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EVALUATION OF THE ENDOMETRIAL CHANGES IN FEMALES DIAGNOSED WITH THE UTERINE LEIOMYOMAS

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Abstract

The female genital tract includes the uterine corpus and cervix. The uterus consists of the endometrium and myometrium which are continuously stimulated by hormones, denuded monthly of its endometrial mucosa and inhabited periodically by foetuses. Together with the lesions that affect the cervix, the lesions of the corpus of the uterus and the endometrium account for most patient visits to gynaecologists. Many treatment options are available nowadays including medical and conservative surgical procedures. Hence based on above findings the present study was planned for Evaluation of the Endometrial Changes in Females Diagnosed with the Uterine Leiomyomas.

The present study was planned in Department of Obstetrics and Gynaecology, Madhubani Medical College and Hospital, Madhubani, Bihar. In the present study 50 cases of the females diagnosed with the uterine leiomyomas were enrolled. 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.The data generated from the present study concludes that 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.

Keywords: Leiomyoma, Endometrium, Menorrhagia, etc.

Introduction

Leiomyomas of the uterus (or uterine fibroids) are benign tumors that arise from the overgrowth of smooth muscle and connective tissue in the uterus. Histologically, a monoclonal proliferation of smooth muscle cells occurs. A genetic predisposition to leiomyoma growth exists. Uterine leiomyomas (fibroids) are the most common benign gynecologic tumors. They primarily affect women of reproductive age, and the estimated incidence of fibroids is over 70% by 50 years of age. [1-4]

Rarely, uterine leiomyomas may undergo malignant degeneration to become a sarcoma. The true incidence of malignant transformation is difficult to determine, because leiomyomas are common, whereas malignant leiomyosarcomas are rare and can arise de novo. [5] The incidence of malignant degeneration is less than 1.0% and has been estimated to be as low as 0.2%.

The preferred imaging modality for the evaluation of uterine fibroids is ultrasonography (US)—specifically, transabdominal and transvaginal US. In some patients, magnetic resonance imaging (MRI) provides additional information. Diffusion-weighted imaging may help evaluate treatment response to uterine artery embolization. [1]

The role of computed tomography (CT) scanning is limited in the detection of uterine fibroids by the similar attenuation characteristics of fibroids and healthy myometrium, although some fibroids may be hypoattenuating. Fibroid calcifications may be more visible on CT scans than on conventional radiographs because of the superior contrast differentiation achieved with CT scanning. [6, 7]

Conventional radiographs have a limited role in the diagnosis of uterine fibroids, because only heavily calcified fibroids are depicted on these scans. Extreme enlargement of the uterus resulting from fibroids may be seen as a nonspecific soft-tissue mass of the pelvis that possibly displaces loops of bowel.

Like radiography, CT scanning also has a limited role in the diagnosis of uterine fibroids. On CT scans, fibroids are

usually indistinguishable from healthy myometrium unless they are calcified or necrotic. Calcifications may be more visible on CT scans than on conventional radiographs because of the superior contrast differentiation in CT scanning.

MRI has an important role in defining the anatomy of the uterus and ovaries, as well as in assessing disease in patients in whom ultrasound findings are confusing. MRI also may be helpful in planning myomectomy, or selective surgical removal of a fibroid. Fibroids appear as sharply marginated areas of low to intermediate signal intensity on T1- and T2-weighted MRI scans. [1, 8, 9, 10]

Data suggest that less stiff fibroids appear lighter on T2-weighted MRI, while stiffer fibroids are darker on T2-weighted images. [8] The intravenous administration of gadolinium-based contrast material usually is not required; however, if it is administered, fibroids usually enhance later than does the healthy myometrium. Fibroid enhancement can be hypointense (65%), isointense (23%), or hyperintense (12%) in relation to that of the myometrium.

Gadolinium-based contrast agents have been linked to the development of nephrogenic systemic fibrosis (NSF) or nephrogenic fibrosing dermopathy (NFD). For more information, see the Medscape Reference topic Nephrogenic Systemic Fibrosis. The disease has occurred in patients with moderate to end-stage renal disease after being given a gadolinium-based contrast agent to enhance MRI or magnetic resonance angiography (MRA) scans. NSF/NFD is a debilitating and sometimes fatal disease. Characteristics include red or dark patches on the skin; burning, itching, swelling, hardening, and tightening of the skin; yellow spots on the whites of the eyes; joint stiffness with trouble moving or straightening the arms, hands, legs, or feet; pain deep in the hip bones or ribs; and muscle weakness.

Ultrasonography is the imaging modality of choice in the detection and evaluation of uterine fibroids. [11-17] Most fibroids are intramural; that is, they are located in the myometrium. However, they can be submucosal or subserosal. Uterine fibroids most often appear on ultrasonograms as concentric, solid, hypoechoic masses. This appearance results from the prevailing muscle, which is observed at histologic examination. These solid masses absorb sound waves and therefore cause a variable amount of acoustic shadowing.

Fibroids may vary in their degree of echogenicity; they can be heterogeneous or hyperechoic, depending on the amount of fibrous tissue and/or calcification. Fibroids may have anechoic components resulting from necrosis. If fibroids are small and isoechoic relative to the uterus, the only ultrasonographic sign may be a bulge in the uterine contour. Fibroids in the lower uterine segment may obstruct the uterine canal, causing fluid to accumulate in the endometrial canal.

The echogenic endometrial stripe may be displaced by a fibroid. Calcifications are hyperechoic, with sharp acoustic shadowing. Diffuse leiomyomatosis appears as an enlarged uterus with abnormal echogenicity. Magnetic resonance-guided high-intensity focused ultrasound has been shown to be successful in reducing the size of fibroids. [14]

Vascular density, ischemic necrosis, and histologic cellular activity score have been found to be statistically significantly associated with some 3D power Doppler ultrasound indices. A high histologic cellular activity score, combining hypercellularity, a fibrosclerosis rate less than 25%, and positive Ki-67 staining, was found in one study to be statistically related in multivariate analyses to high 3D power Doppler VI in spherical samples and vascularization flow index (VFI). Positive CD31 staining was statistically related to high 3D power Doppler VI in spherical samples. In contrast, ischemic necrosis was statistically related to low 3D power Doppler VI in the total volume and VFI. [15]

Of 280 women who underwent magnetic resonance-guided focused ultrasound (MRgFUS), the rate of minor complications was 3.9%, and there were 3 serious complications (1.1%), including one skin burn, a fibroid expulsion, and one case of persistent neuropathy. According to the authors of the study, the nonperfused volume (NPV) achieved following MRgFUS have increased as the experience with this treatment has grown. In a 5-year follow-up study of 162 women, the overall reintervention rate was 58.64%, but in those treatments with greater than 50% NPV, the re-intervention rate was 50%. [16]

The female genital tract includes the uterine corpus and cervix. The uterus consists of the endometrium and myometrium which are continuously stimulated by hormones, denuded monthly of its endometrial mucosa and inhabited periodically by foetuses. Together with the lesions that affect the cervix, the lesions of the corpus of the uterus and the endometrium account for most patient visits to gynaecologists. Many treatment options are available nowadays including medical and conservative surgical procedures. Hence based on above findings the present study was planned for Evaluation of the Endometrial Changes in Females Diagnosed with the Uterine Leiomyomas.

Methodology:

The present study was planned in Department of Obstetrics and Gynaecology, Madhubani Medical College and Hospital, Madhubani, Bihar. In the present study 50 cases of the females diagnosed with the uterine leiomyomas were enrolled. 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.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Females diagnosed with the uterine leiomyomas

Exclusion criteria: Females diagnosed with multiple complications.

Results & Discussion:

Leiomyoma being the commonest benign tumour in middle aged females, is one of the major cause of hysterectomies all around the world. The Leiomyoma also known as fibroids, it is a benign smooth muscle tumour that very rarely becomes cancerous (0.1%). They are perhaps the most common tumour in pre-menopausal women. They can occur at any site or organ, but the more common forms occur in the uterus, small bowel, and the oesophagus. Uterine Leiomyomas are basically spherical masses of smooth muscle cells that can vary greatly in size, ranging from a few millimetres to many centimetres in diameter. Leiomyomas are sharply circumscribed, discrete, round, firm, grey -white tumours. In frequently they can occur in the myometrium or the uterine ligaments.

Leiomyoma of the uterus are the most common indication for hysterectomy all around the world. Uterine Leiomyoma can result in masses associated with a variety of obstetric and gynaecological problems, the most commonly occurring of which are the Abnormal Vaginal Bleeding (including abnormal Menstrual bleeding), Urinary frequency, Asymptomatic pelvic mass, Fetal malpresentation etc.

Table 1: Basic Details

Parameters	No. of Cases
Age:	
30 – 40 years	5
41 – 50 years	22
51 – 60 years	20
61 – 70 years	3
Parity:	
Single	9
Multiple	41
Complaints:	**Observed in No. of Cases**
Menorrhagia	29
Pain in abdomen	13
Mass per vagina	11
Mass per abdomen	10

Table 2: Endometrial area

Endometrial area in Sq. mm	No. of Cases
Less than 1	3
1 – 4	26
4 – 40	18
More than 10	3
Total	50

Table 3: Endometrial phase

Epithelial cell changes	No. of Cases
Absent	10
Present	40

Table 4: Epithelial Cell Changes Present

Epithelial Cell Changes Present	Observed in No. of Cases
Dilated/distorted glands	32
Endometrial glands separated by muscle fibres	21
Endometrial glands parallel to myometrium	12
Focal loss of surface epithelium	20
Decidual cast	3
Polyposis	1
Subtotal glandular atrophy	2
Total glandular atrophy	2

Comparing our case setting to that of Anusha Babu Rajendran [18] et al, and with that of Mannem Chethana et al, the most common type of endometrium associated with a Leiomyoma was P roliferative Endo [19] metrium observed in 44.41% (147 cases), and 33 % in the next one, matching with our most common finding of Proliferative Endometrium, observed in 52% (33 cases) of total 63 cases.

Comparing our case setting with that of L. DELIGDISH AND M. LOEWENTHAL et al [20], and of Mangala Gowri et al [21], there was total endometrial glandular atrophy in 17 (58%) of the 30 cases, and 69.1% putting together the proliferative endometrium and simple hyperplastic endometrium in the next one this being their most common finding respectively, contrasting to our most common finding of Proliferative Endometrium in 33 (52%) out of the 63 cases studied.

Among all the studies carried out on endometrial changes, the most commonly found change was found to be Proliferative Endometrium, with a few exceptions.

Leiomyomas can be located anywhere in the myometrium. Intramural leiomyomas are the most common type. Submucosal leiomyomas compress the overlying endometrium and bulge into the endometrial cavity as they enlarge. Subserosal leiomyomas can become

pedunculated and if the pedicle undergoes torsion and necrosis, the leiomyoma can lose its connection with the uterus, some of them become parasitic in rare instances. The appearance of a leiomyoma is commonly altered by degenerative changes such as hemorrhage, necrosis, edema, myxoid change, hypercellular foci and increase in mitotic activity particularly if they are large or occur in pregnant women or in those patients undergoing high-dose progestin therapy.

Cystic degeneration and calcification can also occur. [22] Uterus comprises of the endometrium and the myometrium. While endometrium undergoes dynamic reorganization through each menstrual cycle in response to the steroid hormone, uterine leiomyomas also frequently occur and show increase in size during pregnancy or on intake of oral contraceptive pills. This is due to the fact that both endometrium and myometrium express higher levels of estrogen and progesterone receptors. The number of receptors has been shown to be higher in leiomyoma tissue when compared to the homologous myometrium. [22] Treatment with gonadotropin releasing hormone agonist (GnRHa) results in shrinkage of leiomyomas facilitating myomectomy and reduce the risk of hemorrhage during surgery. [23] Thus, this explains the importance of sex hormones in the development and maintenance of leiomyomas and their association with endometrial changes.

The probable cause for the endometrial changes could be oestrogen, progesterone and pressure effects, in cases of submucosal fibroids. Deligdish L et al., concluded that there is high oestrogen level in women with fibroids and it is hypothesised that oestrogen is synthesised by the endometrium which is responsible for the growth of the fibroid. [24] Oestrogen and progesterone together play a role in fibroid growth. [25] The oestrogen up regulates both oestrogen receptors and progesterone receptors in the fibroids during proliferative phase which is followed by the progesterone induced mitogenesis during the luteal phase. [26]

Study by Gull B et al., has shown that the tissue concentration of oestrogen receptor and progesterone receptor were more in the leiomyoma when compared with the normal myometrium. [26]

The endometrium is under the cyclical influence of the steroid hormones. There is an entity called the sub-endometrial myometrium which also undergoes cyclical steroid receptor changes in concurrence with the endometrium during the menstrual cycle. [27] There is growing evidence that the leiomyomas are benign tumours arising from this sub-endometrial myometrium Hence the leiomyomas, arising from the sub-endometrial myometrium, also show cyclical changes in the oestrogen and progesterone receptors, during the menstrual cycle, which adds to the evidence that the leiomyomas are not only steroid dependant for their growth but occur in concurrence with the changes in the endometrium. So, it could be said that, oestrogen and progesterone are common factors affecting the leiomyoma and the endometrium.

Uterine fibroids are classified according to their location as submucosal, intramural or subserosal. [28] Submucosal fibroids are the least common type, accounting for just 5% of all fibroids, but they are the most likely to be symptomatic since they project into the endometrial cavity. Submucosal fibroids can occasionally become pedunculated and prolapse into the cervical canal or vagina. [29] Intramural fibroids are the most common type, but they are usually asymptomatic; however, they may cause infertility due to compression of the fallopian tubes. Subserosal fibroids, project exophytically into the abdomen or pelvis and can also become pedunculated, which may be confused with ovarian tumors. Pedunculated subserosal fibroids can undergo torsion and consequent infarction and thus be a cause of severe abdominal pain. [30] Large fibroids often degenerate as they outgrow their blood supply. The various types of degeneration include hyaline, myxoid, cystic and red degeneration. [31] Calcification tends to occur following necrosis. [32]

Although the majority of fibroids are benign, it is thought that some uterine leiomyosarcomas arise in a subset of fibroids. Only about 0.23-0.7% of apparently benign uterine fibroids turn out to be leiomyosarcomas on pathological examination. [33] Most leiomyosarcomas arise de novo . A leiomyosarcoma can be difficult to distinguish from a benign fibroid and this possibility should always be considered in a patient with a rapidly growing uterine fibroid.

Conclusion:

The data generated from the present study concludes that 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.

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