Case Report Two cases of matrix-producing carcinoma showing chondromyxoid matrix in cytological specimens

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Abstract: Matrix-producing carcinoma (MPC) is extremely rare. Limited reports have described the cytological aspects of MPC. Herein, we present 2 cases of MPC, both of which showed ring-enhancement on magnetic resonance imaging (MRI) and chondromyxoid matrix on cytological specimens. In these cases, the diagnosis of MPC was preoperatively suspected. Recognizing extracellular matrix as chondromyxoid matrix on the cytological specimen is important in making a distinction between MPC and mucinous carcinoma. They share some features on cytology and MRI (ring-enhancement) but have different prognoses and involve different approaches for obtaining the histological specimens is that tumor cells usually distribute peripherally in MPC in contrast to the relatively uniform distribution of mucinous carcinoma. Therefore, it would be helpful if the diagnosis of MPC can be suspected by examination of the cytological specimen.

Keywords: Matrix-producing carcinoma, chondromyxoid matrix, mucinous carcinoma, cytology, magnetic resonance imaging

Introduction

Matrix-producing carcinoma (MPC), a type of breast carcinoma that produces chondromyxoid matrix, is extremely rare and accounts for only 0.1% of all breast carcinomas [1]. MPCs have been recently renamed as "metaplastic carcinomas with mesenchymal differentiation" under the broader category of metaplastic carcinomas, according to the World Health Organization classification of 2012 [2]. Metaplastic carcinomas of any type are also rare and account for 1-5% of all breast carcinomas [1]. The metaplastic carcinoma category also includes spindle cell carcinoma, squamous cell carcinoma, and other rarer subtypes [2]. Instead of metaplastic carcinoma with mesenchymal differentiation, we have continued to use the more common term, MPC, which the reader can easily understand.

There have been only a limited number of welldescribed cases showing cytological aspects of MPC [1, 3-5]. Herein, we present the cytological appearance of 2 cases of MPC. The importance of the distinction between MPC and its potential mimicker on cytological specimens, mucinous carcinoma, is further discussed.

Case report

Case 1

A 72-year-old woman presented with a palpable mass in the left breast. A mammography revealed segmental calcifications, and ultrasonography (US) examination showed a mass with dimensions of $25 \times 21 \times 14$ mm in the bottom area of the left breast. Axillary lymph node swelling was not observed on palpation and US. Magnetic resonance imaging (MRI) with contrast enhancement revealed that the mass displayed rim enhancement (Figure 1A). Subsequently, fine-needle aspiration biopsy (FNAB) exhibited atypical epithelial cell clusters with nuclear enlargement and prominent nucleoli separated from apparent chondromyxoid matrix (Figure 2A). MPC was suspected. There was no abnormality noted on blood examination, including tumor markers. A left partial mastec-



Figure 1. Magnetic resonance imaging A, B. A: Case 1; B: Case 2. The masses exhibited rim enhancement.

tomy and sentinel lymph node biopsy was performed. Intraoperative pathological examination of sentinel lymph nodes found the nodes to be free of carcinoma.

The surgically resected specimen showed a mass measuring 24 mm in maximal diameter. In the center of the mass, there is a whitish area surrounded by a tan-colored rim (**Figure 2B**).

The histological examination of the specimen showed that the tumor contained a central area with an abundance of chondromyxoid matrix. Carcinoma cells were predominantly distributed in the peripheral area with only occasional scattered cells in the central area (**Figure 2C**). The carcinoma cells were directly in contact with the chondromyxoid matrix without any spindle cell component (**Figure 2D**). The carcinoma cells were negative for estrogen receptor (ER), progesterone receptor (PgR), and HER2 by immunohistochemical staining. The final diagnosis of the carcinoma was MPC, stage pT2.

The patient was treated with adjuvant chemotherapy. She has been disease-free for 9 months since the operation.

Case 2

A 77-year-old woman presented with a left breast lump. Mammography and US revealed a

mass measuring 30 × 24 × 22 mm, and malignancy was suspected. MRI with contrast enhancement exhibited rim enhancement (**Figure 1B**). FNAB demonstrated atypical epithelial cells within abundant chondromyxoid matrix. Those cells had eosinophilic cytoplasm and showed loose cohesiveness. Their nuclei were enlarged and nucleoli were prominent (**Figure 3A**). The diagnosis of MPC was suspected. There was no abnormality noted on blood examination, including tumor markers. A left mastectomy and sentinel lymph node biopsy was performed. Intraoperative pathological examination of sentinel lymph nodes found the nodes to be free of carcinoma.

The surgically resected specimen showed a mass measuring 30 mm in maximal diameter. The mass was basically whitish with some yellowish areas distributed in the inner part, and some areas of outer part were tan-colored (Figure 3B).

The histological examination of the specimen showed that the tumor contained a central area with an abundance of chondromyxoid matrix and hyalinous matrix. Carcinoma cells were predominantly distributed in the peripheral area; in some parts, they were also present in the inner area, continuous with peripherally situated cellular area (**Figure 3C**). The carcinoma cells were directly in contact with the chon-



Figure 2. Cytological, macroscopic, and microscopic findings of Case 1. A. Cytological specimen. Atypical epithelial cell clusters and chondrmyxoid matrix were present separately (× 100, Papanicolaou staining). Inset: atypical epithelial cell clusters with nuclear enlargement and prominent nucleoli (× 600, Papanicolaou staining). B. The surgically resected specimen showed a mass (arrowheads), in the center of which there was a whitish area surrounded by a tan-colored rim. C. The histological examination of the specimen showed that the tumor harbored a central area with an abundance of chondromyxoid matrix, and that carcinoma cells were predominantly distributed in the pe-

ripheral area with only scattered cells in the central area (× 20). D. Carcinoma cells were in contact with chondromyxoid matrix directly without any spindle cell component (× 400).

dromyxoid matrix without any spindle cell component (**Figure 3D**). The carcinoma cells were negative for ER, PgR, and HER2 by immunohistochemical staining. The final diagnosis of the carcinoma was MPC, stage pT2.

The patient was treated with adjuvant chemotherapy. She has been disease-free for 3 months since the operation.

Discussion

The percentage of the matrixoccupying tumor area of MPC is 2-98% (median 18%) [6]. MPCs with < 10% of matrix account for 44% of cases [6]. Cases with chondromyxoid area < 10% do not display chondromyxoid substance, while those with > 10% occasionally exhibit chondromyxoid substance on FNAB [1]. As matrix is not always observed in FNAB specimens, in such cases, it would be almost impossible to diagnose MPC by cytology.

Preoperative diagnosis of MPC is not easy particularly because it is very rare, in addition to the abovementioned fact. Therefore, physicians are unfamiliar with its diagnosis by FNAB and radiological analysis. Rim-enhancement patterns on MRI which is one of the characteristics of MPC, as shown in our case, can also be observed in mucinous carcinoma [5, 7]. Regarding cytological specimens obtained by FNAB, both



Figure 3. Cytological, macroscopic, and microscopic findings of Case 2. A. Cytological specimen. Atypical epithelial cells within abundant chondromyxoid matrix were observed. Those cells had eosinophilic cytoplasm and showed loose cohesiveness. Their nuclei were enlarged and nucleoli were prominent (× 600, Papanicolau stain). B. The surgically resected specimen showed a mass which was basically whitish with some yellowish areas distributed in the inner part, and some areas of outer part were tan-colored. C. The histological examination of the specimen showed that the tumor contained a central area with an abundance of chondromyxoid matrix and hyalinous matrix.

Carcinoma cells were predominantly distributed in the peripheral area; in some parts, they were also present in the inner area, continuous with peripherally situated cellular area (× 20). D. The carcinoma cells were directly in contact with the chondromyxoid matrix without any spindle cell component (× 600).

MPC and mucinous carcinoma are expected to show extracellular substance: mucinous carcinoma are expected to show abundant extracellular mucin surrounding carcinoma cell clusters and weaker nuclear atypia than MPC [8]. In this case, we could preoperatively suspect the correct diagnosis; cellular atypia which exceeded that of typical mucinous carcinoma hinted towards the possibility of MPC. Subsequently, the presence of chondromyxoid matrix, which is different from mucin whirling around carcinoma cells, further hinted towards the diagnosis of MPC [1, 3-5].

Making the distinction between MPC and mucinous carcinoma would determine where to obtain the histological specimen especially when neoadjuvant therapy is considered after obtaining the cytological diagnosis. Generally in breast carcinoma, the histological specimen must be obtained by biopsy for conducting neoadjuvant therapy. because the status of ER, PgR, and Her2 evaluated by immunohistochemistry affect the treatment option [9]. At the time of obtaining the histological specimen of MPC by biopsy, the following factor should be considered: the inner part of the tumor might not provide enough tumor

cells to be evaluated by immunohistochemistry owing to their predominant existence at the outer part of the tumor. This notion is reinforced by observing the histological specimens of our 2 cases. Meanwhile, tumor cells of mucinous carcinoma usually distribute throughout the tumor [10]. Thus, it is usually not required to consider where to obtain histological specimen in such cases.

From the viewpoint of prognosis, an accurate distinction between MPC and mucinous carcinoma is important. According to a multicenter study, MPC has a worse prognosis than ductal carcinomas in stage pT3 or pT4, but there is no difference in prognosis between MPC and ductal carcinomas in stage pT1 or pT2 [11]. On the other hand, mucinous carcinoma shows a more favorable prognosis than ductal carcinoma [12]. As our 2 cases of MPC were stage pT2, the prognosis might be expected to be similar to that of ductal carcinomas.

In conclusion, the present 2 cases illustrate an exceedingly rare tumor subtype, MPC, especially focusing on cytological analysis as well as MRI findings. Recognizing extracellular matrix as chondromyxoid matrix on the cytological specimen is important in making a distinction between MPC and mucinous carcinoma. They share some features on cytology and MRI but have different prognoses and might involve different approaches for obtaining histological specimens for neoadjuvant therapy.

Disclosure of conflict of interest

None.

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