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Myxofibrosarcoma of the male breast – An infrequent neoplasm: A case report and comprehensive review

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ABSTRACT
Primary breast sarcoma is a rare type of malignancy arising from the mesenchymal tissue of the breast and represent less than 1% of all breast cancers. We report a rare case of myxofibrosarcoma in a 25 year old male patient, who presented with rapidly enlarging mass, in his right breast extending upto right axilla since 5 month, the patient also had history of right breast lumpectomy 2 years back. On the basis of history, clinical examination and fine needle aspiration cytology a provisional diagnosis of stromal sarcoma breast with myxoid change was made. However histopathological examination and the immunohistochemical analysis lead to a conclusive diagnosis of myxofibrosarcoma breast with local recurrence. Myxofibrosarcoma shows a predilection for multiple local recurrences, tendency of low-grade tumour to recur at higher grades and potential metastasis which emphasizes the need for accurate diagnosis and excision in specialized centres.

Keywords: Male breast carcinoma, Myxofibrosarcoma, Stromal tumors.

INTRODUCTION
Myxoid soft tissue tumours are a difficult group of neoplasm from the diagnostic viewpoint, a significant histological overlap is seen, with a wide spectrum of spindle cell tumours showing secondary myxoid change. Angervall et al[1] introduced the term myxofibrosarcoma to delineate this distinct soft tissue tumour, which was earlier termed as the myxoid variant of malignant fibrous histiocytoma.

The rarity of this lesion, tendency to recur at higher grades later and its significant histological overlap with many spindle cell tumours showing myxoid change, prompted us to present this case of myxofibrosarcoma of male breast. Simultaneously we intend to discuss its clinical and histopathological manifestations and implication of immunohistochemistry in reaching to a conclusive diagnosis.

Case presentation
25 year-old male, aware of a tumour in his right breast since 5 months, was admitted to the inpatient department of surgery with complaints of rapid painful enlargement of the tumour. The patient also gave history of prior right breast lumpectomy. On examination a large nodular lump, soft to firm in consistency measuring 26x16 cm, with fungation and ulceration of the skin in the centre, was seen in his right breast extending to the axillary region. No axillary or cervical lymphadenopathy was appreciated. Routine haematological, urinary and biochemical tests were within normal limits. Chest X-ray and CT scan

were normal and there was no evidence of lung or distant metastasis.

The smears prepared from fine needle aspiration tumour yielded scant cellularity, with few atypical spindle cells in a myxoid background suggestive of a stromal sarcoma with myxoid change. Standard modified radical mastectomy [MRM] was performed and the resultant skin defect was covered by the split skin graft.

The excised tumor was large, partially skin covered multinodular mass measuring 22 x 14 x 12 cm; the surface showed, an exophytic growth with ulcerations . Cut section was grayish white with extensive myxoid areas, along with yellowish orange foci of necrosis and hemorrhage [figure 1]. No lymphnodes were received. Sections were given from the different areas of tumor mass, including skin, base and surgical margins.

Paraffin embedded blocks were prepared and the sections were stained with hematoxylin and eosin (H&E) stain. Tumour architecture, differentiation, cellular atypia, mitosis and necrosis were emphasized on histopathological examination. Microscopy revealed hypocellular myxoid and hypercellular areas with curvilinear blood vessels [figure 2], hypercellular areas comprised of atypical round to spindle cells along with multinucleated and floret type giant cells and frequent atypical mitotic figures (average 3/10 hpf). Myxoid change encomprised >50% of the entire tumour area. Necrosis was seen occupying 20 percent of tumour. All the surgical margins were involved by the tumour. Considering the clinical and histopathological features, diagnosis of primary myxofibrosarcoma of the breast was made.

For confirmation of the diagnosis and to differentiate it from other spindle cell neoplasm with myxoid change, immunostaining for vimentin, CD34 and CD68 were done, out of which only vimentin [figure 3] and CD34 gave positive staining while immunomarkers as cytokeratins (CK) [figure 4], S-100, and CD68 were negative excluding the possibilities of metaplastic carcinoma, myxoid liposarcoma or any fibrohistiocytic tumour respectively.

Post-operative period was uneventful, Currently the patient is in follow up and doing well after six months of surgery.

DISCUSSION

Male breast cancer constitutes approximately 1% of all breast cancers; with a rising incidence and awareness of the disease[2-3]. Male breast cancer has a unimodal age-frequency distribution with a peak incidence at 7^{th} decade of life[4]. The common histopathologic type is invasive ductal cancer(93.7%), other types include papillary(2.6%), mucinous (1.8%), lobular (1.5%), and medullary (0.5%) carcinomas.[5] Primary breast sarcomas are rare, histologically heterogenous nonepithelial malignancies that arise from the mesenchymal tissue within the breast, constituting 0.2% to 1.0% of all breast malignancies[5]. Like soft tissue sarcomas originating in other parts of the body, breast sarcomas consist of a heterogeneous group of several subtypes as: liposarcoma, fibrosarcoma, pleomorphic sarcoma, leiomyosarcoma, rhabomyosarcoma, angiosarcoma, osteosarcoma, and sarcomas of uncertain differentiation[6]. Mahalingam SB et al reported a case of myxoid fibrous histiocytoma in a male breast[3]. Myxofibrosarcoma presents as a slow growing, painless mass, comprising malignant fibroblastic cells with variably myxoid stroma[7]. The term myxofibrosarcoma describes a group of fibroblastic lesions that show a spectrum of cellularity, nuclear pleomorphism, and mitotic activity that ranges from a hypocellular lesion with minimal cytologic atypia to a more cellular lesion with features resembeling those of pleomorphic-storiform malignant fibrous histiocytoma (MFH)[1]. However the term is moreover applicable for tumors that are predominantly (>50%) myxoid and of low nuclear grade. It is one of the most common sarcomas affecting patients in sixth to eighth decade of life with a slight male preponderance and is seen exceptionally rare under the age of 20 years[7]. Predominantly these tumours arises in the limbs including the limb girdles (lower > upper extremities) while rarely occur in trunk, head and neck area[7].

Myxofibrosarcomas have higher rate of superficial lesions as compared to other soft tissue sarcomas[8]. Superficially located neoplasms typically consist of multiple, variably gelatinous or firmer nodules, where as deep seated ones often form a single mass with an infiltrative margin. Microscopically, the principal features shared by the tumours of all grades are hypocellular areas, containing thin-walled curvilinear vessels[7]. atypical hyperchromatic spindle and stellate cells with poorly defined cytoplasm.

Myxofibrosarcomas shows gradual progression in cellularity, pleomorphism, mitotic activity and necrosis with time[9]. Tumour cells are consistently positive for vimentin whereas in minority of cases some spindle or larger eosinophilic tumour cells express muscle specific actin and/or alpha-smooth muscle actin, suggestive of focal myofibroblastic differentiation; desmin, and histiocytic markers as- CD68, Mac 387, FXIIIa are consistently negative[9].

Cytogenetic and molecular analysis of myxofibrosarcoma demonstrates a complex karyotype with triploid or tetraploid alterations, ring chromosome formation and various genomic imbalances that includes loss of 6p, gain of 9q and 12q[10]. An isolated case with reciprocal translocation i.e t(10;17)(p11.2;q23) has also been reported by Sawyer and colleagues. Interestingly more complex cytogenetic alteration is observed in cases with local recurrence which implies the multistep genetic progression in myxofibrosarcoma governed by genetic instability[10].

Due to a significant histological overlap of myxofibrosarcoma with many spindle cell tumours showing myxoid change, it is essential to differentiate this sarcoma from its close mimickers as[6,10] i)low grade fibromyxoid sarcoma: pucicellular, with minimal to focal moderate pleomorphism, scant mitotic figures with no atypical one, they show alternating fibrous and myxoid areas while myxofibrosarcoma shows more cellularity, pleomorphic nuclei and high mitotic figures including atypical ones, also the detection of FUS translocation is a strong confirmatory evidence for the diagnosis of this tumour; ii) High Grade Pleomorphic Sarcoma (MFH): distinguished from high grade myxofibrosarcoma by lack of myxoid stroma and organised vascular pattern, also these tumor are moreover deep seated; iii) Myxoid dermatofibrosarcoma (DFSP): these tumour lack cytologic pleomorphism, and arcuate/ curvilinear vascular pattern**;** iv) Aggressive angiomyxoma: have a small bland cells and rare mitotic figures contrasting the large cytologically atypical cells and frequent mitotic figures seen in cases of myxofibrosarcoma; v) Myxoid Liposarcoma: they show frequent lipoblast, a feature lacking in case of myxofibrosarcoms, also these tumours lack pleomorphism and are rarely seen in subcutis. Also they show strong positivity for S-100 immunostaining.

The cornerstone of treatment therapy for myxofibrosarcoma includes complete surgical excision with 2 cms of optimal negative margins[6], implication of adjuvant radiation therapy may decrease the likelihood of local recurrences, particularly in cases where the margins are close or compromised.

The 5-year recurrence-free survival, metastasis-free survival and disease-specific mortality rates were 41%, 90%, and 4.4%, respectively. Tumor size larger than 5 cm, tumor necrosis, and <75% of myxoid areas were significantly associated with disease-specific mortality, the former two factors being the most predictive of metastasis. Local recurrence of myxofibrosarcomas is a widely reported as high as 50-60% cases[6], higher than that of other soft tissue sarcomas[11], in spite of repeated surgery involving wide local excision with negative surgical margins[8]. The tendency of low-grade lesions to recur at higher grades and potential metastatis underlines the need for accurate diagnosis[9]. The most common sites of metastasis are the lungs, although osseous metastasis had also been reported[6]. Metastatic myxofibrosarcomas are frequently refractory to current treatment strategies leading sarcoma related death[12], which mandates lifelong follow up of these patients. Future treatment may lie in developing an understanding molecular basis of the tumour and directing therapies accordingly.

Figures with the legends

Figure 1: cut section: greyish white with extensive myxoid areas, along with yellowish orange foci of necrosis and haemorrhage.

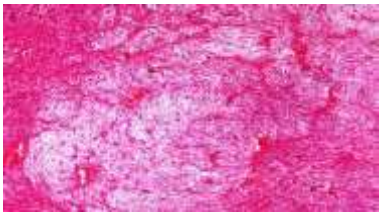

Figure 2 : Section showing hypocellular myxoid and hypercellular areas with curvilinear blood vessels (H&E, x40, x100)

Figure 3: Tumour cells showing viamentin positivity (vimentin, x100).

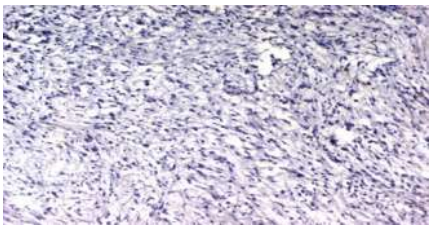

Figure 4: Section showing negative cytokeratin immunostaining (CK, X100)

CONCLUSION

- Myxofibrosarcoma (a distinct stromal sarcoma) of the male breast is an extremely rare occuring entity.
- Immunohistochemistry is helpful in differentiating myxofibrosarcoma from other spindle cell neoplasm with similar histomorphology.
- Myxofibrosarcoma shows a predilection for multiple local recurrences, tendency of low-grade tumour to recur at higher grades and potential metastasis which emphasizes the need for accurate diagnosis and excision in specialized centres.

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