A clinicopathological study of endometrium in hysterectomy specimens with fibroids

Ksheera Cariappa. A[1], Vinay Kumar. R[2,*]

Assistant Professor, Dept. of Pathology, [1]Subbaiah Institute of Medical Sciences, Shivamogga, Karnataka, [2]Koppal Institute of Medical Sciences, Karnataka, India

***Corresponding Author**
Email: viney.dr@gmail.com

Abstract

Introduction: Hysterectomy is the most common gynaecological surgery performed in the peri menopausal and post menopausal women all over the world. The commonest pathologies in such hysterectomies are uterine fibroids. Many times hysterectomies are also performed for dysfunctional uterine bleeding, in which leiomyomas are commonly noted. When such hysterectomy specimen are grossed and sections studied, co-existing endometrial lesions like hyperplasias, metaplasias, malignancies are usually missed due to the significant presence of leiomyoma.

Aim of the Study: The present study intends to unravel all such endometrial pathologies, which would have been missed when there is a co-existing uterine leiomyoma and to categorize these lesions into different groups.

Materials and Methods: The study material was obtained from patients who underwent hysterectomy for leiomyoma from December 2011 to August 2013. 200 hysterectomy specimens were included in the study. Tissue bits from representative areas were taken, microscopic sections obtained and histological features studied.

Results: Leiomyomas occurred mostly in women aged between 41-50 years and in multiparous women. Menorrhagia was the commonest presentation. Endometrial pattern commonly seen was proliferative phase and hyperplasia. Other patterns like endometrial adenocarcinoma, endometrial polyps and pill endometrium were also encountered.

Conclusion: Leiomyomas are estrogen dependent tumours, wherein the endometrium manifests mostly as proliferative phase or hyperplasia suggesting estrogenic prevalence. Findings such as endometrial hyperplasia, polyposis along with distorted, dilated or elongated glands in endometrial curetting could suggest a possibility of uterine leiomyoma.

Keywords: Leiomyoma, Hysterectomy, Endometrium, Hyperplasia, Metaplasia, Carcinoma.

Introduction

Hysterectomy is the most common gynecological surgery performed in the peri-menopausal and post menopausal women all over the world.[1] The commonest indications being uterine fibroids (leiomyomas) followed by DUB(dysfunctional uterine bleeding), in which leiomyomas are commonly noted.[2] During histopathological study of these specimens any co-existing endometrial lesions like hyperplasias, metaplasias, malignancies or tuberculosis are usually missed due to the significant presence of leiomyoma.[2] Other myometrial lesions like adenomyosis also show malignant changes with co-existing benign glandular hyperplasia and atypical complex hyperplasia of the endometrium.[3]

The present study aims to detect all such endometrial lesions which would have been missed when there is a co-existing uterine leiomyoma and to study the endometrium for any associated changes which could help diagnose leiomyoma in curettage samples.

Aims and Objectives

1. To study the various gross and microscopic features of the endometrium and fibroids in all hysterectomy specimen with leiomyomas.
2. To categorize these endometrial lesions into different groups.
3. To study the endometrial changes which help to suggest a diagnosis of uterine leiomyomas on endometrial curettings.

Materials and Methods

The study was undertaken in department of pathology A.J Hospital and Research Centre from December 2011 to November 2013 which included 200 hysterectomy specimens with fibroid, which were obtained from patients admitted in the hospital. The clinical data was obtained from patients or patient records with respect to age, clinical presentation, parity and menstrual phase. The hysterectomy specimens received were cut into two halves were fixed in 10% formalin for 12-24 hours. A detailed gross examination was performed with respect to size and weight of uterus, location and size of fibroids, secondary changes like cystic change, red degeneration, calcification, mucoid degeneration or fatty degeneration and status of endometrium was noted. Tissue bits from representative areas of the fibroids and a minimum of two tissue bits from either side of the endometrium were taken, processed, paraffin blocks prepared and 5 micron thickness sections obtained and stained with hematoxylin and eosin for histopathological examination of the following features.

1. Endometrial parameters- endometrial thickness, phase, number and other histopathological parameters were noted.

2. Myometrial parameters- type/ variant of leiomyoma and secondary/ degenerative changes in the leiomyoma.

The obtained parameters were evaluated using descriptive statistical analysis using the software SPSS ver., 16. Percentage evaluation was used for comparison.

Results

In the present study, patients were aged between 2nd and 6th decades of life with youngest being 27 years and oldest 67 years with Majority (80%) in 3rd and 4th decades of life

Table 1: Age distribution

Age in years	Number	%
21-30	5	2.5
31-40	48	24
41-50	112	56
51-60	30	15
61-70	5	2.5
Total	200	100

159 out of 200 women with leiomyoma were multiparous and constituted 80% of the cases. (Table 3) Excessive bleeding/ Menorrhagia was the commonest symptom among patients with leiomyoma(44%), followed by excessive bleeding with pain abdomen (17%), pain abdomen (16.5%), mass per abdomen (10.5%) and mass per vagina (8.5%). (Table 2)

Table 2: Presenting complaints

Presenting Complaints	Number (n=200	Percentage
Excessive bleeding	88	44
MPA	21	10.5
Pain abdomen/dymenorrhea	33	16.5
MPV	17	8.5
Excessive Bleeding + Pain Abdomen	34	17
Post Menopausal bleeding	7	3.5

Clinical Diagnosis: In the present study, fibroid uterus was the commonest clinical diagnosis (55.5%), followed by dysfunctional uterine bleeding (30%), UV prolapse (17%), post-menopausal bleeding (3.5%) and pelvic inflammatory disease (2.5%). (Table 3)

Table 3: Clinical diagnosis

Clinical Diagnosis	Number	Percentage
Fibroid	111	55.5
DUB	60	30
UV Prolapse	17	8.5
PID	5	2.5
Postmenopausal bleeding	7	3.5
Total	200	100

Weight of the Uterus: Most of the uteri weighed between 100 – 300 grams, which accounted for 86% of the cases. In 6% of the cases, the uteri weighed over 1000 grams and in 6% of cases they were less than 100 gms which constituted the atrophic uteri with fibroids. Maximum uterus weight obtained was 1300 grams.

Number of Fibroids: Most of the uteri showed a single fibroid, accounting for 45%, followed by multiple fibroids >5 in number (Fig. 1) which were seen in 21% of cases. In the remaining 34%, the number of fibroids varied from 2 – 4.

Location of Fibroids: In the present study, 55.5% of the cases had intramural fibroid, 12.5% had subserosal fibroid and 3% had submucosal fibroid with 20% having both intramural and subserosal fibroids. (Table 4)

Table 4: Showing location of fibroids

Location	Number (n=200)	%
Intramural (IM)	111	55.5
Subserosal (SS)	25	12.5
Submucosal (SM)	6	3
Intramural + Subserosal	40	20
Intramural + Submucosal	13	6.5
Submucosal + Subserosal	2	1
IM + SM + SS	3	1.5

Secondary Changes in Fibroid: 13 out of the 200 leiomyomatous uteri showed gross secondary or degenerative changes within the fibroids of which calcification was seen in 4 cases, cystic change in 3 cases, fatty change in 3 cases, myxoid degeneration in 2 cases and infarction in 1 case.

Incidence of Endometrial Polyp on Gross: on gross examination of the cut surface of fibroid uteri, endometrial polyp (Fig. 1) was seen in 27 out of the 200 cases. The largest polyp measured 4 x 2.5 x 2 cms and on microscopy about 10 of them were associated with endometrial hyperplasias, disordered proliferation and carcinomas. 3 were leiomyomatous endometrial polyps.

Histologic type of Leiomyoma: In the present study, 195 (97.5%) out of the 200 cases showed features of usual leiomyoma consisting of anastomosing and whorled fascicles of fusiform cells of a relatively uniform size. These cells contained abundant eosinophilic and fibrillar cytoplasm with elongated nuclei having finely dispersed chromatin with occasional nucleoli. Variants of leiomyomas were seen in 5 cases constituting 2.5%. Of these, 2 cases were myxoid leiomyomas, 2 were leiomyomas with bizarre cells and 1 was a case of cellular leiomyoma.

Secondary Changes in Fibroid on Microscopy: The commonest degenerative changes encountered on microscopic examination of the fibroids were hyaline degeneration (Fig. 2), which accounted for 18%, followed by calcification (Fig. 3) and fatty change 2%. (Table 5)

Table 5: Secondary changes in fibroid and their distribution

Secondary changes on microscopy	Number (n=200)	%
Absent	150	75
Hyalinization	36	18
Calcification	4	2
Infarction	1	0.5
Fatty change	4	2
Cystic change	3	1.5
Myxoid change	2	1

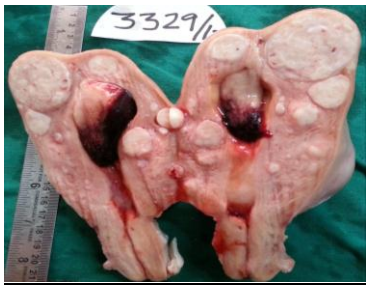

Fig 1: Multiple fibroids in uterus along with a leiomyomatous (submucosal) endometrial polyp

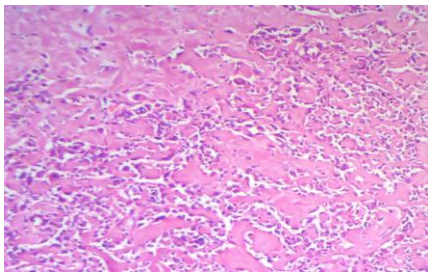

Fig. 2: Photomicrograph of leiomyoma with extensive hyalinization. (H&E, 40x)

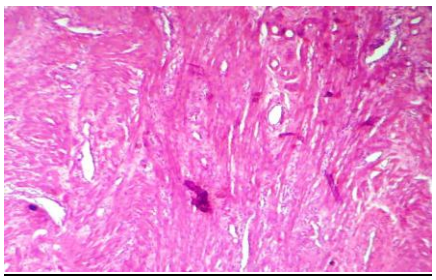

Fig 3: Photomicrograph of leiomyoma with small areas of calcification. (H&E, 40x)

Incidence of Adenomyosis: Adenomyosis was seen on microscopic examination of the myometrium in 22.5% of the cases.

Endometrial Phase on Microscopy: Of the 200 cases, proliferative endometrium was noted in 40%, followed by secretory endometrium in 20%, endometrial hyperplasia in 14%, atrophic endometrium in 11.5% of the cases and endometrial carcinoma in 3% cases.(Table 6) (Fig. 4-6)

Table 6: Showing various endometrial phases and their distribution

Endometrial Phase	Number (n=200)	%
Proliferative	80	40
Secretory	40	20
Simple hyperplasia without atypia	18	9
Complex hyperplasia without atypia	7	3.5
Simple hyperplasia with atypia	2	1
Secretory phase with endometrial polyp	6	3
Proliferative phase with endometrial polyp	9	4.5
SH + Polyp	1	0.5
Pill endometrium	5	2.5
Cystic atrophic endometrium	23	11.5
Endometrial carcinoma	6	3
Disordered proliferative endometrium	3	1.5

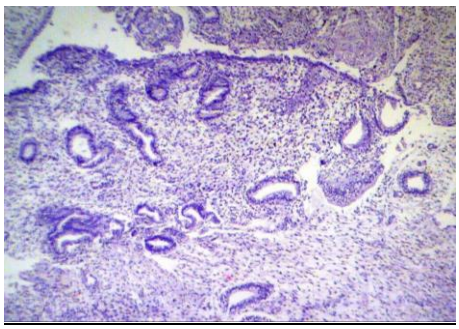

Fig. 4: Photomicrograph showing pill endometrium, with widely spaced glands and decidualised stroma (H&E, 40x)

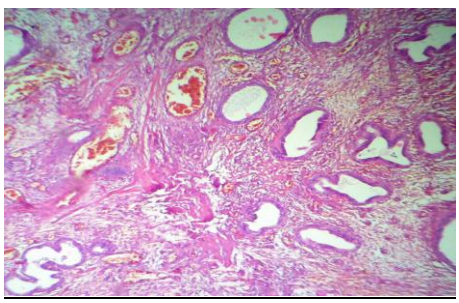

Fig. 5: Photomicrograph showing secretory endometrial polyp. (H&E, 10x)

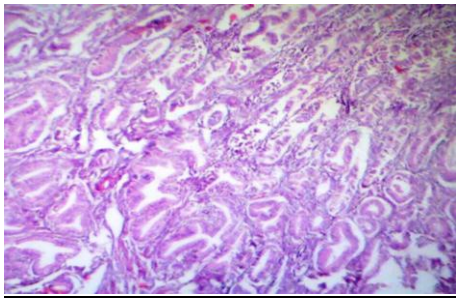

Fig. 6: Photomicrograph showing Simple endometrial hyperplasia without atypia. (H&E 10x)

Discussion

Uterine fibroids are the most common pelvic tumour and the most common noncancerous tumors in women of childbearing age.[4] As many as 1 in 5 women may have fibroids during their childbearing years, and it usually affects women over the age of 30 years.[4,5] It is estimated that 20 to 30% of women above the age of 30 years harbor uterine fibroids.[6]

In the present study, it was observed that uterine leiomyomas were most common in the age group of 31–40 yrs and 41 – 50 yrs accounting for 24% and 56% respectively. As we can see they have increased incidence with age progression and a sharp decline after menopause, as in our study the incidence was 15% between 50 – 60 yrs and 2.5% after 60 yrs.

As seen and understood earlier parity is a protective factor against uterine fibroids. 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.[7] 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.[8]

However, in the present study, majority of the patients were multiparous and constituted 80% and results are comparable with studies by Chhabra & Jaiswal[9] and Rosario Pinto.[10] (Table – 16)

Although a protective effect of parity has been found in many studies, this association remains difficult to interpret because of potential bias.

Estrogen and progesterone appear to be promoters of fibroid growth, acting in concert.[8] Quantitative studies have 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.[8]

Fibroids can present with a variety of complaints. They can present with excessive uterine bleeding, mass per abdomen pertaining to its size, infertility based on its location, mass per vagina, abdominal pain, dysmenorrhea so on and so forth. In the present study the commonest symptom that these patients with fibroids presented was menorrhagia (61%), followed by pain abdomen (33%). In the study done by Gazozai et al[11] it showed that 67% of women who underwent hysterectomy for menorrhagia revealed fibroids. Menorrhagia was the most common symptom noted by Chhabra & Jaiswal[9] and Chethana (Table 17). Dysregulation of the vascular channels along with a number of growth factors in the myomatous uterus is said to be responsible for this symptom.[12] KA Downes et al[13] observed pelvic pain, enlarged uterus and irregular or heavy menstrual bleeding as the presenting signs and symptoms, which were seen in our patients too.

In the present study, majority of leiomyomas were intramural in location constituting 83%, followed by subserosal location 34% and submucosal leiomyomas 11%. We also encountered 3 cases that had multiple leiomyomas in all the 3 locations. Studies done by Chhabra and Ohri,[14] Rosario Pinto[10] also reports intramural leiomyomas as the commonest type observed with an incidence of 73.5%, 47.5% and 73% respectively (Table 18). The incidence of subserosal and sub mucosal leiomyomas in the present study (34%) also correlates with studies of Chhabra and Ohri.[14]

In the present study, the number of leiomyomas in the uteri varied from 1 – 20 which is similar to the studies by Rosario Pinto[10] where the number varied from 1-14 and 1-10 respectively. We have noted an increase in occurrence of multiple leiomyoma in a single uterus as is against the other studies wherein the occurrence of a single fibroid per uteri is high. A single uterus in our study showed as many as 20 fibroids, found in all three locations.

In the present study, menorrhagia was most commonly associated with submucosal and intramural fibroids with a frequency of 85% and 62% respectively which was in accordance with the study done by Rosario Pinto.[10] (Table 20).

67% of the nulliparous women, 76% of the primipara women and 70% of the multiparous women had leiomyomas only at one location. The commonest location was intramural in nulliparous and primipara women with Similar findings in studies by Miura et al.[15]

Miura et al showed that pregnancy and implantation rates were significantly lower in women with intramural myomas. They studied biological factors such as increased accumulation of inflammatory cells within fibroid tissue and corresponding endometrium that might impair fertility. [15] The combined inflammatory reaction of the endometrium and increased PGF2α production could be a possible mechanism in causing either infertility or miscarriage in women harboring submucosal or intramural myoma in their uterus.[15]

There is wide agreement that the incidence of adenomyosis is increased in the presence of leiomyoma. In the present study, the incidence of adenomyosis was

23% which is similar to the findings of Deligdish & Loewenthal[16] in whose study the incidence was about 27%. Adenomyosis was found to be more common among multiparous women similar to study done by Vora et al[17] where the incidence was 74%.

According to Israel et al, every pregnancy increases the chances of endometrial penetration into myometrium. This could be explained on anatomical basis that because of lack of submucosa in the uterus, endometrial glands penetrate into the myometrium easily and get caught as infoldings into the hypertrophied myometrium when it contracts after delivery. This indicates prolonged action of estrogens uninterrupted by progesterone which may be responsible for the development of adenomyosis.[17]

In the present study, usual leiomyomas were the commonest accounting for 97% cases. Variants of leiomyomas were seen in only 5 cases constituting 2.5%. 1 case was of cellular leiomyoma presenting in a 50 year old lady, 2 were myxoid leiomyomas and 2 cases of leiomyoma with bizarre cells showed younger age incidence one was a 29 year old and the other 36 years similar to the studies by Downes & Hart WR.[18]

This study also showed degenerative changes in 50 leiomyomas (25%). Of the degenerative changes, hyaline degeneration accounted for the highest number (72%). Similar to thw studies of Harsh Mohan et al,[19] Manjula[20] and Begum and Khan[21] Larger the leiomyoma, the more likely it is that some form of degeneration will be present. Degeneration in fibroids occurs secondary to inadequate blood supply, which may be hyaline (commonest), myxomatous, cystic, fatty, haemorrhagic or malignant in nature. The type of degenerative change seems to depend on the degree and rapidity of the onset of vascular insufficiency.

In the present study, proliferative and hyperplastic endometrium accounted for 45% and 14% of the cases respectively, accounting together for 59%. Similar findings were also seen in other studies (table 24). 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. The atrophic endometrium associated with leiomyoma seen in 11.5% cases was probably due to the mechanical and hormonal factors.[16]

Of the various forms of endometrial hyperplasia (14%), simple hyperplasia accounted for 10.5%, while complex hyperplasia with or without atypia accounted for only 3.5% similar to the study conducted by Teleman and Mihailovici.[22] The explanation for the above finding is a possible protective role of leiomyoma as a target tissue which capture estrogens. Hence the incidence of complex hyperplasia with or without atypia is less.

One case of endometrium in proliferative phase with tubal metaplasia was also encountered. Among all the types this is the type which is considered as a normal phenomenon, the others commonly seen may be squamous metaplasia, mucinous metaplasia, clear cell metaplasia etc.[23] They are known to occur in hyperestrogenic states hence sharing a common causative factor with uterine fibroids

We also encountered 6 cases of leiomyoma associated with carcinoma endometrium. Of the six cases 4 were well differentiated adenocarcinomas, one was moderately differentiated adenocarcinoma coming under the Type I endometrial carcinomas that are estrogen dependent, we even received one case of papillary serous adenocarcinoma associated with a submucosal fibroid.

There is an increased incidence of endometrial carcinomas in fibroid uterus and both being estrogen dependent is well known. We also know that progesterone antagonizes estrogen-driven growth in the endometrium, and insufficient progesterone action strikingly increases the risk of endometrial cancer.[24]

We observed features of pill endometrium in 2.5% of the cases. It was due to the treatment that these patients were receiving for symptomatic relief. One effective way of treating fibroids is through hormones. 1 case of pill endometrium also showed endometrial polyp. It has been studied by Feely KM et al that there is increased incidence of endometrial polyps in women undergoing HRT.[25] Disordered proliferating endometrium was also seen in 3 cases.

We even encountered 8% cases of endometrial polyps, the overlying epithelium showing predominantly proliferative phase. One case of polyp was associated with simple endometrial hyperplasia. In the study by Mittal K the prevalence of endometrial polyps in the general population is about 24%, age incidence between 40 – 50 years and more frequent in the postmenopausal age.[26] In our study they were seen more in the younger age group.

Few endometrial conditions like tuberculous endometritis, retained products of conception and chronic endometritis were not encountered in this study. But they can be found and easily missed when present in association with leiomyomas.

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Conclusion

This study was undertaken to study the clinico-pathological profile of patients with leiomyoma of the uterus and to characterize the gross and histopathological features of endometrium in these uteri. Hysterectomy remains the widely performed surgery in gynaecological practice even in developed countries for fibroid. Though the histopathological examination correlates well with the pre-operative clinical diagnosis, a number of lesions were also encountered as incidental findings. Hence, every

hysterectomy specimen should be subjected to histopathological examination so as to ensure better post-operative management. Endometrial curettings showing a mixed picture of glandular atrophy, hyperplasia or polyposis along with many distorted, elongated or dilated glands suggest the presence of uterine leiomyoma.

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