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Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Myofibroblastoma, a case report of uncovering this rare mesenchymal tumor

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Abstract

A pathologist stumbles upon a male breast lump not uncommonly.Through the present case report, we uncover one of the rare breast tumors that every pathologist should be aware of, as it is often mistaken for a malignant lesion which in turn leads to radical treatment. To complicate things, this tumor also has multiple morphological variants. Here we present a case of Myofibroblastoma in a middle aged male patient, which was of epithelioid variant. Further the diagnosis was confirmed by Immunohistochemistry. A careful microscopic evaluation in the light of a good clinical history and supporting immunohistochemistry usually clinches the diagnosis.

Keywords: Breast, Myofibroblastoma, Imunohistochemistry.

Received: 29-05-2025; **Accepted:** 29-08-2025; **Available Online**: 17-10-2025

1. Introduction

In the present case report we emphasize the importance of identifying the rare benign tumor, Myofibroblastoma. The literature search shows very few case reports and series of this tumor, especially in this part of the world. We also highlight the difficulty in diagnosing this tumor on FNAC and the clinical dilemma due to unusual presentations. In addition the present case report includes the discussion on the numerous morphological variants of this tumor. Overall the concern is to prevent the over-diagnosis and to keep this differential diagnosis open in an appropriate clinical context.

2. Case Presentation

A 55 years old male patient presented to the clinic with a painless slowly progressive lump in the right breast for 1 year. The lump was in the central sub-areolar region and firm to hard in consistency. The ultrasonography of the right breast showed well defined heterogenous lesion measuring approximately 5.0x5.0cms. The lesion showed increased vascularity. No calcifications were noted. Few lymph nodes were identified in the right axillary region, largest measuring 1.0x0.7cms. A probable diagnosis of neoplastic lesion was made.

The Fine needle aspiration cytology done elsewhere showed dyscohesive sheets of round to oval cells resembling epithelial cells in a background of hemorrhage. An impression suspicious of malignancy was made. Since the “Triple test” was pointing towards a neoplastic lesion, likely malignancy, a wide local excision was done with right axillary lymph node dissection. Grossly the lesion was circumscribed, un-encapsulated, measuring 3.5x2.5x3.0cms, firm to hard with focal yellowish areas as shown in the **Figure 1**.

Microscopically there was a circumscribed lesion composed of oval to polygonal cells arranged in sheets and fascicles (**Figure 2**). The cells had a vesicular nuclei, prominent nucleoli and moderate amount of eosinophilic cytoplasm. There were no atypical mitotic figures. There

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https://doi.org/10.18231/j.ijpo.11493.1746998923

were interspersed, thick hyalinized collagen bundles, mature adipose tissue, focal myxoid change, hemorrhage, fibrosis, and scattered chronic inflammatory cell infiltrate. With clinical history in mind a diagnosis of Myofibroblastoma of Epithelioid type was made suggesting Immunohistochemistry for confirmation and to rule out other mesenchymal tumors. The Immunohistochemistry was performed manually, on sections cut from paraffin blocks, following antigen retrival. Immunohistochemistry showed positivity for Vimentin, CD34, Desmin, ER and PR and negative for Cytokeratin (**Figure 3**). The clones used were V9, QBEnd/10, D33, SP1, SP2 and AE1/AE3 respectively. With this a Final diagnosis of Myofibroblastoma was made.

Figure 1: Cut section of the wide excision specimen showing a well circumscribed gray white to tan lesion with focal yellowish areas.

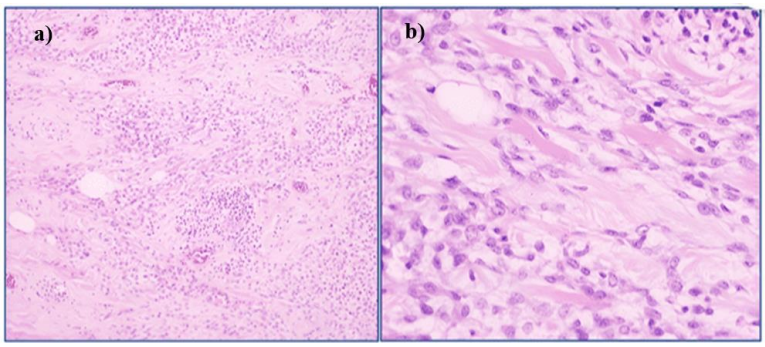

Figure 2: Microscopic image showing sheets of ovoid cells with interspersed adipocytes and chronic inflammatory cells, **a):** 10x, **b**): 40x

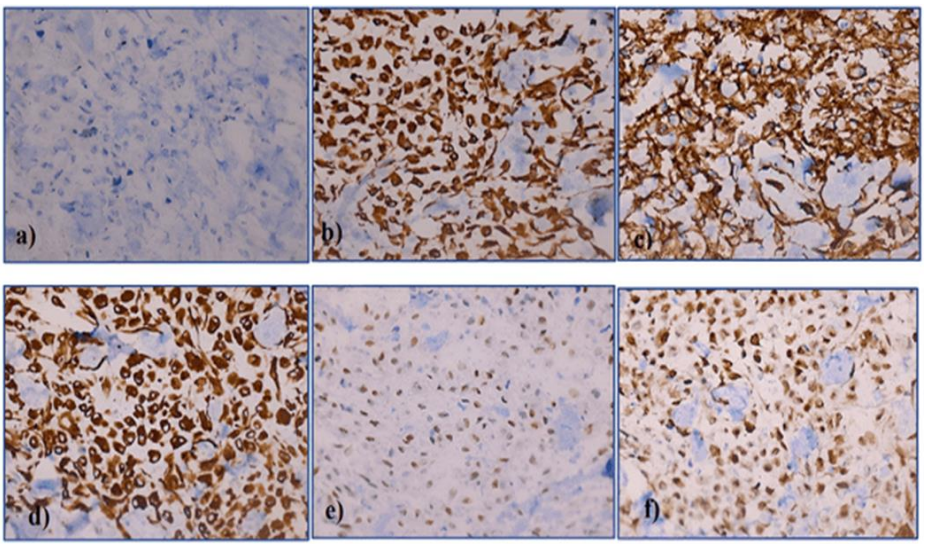

Figure 3: Immunohistochemistry, **a)**: Pan cytokeratin-negative, **b):** Vimentin-positive, **c)**: CD34-positive, **d):** Desmin-positive, **e):** ER-positive, **f):** PR-positive.

3. Discussion

Myofibroblastoma is a benign mesenchymal tumor of the breast. If it occurs elsewhere it is termed "Mammary Myofibroblastoma".[1] The term Myofibroblastoma was first coined by Wargotz et al. in an article where he presented 16 cases of a distinctive type of mesenchymal neoplasm.[2] 68.75% of his cases were males and the average age at the presentation was 63years. However previous report of this case was made for the first time by Toker et al.[3]

Clinically and radiologically the features that point towards benign nature of this tumor are, slow progression, painless, circumscribed lesion with no calcification.[4,5] On ultrasonography, the MFBs are mostly well-circumscribed, homogenous/heterogenous hypoechoic mass, on mammography they are hyperdense mass with no calcification, on MRI they present as homogeneous enhancing mass with internal septations and on CT scan they are non-enhancing solid mass.[6] Most of the tumors range in size from 1.0 to 3.7cms.[7] At this point the differential diagnosis of a circumscribed lesion in male breast are, breast abscess, Hematoma, fibromatosis, granular cell tumor, neurofibroma, lymphangioma, leiomyoma, myofibroblastoma and Invasive ductal carcinoma.[8] Among these, Myofibroblastoma requires only wide local excision as the lesion rarely relapses unless the resection margins are free and there is nearly no malignant transformation.[9] Hence FNAC/ Tru-cut biopsy may be planned before surgery in case of unusual radiological findings as in the present case.[7]

Pathological examination: On FNAC myofibroblastoma shows abundant, randomly arranged single and clustered spindle cells of benign morphology. The cells had elongated/oval nuclei with scant cytoplasm. Nuceli show finely granular chromatin with inconspicuous nucleoli.[10] However the accuracy of FNAC/ Tru-cut biopsy in the diagnosis of Myofibroblastoma is questionable. The reasons being, wide histo-morphological spectrum of the tumor.[11] As in the present case the FNAC findings can be dubious and many cases end up with unnecessary mastectomy and lymph node dissection.

On gross examination, MFB usually presents as a well circumscribed round to oval mass, as in the present case. They have a smooth lobulated external surface. Cut surface is solid, greyish to whitish. Sometimes may show whorling.[6]

Microscopically the typical myofibroblastoma shows intersecting fascicles of bland appearing spindled and epithelioid myofibroblastic cells in a background of collagen bundles. They are unencapsulated with a pushing borders. Atypical mitosis, nuclear pleomorphism or necrosis is generally not visible.[12] The tumor cells of myofibroblastoma are said to arise from the precursor cells of mammary stroma, which are capable of assuming various morphology and able to differentiate along different mesenchymal lineages,[1,13] which explains their morphologic heterogeneity.

The variants of this tumor include fibrous, cellular, infiltrating, myxoid, deciduoid, lipomatous, epithelioid, Hemangiopericytoma like and atypical.[14] Due to this wide spectrum of the morphological appearance, at this point the differential diagnosis include epithelial and mesenchymal tumors. The epithelial tumors that enter the differential diagnosis include, lobular carcinoma and fibromatosis like metaplastic carcinoma. Certain subtypes of invasive ductal carcinoma, especially spindle cell metaplastic carcinoma, can histologically resemble MFB, due to the fasicular arrangement of the elongated cells. Differentiating points on cytology are that the malignant epithelial cells show marked atypia, prominent nucleoli and atypical mitosis, however the MFB cells are bland with vesicular nuclei and lack atypical mitosis. Histologically the invasive carcinoma shows infiltrative border with a desmoplastic stromal reaction and MFB has a pushing, well-circumscribed borders. Immuno-histochemistry stains show cytokeratin positive and CD-34 negative in invasive carcinoma and cytokeratin negative and CD-34 positive in MFB.[15] On the other hand the various mesenchymal tumors that mimic this tumor are intramammary lipoma, inflammatory myofibroblastic tumor, Fibromatosis, Solitary fibrous tumor, Low-grade fibromyxoid sarcoma.[13] The desmoid fibromatosis is negative for CD34 and they express beta-catenin. Solitary Fibrous Tumor shows STAT 6 positivity, which is negative in MFB. In the present case the cells had an epithelioid morphology and there were scattered mature adipocytic clusters.

Myofibroblastoma was originally thought to be associated with Solitary fibrous tumor, however upon study of molecular mechanisms, i.e chromosomal deletions of 13q14, they are now found close to spindle cell lipoma and cellular Angiofibroma.[16] Mammary myofibroblastoma are thought to arise in response to TGF-beta 1 secreted by injured myofibroblasts.[17] As discussed earlier, MFBs are known to arise from progenitor cells capable of differentiation into various forms, which has a great potential to be harnessed for organoid culture models.[13,18]

4. Conclusion

Due to the morphological heterogeneity the pathologists should be aware of the variants, which will in-turn avoid the overdiagnosis. Also at this point it is safe to say, large scale studies are needed to assess the utility of doing an immunocytochemistry on cell block samples for definitive diagnosis.

5. Abbreviations

FNAC: Fine Needle Aspiration cytology; IHC: Immunohistochemistry; MFB: Myofibroblastoma

6. Author Contribution

Mention all authors' contribution to justify authorship for this article.

1. SAN: Conceptualizing and Writing up the content, collection of reference articles and supervising the progress.
2. TS: Writing up the content, collection of reference articles and proof-reading.
3. KKNS: Providing the clinical details of the case and proof-reading.

7. Source of Funding

None.

8. Conflict of Interest

None.

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Cite this article: Narayana SA, Syed T, Nayak KKS. Myofibroblastoma, a case report of uncovering this rare mesenchymal tumor. *Indian J Pathol Oncol*. 2025;12(3):271–274.