Original Article

Endometrial Changes in Uterine Leiomyomas

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ABSTRACT

Background: *Uterine leiomyomas are steroid dependent tumours. The endometrium responds cyclically to these hormones. This study thus reviews histopathologic changes in endometria of leiomyomatous uteri.*

Objectives: *To Study histopathologic changes in endometria of leiomyomatous uteri. Identify endometrial changes which help to suggest a diagnosis of uterine leiomyomas on endometrial curetting.*

Methods: *100 cases of leiomyomatous uteri were studied. Parameters were evaluated by descriptive statistical analysis. Chi-square/ Fisher Exact test was used to find the significance. 95% Confidence Interval has been computed to find the significant features.*

Results: *Leiomyomas commonly presented between 41-50 years, mostly in multiparous women as menorrhagia. Proliferative / hyperplastic endometrium was usually seen. Other epithelial cell changes seen were dilated, elongated or distorted glands, glands parallel to muscle fibres and glands separated by muscle fibres.*

Conclusions: *Leiomyomas are steroid dependent tumours wherein the endometrium manifests mostly as proliferative phase or hyperplasia suggesting estrogenic prevalence. Association with multiparity explains the need for progesterone in maintenance of leiomyomas. Mixed findings such as few glands showing a particular menstrual phase admixed with some showing atrophy or polyposis, together with distorted, dilated or elongated glands and muscle fibres between glands in endometrial curetting, could suggest a possibility of uterine leiomyoma. The study is useful where other diagnostic modalities are a matter of concern in the evaluation of menorrhagia, and leiomyomas being the most common cause for menorrhagia.*

Key words: *Leiomyoma, Endometrium, Menorrhagia.*

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INTRODUCTION

The endometrium is a dynamic tissue showing structural reorganisation with each menstrual cycle in preparation for implantation, in the absence of which the superficial layer is partially/ completely shed and remodelled in preparation for the next cycle. Many compounds exert local effects which are important for

implantation and maintaining the integrity. The important hormones include estrogen and progesterone.[1] Uterine leiomyomas account for more than 75 % of the benign tumours in women of reproductive age group. They are dependent upon the steroid hormones for their growth and maintenance.

At R.L Jalappa hospital and research centre, a referral hospital in Kolar attached to Sri Devaraj Urs Medical college, hysterectomies are mostly performed for the management of leiomyomas and dysfunctional uterine bleeding. Hence, this study will identify the histopathologic changes in endometrium of leiomyomatous uteri, which can be useful in peripheral centres where other diagnostic modalities are a matter of concern and in endometrial curetting done to evaluate cause of menorrhagia.

AIMS AND OBJECTIVES

1. To study the histopathological changes in endometrium in association with uterine leiomyomas.
2. To identify endometrial changes which help to suggest a diagnosis of uterine leiomyomas on endometrial curetting.

METHODS

The study included 100 cases in which uterine leiomyomas were present. Brief clinical data with respect to age, clinical presentation, parity and menstrual phase was obtained. The specimens were processed as per standard grossing protocols. Gross examination was performed with respect to size and weight of uterus, location of fibroids and endometrial polyp if any was noted.

Tissue bits from the fundic endometrium, tissue from both sides of endometrial canal & endometrium subjacent to sub mucosal leiomyoma were taken for histopathological examination, processed and sections of 5 micron thickness stained with haematoxylin and eosin were studied as under:

1. Endometrial parameters- thickness of endometrium, phase, number and appearance of glands within the given area and stromal changes.
2. The endometrial area was calculated using a standard 2-mm length multiplied by the measured width.[2]

The parameters were evaluated using descriptive statistical analysis. Significance was assessed at 5 % level of significance. Chi-square/ Fisher Exact test have been used to find the significance of study parameters on categorical scale between two or more groups. 95 % Confidence Interval has been computed to find the significant features. CI with lower limit more than 50 % is associated with statistical significance.

RESULTS

Age: In the present study, patients with leiomyoma were aged between 3rd and 7th decades of life. Majority of the patients (84 %) were in 4th and 5th decades of life.

Parity: 81 out of 100 women with leiomyoma were multiparous accounting for 81 %.

Presenting complaints: Menorrhagia was the commonest symptom (58 %), followed by pain abdomen (26 %), mass per vagina (22 %) and mass per abdomen (21 %).

Endometrial area: Majority of the leiomyomatous uteri showed an endometrial

area ranging from 1-4 sq.mm (50 %) (table 1), followed by an area ranging from 4-10 sq.mm.

Endometrial phase on microscopy: Proliferative endometrium was noted in 33 %, secretory endometrium in 29%, endometrial hyperplasia in 24 % and atrophic endometrium in 14 % of the cases. (Table 2)

Endometrial epithelial cell changes: Dilated or distorted glands and arrangement of glands parallel to the long axis of myometrium were seen in 53 % of the cases and 31 % of the cases showed endometrial glands separated by muscle fibres. These features were noted in the endometrium on the same side as the leiomyoma and in the fundic endometrium. 79 out of the 100 uteri showed a combination of these features in the endometrium. These changes did not show any association with the size of the leiomyomas. (Table 3)

DISCUSSION

1. Age

In the present study, leiomyomas was seen to be more common in the 4th and 5th decades. Cumulative stimulation by estrogen and progesterone and hormonal factors associated with peri-menopause are important modulators which are associated with presentation of fibroids in women aged between 20-30 years and in late reproductive years respectively.[3]

2. Parity

Studies have reported the risk of uterine leiomyomata to be 20-50% lower among women who have ever given birth compared to nulliparous women, and the risk appears to decrease with increasing parity.[4,5,6] The explanation cited was that pregnancy reduces the time of exposure to unopposed estrogens, whereas nulliparity or reduced fertility may be associated with anovulatory cycles characterized by long term unopposed estrogens.[3]

However, in the present study, the majority of the patients were multiparous (81 %), which is similar to studies by Chhabra & Jaiswa l[7] and Rosario Pinto.[8]

Rein et al studied the factors involved in initiation and growth of leiomyoma. Traditionally, estrogen was considered the major promoter of myoma growth. However, their studies presented the clinical, pathological and molecular biochemical evidence suggesting that progesterone, progestins, and the progesterone receptors promote cellular proliferation in leiomyoma.[9,10] Estrogen and progesterone appear to be promoters of fibroid growth, acting in concert. The estrogen up-regulates both ERs and PRs during proliferative phase which is followed by the progesterone-induced mitogenesis during the luteal phase.[3]

The quantitative studies have also revealed the tissue concentrations of estrogen, progesterone and their receptors, ER and PR respectively, to be significantly higher in the leiomyomatous uteri in comparison with normal uteri.[3,11]

Thus, from above studies, it can be concluded that growth of fibroids are regulated both by estrogen and progesterone. Further, progesterone is known as the hormone of pregnant uterus. This provides a probable explanation for the increased incidence of fibroids among the multiparous women, who probably acquire increased levels of estrogen, progesterone and their receptors, ER and PR,

Table 1: Endometrial area

Endometrial area (Sq. mm)	Number (n=100)	%
<1	7	7.0
1-4	50	50.0
4-10	36	36.0
>10	7	7.0

Table 2: Endometrial phase

Epithelial Cell Changes	Number of patients (n=100)	%
Absent	21	21.0
Present	79	79.0
• Dilated/ distorted glands	53	53.0
• Endometrial glands separated by muscle fibres	31	31.0
• Endometrial glands parallel to myometrium	53	53.0
• Focal loss of surface epithelium	7	7.0
• Decidual cast	1	1.0
• Polyposis	3	3.0
• Subtotal glandular atrophy	4	4.0
• Total glandular atrophy	13	13.0

Epithelial cell changes are 79.0% with 95%CI (70.02-85.83%) which is statistically significant

Table 3: Comparison of endometrial epithelial cell changes in uteri with submucous leiomyoma and other locations

Epithelial cell changes	Total number of cases	Location		P value
		Submucosal (n=21)	Others (n=79)	
1. Dilated/ distorted glands	53	8 (38.1 %)	45(56.9 %)	0.124
2. Endometrial glands parallel to myometrium	53	8(38.1 %)	45(56.9 %)	0.124
3. Endometrial glands separated by muscle fibres	31	6(28.6 %)	25(31.6 %)	0.787
4. Total glandular atrophy	13	12(57.1 %)	1(1.3 %)	<0.001**
5. Focal loss of surface epithelium	7	1(4.8 %)	6(7.6 %)	1.000
6. Subtotal glandular atrophy	4	4(19.1 %)	0	0.002**
7. Polyposis	3	2(9.5 %)	1(1.3 %)	0.111
8. Decidual cast	1	0	1(1.3 %)	1.000
9. Absent	21	1(4.8 %)	20(25.3 %)	0.066+

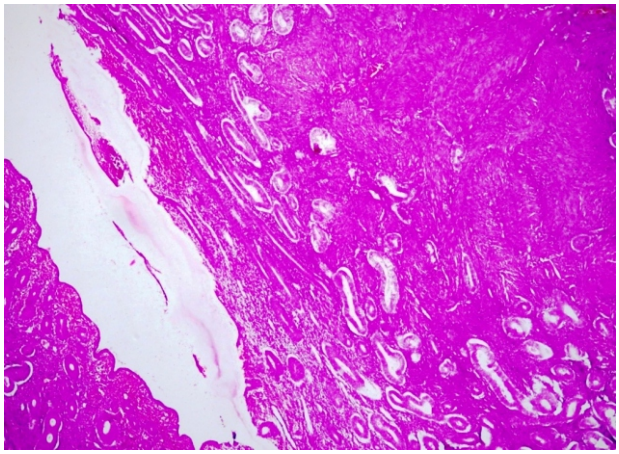

Fig 1: Endometrium showing elongated glands parallel to myometrium (H&E, LP)

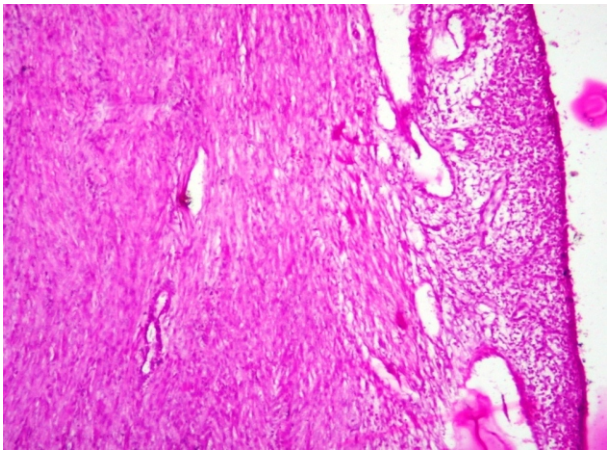

Fig 2: Total glandular atrophy of endometrium overlying submucous leiomyoma (H&E, LP)

with each pregnancy.

3. Presenting complaints

Approximately 30% of women with fibroids have been reported to have menstrual abnormalities, most often menorrhagia.[12,13] In the present study, majority of the patients with leiomyomas presented with menorrhagia (58%) which is similar to the study by Chhabra and Jaiswal[7].

Menorrhagia may occur when endometrial cavity surface area is expanded by submucous

fibroids. However, often submucous fibroids are not present, but extensive uterine bleeding exists. The increased bleeding maybe due to either increased vascularity of the uterus or anovulatory cycles. Fibroids arising at various sites in the uterus could cause congestion and dilatation of endometrial venous plexuses by impinging and obstructing veins in the myometrium. The resultant obstruction could cause endometrial venule ectasia which may play a role in enhanced uterine bleeding. [13]

4. Comparison of the endometrial phase in leiomyomatous uteri:

In the present study, proliferative and hyperplastic endometrium accounted for 33% and 24% of the cases respectively, accounting together for 57%. Similar findings were also seen in other studies.[14,15] The probable cause may be the hyperestrogenic state responsible for the proliferative phase and hyperplastic lesions which may also be the causative factor of the organic lesion as well.[13]

The atrophic endometrium associated with leiomyoma which accounted for 14% in the present study was probably due to the mechanical and hormonal factors.[16]

5. Endometrial epithelial cell changes:

Of the various epithelial cell changes, total or subtotal glandular atrophy were most commonly seen in uteri having submucous leiomyoma and showed significant correlation ($p<0.001$) (Table 4). These results are found to be comparable with the findings of the studies conducted by Deligdish & Loewenthal[16], Sharma et al[17]and Patterson-Keels et al.[2]

Further, other features such as dilated/ distorted glands and glands parallel to long axis of myometrium were noted in endometrium irrespective of the location of leiomyomas. These findings were present in 79% of the cases with 95% CI (70.02-85.83%) which is statistically significant. (Table 3)

Studies involving a topographical investigation of the pathological changes of the endometrium with special reference to the site of myomata within the uterus have shown different pathological patterns in the endometrium. These could be a result of mechanical factors and hormonal factors. Atrophy of the endometrium, elongation and distortion of the glands could result from mechanical pressure exerted by the nodular mass of the myoma on the overlying or nearby endometrium. Cystic glandular hyperplasia, edema and haemorrhage can result from hormonal disturbances, mainly hyperestrogenism.[16,17]

However, the action of both the factors, mechanical and hormonal is complex. Atrophy may result not only from mechanical pressure but also from postmenopausal hormonal insufficiency. Glandular hyperplasia or polyposis, mainly in the endometrium at the edge of a myoma, may not only be the expression of estrogen hyperactivity, but also the result of mechanical forces upon the endometrium.[16]

CONCLUSION

Uterine leiomyomas mostly presented in multiparous women. Proliferative endometrium and endometrial hyperplasia accounted for 57%,, of the cases suggesting an estrogenic prevalence. Different patterns are seen in the endometrium of leiomyomatous uteri as a result of mechanical or hormonal factors such as dilated/ distorted glands, glands parallel to long

axis of myometrium, glands separated by muscle fibres, focal total or subtotal glandular atrophy and polyposis which are statistically significant in identifying uterine leiomyoma. Further, total and subtotal endometrial glandular atrophy showed significant association with submucosal leiomyoma.

Thus, if endometrial curettings show a mixed picture of few glands showing a particular menstrual phase admixed with some showing atrophy or polyposis, together with distorted, dilated or elongated glands and muscle fibres between glands, one can suggest a possibility of uterine leiomyoma. The study is useful where other diagnostic modalities such as ultrasound and hormonal assays are not available and in endometrial curettage done for evaluation of menorrhagia, leiomyomas being the most common cause for menorrhagia.

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