A Case of Pure Mucinous Breast Carcinoma in a 25-Year-Old Female Who Showed Complete Pathological Response to Neoadjuvant Chemotherapy despite Poor Clinical Response

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Established Facts

- Mucinous breast carcinoma is a rare histological subtype in young patients and usually presents without lymph node involvement.
- The pathological characterization of response to neoadjuvant chemotherapy (NAC) in mucinous breast carcinoma is rarely reported.

Novel Insights

- This case report presents pure mucinous breast carcinoma in a 25-year-old female with axillary lymph node metastasis.
- Complete pathological response of pure mucinous breast carcinoma to NAC was found despite poor clinical response.

Keywords

Mucinous breast carcinoma · Neoadjuvant chemotherapy · Complete pathological response

Abstract

Introduction: Mucinous breast carcinoma is a rare histological subtype of primary breast cancers accounting for 1–6%. It is a rare histological variant in young patients and usually presents without lymph node involvement, and its pathological response to neoadjuvant chemotherapy is rarely reported. **Case Presentation:** Pure mucinous breast carcinoma in a 25-year-old female was treated with neoadjuvant chemotherapy every 3 weeks for 8 cycles. After the fifth cy-

cle, the mass size showed no change. We performed modified radical mastectomy in the left breast and axillary lymph node clearance. However, the pathological report showed a complete elimination of both the breast tumor and axillary lymph nodes, which were filled with mucus but did not contain malignant cells. **Discussion:** Chemotherapy was profoundly effective against the tumor cells, but ineffective against large amounts of extracellular mucus. Even though the cancer cells were sensitive to chemotherapy, the volume of mucinous cancer could not be reduced. **Conclusion:** In summary, the evaluation criteria of tumor response to chemotherapy based on maximum diameter only should be considered insufficient for mucinous carcinoma.

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Introduction

Mucinous carcinoma of the breast (MBC) is a rare histologic subtype accounting for 1–6% of all primary breast cancers [1]. These tumors frequently develop in postmenopausal females and are rarely reported in young patients [1, 2]. They usually have a better prognosis without lymph node involvement in contrast to the non-special type [3, 4]. Neoadjuvant chemotherapy (NAC) is the standard of care for patients with stages II and III breast cancer who might benefit from breast-conserving surgery after downstaging of their disease [5–7]. Response and histological changes after NAC have been widely reported, mostly in invasive ductal carcinoma. However, NAC is not usually used in mucinous carcinomas because they present as small, slow-growing, and human epidermal growth factor receptor 2 (HER2) negative [4, 5] tumors. Therefore, there is a lack of pathological characterization of response to NAC in MBC. In this study, we report a 25-year-old Chinese female with a pure mucinous breast carcinoma (PMBC) and axillary lymph node metastasis who showed pathological complete response (pCR) to NAC despite poor clinical response.

Case Presentation

A 25-year-old female presented with a 3-year history of a slow-growing mass in her left breast. Her past medical history was unremarkable. Clinical examination revealed a large regular mass in the upper outer quadrant of the left breast and palpable ipsilateral axillary active lymph nodes. Ultrasonography revealed an irregularly shaped, hypoechoic lesion with mixed solid and cystic components at the 12–1 o'clock position in the left breast, measuring 60 × 18 × 45 mm in diameter (Fig. 1). In addition, there were three abnormal left axillary lymph nodes, suggestive of significant lymph node metastasis. Magnetic resonance imaging (MRI) revealed a hypointense, irregular mass measuring 58 × 20 mm in the left breast laterally that showed mild enhancement in contrast sequences and a slightly hyperintense sequence on T2 and multiple enhanced left axillary lymph nodes (Fig. 2). The patient underwent core needle biopsy of the left breast mass and fine-needle biopsy of the nodes in our hospital (Fig. 3), and both showed that at least 90% of the contents in PMBC were mucinous. Immunohistochemical analysis of the left axillary lymph node resection biopsy revealed that 90% of the tumor cells were strongly positive for estrogen receptor (ER) and progesterone receptor (PR), but negative for HER2 (Fig. 3). The patient's TNM staging was cT3N1M0, and stage IIIA was confirmed [8]. Therefore, she received NAC consisting of 4 cycles of epirubicin 90 mg/m² (intravenous) plus cyclophosphamide 600 mg/m² (intravenous), followed by 4 cycles of paclitaxel 180 mg/m² (intravenous) every 3 weeks prior to surgery. After cycle 4 (12 weeks), the tumor size remained unchanged by breast ultrasound examination. MRI revealed an unenhanced mass in the left breast, approximately 60 mm in diameter, and a higher hyperintense sequence on T2 (Fig. 2). After cycle 5 (15 weeks), ultrasound examination showed that the mass size was still unchanged. Based on the patient's strong wish, we performed modified radical mastectomy (retains the areola and nipple) of the left breast and axillary nodes

Fig. 1. a Ultrasonography revealing an irregularly shaped, hypoechoic lesion with mixed solid and cystic components at the 12–1 o'clock position in the left breast, measuring >5 cm in diameter (white arrows).

clearance in November 2018. The pathological report showed a complete elimination of both the breast tumor and axillary lymph nodes, which were filled with mucus but did not contain malignant cells (Fig. 4). A 60-mm mucin lake matched the original tumor size. Mucin was also seen in 2 of the 6 axillary lymph nodes, both of which were filled with mucus and were thought to be a response to chemotherapy. Interestingly, residual mucin was co-located with the initial tumor in the breast as well as in the axillary lymph nodes. The pathological assessment of the therapeutic response was pCR [9, 10], pathological staging was ypT0N0M0 [5, 11]. Postoperatively, she continued to receive the remaining 3 cycles of paclitaxel (180 mg/m²) every 3 weeks. The chemotherapeutic course was completed in February 2019, and the toxicities were tolerable. She then received adjuvant radiotherapy. The patient is alive for 15 months from the initial diagnosis, without evidence of relapse.

Discussion

This case report is interesting for two reasons: first, it shows a PMBC in a 25-year-old female with axillary lymph node metastasis, which is a rare variant reported in young patients; second, although the clinical response was poor, pCR to NAC was found in this PMBC case.

MBC is a rare entity, representing 1–6% of the invasive breast carcinomas. It is defined as nests of cells floating in lakes of mucin [1]. There are two histologic subtypes: pure mucinous carcinoma when mucous components account for >90% of the tumors, and mixed mucinous carcinoma when the mucin is >50 but <90% [11, 12]. In this case, the core biopsy showed that >90% of the tumor tissue was mucus, consistent with the diagnosis of PMBC. Previous studies reported that PMBC is frequently found in postmenopausal patients, and its

Fig. 2. **a, b** Contrast-enhanced MRI scan showing mild enhancement in both the left breast tumor and the left axillary lymph nodes (prior to chemotherapy). **c, d** Contrast-enhanced MRI scan showing no enhancement in both the left breast tumor and the left axillary lymph nodes (after chemotherapy).

Fig. 3. Core biopsy. **a** Panoramic view of the tumor that is composed of multiple groups of neoplastic cells immersed in extracellular mucin ($\times 4$). **b** A left axillary swollen lymph node resection biopsy showing mucin lakes with cellular characteristics of the tumor ($\times 20$). **c** Ninety percent of the neoplastic cells are ER positive ($\times 40$). **d** Ninety percent of the neoplastic cells are PR positive ($\times 20$). **e** Ninety percent of the neoplastic cells are HER-2 negative ($\times 10$).

Fig. 4. Surgical resection. Mucinous lakes with no tumor cells in the breast tumor after NAC treatment (×4), corresponding to pCR.

prevalence in females younger than 35 years is 1% [2, 13]. MBC could be easily misdiagnosed as benign lesions because of its slow growth and well-circumscribed margins [2, 14], which are classified as low-grade tumors. Lymph node metastasis is rare, even with large primary pure or mixed MBC [11]. It was reported to be <5% in PMBC patients with axillary lymph node metastasis, which implied a favorable prognosis [15]. However, the only poor prognostic factor is lymph node involvement [1, 16]. Komenaka et al. [2] reported that the number of axillary lymph nodes involved was the only significant predictor of death. MBC shows a high probability of benignity but can also be a rare histological variation of a malignant tumor, which is not common in young patients. Therefore, a differential diagnosis of breast lumps in young patients is very important [17, 18].

NAC has become standard therapy for locally advanced or large operable breast cancer, leading to significant regression of cancer and thus making breast-conserving surgery possible [5–7]. As we know, few literature reports present the typical responses of MBC to NAC. The typical immunoprofile for PMBC is ER and/or PR positive and HER-2 negative [3, 4, 19]. These biological features suggest that NAC is not usually used in mucinous carcinoma [4, 5]. However, our patient did not meet the above criteria, as she had a large breast mass with axillary lymph node metastasis that suggested a more aggressive cancer. Fortunately, she showed a pCR after NAC. Clinical and radiological evaluations of the response to NAC are based on residual tumor size, and the correlation with pathologic response is often inaccurate. Tumor size remains the gold standard for evaluating residual tumor after chemotherapy [20]. Rajan et al. [21] reported that chemotherapy can significantly re-

duce the number of cells but has little effect on the overall size of some tumors. In other words, chemotherapy has a strong inhibitory effect on tumor cells but is ineffective against large amounts of extracellular mucus. Therefore, mucus is an important component of the residual tumor. In addition, the residual tumor may be associated with chemotherapy-induced tumor cell necrosis, fibrosis, or fibrocystic changes. These secondary changes may lead to an overestimation of the residual tumor size at the macroscopic level [22]. This phenomenon results in a discrepancy between the residual tumor size and the effect of chemotherapy. However, the pathological diagnosis is usually made by core biopsy before chemotherapy that, however, represents a tiny proportion of the whole tumor. Therefore, it is difficult to determine whether these obvious changes reflect the heterogeneity of the primary tumor or the response to chemotherapy. Furthermore, based on our patient alone, we cannot recognize the general trend of chemotherapy response. However, pathological examination indicates that the size of mucinous carcinomas may not be reduced even if the tumor cells are sensitive to chemotherapy.

Conclusion

In summary, maximum diameter may be an inadequate criterium to evaluate mucinous carcinoma response to chemotherapy. More detailed studies are needed to evaluate the pathological response of mucinous breast carcinoma to NAC.

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Statement of Ethics

We declare that the patient agreed to the description and publication of her case (including the publication of the pictures).

Disclosure Statement

There are no conflicts of interest for all authors.

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Author Contributions

Pei Du, Lucou Chen, and Chunjie Hou designed the research. Jinglan Tang and Ying Liu collected and organized the MR images. Qiaohong Hu collected and organized the ultrasound images. Hongfeng He and Kefeng Lu collected and organized the pathological images and results. Pei Du and Lucou Chen wrote the manuscript. All authors performed critical revision of the final manuscript. Pei Du, Lucou Chen, and Chunjie Hou supervised the study.

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