PROSPECTIVE STUDY OF UTERINE LEIOMYOMAS IN A TERTIARY CARE HOSPITAL

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ABSTRACT: BACKGROUND: Fibroids are benign smooth muscle neoplasms that may occur singly, but more often are multiple. Uterine tumors are the most common and the leading cause of hysterectomy in women. METHODS: The present study is a prospective study conducted in the department of pathology, Andhra Medical College, King George Hospital, Visakhapatnam in the period of one year, from March 2014 to March 2015. RESULTS: We received a total of 368 hysterectomy and 5 myomectomy specimens during this period, out of which, 249(66.7%) were single and 124(33.3%) were multiple. The age group ranged from 20 to 69. The most common location was intramural 243(65.1%) cases, subserosal were 51(13.7%), submucosal were 18(4.8%), cervical were 7(1.8%) and 2(0.5%) were broad ligament fibroids. The size ranged from as large as 19 cm to as small as seedling fibroids of size 0.1cm. Microscopically, the most common degeneration was hyaline degeneration 80 cases, 5 myxoid, 5 cystic and one case of chondroid degeneration. 6 cases showed calcifications. The most common age group was seen in the age group of 40-49 which were 207 cases (55.5%). 51(13.7%) cases were associated with adenomyosis. The results from our study were comparable with those reported in literature and provide a simple integrated pathogenetic view for further thinking, to establish new therapeutic options. CONCLUSIONS: The clinico-social and economic burden of uterine leiomyomas is increasing and requires future studies to clarify the etiopathogenesis and elaborate new and effective therapies for this condition. KEYWORDS: Uterine leiomyoma, Intramural leiomyomas, Histopathological variants.

INTRODUCTION: Leiomyomas of the uterus are extremely common neoplasms. The overall incidence is between 4% and 11%, but it rises to nearly 40% in women over the age of 50 years.1 Uterine tumors are the most common and the leading cause of hysterectomy in women. They are benign smooth muscle neoplasms that may occur singly, but more often are multiple.

Although the precise cause of leiomyoma is unknown, advances have been made in the understanding of the hormonal factors, genetic factors, growth factors, and molecular biology of these benign tumours.2

In this article, we propose as the major problem of research, a histological and clinical statistical study of uterine leiomyomas, obtained from the Department of Pathology, Andhra Medical College, King George Hospital, Visakhapatnam in the period of one year from March 2014 to March 2015.

The motive for choosing this study is determined by the fact that uterine leiomyoma still influences with their high frequency, limited possibilities of conservative treatment and surgery performed often unnecessarily leading to mental and economic trauma to many women.
AIMS:  
1. To study the histological patterns of leiomyomas in our Institute.  
2. To study the prevalence of leiomyomas in various age groups.  
3. To evaluate clinical characteristics and management outcome.

METHODS: This is a prospective study conducted in the Department of Pathology, Andhra Medical College in the period of one year from March 2014 to March 2015. We received a total of 373 specimens during this period. All the specimens were grossed according to standard grossing protocols. Formalin fixed paraffin embedded sections were stained with haematoxylin and eosin and examined microscopically.

RESULTS: We received a total of 373 specimens during the period of one year, out of which 368 were hysterectomy and 5 were myomectomy specimens, and out of which 249(66.7%) were single and 124(33.3%) were multiple in number. The most common age group were seen in the age group of 40-49 which were 207 cases (55.5%) (Table 1).

The most common clinical symptom was menstrual disturbances – menorrhagia (53.3%), abdominal lump (23.4%), mass protruding at the introitus (11.2%) and pressure symptoms on adjacent viscera - bladder, ureters and rectum (12.2%), other clinical presentation was backache and abdominal pain.

The most common location was intramural 243(65.1%) cases, subserosal were 51(13.7%), submucosal were 18(4.8%), cervical were 7(1.8%) and 2(0.5%) were broad ligament fibroids. The size ranged from as large as 19 cm to as small as seedling fibroids of size 0.1cm. 51(13.7%) cases were associated with adenomyosis (Fig 9, 10).

Secondary changes were observed in 98 cases (26.2%) of which hyaline degeneration was the most common which was seen in 80 cases (81.6%), the others were five myxoid, five cystic, one case of chondroid degeneration, one case of fatty degeneration and 6 cases showed calcifications. One case of clinically diagnosed fibroid turned out to be low grade stromal tumour.

DISCUSSION: The first step in the evaluation of a uterine smooth muscle tumor is to be sure that the lesion in question is composed of cells demonstrating smooth muscle differentiation.[3]

An understanding of the etiology of fibroids remains elusive.[4] Several theories about the initiators of fibroids have been proposed. Rein[5] stated that increased levels of estrogens and progesterone could result in an augmentation of mitotic rate that could be responsible for somatic mutation. Richards and Tiltman found increased concentration of receptors for estrogens (ER) in certain regions of the myometrium.[6] Another interesting theory underlines that the pathogenesis might be similar to a response to injury;[7] ischemic damage could be linked to release of increased vasoconstrictive substances at the time of the menses. Smooth muscle cells of the myometrium could react to injury with the synthesis of extracellular fibrous matrix.[8] After vascular damage, basic fibroblast growth factors are overexpressed in leiomyomas.[9,10]

The wide spectrum of clinical and genetic heterogeneity of uterine leiomyomas underscores the importance of continued investigation to determine the various molecular etiologies that result in leiomyoma development.[11]
Grossly, the cut surface of a typical leiomyoma has a raw silk appearance.[1] They are sharply circumscribed, discrete, round, firm, gray-white tumors varying in size from small, barely visible nodules to massive tumors that fill the pelvis. (Fig. 1) Whatever their size, the characteristic whorled pattern of smooth muscle bundles on cut section usually makes these lesions readily identifiable.[12] Microscopically, the tumor is formed by interlacing bundles of smooth muscle cells separated by a greater or lesser amount of well-vascularized connective tissue.[1] (Fig. 3, 4)

The tumor may grow symmetrically, remaining within the myometrial wall, when it is called 'intramural' or 'interstitial'. If the tumor grows outwards towards the peritoneal surface, it shows itself as a bossy growth and it is termed 'subserous'. Uterine contractions may force the myoma towards the cavity where it is covered only by thin endometrium, it is then called 'submucous' myoma.

Many variations of leiomyomas exist, most of these are the result of secondary changes and are detectable in approximately 65% of cases. These include hyaline degeneration (Fig. 5), myxoid changes (Fig. 7, 8), calcification, cystic changes and fatty metamorphosis.[1]

We have received one case of cellular leiomyoma showing increased cellularity but no coagulative necrosis, atypia, or an excessive number of mitotic figures.[1] (Fig. 2, 6)

Differential Diagnosis: Considerations in the differential diagnosis of leiomyoma include other non–smooth muscle neoplasms, particularly endometrial stromal tumors, and leiomyosarcoma.

Smooth muscle cells can also resemble endometrial stromal cells by losing much of their characteristic eosinophilic, fibrillary cytoplasm and by developing closely approximated round to oblong nuclei of the type more often seen in endometrial stromal cells. A feature that favors smooth muscle differentiation is the presence of thick-walled vessels within the lesion; the vessels in stromal tumors are mainly thin-walled arching capillaries. A fascicular arrangement of the constituent cells also favors a smooth muscle tumor.[3]

The histopathologic diagnosis of uterine leiomyosarcoma is usually straightforward since most clinically malignant smooth muscle tumors of the uterus show the microscopic constellation of hypercellularity, severe nuclear atypia, and high mitotic rate generally exceeding 15 mitotic figures per 10 high-power-fields (MF/10 HPF).[13]

Most of the patients in our study have small fibroids. On rare occasions, however, fibroids can grow extremely large. It is in these cases that treatment is not standardized because proper management of patients with very large fibroids is complex and requires exceptional skill.[14]

Considering that leiomyomas are characterized by increased cell proliferation and tissue fibrosis, antiproliferative and/or antifibrotic agents could be emerging target for leiomyoma treatment. Surgery is definitive treatment for fibroid management, and various minimally invasive procedures have been developed.[15]

The results from our study were comparable with those reported in literature and provide a simple integrated pathogenetic view for further thinking, to establish new therapeutic options.

CONCLUSION: The clinico-social and economic burden of uterine leiomyomas is increasing and requires future studies to clarify the etiopathogenesis and elaborate new and effective therapies for this condition.
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| Age group | Number | % |
|-----------|--------|---|
| 20-29     | 20     | 5.4 |
| 30-39     | 112    | 30 |
| 40-49     | 207    | 55.5 |
### Table 1: Age distribution of uterine leiomyomas

| Age Range | Count | Percentage |
|-----------|-------|------------|
| 50-59     | 28    | 7.5        |
| 60-69     | 6     | 1.6        |

Fig. 1: Gross photograph of leiomyoma measuring 16 x 12 cm, cut section circumscribed and gray-white

Fig. 2: Gross photograph of cellular leiomyoma measuring 4 x 4 cm, cut section grey white & foci of yellowish areas

Fig. 3: Microphotograph showing circumscribed tumor composed of uniform sheets of smooth muscle cells. H & E 100x
Fig. 4: Microphotograph showing uniform sheets of spindle cells arranged in fascicular pattern. H & E 100x

Fig. 5: Microphotograph showing leiomyoma with extensive areas of hyalinization H & E 100x

Fig. 6: Microphotograph of cellular leiomyoma showing increased cellularity. H&E 100x
Fig. 7: Microphotograph showing areas of hyalinization and spindle cells. H & E 100x

Fig. 8: Microphotograph showing leiomyoma with myxoid change. H&E 100x

Fig. 9: Microphotograph showing adenomyosis. H&E 40x
Fig. 10: Microphotograph showing adenomyosis with endometrial glands surrounded by endometrial stroma. H & E 100x

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