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Case Report

A rare case of metaplastic carcinoma of the breast that could be diagnosed with preoperative core needle biopsy and the improbability of skin invasion

Keiichi Takahashi*

Takahashi Breast and Gastroenterology Clinic, Osaka, Japan

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ABSTRACT

Background: Metaplastic carcinoma of the breast (MCB) is a rare type of breast cancer that accounts for 1% of all cases of invasive breast cancer. This MCB is categorized into special types of breast cancers.
MCB is characterized by the presence of multiple components and transitional cells between two tissue types, because the tumor cells differentiate in different directions and degrees into a variety of cells other than glandular cells. However, MCB is often misdiagnosed preoperatively as ordinary breast cancer based on several tissue imaging findings. The diagnosis of MCB is highly difficult with cytology and even with core needle biopsy (CNB). The diagnostic rate of MCB with CNB is as low as 40%, with the remaining 60% diagnosed as ordinary mammary duct carcinoma.
MCB is unlikely to respond to anticancer drugs, surgery as the initial treatment is prioritized over preoperative anticancer drug therapy. Therefore, accurate preoperative diagnosis is important.
To date, no report has described the likelihood of skin invasion in a patient with MCB.
Case presentation: This case report describes a 67-year-old woman with an unremarkable past or family history, who visited the author's clinic after noticing a swelling of her right nipple and a lump located around her right nipple 2 months previously. CNB was performed.
Results: The pathological findings of the CNB specimen indicated metaplastic carcinoma. Metaplastic carcinoma with sarcomatoid changes, i.e., spindle cell carcinoma or matrix-producing carcinoma, was suspected. There was no skin invasion despite the presence of both a large mass and large swelling of the nipple in this patient.
Conclusions: For MCB, preoperative anticancer drug therapy could be avoided and surgery may be considered the initial treatment.
Despite the presence of a large mass, MCB may be less likely to cause skin invasion than ordinary breast cancer of the same size.

1. Introduction

Breast cancer originates from glandular epithelial cells, therefore, most breast cancers are adenocarcinomas. However, the epithelium of adenocarcinoma may exhibit a proliferative pattern of non-glandular structures accompanied by metaplastic changes in the squamous epithelium, spindle cells, bone, or cartilage in part or entirely [1–4]. Previously, these cancers were classified as squamous cell carcinoma, spindle cell carcinoma, or cancer accompanied by osseous or cartilaginous metaplasia,; however, they were collectively classified as MCB in 2003 according to the World Health Organization classification. It is a serious concern that MCB is often misdiagnosed preoperatively as ordinary breast cancer. Since anticancer agents are not effective for MCB, surgery must be the preferred first choice treatment over preoperative anticancer drug therapy.

To date, no report has described both the likelihood of skin invasion and its incidence in a patient with MCB.

Herein, a case of MCB identified using CNB is reported.

2. Case presentation

The present patient was a 67-year-old woman with unremarkable past or family history, who visited the author's clinic after

Abbreviations: MCB, Metaplastic carcinoma of the breast; CNB, Core needle biopsy; MMG, Mammography; US, Ultrasonography.

* Takahashi Breast and Gastroenterology Clinic, Yamazaki Seiren Bldg. 2F, 6-2-22, Uehonmachi, Tennoji-Ku, Osaka City, Osaka, 543-0001, Japan.
E-mail address: takahashi-nyusen@dolphin.ocn.ne.jp.

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noticing a large swelling of her right nipple and a lump around her right nipple 2 months previously. There were no retraction and invasion of the skin, and no papillary secretions. Several axillary lymph nodes were swollen. Mammography (MMG) revealed a tumor shadow measuring 37 mm in diameter in the left S region, which was diagnosed as category 5 (Fig. 1a and b). Ultrasonography (US) showed a poorly demarcated mass measuring 33.4 × 36.8 × 34.9 mm with irregular margins and inhomogeneous content in the right EABCD region (Fig. 2a and b). Color Doppler US showed a hypervascular pattern (Fig. 2c).

CNB was performed. The linear shadow passing from the right side transversely and slightly obliquely downwards anterior to the tumor in Fig. 2d was the needle used in the biopsy. The needle passed through the solid tumor steadily and accurately (Fig. 2e).

The pathological findings of the CNB specimen indicated metaplastic carcinoma. Highly polymorphic cells accompanied by necrosis and degeneration were found to have proliferated in sheet formations. Basophilic extracellular matrix was observed between the cells. The connectivity of the tumor cells was poor. Intraductal components of high-grade ductal carcinoma in situ showing solid proliferation of atypical epithelial cells were found. On the basis of these findings, metaplastic carcinoma with sarcomatoid changes, i.e., spindle cell carcinoma or matrix-producing carcinoma, was suspected (Fig. 3a, b, c, d).

Computed tomography examination showed a lobulated mass around the right nipple. The marginal contrast effect was outstanding, but the inside of the tumor was relatively uniform, and the contrast effect was poor. These findings did not lead to a diagnosis of the specific breast cancer type. There was no infiltration of large pectoral muscles. The right axillary lymph nodes were swollen (Fig. 4a and b). Magnetic resonance imaging showed that the tumor was lobulated and the boundary of the major axis 53mm with infiltration just below the nipple was partially unclear. The particular breast cancer type could not be diagnosed on the basis of these findings (Fig. 5).

The patient underwent right mastectomy and right axillary lymph node dissection. The surgical findings were as follows: tumor size, 6.50 × 6.00 × 3.00 cm, metaplastic carcinoma, negative for estrogen receptor (ER), negative for progesterone receptor (PgR), negative for human epidermal growth factor receptor 2 (HER2), ly1, vo and negative resection margins. There were 25 metastatic lymph nodes (25/37), with levels I (16/27), II (2/3), III (6/6), and Ic (1/1).

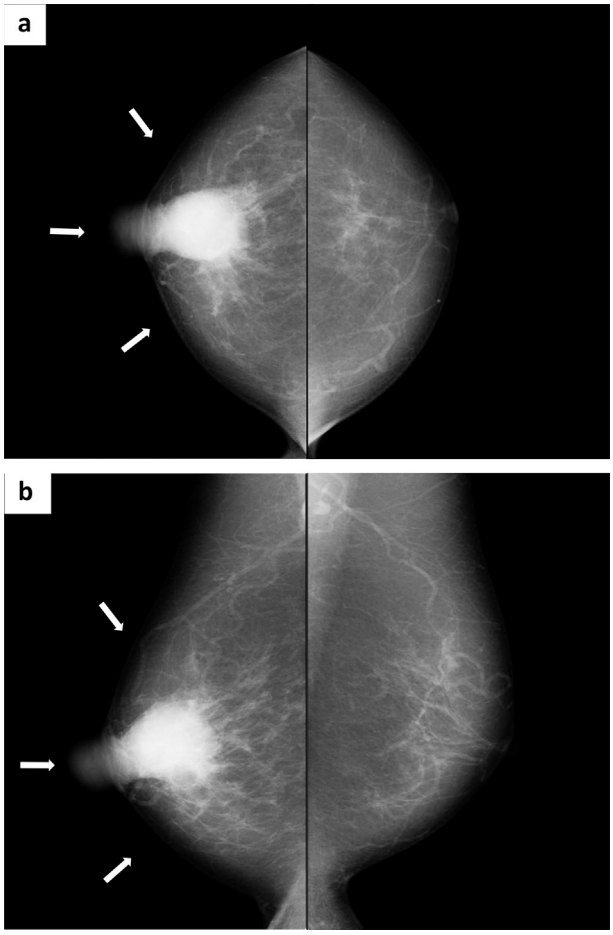

Fig. 1. Mammography; (a, b). Mammography revealed a tumor shadow measuring 37 mm in diameter in the left S region, which was diagnosed as category 5.

3. Discussion

MCB is a rare type of breast cancer that accounts for 1% of all cases of invasive breast cancer [1,5–8]. This tumor is characterized by the presence of multiple components and transitional cells between two tissue types, because the tumor cells differentiate, in different directions and degrees, into a variety of cells other than glandular cells.

MCB exhibits the histological patterns of epithelial tumors and is included in the category of special breast cancers.

MCB usually presents as a palpable mass and occurs among women older than 50 years [9,10]. Further, it is characterized by a larger size and more rapid growth than ordinary invasive ductal carcinoma [11–14].

The tumor is clearly demarcated, and the cut surface is solid and may be glossy or may show cystic changes according to the histological type. The metaplastic component is considered to be derived from the adenocarcinoma component, usually showing a wide variety of transitional features. Although there are no definite diagnostic criteria for metaplastic carcinoma, its diagnosis is generally made when metaplastic components constitute most of the tumor. In metaplastic carcinoma, the tumor cells develop in different directions and show different degrees of differentiation into cells other than glandular cells. Therefore, from a developmental viewpoint, metaplastic carcinomas are classified into pure epithelial metaplastic carcinomas (which show epithelial differentiation such as squamous cell, adenosquamous, or spindle cell carcinoma) and mixed epithelial/mesenchymal metaplastic carcinomas (which include mesenchymal differentiation, such as bone/cartilage metaplasia). These classifications are based on the concept of metaplastic carcinoma originally reported by Wargotz et al., in 1989.

Most metaplastic carcinomas consist of various proportions of squamous metaplasia, spindle cell, bone/cartilage metaplasia, and matrix components. Therefore, they vary in morphology and are considered to have no specific cytological characteristics.

For this reason it is difficult to diagnose MCB, which shows a variety of tissue imaging findings, with cytology [5,7,11,15], and even more difficult with CNB. The diagnostic rate of MCB with CNB is as low as 40%, with the other 60% diagnosed as ordinary mammary duct carcinoma [7,11]. Because MCB is unlikely to respond to anticancer drugs, achieving a pathological response of less than 10% [7,16–18], surgery as the initial treatment is prioritized over preoperative anticancer drug therapy. Therefore, accurate preoperative diagnosis is important.

However, the diagnosis of MCB cannot rely on imaging features alone because MCB has no distinctive imaging findings [1,2]. Neither MMG nor US have provided specific images [19]. MCB

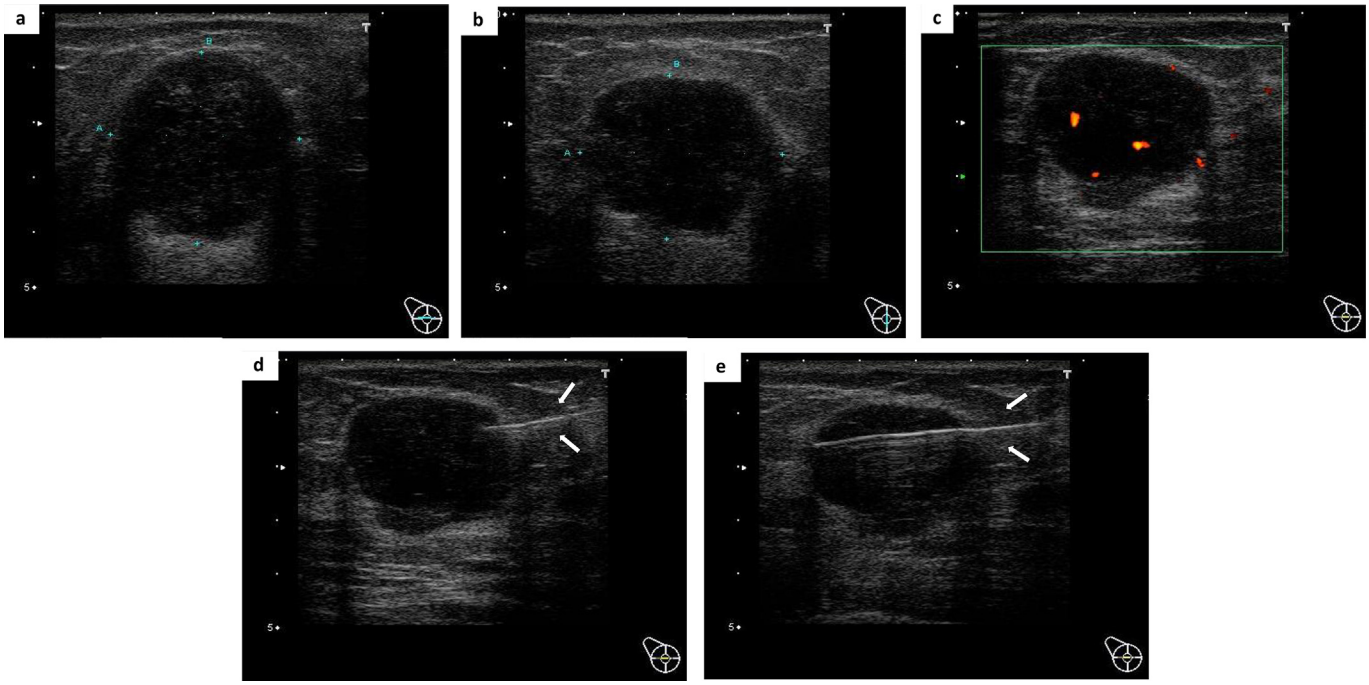

Fig. 2. Breast ultrasonography; (a, b). Ultrasonography showed a poorly demarcated mass measuring 33.4 × 36.8 × 34.9 mm with irregular margins and inhomogeneous content in the right EABCD region. **c.** Color Doppler US showed a hypervascular pattern. **d.** The linear shadow passing from the right side transversely and slightly obliquely downward anterior to the tumor is the needle used in the biopsy. **e.** The needle passed through the solid tumor steadily and accurately.

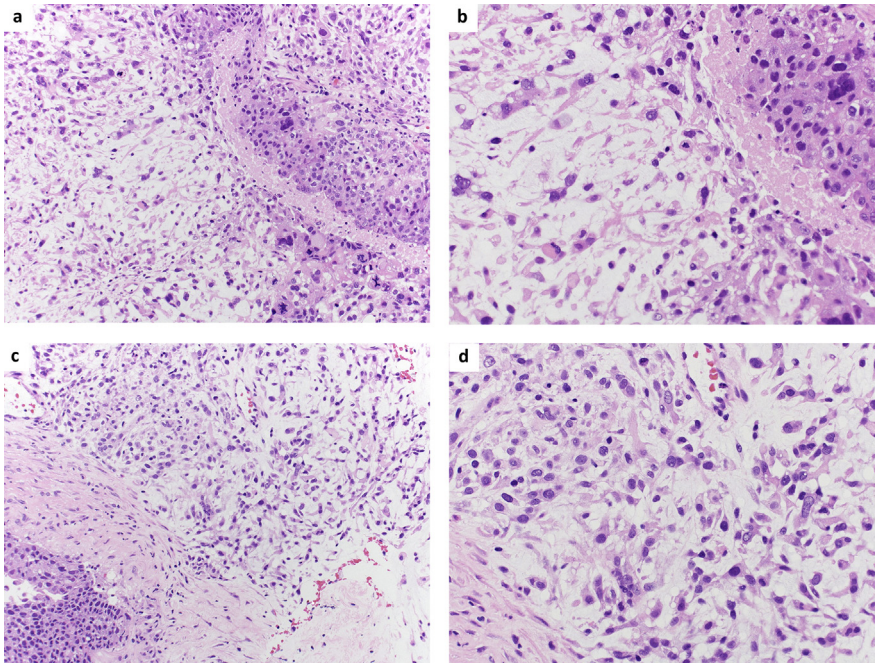

Fig. 3. Pathological analysis; (a, b, c, d). (3a: 【H-Estain, x200】, 3b: 【H-Estain, x400】, 3c: 【H-Estain, x200】), 3d: 【H-Estain, x400】. The pathological findings of the CNB specimen indicated metaplastic carcinoma. Highly polymorphic cells accompanied by necrosis and degeneration were found to have proliferated in sheet formations. Basophilic extracellular matrix was observed between the cells. The connectivity of the tumor cells was poor. Intraductal components of high-grade ductal cancer in situ (DCIS) showing solid proliferation of atypical epithelial cells were found. Based on these findings, metaplastic carcinoma with sarcomatoid changes, i.e., spindle cell carcinoma or matrix-producing carcinoma, was suspected.

demonstrates several benign features similar to those of ordinary breast cancer in MMG and US, and subsequently may be misdiagnosed as benign lesions [12,13]. This makes preoperative diagnosis even more difficult.

In most cases, the tumors are triple negative tumors, i.e., immunohistologically negative for ER, PR, and HER2/neu [11,14], and the prognosis is reportedly poorer than that of other histological types. The incidence of axillary lymph node involvement is

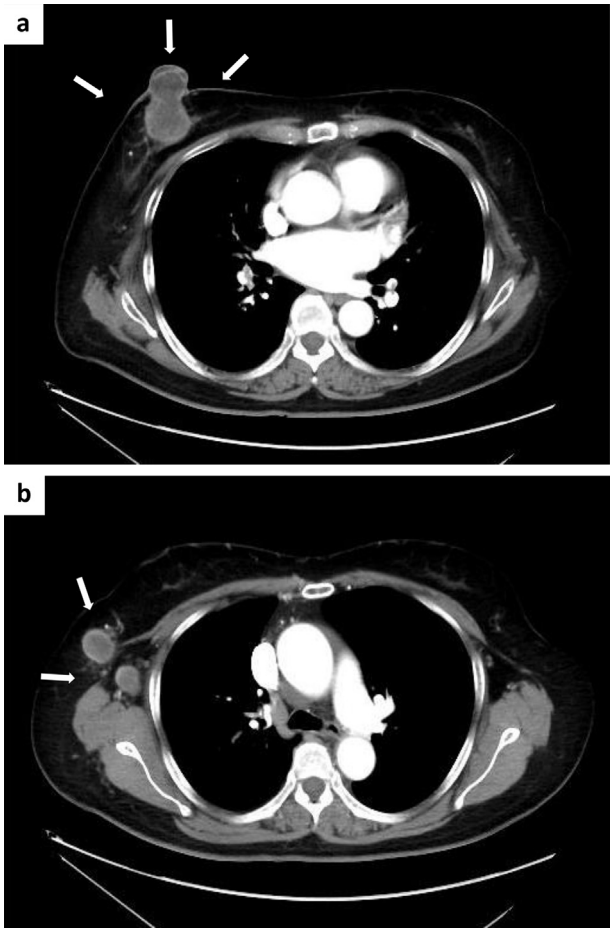

Fig. 4. Computed tomography; (a, b). Computed tomography examination showed a lobulated mass around the right nipple. A marginal contrasting effect is outstanding, but the inside is relatively uniform, and the contrasting effect is poor. It does not lead to a diagnosis of the specific breast cancer type. There is no infiltration of large pectoral muscles. Right axillary lymph nodes are swollen.

Fig. 5. Magnetic resonance imaging. Magnetic resonance imaging examination showed the tumor is lobulated and the boundary of the major axis 53 mm with nipple infiltration just below the nipple is partially unclear. It cannot be diagnosed to be specific findings in a particular breast cancer tissue type.

variable ranging from 8% to 40% [9,11,14,20,21]. There is high hematogenous metastatic potential to the lung and bone rather than lymphatic spread [10,19,21]. Local recurrence and distant metastasis were frequently found in more than half of MCB cases during 5 years of follow-up [22–24].

To date, no report has described both the likelihood of skin invasion and its incidence in a patient with MCB.

In this case, no skin invasion was observed despite the presence of both a large mass and large swelling of the nipple. The tumor proliferation mechanism of MCB is somewhat different from that of an ordinary ductal carcinoma of the breast [8].

This may be related to the lower incidence of lymph node metastasis than that of typical ductal carcinoma. MCB may be unlikely to cause direct skin infiltration despite the presence of a large mass.

Patients with MCB have worse outcomes in terms of 5-year survival rates, ranging from 49% to 68% [21,23]. According to Wargotz et al., the prognosis varies among different histological subclassifications, with the 5-year survival rate being 63% for squamous cell carcinoma and 64% for spindle cell carcinoma. The tumors often test positive for cytokeratin (CK)5/6, CK14, epidermal growth factor receptor, and p63 [5,7,22,25]. Although high-grade tumors are frequent, mild nuclear atypicality is exceptionally seen in low-grade adenosquamous carcinoma and fibromatosis-like metaplastic carcinoma.

MCB is less responsive to neoadjuvant presurgical chemotherapy [3,7,15,17,18], achieving a pathological response of less than 10% [7,8]. Therefore, priority should be given to initial surgery [7,8]. Furthermore, adjuvant chemotherapy is also unsuccessful [3,8,26].

The prognosis of patients is influenced by the type of existing metaplastic components; therefore, it is necessary to perform appropriate histopathological subclassification.

4. Conclusion

MCB is often misdiagnosed preoperatively as ordinary breast cancer.

MCB may be less likely to cause skin invasion despite the presence of a large mass than ordinary breast cancer of the same size.

Because anticancer agents are ineffective for MCB, surgery must be selected as the initial treatment. Moreover, depending on the case, postoperative adjuvant chemotherapy should not be used. Patients receiving postoperative adjuvant chemotherapy should be selected carefully.

If the preoperative histological examination shows the presence of components such as squamous epithelium, spindle cells, or metaplastic stroma even in small amounts, extensive sampling through surgical biopsy should be proactively recommended to avoid misdiagnosis. Increasing the awareness of MCB might reduce the probability of misdiagnosis.

When a tumor presents a variety of histological features, it is important to exercise caution in the diagnosis and treatment while considering the possible differential diagnosis of MCB, despite the rarity of this tumor.

The patient provided her informed consent for the publication of her clinical details and any accompanying images about this case report.

Ethical approval

IRB/Ethics Committee ruled that approval was not required for this study.

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Author contribution

Keiichi Takahashi.

Conflict of interest statement

The author declares no conflict of interest.

Guarantor

Keiichi Takahashi.

Research Registration Number

Not applicable.

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