absence of atypia; (c) Photomicrograph of a palisaded (neurilemmoma-like) leiomyoma.

Variants of leiomyoma: we observed 09 types of variants of leiomyoma in the present study of the total 79 leiomyomas (Figure 4), which included following types of variants- cellular leiomyoma (6.33%), diffuse

leiomyomatosis (5.05%), apoplectic leiomyoma (3.8%), Cotyledonoid leiomyoma (3.8%), palisaded leiomyoma (2.53%), vascular leiomyoma (3.8%), intravascular leiomyoma (2.53%), mitotically active leiomyoma (1.27%) and atypical leiomyoma (1.27%) (Figure 5).

Associated myometrial pathology in leiomyomas: adenomyosis was found associated with leiomyoma in 15 cases (19.23%).

DISCUSSION

Leiomyomas continue to be a major cause of morbidity in perimenopausal women. Limited data is available from our community regarding clinicopathologic patterns of uterine leiomyomas. This study was conducted to analyze the clinicopathologic spectrum of uterine leiomyomas with regards to their presentation, location, associated changes and variants, and to compare our findings with those of other similar studies from different parts of the world.

The ages of the patients ranged from 18-62 years. The average age of patients was 45.82 years. Highest numbers of patients included in this study were between 41-50 years (46.82%). These findings were similar to that observed by Gupta et al (51.40%), Rather et al (47.27%), Vaidya et al (45.63%) and Rizvi et al (44.56%).[10-13] In other studies, 31-40 years age group was mainly affected-Karthikeyan et al (46.15%), Gowri et al (41.3%).[14,15]

In this study, menorrhagia was the commonest presenting symptom seen in 37.97% cases, followed by dysmenorrhea in 18.99% cases. Menorrhagia was also the presenting complaint in studies by Sarfraz (68%), Karthikeyan (62.5%), Rather (35.43%), Gowri (49.03%) and Manjula K (35.4%).[11,14-17]

The most common preoperative diagnosis was fibroid uterus in 44% cases followed by utero-vaginal prolapse in 20 % cases, dysfunctional uterine bleeding in 19% cases and pelvic inflammatory disease in 17 % cases. These findings are consistent with the data reported by Vaidya et al (42.96% and 18.95%), Siwatch et al (39% and 22.6%), utero-vaginal prolapse was the commonest indication in a study by Jha et al (37.1%), Gupta et al (40.0%).[10,12,18,19]

In the present study, out of 79 cases of leiomyomas, 45 (56.96%) were single and 34 (43.04%) were multiple. In a study by Sarfraz et al (2010) multiple leiomyomas were seen in 60.87% cases.[16] Abraham and Saldanha 20 observed solitary leiomyoma in 42.5% cases and multiple leiomyomas in 57.5%.

The most common site of leiomyomas in our study was intramural (57.43%) followed by subserosal leiomyomas (30.69%), sub mucosal leiomyomas (8.91%) and broad ligament leiomyomas (2.97%). Jung et al observed intramural fibroids in 55.7% cases, subserous fibroids in 16.3% cases, 15.6%, and submucosal fibroids in 12.4% cases respectively.[21] Intramural leiomyomas were also the commonest types in studies by Gowri et al (48%) and Rosario et al (52%).[15,22] Abraham and Saldanha observed intramural fibroids in 61.5% cases, subserosal leiomyomas in 9% cases and submucosal leiomyomas in 5% cases.[20]

In the present study, degenerative changes were observed in 13 leiomyomas (16.46%). Among these, 6.33% showed hyaline change which constituted the most common degenerative change observed in this study, 6.33% showed myxoid change, 3.8% showed calcification, 3.8% showed cystic and 2.53% demonstrated red (carneous) degeneration. Jung at al found secondary (degenerative) changes in 9.2% cases and the most common change was hyaline degeneration (5.7%).[21] Gowri et al reported secondary changes in 22.6% cases with hyalinization (16.9%) being the commonest secondary degenerative change followed by cystic (3.5%) and myxoid (1.6%) change.[15] Abraham and Saldanha observed secondary changes 22.2% cases; among these 49% showed hyaline change, 4.9% showed myxoid change, 4.9% showed calcification, 3.35 showed red degeneration and 4.9% showed hydropic change.[20]

In the present study, 09 variants of leiomyoma were seen in 24 cases out (30.38%) of the total 79 leiomyomas, which included following types of variants-cellular leiomyoma (6.33%), apoplectic leiomyoma (3.8%), diffuse leiomyomatosis (5.05%), cotyledonoid leiomyoma (3.8%), palisaded leiomyoma (2.53%), vascular leiomyoma (3.8%), intravascular leiomyoma (2.53%), mitotically active leiomyoma (1.27%) and atypical leiomyoma (1.27%). Abraham and Saldanha in their study encountered leiomyoma variants in 7.5% cases, which of which 78% were cellular leiomyomas, 9.5% were lipoleiomyoma and 4.7% were bizarre (symplastic) leiomyomas and 2.3% were epithelioid leiomyomas.[20] Manjula K et al in their study observed leiomyoma variants in 4.55% cases, which included-Lipoleiomyoma (2.05%), myxoid (0.91%), hemorrhagic cellular (0.45%), cellular (0.22%), epithelioid (0.22%), bizarre (0.22%), palisaded (0.22%) and lymphocytic infiltrated (0.22%) variants.[17]

CONCLUSION

Leiomyoma is the most common benign tumor of the pelvis. They are commonly seen in perimenopausal females and present with menorrhagia, pain in abdomen or dysmenorrhea. Intramural site was the most common location, hyaline change was the most common degeneration and cellular variant was the most common subtype seen in our study. The treatment modalities are chiefly hysterectomy, myomectomy or drug therapy (GNRH analogues), depending on various factors like parity, size, symptomatology, etc. Also, the pathologist needs to be cautious while diagnosing cases of atypical, mitotically active or bizarre leiomyoma's due to their

morphologic homogeneity with STUMP and leiomyosarcoma.

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