Case Report

Cytopathological features of matrix-producing carcinoma of the breast

ABSTRACT
Matrix producing carcinoma (MPC) of the breast is a very rare subtype of metaplastic carcinoma with heterologous elements, which comprises <0.1% of invasive breast carcinomas. There are very few reports describing the cytological features of MPC. In this article, we aimed to discuss cytological, histopathological and immunohistochemical features of this rare entity in a 59-year-old woman.

Key words: Aspiration cytology; carcinoma; matrix producing; metaplastic

Introduction
Matrix producing carcinoma (MPC) of the breast is a rare variant of metaplastic carcinoma with a total of approximately 240 cases have been reported to date. [1] It was first described by Wargotz and Norris in 1989. [2] Direct transition of carcinomatous elements to cartilaginous or osseous matrix without an intervening spindle cell component make the major diagnostic histopathologic criteria. [3] Reports dealing with cytological features of MPC are far more scarce with only a few cases reported to date. [3-5]

The cellular origin of the MPC remains unclear. [6] It has been suggested that the tumor cells have the features of both epithelial and mesenchymal cells. [3,6]

Herein, we report a case of a MPC in a 59-year-old woman with cytological, histopathological and immunohistochemical findings.

Case Report
A 59-year-old woman presented with a palpable, hard nonmobile mass in her left breast. The skin over the mass was normal, and the nipple was not retracted. No axillary lymphadenopathy was present. Fine needle aspiration (FNA) of the mass was performed. FNA smears showed ovoid to cuboidal shaped and spindly cells with bland nuclear features embedded in a chondromyxoid background. These cells also formed sheet-like clusters [Figure 1a]. Between these neoplastic tissue fragments, loosely cohesive, highly pleomorphic epithelial cells with hyperchromatic and angulated nuclei were present [Figure 1b]. In some microscopic fields, a transition could be observed between epithelial cells and the matrix-stromal complex. Some chondrocyte like cells were found to be present in the metachromatic extracellular matrix [Figure 1c]. One of the aspirates was mostly composed of necrosis [Figure 1d]. Cytological findings indicated the possibility of a matrix-producing variant of metaplastic carcinoma.

Breast conserving surgery was performed. The tumor was 2 cm in its greatest dimension. Histopathological examination showed invasive carcinoma with an abrupt transition to chondromyxoid matrix without an intervening spindle cell component [Figure 2a and b].

Medium to large sized chondrocyte-like tumor cells embedded in a chondromyxoid matrix sometimes formed
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discrete nodules [Figure 2a]. Focal areas of the matrix ranged from mucoid appearing to hyaline cartilaginous matrix [Figure 2c]. The chondromyxoid matrix was multifocal and mostly of high grade and showed direct transition to a carcinomatous component, which was composed of high grade undifferentiated mammary carcinoma with necrotic areas [Figure 2d]. The tumor cells were negative for estrogen and progesterone receptors and were also negative for cerb-B2. Overt carcinoma cells of the tumor diffusely stained by pancytokeratin and epithelial membrane antigen (EMA) while focal positivity was present in matrix producing areas. S100 protein was diffusely positive in both compartments. Two sentinel lymph nodes dissected were negative.

The patient was treated with six cycles of chemotherapy and local radiation therapy and is well after surgery for 30 months.

Discussion

As a rare entity, cytopathological features of MPC of the breast are limited to individual case reports. In cytological smears, cuboidal to oval and sometimes spindly shaped tumor cells as single or in sheets of cells embedded in a myxoid matrix devoid of any sarcomatous spindle cells are the hallmarks of MPC. If FNA biopsy sample shows myxoid matrix material, this should be a clue to the presence of a mesenchymal component in a breast mass. Based on the cellular components of the smears, differential diagnosis can vary. One of the differential diagnoses is the conventional metaplastic carcinoma with myxoid chondrosarcomatous differentiation. In such cases, diagnosis depends on the identification of sarcomatous spindle cells or osteoclastic cells.

Malignant phyllodes tumor should also be considered in the differential diagnosis due to the presence of various type of sarcomatous elements. However, the epithelial component, which is represented by sheets of epithelial cells and small, round/oval nuclei is benign in malignant phyllodes tumor, whereas the epithelial component of MPCs consists of moderately to poorly differentiated adenocarcinoma. Fat necrosis is another entity that can mimic metaplastic carcinoma, due to the presence of bizarre spindle and giant mesenchymal cells, as well as an atypical reactive epithelium.

The nature of the matrix component is changeable, which could be a mixture of cartilage and osteoid, mainly osseous metaplasia or mainly cartilaginous. Wargotz and Norris suggested that tumor cells of MPC might be of epithelial myoepithelial derivation according to the findings on electron microscopy. On the other hand, Okuyama et al. found that of the eight MPCs, none of the overt carcinoma cells stained with myoepithelial markers. Metastatic breast cancer is usually regarded as triple negative breast cancer or basal-like breast cancer. This could be important to explore the etiology of metaplastic change. It is proposed that basal-like cancers may undergo epithelial-mesenchymal transition, which also has been reported to be an etiological factor in metaplastic carcinoma. Our case was also a triple negative breast cancer with both epithelial and mesenchymal compartments staining positive with pancytokeratin, EMA (overt carcinoma cells were diffusely positive, chondromyxoid areas were focally positive) and S100 (both components diffusely positive).
Histologically carcinomatous component of MPC’s consists of moderately to poorly differentiated adenocarcinoma, which usually shows central necrosis. The metaplastic chondromyxoid matrix may show a range of pleomorphism and cytological atypia. Atypical cartilaginous matrix namely the “high grade matrix”, has been shown to be an adverse prognostic factor among patients with MPC[2] whereas Downs-Kelly et al.[10] found no correlation between matrix grade and tumor recurrence. Furthermore, high proportion of matrix was found to have a more favorable clinical course.[10]

Prognostic data regarding MPC is conflicting. Equivalent to or more aggressive behavior than invasive ductal carcinomas matched for patient age, stage and tumor grade have been reported.[1,10] Locoregional recurrence rates were also found to be strikingly higher.[2] Postoperative radiation therapy after breast conserving surgery seems to be important for controlling local disease as a high rate of locoregional recurrences were detected without postoperative radiation.[2] Since most of these tumors are hormone receptor, and HER2 negative, systemic chemotherapy after surgery is the mainstay of treatment.[1] As is the case in our patient, axillary lymph node metastases tend to be rare in MPC.[1,2,10] However, aggressive systemic therapy is also thought to be necessary regarding the high rate of distant recurrences in spite of the absence of lymph node metastases.[2]

Conclusion

Matrix producing carcinoma is very rare but at the same time an aggressive subtype of metaplastic carcinoma. This subtype of metaplastic carcinoma should be kept in mind when chondromyxoid ground substance is seen in cytological slides. Accurate preoperative diagnosis of this rare tumor could also be achieved when all cytologic criteria is carefully evaluated in FNA biopsy samples of the breast.

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