HISTOMORPHOLOGICAL STUDY OF DEGENERATIVE CHANGES IN LEIOMYOMA OF MYOMETRIUM

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ABSTRACT

Degenerative changes are encountered relatively frequently in uterine leiomyomas. The nature of the change varies according to the degree and rapidity of onset of vascular insufficiency and is found in one or several of a group of fibroids. In some instances degeneration is associated with acute and severe symptoms. All these features maybe encountered in malignant tumours and therefore thorough sampling of lesions with unusual gross appearance is imperative. Further, in the presence of extensive degeneration, it is difficult to identify the smooth muscle nature of the lesion. The present study is proposed to be undertaken, because the gross and microscopic appearances of degeneration may simulate malignant tumors, the diagnosis of these tumors carry better prognosis requires detailed morphological study.

Keywords : degenerative changes, Leiomyoma, Smooth muscle cells.

INTRODUCTION

Leiomyomas are the commonest tumors found in women. They occur in 20-25% of women over the age of 30 years. Leiomyomas most frequently are solid and white, and have a whorled cut surface. Deviation from this gross appearance is common, is usually the result of a variety of alterations which have been grouped together under the term 'degeneration .'[1,2]

Degeneration is important for two reasons. First, the gross and microscopic appearances of degeneration may simulate malignant tumors; moreover, degenerative changes may cause confusion in the interpretation of ultrasonograms.[3,4] Second, discerning smooth muscle differentiation in neoplasms with extensive degeneration may be difficult. Because of similarities in gross appearance between some leiomyosarcomas and leiomyomas with degeneration.[5]

METHODOLOGY

This prospective study consists of 1845 hysterectomy and myomectomy specimens collected over a period of two years. Brief essential clinical history and finding were recorded : patient's age, clinical presentation, uterine size, etc.

Following the receipt of surgical specimens in 10% formalin at the Department of Pathology, a detailed gross examination including size, appearance, external surface were noted. The specimens were allowed to fix in 10% formalin for 24-48 hours. Multiple parallel sections were made and each surface were examined. A detailed gross morphology of myometrial neoplasms were noted, which included location, number, size and secondary degenerative changes like haemorrhage, cystic change, calcification, fatty degeneration and mucoid degeneration.

The tissue bits from representative areas were taken for histopathological examination and paraffin blocks prepared, the number of blocks prepared depended upon the size and

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morphology of tumors. Multiple sections of five microns thickness were cut and routinely stained with haematoxylin and eosin stain. The following histological features were studied and recorded : the degree of cellularity, presence or absence of degeneration, type of degeneration, mitotic index, the degree of cytologic atypia if any, the presence or absence of necrosis and type of necrosis, the status of the margins of the tumor with the surrounding myometrium and presence of intravascular invasion by tumor.

RESULTS

Hysterectomy is the commonest surgical operative procedure encountered in gynaecological practice. This prospective study on degeneration in leiomyoma of myometrium was undertaken in the Department of Pathology, J.J.M. Medical College, over a period of two years.

Of the total 12,285 surgical specimens received for histopathological examination in the Department during the study period, 1832 were hysterectomies and 13 were myomectomy specimens. The neoplastic lesions of myometrium were diagnosed in 441 (23.90%) of the total 1845 specimens. Benign tumours were diagnosed in 440 cases, and all the benign tumours were leiomyomas except one case of adenomyoma. Malignant tumour of the myometrium was diagnosed in one hysterectomy specimen out of 1845 specimens studied (0.054%).

AGE : Age of the patients with leiomyoma were between 2nd to 6th decade of life. Youngest was 23 years and the oldest was 62 years. Majority of the patients (87.49%) were in 4th and 5th decade, with peak incidence in the 4th decade (47.72%), while only two patients were in 7th decade (Table – 1).

TABLE – 1 : AGE DISTRIBUTION

Age Range	No. of Cases	Percentage
10 – 20	0	0
21 – 30	25	5.68
31 – 40	210	47.72
41 – 50	175	39.77
51 – 60	27	6.13
61 – 70	2	0.45
> 70	0	0
Total	439	100.00

Out of 439 cases of leiomyomas, 320 cases were single and located in different parts of the myometrium. 213 cases were intramural, 60 were subserosal and 47 were submucosal in location. Remaining 119 cases showed leiomyomas in more than one location, of which combined subserosal and intramural location was commonest. Thus of the total 439 cases of leiomyomas, 320 (72.89%) were single and 119 (27.10%) were multiple.

Intramural leiomyomas varied from 7 mm to 14.5 cms in diameter. Subserosal leiomyomas varied from 6 mm to 13 x 10 x 9.5 cm in size. Submucosal leiomyomas varied from 6 mm to 5 cm in diameter.

DEGENERATIVE CHANGES IN LEIOMYOMA :

23 leiomyomas showed gross degenerative changes, out of which mucoid degeneration was seen in 8 cases, cystic degeneration in 6 cases, fatty change in 4 cases, calcification in 4 cases and red degeneration in 1 case.

Microscopically, Degenerative changes were observed in 260 leiomyomas (59.22%). Among these 211 leiomyomas showed predominantly hyaline degeneration. Remaining 40 leiomyomas were associated with other degenerative changes: myxoid, calcification, cystic, fatty, haemorrhagic, oedema, necrosis and red degeneration (Table – 2).

TABLE – 2 : DEGENERATIVE CHANGES IN LEIOMYOMA

Degenerative Changes	No. of Cases	Percentage
Hyaline degeneration	211	48.06
Myxoid degeneration	14	2.26
Fatty degeneration	9	2.05
Calcification	7	1.59
Cystic degeneration	7	0.91
Haemorrhage	4	0.91
Hyaline necrosis	2	0.45
Hydropic degeneration	5	1.13
Red degeneration	1	0.22

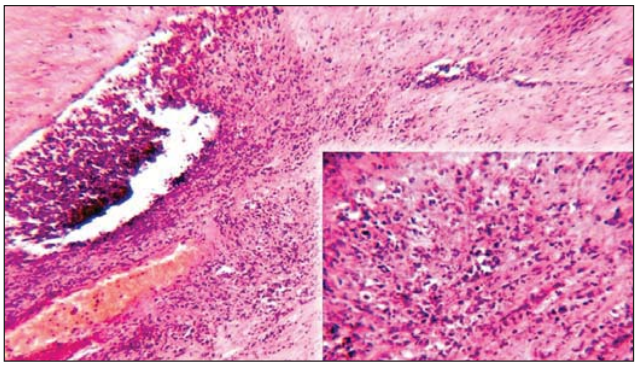

Fig -1 : Hyaline Necrosis - H&E - 100x, Inset - 400x

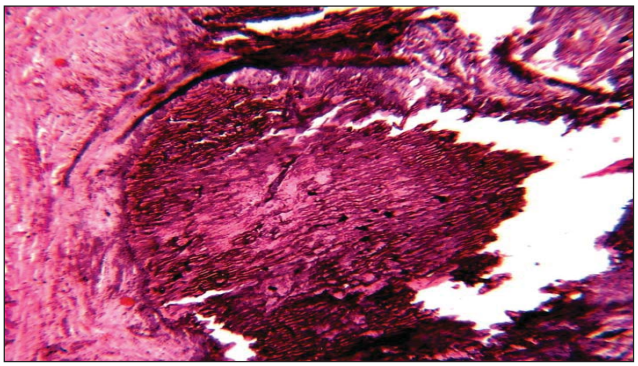

Fig -2 : Calcification - H&E 400x

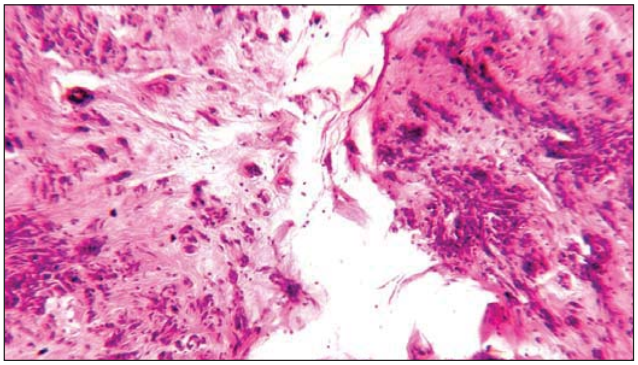

Fig -3 : Hydrophic Degeneration - H&E 400x

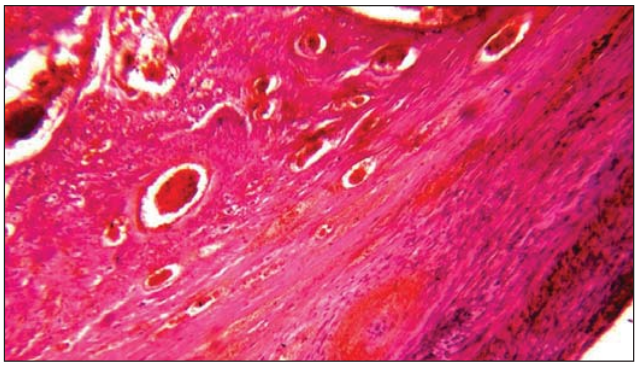

Fig -4 : Red Degeneration - H&E 100x

Hyaline degeneration was observed in 220 leiomyomas constituting 48.06% of the total leiomyomas. Grossly the mean size of these leiomyomas was 4.8 cms. Out of 7 cases with calcification, 4 were detected grossly and 3 showed microscopic foci of calcification. There were 14 cases of myxoid degeneration, 8 were detected grossly, 6 showed microscopic foci. There were 9 cases of fatty degeneration, 4 were detected grossly, 5 cases showed microscopic foci. There were 7 cases of cystic degeneration, 6 were detected grossly, 1 showed microscopic foci and was associated with hyaline degeneration. Out of 4 haemorrhagic degeneration, 2 cases were detected grossly and 2 showed microscopic foci of haemorrhagic degeneration.

DISCUSSION

AGE : In the present study, the youngest was 23 years and oldest was 62 years. The highest incidence (47.72%) was observed between 31-40 years. This age incidence correlates well with observations made by Rosario Pinto6 and Ramesh7 (Table – 3).

TABLE – 3 :
AGE INCIDENCE OF LEIOMYOMAS IN VARIOUS STUDIES

Age	Rosario Pinto[6] (%)	Ramesh[7] (%)	Present Study (%)
10 – 20	-	-	-
21 – 30	14.92	10.50	5.68
31 – 40	44.7	49.37	47.72
41 – 50	41.3	34.08	39.77
51 & above	4.6	06.06	6.58

Degenerative Changes in Leiomyomas : Hyaline degeneration was the commonest degenerative change which was seen in 211 leiomyomas and thus constituted 48.06%. Similarly, Zaloudek et al8 higher incidence of hyaline change. However Rosario Pinto6 noted low incidence of hyaline change (Table 4).

Zaloudels et al[8] noted 60% of leiomyomas with hyaline changes, cystic change in 4%, calcification in 10% and haemorrhage in 11%. The low incidence of calcification was observed (1.59%) in the present study correlates well with other studies (Table 4).

TABLE – 4 : SHOWING COMPARATIVE INCIDENCE OF DEGENERATIVE CHANGES IN VARIOUS STUDIES

Degenerative Changes	Ramesh[7] (%)	Zaloude KK et al[8]	Present Study (%)
Hyaline degeneration	41.71	60.0	48.06
Myxoid degeneration	2.55	-	2.26
Calcification	2.22	10.0	1.59
Cystic degeneration	3.50	4.0	0.91
Haemorrhagic degeneration	0.64	11.0	0.01
Hyaline necrosis	-	-	0.45
Hydropic degeneration	-	-	1.13
Red degeneration	-	-	0.22

A variety of degenerative changes are encountered in leiomyomas. As leiomyoma enlarges, they outgrow their blood supply, which results in various types of degeneration. Degeneration, though often central first, may be diffuse. Fibroids at any site are subject of degenerative change but those with a pedicle are particularly susceptible. The nature of the change varies according to the degree and rapidity of onset of vascular insufficiency and is found in one or several of a group of fibroids. Most forms of degeneration are the result of replacement of smooth muscle cells by hyaline, collagen, blood, calcium, mucopolysaccaride, or a combination of these.[9, 10, 11]

Eosinophilic glassy or fibrillar material replaces muscle fibers in hyaline degeneration. Hyalinization can result in tumor cell necrosis (hyaline necrosis Fig1). It should not be mistaken for coagulative tumor cell necrosis seen in leiomyosarcoma.[9,11] In coagulative tumour cell necrosis, there is an abrupt transition between necrotic and preserved cells. The hematoxyphilia of the nuclei is often retained in the necrotic cells and there is no associated inflammation. The characteristic low power microscopic pattern is one of the blood vessels cuffed by viable cells surrounded by a sea of necrotic tumor. Coagulative tumour cell necrosis is commonly present in clinically malignant smooth muscle neoplasms. In contrast, hyalinising necrosis has a distinctly zonal pattern with central necrosis, a more peripheral zone of granulation tissue, and at the periphery, a viable amount of hyaline eosinophilic collagen interposed between the central degenerated region and peripheral preserved smooth muscle cells.[12,13,14]

When hyaline liquefies, cysts are often produced (cystic degeneration). Myxiod change is characterized by a fibrillar matrix containing scattered cells with elongated nuclei and tiny wisps of cytoplasm. It must be distinguished from myxiod leiomyosarcoma.[14,15] Calcification is common in fibroids of postmenopausal women, and also is liable to occur following necrosis. . Histologically appears as purplish amorphous lake with haematoxylin (Fig 2). Ossification may appear in a calcified area.[5]

Hydropic degeneration refers to the accumulation of abundant edema fluid, typically associated with variable amounts of collagen(Fig 3) . It is usually a focal finding on both gross and microscopic examination of otherwise

typical uterine leiomyomas. 15 Hydropic degeneration can sometimes cause significant diagnostic confusion, in particular when it occurs in a perinodular distribution.[16]

Red degeneration (necrobiosis) is a form of degeneration that occurs commonly in pregnancy, and the process is often the cause of pain and fever. Microscopy shows central area of necrosis with peripheral inflammation and granulation tissue – like reparative response (Fig 4).[5,8]

Degenerative changes within leiomyomas, particularly necrosis and alterations in cellularity, have been described following treatment with gonadotrophin releasing hormone analogue.[17] The typical appearance of leiomyomas are easily recognized on imaging. However, the atypical apprarances that follow degenerative changes may result in heterogenous or unusual presentations that may lead to a diagnostic dilemma. [4]

The morphological alterations induced by degeneration must not lead to interpretation of smooth muscle tumor as another type of neoplasm or to a diagnosis of leiomyosarcoma. Assessing the frequency of mitotic figures, determining if necrosis present and if so, its type, and an assessment of cytological atypia are of great aid in this regard. All myometrial neoplasms which deviate from the classic whorled appearance of leiomyoma should be extensively sampled and examined histologically.

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