Metaplastic Breast Carcinoma (MBC), Primary Squamous Cell Carcinoma Subtype in A 49-Year-Old Woman: A Case Report

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ABSTRACT

Introduction: Metaplastic Breast Carcinoma (MBC) is quite a challenging case because metaplastic breast cancer is one of the rarest subtypes of invasive breast cancer. It is reported that MBC occurs only 0.2 to 1% throughout the world. The metaplastic changes can be squamous cells or other mesenchymal cell types. Clinically, MBC presents as a large palpable mass and may be associated with rapid growth. The size of MBC tends to be larger compared with other types of invasive breast cancer ranging from 1 to more than 10 cm. Although there are several main categories of MBC, some carcinoma can be difficult to classify due to their unusual histologic patterns. This case report study is to provide a clinicopathological overview and approach to MBC.

Case Presentation: We reported a 49-year-old woman who suffered from a breast mass that rapidly grew for less than one year. The microscopic findings showed squamous cell carcinoma. While molecular studies revealed triple negative results for hormone receptors although Human Epidermal Growth Factor Receptor 2 (HER2) overexpression was unusual (< 5%). Then, we confirmed with chromogen in situ hybridization (CISH) and there was no gen amplification for HER2. Microscopically, we found ductal carcinoma in situ and this finding supported breast origin.

Conclusions: Metaplasic carcinoma did not have any specific and distinctive signs clinically. Metaplasic carcinoma can be monophasic (with only a metaplastic component) or biphasic with two or more components. As treatment options, our patient received conventional chemotherapy. Metaplastic breast cancer is reported to have a lower response rate to conventional adjuvant chemotherapy and worse clinical outcome after chemotherapy than other forms of triple-negative breast cancer.

INTRODUCTION

Metaplastic breast carcinoma (MBC) is a heterogeneous group of invasive breast cancer characterized by their differentiation of the neoplastic epithelium towards squamous cells and/or mesenchymal-looking elements, including but not restricted to the spindle, chondroid and osseous cells [1]. MBC is a rare case because there are only 0.2 to 1% of MBC cases in the world were reported [1,2]. Clinically, MBC is similar to those estrogen receptor (ER) negative invasive breast cancer of no special type. Unfortunately, it is more likely to happen in an advanced stage. The most common presentation of MBC is a palpable mass with characteristics of a large-sized tumor and rapid growth [2,3].
pathognomonic mutations for metaplastic carcinomas have yet been identified. MBC encompasses a heterogeneous group of carcinomas that has features that overlap with squamous carcinoma of skin, sarcoma, and phyllodes tumors. The prognosis for some types of MBC is significantly worse than for non-MBC [1,5,6]. Subtypes with favorable prognoses are important to recognize. Therefore, we eagerly make this case study report which aims to provide a clinicopathological overview and approach to MBC. Here, we report metaplastic squamous cell carcinomas in a 49-year-old woman.

CASE PRESENTATION

A 49-year-old woman came to the hospital with a chief complaint of a lump on her left breast which has lasted for 10 months ago. She said that it started with a small lump and got bigger in the last 6 months. She had no history of breast cancer in her family. Her first menarche was at the age of 15 years old and she didn’t use any hormone replacement therapy yet. The patient and her husband decided to take traditional treatment in her village, but it has been worse since a month ago. She suffered from pain and her skin was ulcerated, filled with whitish discharge, and easily bleeding (Figure 1). Clinically, the patient was diagnosed with malignant tumor mammae sinistra T4N0Mx. The oncologist decided to do a mastectomy. The specimen was then sent to a pathology anatomy laboratory.

Macroscopically, the tumor size was huge. It was 18.5 x 5, 5 x 3.5 cm, and was 780 grams (Figure 2). It had fleshy color and easily bled. The tumor was continuously fixated in formalin buffer 10% for about 1 x 24 hours. At the incision, most components were solid. In addition, it also had a 5-centimeter-cystic space that contains brown liquid.

Microscopic examination revealed neoplastic cell proliferation arranged in solid, trabecular, and nested pattern infiltrative through fibrous stromal component, tubular component less than 10% (Figure 3). Morphologically, the cells are polygonal with eosinophilic cytoplasm. The nuclei were round to oval. While the nuclei membrane was irregular, the nuclear to cytoplasmic ratio increased with moderate nuclei pleomorphism. The nuclei chromatin was vesicular with single to multiple prominent nucleoli. A focal keratin pearl was observed (Figure 4). Mitosis was 25 per 10 high power fields. There was also ductal carcinoma in situ with cribriform patterns which showed the proliferation of cells limited at the mammary ductal lobular system with intermediate nuclear grade and moderate variability in shape, size, and polarization (Figure 5). At other focus, there was also angiovascular invasion by tumor cells. The tumor-infiltrating lymphocyte (TILs) was light in the peritumoral area.

![Figure 1. Pre-treatment breast tumor](image1)

![Figure 2. Macroscopic tumor post-mastectomy](image2)

![Figure 3. Tumor cell in solid, nest, and trabecular pattern with pleomorphic nuclei and broad eosinophilic cytoplasm (H&E staining, 100x magnification)](image3)

![Figure 4. Tumor cell with squamous morphology (insert and arrow) and scattered keratin pearl (head arrow) (H&E staining, 100x magnification)](image4)
The patient continued to do molecular testing. The result showed that estrogen receptor/progesterone receptor (ER/PR) was <1% negative (Figure 5) and HER2 +2 (Figure 6). For HER2 due to score +2, then it was continued with immunopathology chromogen in situ hybridization (CISH) which the probe results were; zydot 2C HER2/CEN17. The result of counting on 20 nuclei of tumor cells was the HER2 with a score was 29. The total Centromere of Chromosome 17 (CEN17) score was 24 and the ratio of HER2/CEN17 was 1.2. Thus, it can be concluded that there was no gene amplification of HER2.

DISCUSSION

The case was quite challenging because metaplastic breast cancer was one of the rarest subtypes of invasive breast cancer [1]. Metaplastic carcinoma constitutes a group of histopathologically distinct patterns with different outcomes although there is often an overlap [1,7]. Clinically, metaplastic carcinoma did not have any specific and distinctive signs. The tumors can be either present as well-circumscribed, circumscribed masses, or display indistinct and irregular borders [1,8]. Theoretically, cystic degeneration is common, in particular metaplastic carcinoma with squamous carcinoma. Compared with invasive breast carcinoma of no special type, metaplastic carcinoma tends to be large with the mean size of 3.9 cm, ranging from 2 to >10 cm. Metaplastic carcinoma can be monophasic (with only a metaplastic component) or biphasic with two or more components [9]. The WHO classification of tumor editorial board has maintained a descriptive classification system which is based on the type of metaplastic element. They are low-grade adenosquamous carcinoma, fibromatosis-like metaplastic carcinoma, spindle cell carcinoma, squamous cell carcinoma, and mixed metaplastic carcinoma [1,10].

Here, we found metaplastic squamous cell carcinoma, and for diagnosis or primary squamous cell carcinoma of the breast to be rendered, we already ruled out the primary cutaneous or metastatic squamous cell carcinoma from another site like lungs and cervixes. in a differential diagnosis, squamous cell carcinoma of the skin can arise from mammary skin or cutaneous appendages. We already ruled it out through clinical history which was based on anamnesis the first sign and symptom as a breast mass that continuously grew rapidly for less than 1 year. Skin carcinoma was generally first noted as an epidermal mass. Therefore, we did a careful examination for in situ carcinoma associated with skin or cutaneous appendages. Another differential diagnosis is metastatic origin of squamous cell carcinoma from lung and cervix organs. We do have a thorax x-ray imaging and gynecology examination which did not find any other tumor mass. Microscopically, we found a precursor lesion ductal carcinoma in situ as shown in Figure 3. The evidence of DCIS as a precursor lesion, in this case, supported its classification as MBC.

Mostly, more than 90% of metaplastic carcinoma was lack of expression of ER, PR, and ERBB2 (HER2). In our cases, our molecular examination showed a negative expression of ER and PR. However, at HER2 expression, we found +2, and then it was continued with CISH. Finally, it can be concluded that there was no gene amplification of HER2. Based on the clinicopathological results and molecular findings, the tumor had Nottingham grade 3 with pathological staging pT4NxpMx. We also found angiovascular invasion microscopically. Although lymph node metastasis was rare, distant metastasis at the lung and brain could be found.

There are no prognostic and predictive markers of therapeutic response supported for patients with metaplastic breast cancer [1,7,8]. Retrospective analysis has suggested that specific subtypes probably have distinct outcomes. Among the type of metaplastic carcinoma, high-grade spindle cell, squamous cell, and high-grade adenosquamous carcinoma are associated with the worse prognostic [1,6]. There is no difference
found in 5-year survival between positive hormone and negative hormone of metaplastic carcinoma. However, there was evidence that the rare forms of HER2-positive metaplastic carcinoma might be associated with a better outcome triple negative metaplastic carcinoma [1,4].

During treatment options such as triple-negative breast cancer, our patient received conventional chemotherapy consisting of doxorubicin in combination with cyclophosphamide and 5-fluorouracil. Although metaplastic breast cancer was reported to have a lower response rate to conventional adjuvant chemotherapy and worse clinical outcome after chemotherapy than other forms of triple-negative breast cancer. Some studies showed that adjuvant radiation improved both overall and disease-specific survival for all patients who were undergoing treatment for MBC. Patients receiving radiotherapy demonstrated 36% and 26% decrease in death from any causes and breast-related mortality, respectively. Our patient did not receive any adjuvant radiotherapy for MBC. In some literature, a significant survival advantage was observed in high-risk patients who were treated with mastectomy and adjuvant radiotherapy when they had tumors ≥ 5 cm and/or ≥ 4 metastatic axillary lymph nodes and chest wall invasion [1,3,8].

CONCLUSIONS

Metaplastic carcinoma does not have any specific and distinctive signs clinically. It is quite challenging to determine that squamous cell carcinoma is of breast origin. However, the evidence of ductal carcinoma in situ as a precursor lesion, in this case, supports its classification as MBC. Among the types of metaplastic carcinoma, squamous cell carcinoma is associated with the worse prognostic. As a treatment option, for triple-negative breast cancer, our patient receives conventional chemotherapy without any radiotherapy approach.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this paper.

Acknowledgment
There are no grants or funds that need to be acknowledged in this study. However, we would like to thank our patient for allowing us to report her case for educational purposes.

REFERENCES