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Mucinous carcinoma of the male breast

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Sir,

A 35-year-male with a history of slow growing, painless lump in the right breast since 2 years was presented. On examination the lump was found to be firm, nodular, non-tender and measured 4×3 cms. Axillary lymph nodes were not palpable. Systemic examination was normal.

The routine investigations were normal. Aspiration was done using a 22-G needle and a 10-cc syringe. The aspirate was mucoid. Multiple smears were prepared and stained with Hematoxylin and Eosin (H&E), May–Grunwald–Giemsa stain and Meyers mucicarmine stain. The smears were highly cellular. The tumor cells were arranged as 3-D balls, pseudo-papillary structures and angulated papillae entangled in pools of mucin [Figure 1]. The tumor cells had clear to eosinophilic cytoplasm with the nuclei having fine chromatin and indistinct nucleoli. Abundant extracellular mucin, confirmed with mucicarmine stain, was observed.

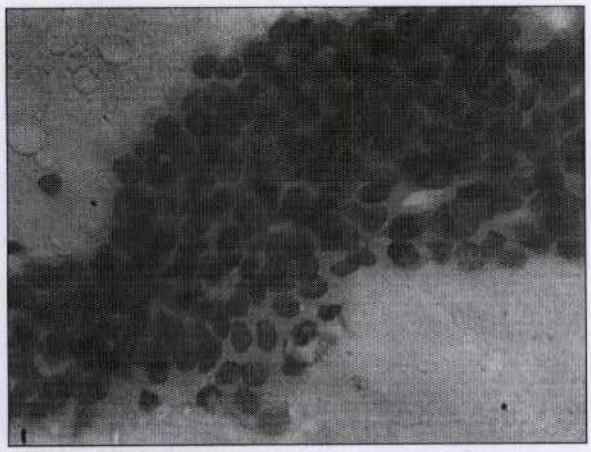

Figure 1: Microphotograph showing tumor cells arranged as 3-D balls, pseudopapillary structures and angulated papillae in pools of mucin (H&E, ×400)

[Figure 2] Cytomorphologically a diagnosis of mucinous carcinoma (Grade 2 was made).

Mastectomy specimen received measured 12×6×3 cms. Nipple and areola were normal. Cut-section showed a circumscribed gray white nodule 4×3×1 cms. The cut-surface was translucent with ill-defined margins. No lymph nodes were identified. Histopathological examination showed features of

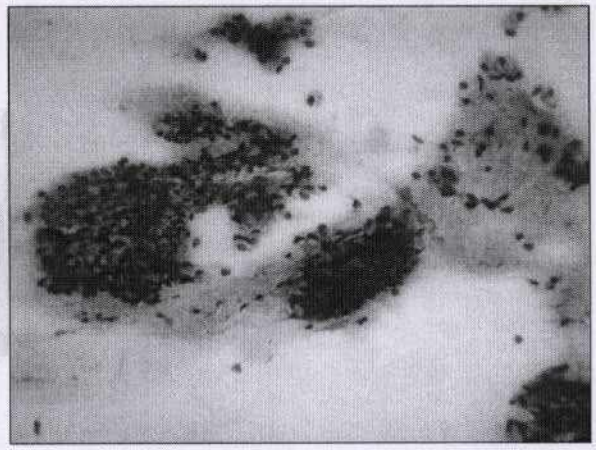

Figure 2: Microphograph showing tumor cells floating in a mucinous background (Mucicaramine ×400)

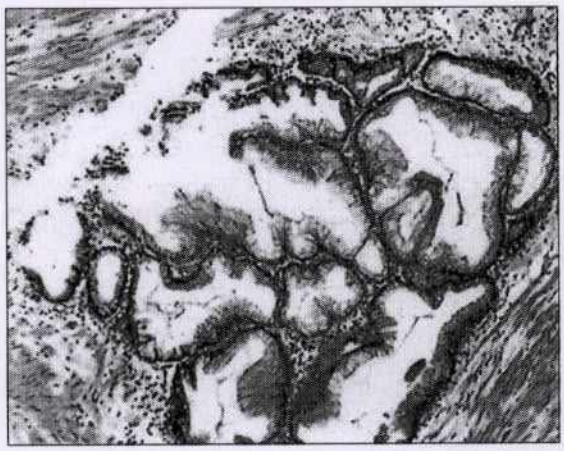

Figure 3: Microphotograph showing histopathological features of mucinous carcinoma (H&E, ×400)

mucinous carcinoma with tumor cells arranged in a variable pattern of cell balls, pseudo-papillae, cohesive clusters and singly with the retraction spaces around the tumor cell showing abundant mucin. [Figure 3]. The neoplastic cells were positive for estrogen (ER) and progesterone receptors (PR). Post-operative period was uneventful and the patient is having a regular follow-up.

Male breast carcinoma accounts for less than 1% of all breast cancers.[1] Mucinous carcinoma constitutes not more than 0.5% among the histological variants, commonest being the infiltrating duct carcinoma (80.5%).[1] If more than 90% of the tumor area consists of mucinous element, a diagnosis of pure mucinous carcinoma is considered which has a better prognosis.[1] In their study, Bhagat *et al*[2] found 14 cases of malignant mammary tumor in men of which only one case of mucinous carcinoma was reported. Visfeldt *et al*,[3] had found five cases of mucinous carcinoma out of 187 male breast carcinoma. High-risk genetic factors for male breast cancer include BRCA2 mutations, Klinefelter syndrome, hormonal imbalances, radiation exposure and family history.[4]

Majority of the mammary mucinous tumors in men are ER-positive, which, however, does not correlate with a better prognosis and are often associated with a higher stage of the disease.[5] Additional immunohistochemical features of male breast cancer include over expression of p^{53} and Erb-B2, which are associated with survival and cell proliferative activities.[5] Worse prognosis in men is due to anatomic factors (i.e., paucity of breast tissue and close tumor proximity to skin and nipple, facilitating dermal lymphatic spread and early regional and distant metastasis) and delayed diagnosis.[5] Modified radical mastectomy, combined with sentinel-node biopsy, is the standard treatment.

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Benign Sertoli cell tumors, not otherwise specified (NOS) and sclerosing sertoli cell tumors (SSCT) are rarely considered for differential diagnosis.[6] Terayema *et al.* [7] suggested that coffee-bean nuclei and nuclear indentations be made the diagnostic criteria for Sertoli cell tumor (NOS). However, the presence of monolayered sheets and the lack of the characteristic nuclear features favor a diagnosis of AT over SSCT.

USG findings along with cytological features help to evolve an organ-sparing surgical approach as noted in case 2.[8] USG-guided aspiration cytology with immediate surgery including the excision of needle track can follow if malignancy is detected. This is because a delayed diagnosis of malignancy is more harmful than the hypothetical risk of tumor spread by aspiration cytology.[9,10]

Hence, these cases have been presented to highlight the importance of FNAC in the preoperative diagnosis of adenomatoid tumors, which can help to plan surgery as complete excision of the benign tumor gives good prognosis without recurrence. Also, we report here testicular AT, which is a relatively rare site.

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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

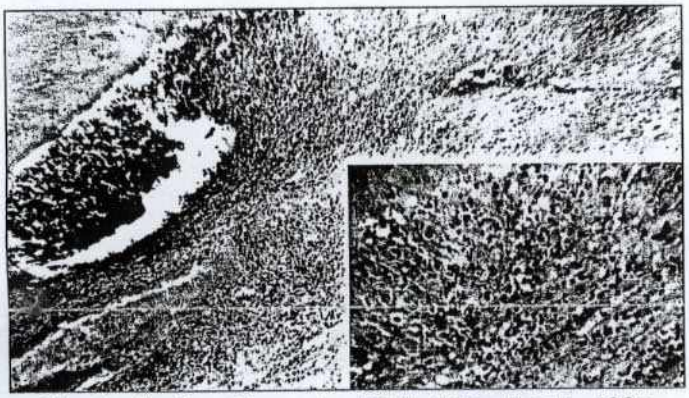

Fig -1 : Hyaline Necrosis - H&E - 100x, Inset - 400x

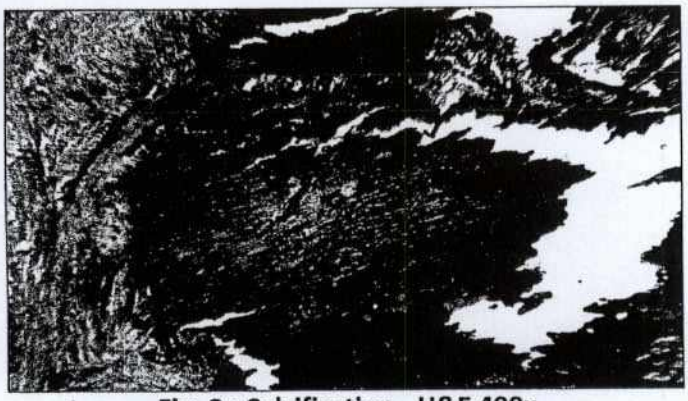

Fig -2 : Calcification - H&E 400x

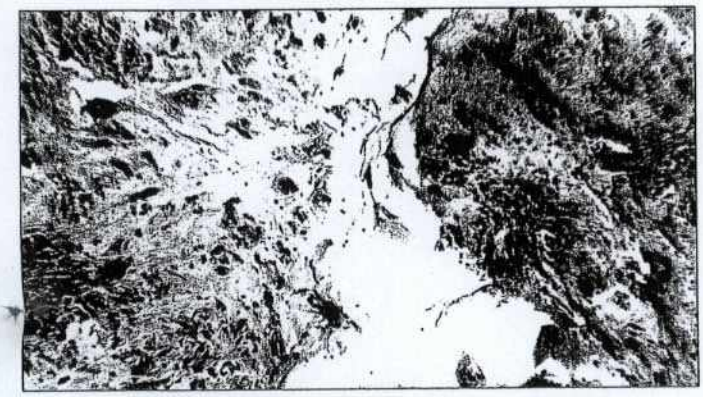

Fig -3 : Hydrophic Degeneration - H&E 400x

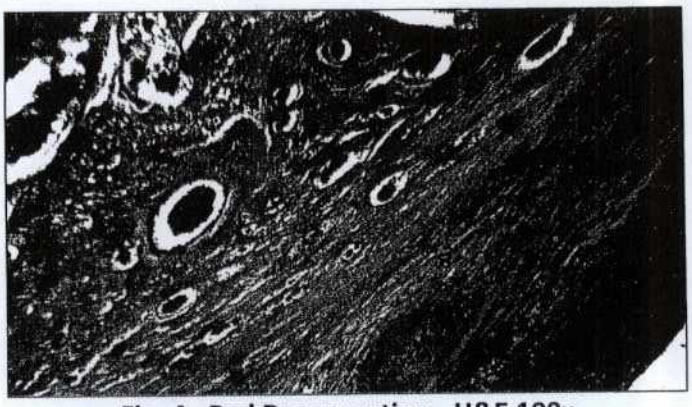

Fig -4 : Red Degeneration - H&E 100x

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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