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DIAGNOSTIC PERPLEXITY: METAPLASTIC CARCINOMA OF BREAST VERSUS MALIGNANT PHYLLODES TUMOR OF BREAST

Breast Surgery

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ABSTRACT

Metaplastic breast carcinoma is an uncommon breast neoplasm constituting less than 1% of all breast cancers. It is more aggressive and has poorer prognosis than other breast carcinomas. It has variable and similar presentation to others. With this case report of a 76-year-old female who presented with a large tender rapidly progressive erythematous lump, we aim to reveal the rarity in pathologic and clinical features of the metaplastic breast carcinoma and its similarities to malignant phyllodes tumor of breast. It has been later diagnosed post operatively as Metaplastic carcinoma of breast. Immunohistochemistry plays an important role in its diagnosis.

KEYWORDS

Metaplastic carcinoma of breast, spindle cell, malignant phyllodes tumor, pan CK positivity, CK 14 positivity, Ki67 index, monoclonal cell origin

INTRODUCTION

0.3% of all breast tumors are metaplastic carcinomas, an uncommon type of the disease.[1] These breast tumors are a heterogeneous group that show a diversity of histological characteristics and seem to have both epithelial and mesenchymal origins. There is little information available regarding patient demographics, presentation, tumor features, prognosis, and treatment patterns because it was not recognized as a unique histopathologic subtype until 2000. MBC is divided by the World Health Organization into two types: pure epithelial and mixed epithelial and mesenchymal type[2]. Squamous cell carcinoma (SCC), adenosquamous carcinoma (ASC), and adenocarcinoma with spindle cell differentiation (SPC) are subclasses of the epithelial-type MBC, while carcinosarcoma (CS) and carcinoma with osseous and chondroid metaplasia are subclasses of the mixed-type MBC (COC). These are myoepithelial and cytokeratin marker-positive tumors that are triple negative.[3]

CASE REPORT

We report a case of 76 years old female who came with the history of breast lump of size 5*5 cm in upper outer quadrant in her Right breast for 2 years, which was initially smaller in size and progressed to the present size. She had history of dull aching continuous pain associated with the right breast lump. Before an year she got diagnosed as ?Benign Phyllodes tumor/? Malignant Phyllodes tumor of right breast. It was diagnosed by histopathological examination of specimen from a core needle biopsy. She presented to us with a breast lump of size 5*5cm which was variable in consistency, firm to hard and cystic in consistency. On first presentation, there was dilated veins over her right breast with slight redness seen at 9-11 O' clock position in her Right breast with the presence of mild Peau-de-orange appearance. The lump was not fixed to the chest wall and no axillary lymphadenopathy was observed. The Figure 1 shows the clinical picture on first presentation. Later within a month the lump became more erythematous, increasing in intensity from 6-12 O'clock position of her right breast involving the nipple areolar complex. Peau-de-orange appearance also deepened. The Figure 2 represents this. She is a known diabetic and on OHAs for 20 years. She is a known hypertensive and on medication for the past 30 years.

Radiologically the lump showed evidence of 7.6*6.1*6 cm heteroechoic lesion with internal cystic spaces noted extending from 7-12 O' clock position with internal vascularity in the solid components. The impression was BIRADS IV B, features suggestive of Phyllodes Tumor of Right Breast.

The impression of the second core needle biopsy was? Malignant Phyllodes tumor of Right Breast/ Metaplastic carcinoma of right breast. Image guided third core needle biopsy histopathological examination has the impression based on histomorphology showing occasional acini lined by bilayered epithelium and immunohisto-chemistry showing CD 34 negativity in tumor cells and Ki67 30%, as? Malignant Phyllode tumor/ ?Metaplastic carcinoma of right breast.

After obtaining the tumor board policy, we proceeded with right modified radical mastectomy. The post operative histopathological examination report was Grade III Metaplastic carcinoma, Unifocal; Nottingham prognostic index: 6.8. Pathological staging was PT_3 N_0 M_x . the post operative period was uneventful and the patient was started on adjuvant chemotherapy.

Figure 1: Preoperative clinical picture on presentation

Figure 2: Preoperative clinical picture after 1 month with erythema and peau-de-orange appearance

DISCUSSION

Metaplastic carcinoma of breast is a theraupeutically challenging and aggressive type of heterogenous group of neoplasm of breast. It is triple negative carcinoma of breast which has transformation either a part or all of its galndular carcinomatous component into either non glandular or metaplastic carcinomatous component. They are histomorphologically heterogenous and comprise low and high grade tumors. The current 4th edition of World Health Organization classification for Metaplastic carcinoma of breast has 5 subsets: 1)low grade adenosquamous carcinoma 2)fibromatosis-like metaplastic carcinoma 3)squamous cell carcinoma 4)spindle cell carcinoma 5)carcinoma with mesenchymal differentiation.

The low grade adenosquamous carcinoma is a variant of Metaplastic carcinoma which has in a bland appearing backgroud of spindle cells, glandular and squamous differentiation. The low grade variant of Fibromatosis-like Metaplastic carcinoma of breast, has resemblance to desmoid type fibromatosis histopathological examination. It has bland spindled morphology with the presence of atypical ducts or ductal carcinoma insitu in between. The sqamous cell carcinoma of Metaplastic carcinoma of breast accounts for 0.1% which arise from metaplastic squamous epithelium. The carcinoma with mesenchymal differentiation is composed of a mixture of differentiated mesenchymal components, including osseous, chondroid, rhabdomyoid and neuroglial elements.[4] The Immunohistochemistry of Metaplastic carcinoma of breast may have heterogenous positivity for cytokeratin, vimentin, SMA and Pan-keratin; ER, PR, HER2 Neu negativity.

To explain how biphasic components can coexist, three main proposals have been put forth [5]. According to the collision theory for a biclonal origin, the CC and HSC are synchronous growth from different progenitor cells and collide to create a single tumour. According to the combination theory for a monoclonal origin, the CC and HSC are both descended from a single multipotent progenitor cell. According to the conversion/metaplastic theory for a monoclonal origin, the CC undergoes a metaplastic or conversion phase that results in the HSC.[6]

The phyllodes tumor of breast is a biphasic fibroepithelial neoplasm with epithelial patterned as leaf and with stromal proliferation. Their epithelial component is benign and the myopeithelial layer is preserved (may be attenuated). Their histomorphology may also have cystic degeneration, hemorrahge, stromal hyalinization and myxoid change. The Phyllodes tumor can be calssified into benign, borderline or malignant based on the decrease in the epithelial component with stromal outgrowth. The other features to classify them into malignant Phyllodes tumor of breast is with marked stromal atypia, cellularity, increased mitotoc count ≥10/10 High Power Field or ≥5/mm^2, diffusely permeative tumor border and occasional presence of malignant heterologous elements.[22] The Immunohistochemistry of Phyllodes tumor is negative for cytokeratin, CD 34, Bcl-2 positive in ductal component.

In our case, the section studied in the second core needle biopsy showed fibro collagenous and fibrofatty tissue with a neoplasm composed of ovoid to spindle cells with a high nuclear cytoplasmic ratio and marked nuclear atypia. Image guided third core needle biopsy histopathological examination has microscopic description as, multiple sections studied shows breast parenchyma with a neoplasm composed of cells arranged predominantly in sheets. The neoplastic cells are ovoid to spindle having moderate eosinophilic cytoplasm and pleomorphic hyperchromatic nuclei. Atypical mitotic figures noted. Intervening stroma shows desmoplasia, extensive areas of necrosis, congested blood vessels, areas of hemorrhage and focal lymphoid aggregates. IHC was CK 5/6-negative, CD 34- negative in stromal cells (positive in vessels), Ki67- 30%.

The post operative histopathological examination, gross description has modified radical mastectomy specimen measuring craniocaudally 28cm, mediolaterally 33 cm, Antero posteriorly 12 cm, with overlying skin measuring 23*17cm, skin showing a nodule in upper outer quadrant measuring 5*4*3.5cm. Nipple areolar complex unremarkable. Cut surface of nodule- shows cystic space filled with tumor and necrosed areas. On cut surface, tumor of size 14*9*8cm, fleshy bulging in nature, cystic with areas of necrosis present in upper outer quadrant. Tumor is 2cm from superior margin, 2.5cm from inferior margin, 8cm from medial margin, 9cm from lateral margin, <0.1cm from anterior skin margin, and 1cm from posterior margin. The microscopic examination has a unifocal tumor in the right breast of size 14*9*8cm with histomorphology similar to the third small biopsy showing sheets of neoplastic cells which spindle having pleomorphic hyperchromatic nuclei and extensive areas of necrosis with congested blood vessels in the stroma.

Immunohistochemistry was Ck 5/6, CD34, CK7, CK 19, ER, PR, H2N- negative and Pan CK-moderate to strong positivity in 20% of tumor cells, CK 14-weak positivity in 30% of tumor cells, Ki67-60%. Tumor free margin with no lymphovascular or perineural invasion of histological type Metaplastic Carcinoma of spindle cell carcinoma subtype of right breast of Grade III histologic grade. The Nottingham prognostic index: 6.8. Pathological staging was $PT_3 N_0 Mx$.

Thus, for difficulty in differentiation of Metaplastic carcinoma of breast and Malignant Phyllodes tumor of breast is because, the heterogenous component containing malignant cells for both epithelial and mesenchymal component in a Metaplastic carcinoma of breast can be determined and confirmed only with multiple sections taken from the full specimen. In case of malignant phyllodes tumor of breast the malignant cells are only from the stroma whereas the epithelial cells are benign. Though lack of cytokeratin exposure can exclude the diagnosis of Phyllodes tumor, the expression of cytokeratin in Metaplastic carcinoma of breast is heterogenous, thus limiting its diagnosis with small biopsy. Malignant heterologous component can also be present in case of the malignant Phyllodes tumor of breast. The IHC marker which helped in clinching the diagnosis of Metaplastic carcinoma of breast is CD34 and Bcl-2 negativity, in our case, CD34 is negative(positive in case of malignant Phyllodes tumor of breast).

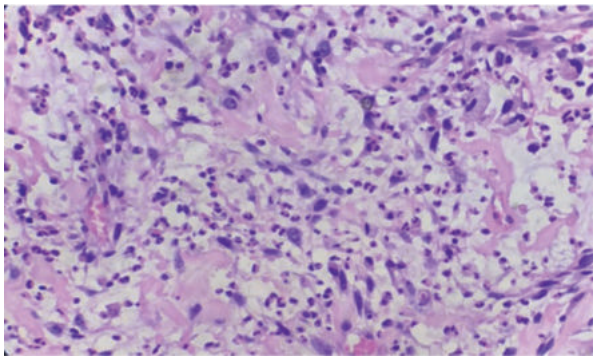

Figure3: Histomorphology examination (High power)

Figure 4: ER -Negative

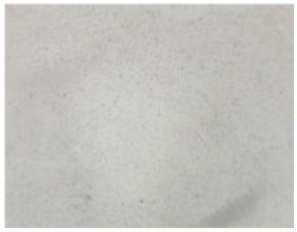

Figure 5: PR -Negative

Figure 7:CK 5/6 -Negative

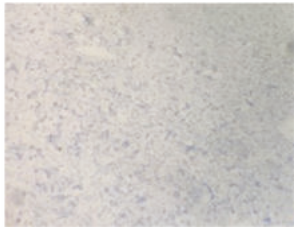

Figure 6: HER2 Neu - Negative

Figure 8: CK 7 -Negative

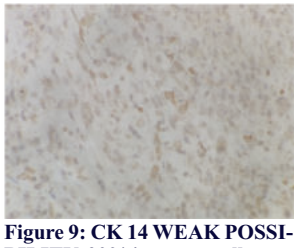

Figure 9: CK 14 WEAK POSSIBILITY 30% in tumor cells

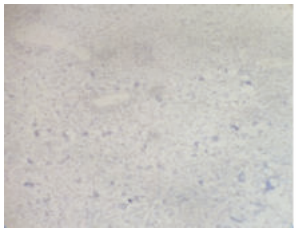

Figure 10: CK 19 -Negative

Figure 11: CD 34 -Negative

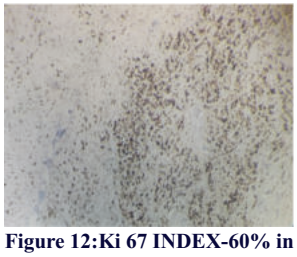

Figure 12:Ki 67 INDEX-60% in tumor cells

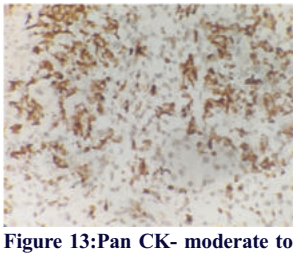

Figure 13:Pan CK- moderate to strong posibility in 20% of tumor cell

CONCLUSION

This case is presented for its rarity and to highlight the difficulties and limitations in its diagnosis with small biopsy. Thus, immunohistochemistry plays an important role in its definitive diagnosis. For any rapidly growing breast lump we should also have high degree of suspicion for Metaplastic carcinoma of breast. Though it has poor prognosis, it should be treated and managed like invasive breast carcinoma followed by adjuvant chemotherapy. Targeted therapy which is under evaluation might prove to beneficial in the future.

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