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Neoadjuvant Therapy for HER-2 Positive Acantholytic Squamous Cell Carcinoma of the Breast: A Case Report

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1. Abstract

HER2-positive breast ASCC is exceptionally rare, its clinicopathological characteristics are insufficiently studied, and the implications of neoadjuvant therapy, comprising targeted treatment against HER2. Here we reported that a 58-year-old woman with a histopathological diagnosis of HER2-positive ASCC gave a neoadjuvant therapy of albumin-paclitaxel, carboplatin in conjunction with trastuzumab every 3 weeks. After mastectomy and axillary lymph node dissection, immunohistochemical diagnosis of ER, PR, and HER2 was positive, followed by 17 cycles of trastuzumab therapy and no indications of disease were detected. So this neoadjuvant therapy is of high value in HER2-positive ASCC patients.

2. Introduction

Squamous Cell Carcinoma (SCC) of the breast is an uncommon malignant tumor. The diagnostic condition is: 1) more than 90% of SCC malignant cells, 2) tumors independent of the overlying skin and nipple, and 3) other parts of primary SCC that need to be excluded. These tumors are believed to represent less than 0.1% (0.04% to 0.075%) of all malignant breast cancers [1]. SCC has several histopathological variants such as warts, spindle-shaped, basaloid, adenosquamous, adenoid, and undifferentiated types [2]. In 1947, ASCC represents a malignant epithelial tumor with a strong glandular pattern extending into the dermis, also called adenocaanthoma of the sweat gland. Almost two decades years, Muller reported about the tumor and its microscopic details related to epidermis, the existence of pseudoglandular elements, dyskeratosis, acantholysis, atypical mitosis, multiple parts of cell morphology, perineural extension. Thereafter, it was considered as a rare variant of SCC, also known as epithelium dyskeratoticum suffragans, adenoid squamous cell carcinoma, acantholytic squamous cell carcinoma, pseudoglandular squamous cell carcinoma. The tumor has distinctive histology compared to classic SCC, although its aggressiveness has been interpreted differently by several authors [3]. Clinical and radiological features are nonspecific, the tumors are resistant to therapy, and the prognosis is poor. The significance of this case lies in its rarity and good therapeutic effect.

3. Case Presentation

In November 2020, a 58-year-old female patient was confirmed the right breast lump for 4 years, accompanied by skin swelling and ulceration for 1 week. She has no family history of breast cancer and physical examination of the breast revealed a right breast mass approximately 8 cm×7 cm in size, the skin overlying the mass was dark red, and the central area erupted approximately 2 cm×2 cm in size. Pus and blood flowed out, and the right axillary lymph node was not swollen. Breast ultrasound showed a hypo-

echoic, heterogeneous solid mass. MRI confirmed the right breast mass with necrosis and invasion of surrounding tissue, adjacent skin, and breast fascia. No abnormalities were observed in the rest of the body. Due to the skin tear of the right breast mass, the wound was cleaned and the skin and tumor tissue was examined. Pathology suggests carcinoma of metaplasia considering ASCC. The immunohistochemical (IHC) staining presented ER; -, PR; -, HER2; 2~3+, Ki67; approximately 30% positive, CD34; positive vascular endothelium, S-100; -, HMB-45; -, Melan-A; -, respectively (Figure 1). Based on the above results, we diagnosed locally advanced (T4N1M0) HER2-positive breast cancer ASCC.

She started neoadjuvant treatment with albumin-paclitaxel (260 mg/m2), carboplatin (AUC=5), and trastuzumab (8mg/kg for the first dose and 6mg/kg for the second dose) every 21 days with no obvious side effects in November 2020. After 6 treatment cycles and periodic imaging assessment of efficacy, ultrasound showed that the mass decreased from 8.5 cm×6.3 cm to 1.5 cm×0.4 cm. MRI showed the reduction from 8 cm×6.5 cm to 2.4 cm×1.5 cm, the mass completely disappeared and the injured skin healed (Figure 2). A right mastectomy and a grade III axillary lymph node dissection were performed. The tumor stage was down to stage 0, ypTisN0cM0. After NAC, the pathology found interstitial fibrosis, histiocytic and multinucleated giant cell reaction, local hemorrhage, hemosiderin cell deposition, noninvasive cancer, and a small number of moderate ductal carcinoma in situ. A total of 37 axillary lymph nodes had no cancer metastasis (Figure 3). IHC: Catheter in situ: ER (30% moderate), PR (5% moderate), HER2 (3+), Ki-67 (approximately 30% negative), CK5/6 (-); myoepithelial: P63 (+), calponin (+); multinucleate giant cell infiltration area: AE1/AE3 (-), CD68 (histiocyte-). According to the Residual Cancer Burden scoring system recommended by the International Breast Collaborative Group for assessing the effectiveness of neoadjuvant therapy, it was determined that the invasive lesion had achieved complete remission. She received no radiation therapy for the right chest wall nor the right supraclavicular bone. Trastuzumab was continued for 17 cycles. According to the postoperative pathological results, ER and PR were positive, so anastrozole 1mg orally for endocrine treatment of breast cancer was added once. The patient was examined every three months and followed up for 1.5 years, but there was no recurrence and metastasis.

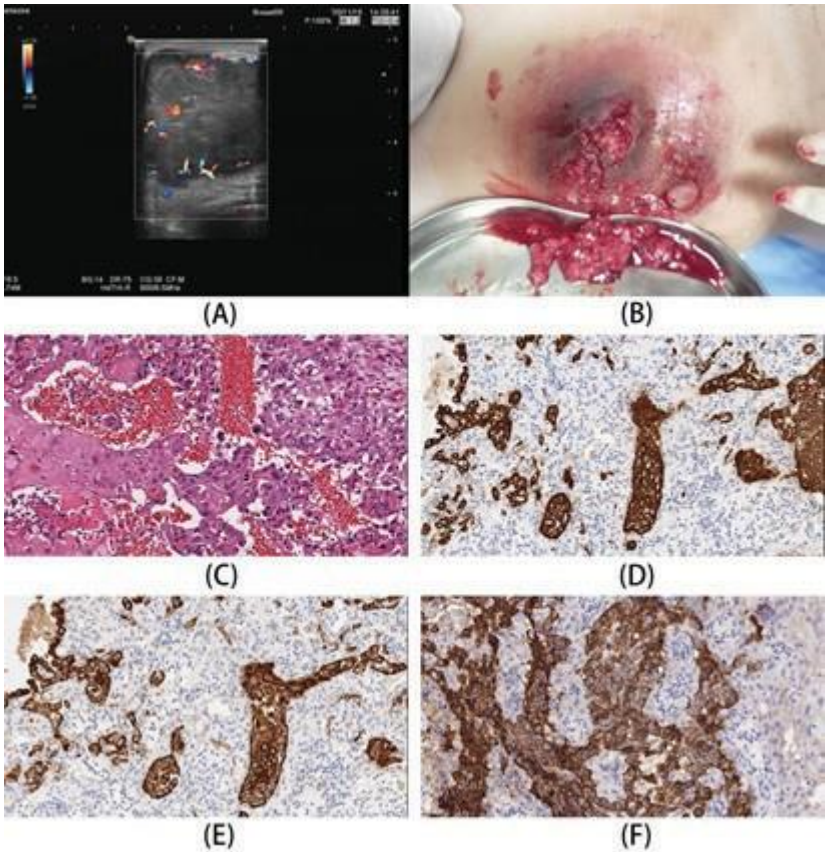

Figure 1: (A) Breast ultrasound revealed a 72-mm hypoechoic and heterogenous solid mass; (B) Right breast tumor biopsy and debridement under local anesthesia; Pathological results of the tissue biopsy in November 2020 (C-F). (C) Cyst in the upper quadrant of the right breast, acantholysis of squamous cell showing pseudoadenoid structure. (×20, Hematoxylin and Eosin staining). (D) Tumor cell CK5/6 staining membrane positive EnVision method (×20, IHC staining). (E) CK5/6 showed strong expression in the cancer (×20, IHC staining). (F) HER2 positive tested in the squamous cell carcinoma. HER2 immunohistochemistry showed 3+ immunoreactivities within the circumferential membrane of the tumor cells (×20, IHC staining).

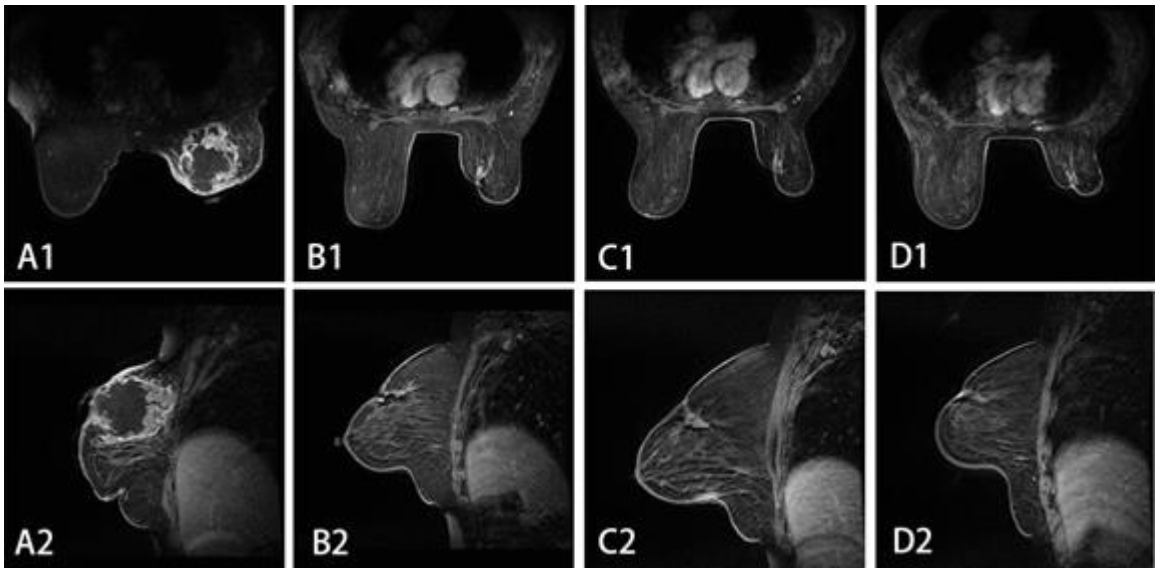

Figure 2: MRI showed the mass was considerably reduced after chemotherapy. A1-2: before chemotherapy, B1-2: 2 cycles, C1-2: 4 cycles, D1-2: 6 cycles.

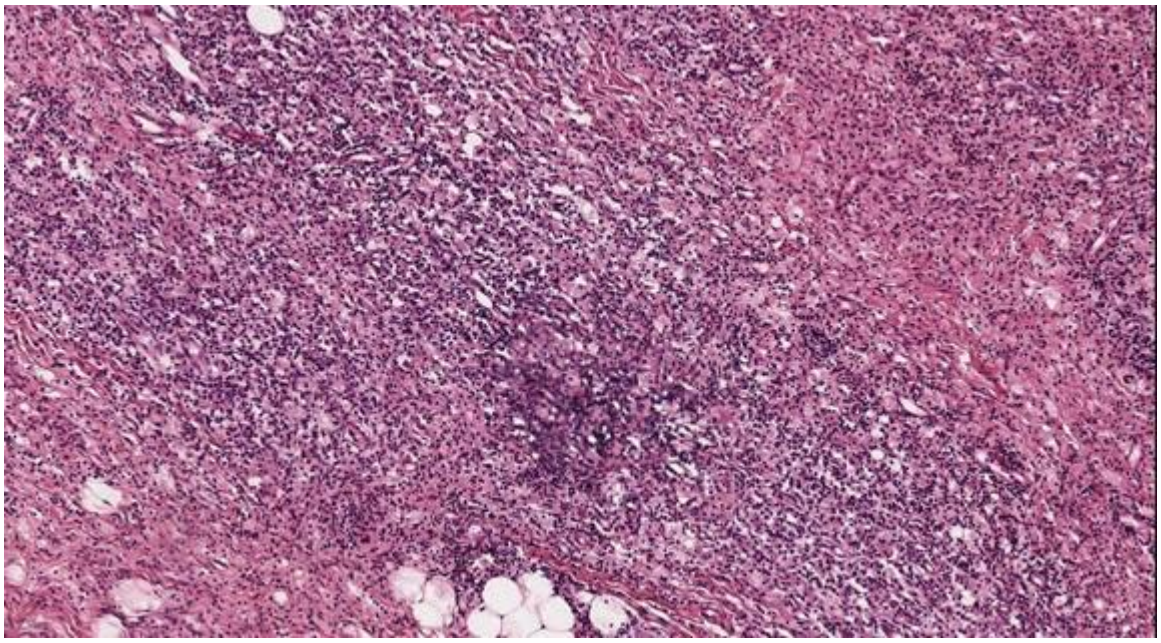

Figure 3: Postoperative pathology showed interstitial fibrosis, histiocyte, multinucleated giant cell response, and no invasive carcinomain. (×20, Hematoxylin and Eosin staining)

4. Discussion

ASCC of the breast is a distinct tumor entity that has been classified as a variant of SCC published World Health Organization classification of tumors of the breast and female reproductive system [4]. As for the cause of breast SCC, most experts feel that it is triggered by ductal dilatation and squamous cell metaplasia of ductal epithelium based on benign lesions such as chronic inflammatory abscess and adenosis of breast cyst, followed by malignant conversion of metaplasia of squamous epithelium, and several cases of primary breast SCC are first before, there were numerous benign breast lesions, such as breast abscess, etc [1]. The histologic feature of ASCC is due to the loss of cohesion between tumor cells with typical pseudoglands and pseudovascular structures, therefore it may be important to make the differential diagnosis using IHC to rule out eccrine neoplasia and vascular sarcomas may be important [5]. Pathologists are usually able to identify them by immunohistochemical staining with an extensive bioptic examination and endothelial lineage (using CD31 and CD34), cytokeratin (high molecular weight cytokeratin) [6]. Cystic degeneration is related to primary SCC, but not to metastatic SCC, and the presence of SCC in situ in the lining epithelium of the cystic degeneration is an essential component in the diagnosis of primary SCC of the breast [7]. In this case, a large cyst is formed in the right breast, and the tumor can be seen with squamous epithelial carcinoma components and pseudoadenoid structures, and IHC can see vascular endothelial CD34, high molecular weight cell keratin (CK5/6), and broad-spectrum cell keratin (AE1/AE3), which are all positive, consistent with the literature.

Primary SCC of the breast is generally triple-negative [8], and Ki-67, P63, and EGFR are highly expressed [9, 10]. There are only a few reported cases of primary SCC of the breast with an unusual "basal-HER2" phenotype [11]. The study of metastasis of lymph nodes is rarely reported [12]. In this case, the patient had ER, PR negative, high Ki-67, and myoepithelial P63 positive, essentially consistent with the literature, and no metastasis in ipsilateral axillary lymph nodes. Only HER2 is positive, which is rare in ASCC.

The treatment of primary SCC of the breast is not yet standardized due to its low incidence. Patients receiving adjuvant chemotherapy have significantly improved disease-free survival and overall survival compared to patients not receiving chemotherapy. However, Pandey et al. found that the survival rate of some patients who received adjuvant chemotherapy did not improve, and they believed that the response to chemotherapy varies from person to person [13]. Zhu L was analyzed with the national cancer database and only 20% of patients with squamous cell carcinoma responded to NAC [14]. Most scholars believe that breast SCC is not sensitive to NAC [15, 16]. However, some authors have reported that patients with breast squamous cell carcinoma have achieved pathological complete remission with NAC, and Aya Noro et al. also said that epirubicin in combination with cyclophosphamide is ineffective, and the use of paclitaxel is effective. Applications such as cisplatin and fluorouracil such as Dejager D have also reached PCR [17, 18]. The efficacy of targeted therapy for HER2-positive squamous cell carcinoma is unclear, particularly in neoadjuvant therapy. Some doctors believe there is drug resistance, but Yuki Usui reported a case of applying dose-dense doxorubicin and cyclophosphamide, followed by pertuzumab and trastuzumab plus docetaxel, achieving complete pathological remission [19]. Zhu L's research suggests that endocrine therapy is necessary for breast cancer in primary SCC [14] and the importance of treating this disease has been rarely reported. The inconsistency in the effects of the above treatment methods indicates that the treatment of ASCC requires the accumulation of more cases and experience. In this case, due to the irreversible nature of the mass, we tried neoadjuvant therapy, which confirmed the excellent effect of albumin-paclitaxel, cisplatin, and trastuzumab in the treatment of HER2-positive squamous cell carcinoma. Postoperative pathology suggested that there was still a small amount of carcinoma in situ in the lesion, ER and PR were highly expressed, and the addition of anastrozole can reduce the risk of recurrence and metastasis. We will continue to track patients for long-term efficacy.

5. Conclusion

Indeed, ASCC is rare breast cancer with tumor heterogeneity and variable prognosis, which requires further understanding of its pathological features and therapeutic approaches. In this case report, we have described a standard sample of HER2-positive breast ASCC treating it with a newer adjuvant treatment approach and achieving good results.

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