Infiltrating Myoepithelial Carcinoma of the Breast with plasmacytoid features: A diagnostic challenge

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ABSTRACT: Infiltrating myoepithelial carcinoma remains an exceptional entity. Spindle cell morphology seems to be more prominent. However, rhabdoid, epithelioid and plasmacytoid morphologies may be seen. In some cases, this tumor may appear as poor differentiated intraduct carcinoma. Immunohistochemistry is very useful to confirm the diagnosis. Local recurrence and distant metastases are common but treatment is not consensual.

We report a case of a 40-year-old woman with an unusual myoepithelial carcinoma. The diagnosis was canceled by the histopathological and immunohistochemical examination of the resected specimen.

We discuss clinical and pathological features of myoepithelial carcinoma, which are very important to know by young pathologists.

KEYWORDS: Myoepithelial Carcinoma, Plasmacytoid, Breast, Immunohistochemistry.

1 INTRODUCTION

Myoepithelial Carcinoma (Malignant myoepithelioma (MMB) is a malignant neoplasm composed exclusively by myoepithelial cells. Although a similar entity is well known to occur in the salivary gland [1], Myoepithelial Carcinoma of the breast is very rare. A fewer than forty published clinical cases have been reported in the English literature through a Pubmed research [2]. These tumours display different morphologies including spindle cell, clear cell, rhabdoid, epithelioid, and plasmacytoid forms. A mixed pattern of these morphologies is current [3, 4]. We report this new case in the aim to define this rare entity, to discuss differential diagnosis, immunohistochemical profile, prognosis and treatment.

2 CASE REPORT

We present a case of a 40-year-old woman, who had a gradually enlarging lump in her left breast three months ago. She had no personal or family history of breast or ovarian cancer. Except this suspect mass, she was in good health. The physical exam showed an asymmetry at the expense of the left breast upper area. The mass was firm and well-circumscribed. It measured 4x3x2 cm with multiple axillaries lymphadenopathies. An ultrasound exam and Mammography showed a suspected and diffuse density area of about 4,5 cm in the upper outer quadrant of the left breast. The conclusion of radiologist was malign finding (BI-RADS 6). A core needle biopsy (CNB) was performed and showed a poor differentiated carcinoma (SBR 3). Based on this data, radical mastectomy became more appropriate. At gross examination, the mastectomy measured 20 x15 cm. The tumour located in the upper outer quadrant. It was blackish measured 3 cm in the greatest dimension. There were mastopathy lesions with cystic changes in the others quadrants. Multiple sections were studied and they showed breast tissue with an irregular dense proliferation which was composed of epithelioid to plasmacytoid cells with moderate amounts of cytoplasm and pleomorphic vesicular nuclei and distinct nucleoli. Many foci displayed cells with clear cell changes (Figure 1; 2). Mitotic
figures were frequent (15 mitotic figures per 10 high power fields) with numerous abnormal mitoses. The tumour infiltrate diffusely the stroma. No lymphovascular emboli or perineural spread was seen. All the surgically resected margins were uninvolved by the neoplastic process. Other findings included atypical ductal hyperplasia and periductal mastitis were seen. The sentinel axillary lymph node showed 23 metastatic nodes with capsular effraction and vascular invasion.

Immunohistochemistry was performed and the tumour cells were seen to be strongly positive for S-100, P63, CK, SMA and weakly positive for E-cadherine with an increased positivity for Ki-67 that provided the high proliferation index (Figure 4). The neoplastic cells were negative for ER, PR, HER-2/neu, CK8/18, LCA, CD163, Melan 1, desmine and myogenine.

The histology and accompanying immunohistochemical staining patterns were consistent with an infiltrating myoepithelial carcinoma with plasmacytoid changes of the breast.

Total body CT scan didn’t show any distant metastasis. The patient had an uneventful postoperative stay. She received an adjuvant chemo-radiotherapy (three cycles of paclitaxel and carboplatin). She is still alive without local recurrence.
3 Discussion

Myoepithelial carcinoma of the breast is an extremely rare tumour. A limited number of published reports have described this entity. Sarkar and Lallenbach [5] were the first who described various amounts of myoepithelial cells with different morphologies in 1966. It’s a benign counterpart “adenomyop epithelioma”. It’s is also a rare tumour of the breast, reported for the first time in 1970 [6]. The WHO classification of breast tumors (4th edition) has included MMB under category of metaplastic carcinoma of no special type [7]. It’s mostly seen in women aged 25–81 years old [2]. This tumor usually discovered clinically within the manual palpation.

Radiologic features are not specific. It presents as poorly-circumscribed masses measuring 10 to 48 mm (middle of 26 mm) [8]. FNA specimen shows a biphasic pattern with or without tumor necrosis or mitotic figures [4]. Microscopically, MMB shows infiltrating spindle tumor cells with prominent cytologic atypia, increased mitotic activity (more than 3–4/10 HPF) and definitely infiltrating tumor borders [3]. However, myoepithelial cells may adopt a number of different morphologies including spindle cell, clear cell, epithelioid, rhabdoid and plasmacytoid forms [9]. In a study by Hornick and Fletcher, over half of their 101 cases of soft tissue myoepitheliomas actually showed a mixed pattern of these four morphologies [10]. Whereas the MMB reported by Sauer described both the spindle cell and epithelioid (“polygonal”) cell populations [11], the intraductal case reported by Tamai et al. lacked only the plasmacytoid cell type [12]. The heterogeneity with the myoepithelial cells can therefore complicate the diagnostic process for myoepithelial carcinoma even further, obviating a need to use the immunohistochemistry and to expand the differential diagnosis.

On immunohistochemistry, tumor cells represent strong positivity of myoepithelial markers, such as smooth muscle actin, calponin, vimentin, S-100, p63, WT1, NGFR, CD10 and EGFR. They variably show staining for epithelial markers, such as cytokeratin [AE1/AE3 + 8/18] or epithelial membrane antigen. Additionally, increased positivity for Ki-67 provided evidence for a high proliferation index among the neoplastic cells [1, 2, 3]. MMB are completely negative for hormone receptors [6].

Under electron microscopy, well-formed desmosomes and hemidesmosomes together with pinocytic vesicles, plentiful rough endoplasmic reticulum and 6 nanometer microfilaments are seen [6].

Molecular abnormalities of myoepithelial carcinoma showed the point mutation of p53 gene. Angele and al [10], have also reported that p53 protein was negative in benign myoepithelial lesions but overexpressed in 44.4% of malignant myoepithelial tumors of the breast.

Increasing research had identified ME cell specific genes like S100A2, LGALS7, CSTA and BPAG [4]. The expression of SPARC (osteonectin) is known to independently portray a poor prognosis in breast carcinoma, which is irrespective of the ER/PR status. These markers can be used in the identification of the myoepithelial cells as well [4].

Identification and further research on the genesis of these tumors could help to discover new molecular targets for its management [2].

The differential diagnosis from spindle cell/metaplastic carcinomas, primary spindle cell sarcomas or malignant fibrous histiocytoma of the breast is challenging all may demonstrate atypical spindle cells along with other common stigmata of cancer like necrosis and mitotic activity [1, 2, 6, 7]. So, these tumors are almost impossible to differentiate without immunohistochemistry. In some instances, the presence of such features as a chondromyxoid background and atypical multinucleated giant cells in a case of metaplastic carcinoma may generously help in eliminating MEC.

In this case, it may be appropriate to entertain the diagnosis of lobular carcinoma or metastatic melanoma, simply because some of the tumor cells in our case displayed plasmacytoid morphology. The presence of signet-ring cells in lobular carcinoma and intracytoplasmic pigment in melanoma can distinguish these entities from MEC [3].

In our case, the positivity for cytokeratin, SMA, S100 and CD10 clearly proved the myoepithelial origin of this tumour.

Myoepithelial carcinomas are treated mainly by wide local excision, lymph node dissection and adjuvant chemotherapy [1, 13, 14]. There are not sufficient data available to define the role and effectiveness of first-line chemotherapy, although it remains the only therapeutic choice in cases with distant metastasis or recurrence disease. Taking into consideration the unresponsiveness of the tumor to neoadjuvant therapy, there was an alteration of regimens postoperatively (Ola A. Harb et al. Papazian et al. and Dsouza S et al.) [1, 2, 6].

However, none of the chemotherapy protocols have been efficient (including carboplatin, paclitaxel, doxorubicin, cyclophosphamide, gemcitabine and oral capecitabine) [15].

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The effectiveness of hormone therapy is unknown, since the tumor was triple-negative, so hormone therapy doesn’t helpful [16]. Up to date, several cases of local recurrence or metastasis have been reported, so myoepithelial carcinoma should be carefully examined and needed to close follow up. They adopt an aggressive clinical course with an outcome comparable to poorly differentiated adenocarcinoma of the breast. Two and five years survival is 88% and 55% respectively [2]. Ola A. Harb and al. also suggested that a tumor of more than 2 cm confers poor prognosis [17,18].

4 CONCLUSION

The ambiguous biological behaviour of this unusual cancer improves to confirm the diagnosis by immunohistochemistry. A multidisciplinary treatment approach is strongly recommended.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES


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