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MALIGNANT MYOEPITHELIOMA OF BREAST: A RARE CASE REPORT AND REVIEW OF LITERATURE

Pathology

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ABSTRACT

Malignant myoepithelioma of the breast is an extremely rare neoplasm arising from myoepithelial cells that possess both epithelial and smooth muscle characteristics. This report presents the case of a 43 year old female with a painless, progressively enlarging lump in the right breast. Histopathological examination revealed malignant spindle and epithelioid cells in a chondromyxoid stroma with high nuclear cytoplasmic ratio and pleomorphism. Immunohistochemistry demonstrated strong positivity for S-100, Smooth muscle actin (SMA), calponin, vimentin, and p63, confirming myoepithelial origin, while estrogen receptor (ER), progesterone receptor (PR), and cytokeratin 5/6 were negative. The patient underwent modified radical mastectomy following neoadjuvant chemotherapy, with six metastatic lymph nodes identified. Literature review emphasizes the diagnostic challenge of distinguishing this entity from other spindle cell lesions of the breast. Early recognition through immunohistochemistry and a multidisciplinary therapeutic approach are crucial for management and improving patient prognosis.

KEYWORDS

Malignant Myoepithelioma, Breast Tumour, Immunohistochemistry

INTRODUCTION

Myoepithelium provides a physical barrier between a basement membrane and luminal epithelial cells located in the breast throughout the mammary duct system including ducts and lobules [1]. Myoepithelial cells have dual characteristics of epithelial and smooth muscle cells. Therefore, carcinoma arising from myoepithelial cells have both epithelial and smooth muscle component but there is no ductal differentiation [2]. The most common location of myoepitheliomas is salivary gland with some extra-salivary locations like soft tissues, skin, breast and lung [3,4,5]. Myoepithelial cells are present in the breast but pure myoepithelial neoplasms of breast are not common and hence very limited case studies are present in literature. Malignant myoepithelial cells are spindle shaped but can be polygonal occasionally. Increased cellularity, high N:C ratio, mitotic activity, infiltrative growth pattern, necrosis, hemorrhage and locoregional spread points towards the diagnosis of malignancy in breast [6,7]. Myoepithelioma presents as a nodular tumor with areas of necrosis and hemorrhage and microscopic examination with spindle cells and epithelioid cells entrapping normal breast tissue. We present a rare case of malignant myoepithelioma of breast with special emphasis on the importance of immunohistochemistry in reaching the diagnosis and differentiating it from other spindle cell lesions of breast.

Case Presentation

A 43 years old female patient presented to the surgery outdoor department with complaint of a painless lump in the right breast, which was gradually increasing in size for 5-6 months. There was no discharge from the nipple. She was non-smoker, non-alcoholic and vegetarian. She gave history of conception after treatment for primary infertility. She had undergone hysterectomy 6 years ago after the child birth. There was no family history of breast cancer. The lump measured 8x7 cms on palpation. On examination, lump was firm, mobile and non tender without involvement of nipple and skin.

CT Scan revealed a relatively well defined lesion having heterogenous density with lobulated margins and evidence of calcification with loss of fat planes in chest wall of right breast. Few heterogenously enlarged lymph nodes were noted in right axillary and interpectoral region. There was no evidence of pleural and pericardial effusion.

Cytological smears from lump breast were highly cellular comprising of loose and cohesive clusters and single scattered atypical cells. The atypical cells had high N:C ratio, moderately pleomorphic nuclei, reticulogranular chromatin with nucleoli in some. These atypical cells were embedded in a background of abundant mucin like material. Cytological features were suggestive of carcinoma breast with mucinous component. Consequent upon which, the patient received 8 cycles of neoadjuvant chemotherapy before going in for modified radical mastectomy.

Right modified radical mastectomy was performed, serial sections of which revealed multiple firm, grey white areas measuring 8x8x8 cm involving almost the whole of breast leading to nodular appearance of overlying skin. On microscopy, sections from the tumour area showed sheets, nests, thin anastomosing cords and tubules of round to oval to spindle malignant cells embedding in chondromyxoid stroma, at places having high N:C ratio, vesicular nuclei, prominent nucleoli in some and scanty to moderate cytoplasm. Few benign duct acini were also seen in surrounding breast tissue. Overlying skin, resected base and nipple areola complex were free from tumour infiltration. Metastatic deposits were seen in six lymph nodes (6/22).

On Immunohistochemical staining, the atypical cells were positive for S-100, smooth muscle actin (SMA), p63, Calponin, Vimentin with focal positivity for CK and Ki67<10%. ER, PR, EMA, CK5/6 were found to be negative.

Review of Literature

Lingamfelter et al in Kansas City School of Medicine and Trauma Medical Centers, Missouri, USA, presented the cytological findings from a case of infiltrating myoepithelial carcinoma of breast in a 52 years old female and provided a histologic correlation with subsequent biopsy and mastectomy specimens. They concluded that the cytology specimens displayed more myoepithelial cellular heterogeneity as compared to histopathology sections. Cytologic features include hypercellularity, pleomorphic spindle cells, and mitotic activity [8].

Endo et al presented a case and discussed its biological behavior and treatment taken by patient including breast conservation surgery, adjuvant radiotherapy. Patient had 4 regimens of chemotherapy including combination of doxorubicin and cyclophosphamide for 20 months after the diagnosis of metastatic disease. The diagnosis of

myoepithelial carcinoma was established on histological and immunohistochemical results [2].

Papazian et al discussed a case of 74 year old woman who was admitted with inflammatory like cancer of breast with invasion of chest wall and axillary lymph node metastasis. They established the diagnosis of malignant myoepithelioma of breast by histological examination and revealed a tumor composed of epithelioid and spindle cells with moderate to marked nuclear atypia, with foci of hemorrhage and necrosis. Furthermore, the tumor cells were immunoreactive for vimentin, p63, p53, CD10, cytokeratin (CK) 8/18, CK AE1/AE3 and S100 [9].

Harb et al confirmed a case of malignant myoepithelioma of breast using immunohistochemistry. The malignant cells revealed diffuse expression of p63, SMA, S-100 in addition to high Ki-67 labelling index. They concluded that malignant myoepithelioma of breast is extremely rare entity and it should be suspected during differential diagnosis of any malignant spindle cell tumor of breast [10].

In our case, the clinical features, macroscopic features and microscopic features pointed towards the differential diagnosis of malignant myoepithelioma of breast. Immunoreactivity to S-100, smooth muscle actin (SMA), calponin, vimentin, p63 and focal positivity for CK helped in establishing the diagnosis.

DISCUSSION

Malignant myoepithelioma of breast is an extremely rare and aggressive neoplasm. It is difficult to diagnose and treat this malignant neoplasm.[1,7,11] There are limited number of published reports in literature describing myoepithelial carcinomas of breast [1]. It is difficult to differentiate it from other spindle cell lesions. According to Tavassoli, there are three types of myoepithelial lesions in the breast: myoepitheliosis, adenomyoepithelioma, and malignant myoepithelioma [12].

Myoepitheliosis and Adenomyoepithelioma consist of significant population of myoepithelial cells admixed with epithelial cells. Myoeptheliosis is often multifocal and is microscopic proliferation of myoepithelial cell in and around small ducts. On the other hand, adenomyoepithelioma is well circumscribed with fibrous capsule and closely packed cells with no invasive growth, no mitotic figures, and no atypical features [13, 14]. Malignant myoepithelioma of breast is a rare tumour seen in women between 25-81 years of age and is composed of sheets and nests of round to oval atypical spindle cells embedded in chondromyxoid stroma with atypical mitotic figures. Usually, the lesion is multinodular with areas of necrosis and hemorrhage [9]. In our case, the clinical manifestations, the microscopic examination and immunohistochemistry (IHC) contributed to the diagnosis of malignant myoepithelioma. IHC played an important role in confirming the diagnosis. The tumor cells were immunoreactive to S-100, SMA, Calponin, Vimentin, p63 with focal positivity for CK and were negative for ER, PR, Her2neu, EMA, CK5/6 with Ki-67 proliferation index around 10%.

Morphologically, it is important to distinguish myoepithelial carcinoma from other spindle cell lesions of breast like monophasic sarcomatoid carcinoma, fibromatosis and primary spindle cell sarcoma [15]. Overlap of histological features may lead to difficulty in correct diagnosis by histopathology alone, e.g., Monophasic sarcomatoid carcinomas contain negligible amount of epithelial component. It can be challenging to distinguish some of these from myoepithelial carcinoma since these co-express actin immunoreactions. So, the diagnosis is made using antibodies to keratin of variable molecular weight. [1]

Fibromatosis on the other hand is composed of proliferation of myofibroblasts and fibroblasts but with minimal pleomorphism and absence of mitotic figures indicating benign nature. It often expresses actin with occasional positivity for S-100 and desmin but does not express cytokeratins on immunohistochemistry [16,17].

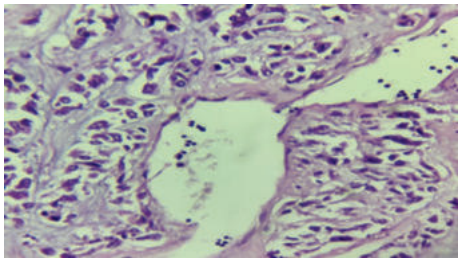
Pure Spindle cell sarcomas, such as fibrosarcomas and dedifferentiated liposarcomas, are generally negative for CKs. Other sarcomas like leiomyosarcoma and rhabdomyosarcoms express specific muscle markers. These sarcomas should only be diagnosed after being distinguished from resembling lesions [1, 9].

S-100 protein, high molecular weight cytokeratins, smooth muscle actins, type IV collagen and laminin are currently popular myoepithelial markers but have insufficient sensitivity and specificity. On the other hand p63, a homologue of p53 is a sensitive and relatively specific marker of myopeithelial cells [18].

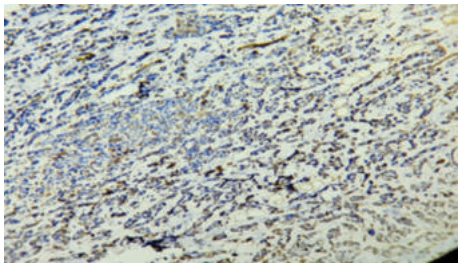
CONCLUSION

Malignant myoepithelioma is an extremely rare tumor of breast and is difficult to diagnose and should be kept in differential diagnosis in malignant spindle cell neoplasm of breast. An aggressive course with both locally invasive and extensive metastatic potential characterizes myoepithelial cancer [19,20]. The preferred treatment of choice is surgery. The use of neoadjuvant chemotherapy is frequently used to reduce local recurrence. Till date there is limited data available on the biological behavior of malignant myoepithelioma of breast.

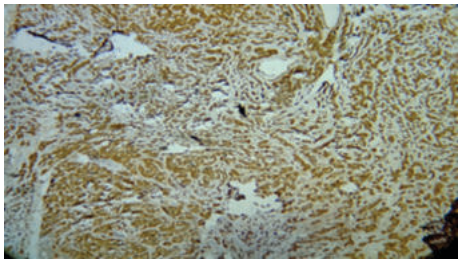
Therefore a multidisciplinary approach would be beneficial for improved survival of patients.



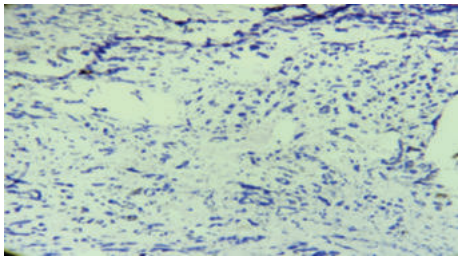
H & E (400x) showing sheets and thin anastomosing cords and tubules of malignant cells having high N:C ratio, prominent nucleoli and scant to moderate cytoplasm.



Immunohistochemistry (IHC) showing positivity to Vimentin.



Immunohistochemistry (IHC) showing positivity to S100.



Immunohistochemistry (IHC) showing positivity to SMA.

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