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Case Report

A case of breast primary neuroendocrine carcinoma treated with neoadjuvant endocrine therapy

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Abstract: Breast primary neuroendocrine carcinoma is a very rare type of invasive mammary carcinoma and there is no uniform criterion on the treatment. Here, a case of breast primary neuroendocrine carcinoma is reported showing a remarkable response to three months of neoadjuvant endocrine therapy. A 28-year-old woman with a large mass of 7.0 cm × 4.5 cm in her right breast was reported. The patient was pathologically diagnosed with breast primary neuroendocrine carcinoma and the stage was cT3N0M0 IIIA. Immunohistochemistry detection demonstrated 90% positivity for ER and 60% positivity for PR. The patient received three months of neoadjuvant endocrine therapy with goserelin and letrozole. The maximum diameter of the tumor decreased from 7.1 cm to 1.5 cm. The patient sequentially underwent total mammectomy and breast augmentation by one-stage silicon gel filling operation. Postoperative pathology showed invasive breast carcinoma with neuroendocrine differentiation. No hemorrhage and necrosis was observed in the specimen. Moreover, no enlargedaxillary lymph node was found. Pathologicalstaging was pT1N0M0 IA. And the patient recovered well after the operation. There have been no reports on using neoadjuvant endocrine therapy to treat breast primary neuroendocrine carcinoma.In the present case, the efficacy of neoadjuvant endocrine therapy was demonstrated for treatment ofhormone receptor positive breast primary neuroendocrine carcinoma, which provided a good reference for similar cases.

Keywords: Breast primary neuroendocrine carcinoma, neoadjuvant endocrine therapy, case report

Introduction

Primary neuroendocrine carcinoma of the breast (NECB) is rare and was first described by Feyrter and Hartmann in 1963 [1]. Because NECB has rare histological types, this presents a challenge to the practicing clinician who must adopt a cautious attitude for surgical treatment, axillary staging, and adjuvant therapy, as well as counsel patients as to their expected disease course and prognosis. For this reason, the treatment and prognosis of NECB deserve in-depth discussion. Our case showed good correlation between NECB and neoadjuvant endocrine therapy.

Case presentation

A 28-year-old female patient complained of a painless mass in the right breast for one year before hospitalization. There was no depression in the nipple. No evident abnormality was detected in the shape of both breasts by physical examination. A segmented mass with a size of 7.0 cm × 4.5 cm exhibiting clear border, hard texture, irregular shape and poor mobility in the outer quadrant of the right breast. Axillary and supraclavicular lymph nodes were not palpable.

The patient did not present positive medical history and family history of breast, colon, ovarian, or other cancers. Breast ultrasound results showed an irregular hypoechoic substantial mass with an irregular shape and a slightly serrated border, posterior echo attenuation, and abundant blood supply. The size of the mass was 7.1 cm × 5.3 cm × 4.2 cm. Both sides of the axilla showed no abnormal lymph node. Enhancement MRI results showed a lobulated lump with amaximum section size of 5.7 cm × 3.5 cm in the outer quadrant of the right

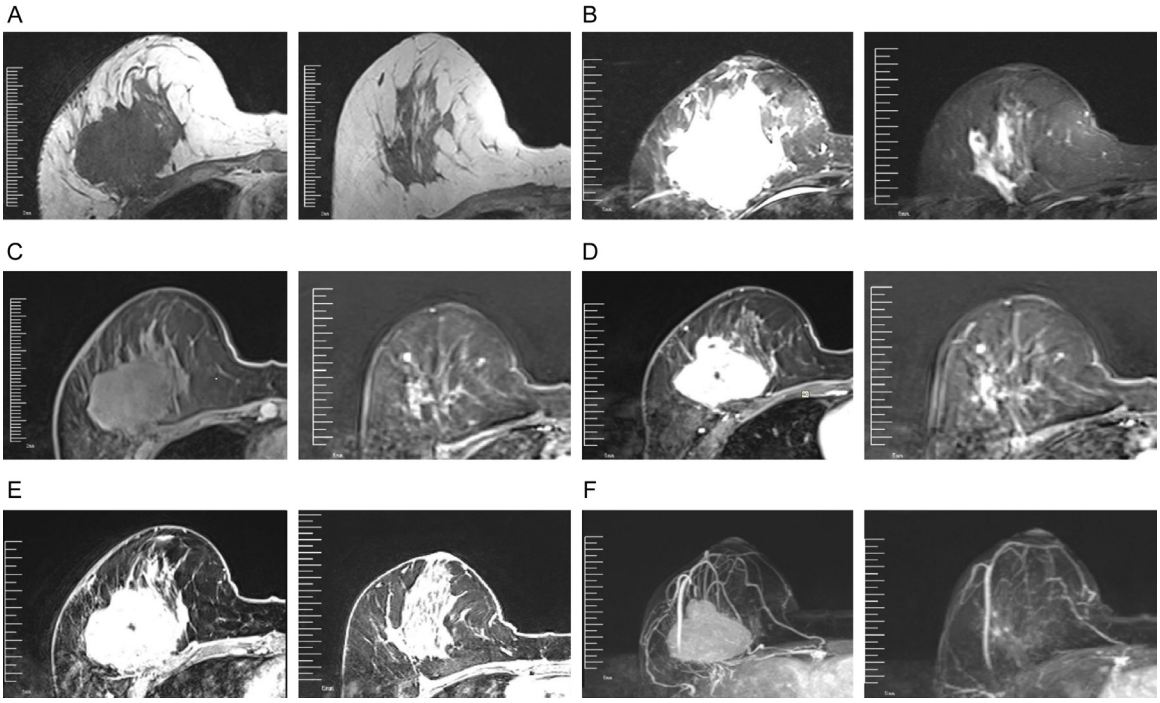

Figure 1. MRI was performed using the 3.0-T system. A. On axial non-fat-saturated T1-weighted images, mass shows round, smooth, homogeneous, low signal intensity. B. On axial fat-saturated T2-weighted images, mass shows high signal intensity. C. Axial fat-saturated pre-contrast-enhanced. D. Early (2 minutes) contrastenhanced. E. Delayed (6 minutes) contrast-enhanced axial T1-weighted images after bolus administration of gadolinium-based contrast agent show heterogeneous enhancement. A cloudy-like area without potentiation can be seen in the enhancement area, and images reveal fast-in and fast-out pattern enhancement. F. On delayedcontrast-enhanced axial T1-weighted image reconstruction, shows a well-defined irregular heterogeneous enhancing mass in right breast parenchyma.

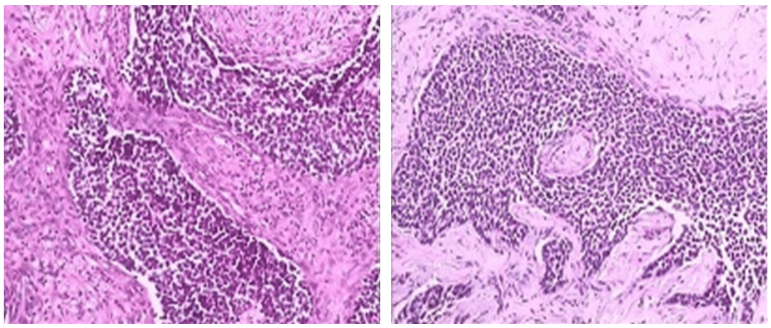

Figure 2. CT also showed an obvious abnormal mass in the breast. CT images indicated clearly that the mass was significantly reduced after three months of neoadjuvant endocrine therapy.

breast. The lump displayed unclear contours (**Figure 1**). CT also showed an obvious abnormal mass in the breast (**Figure 2**). X-ray examination results did not show any abnormity in the lungs and bones, abdominal echography results did not show any abnormal changes in the liver, biliary system, and pancreas.

The patient was diagnosed with histologically with poorly differentiated neuroendocrine carcinoma and was subjected to core needle biopsy (**Figure 3**) in the breast mass. The IHC results demonstrated 90% positivity for ER, 60% positivity for PR, HER-2 positive (++), positivity for CgA, negative for Syn, weakly positive for 34β12 and 50% positivity for Ki-67.

The patient was diagnosed with cT3N0M0 IIIA and received three months of neoadjuvant endocrine therapy with goserelin and letrozole. The maximum diameter of the tumor decreased from 7.1 cm to 1.5 cm (**Figure 4**). Enhancement MRI results showed a mass with a maximum section size of 17 mm × 18 mm in the outer quadrant of the right breast. Ultrasound results showed that the tumor mass became smaller with a size of 1.5 cm × 0.7 cm. The therapeutic response was evaluated as partial response with a 70.18% reduction in tumor size according to the RECIST criteria.

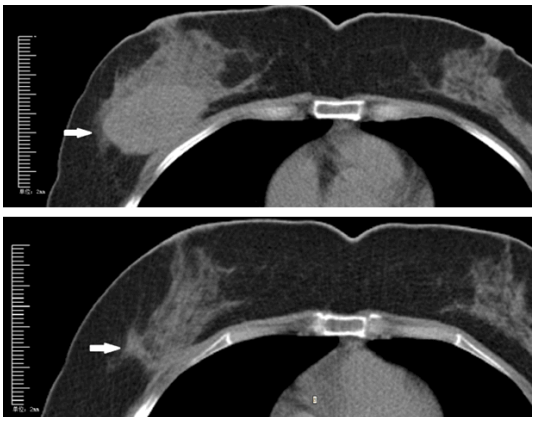

Figure 3. The patient that was diagnosed histologically with poorly differentiated neuroendocrine carcinoma was subjected to core needle biopsy in the breast mass. The tumor cells were small, and there was no obvious necrosis of the tumor cells, and there was no obvious nerve and vascular invasion in the puncture.

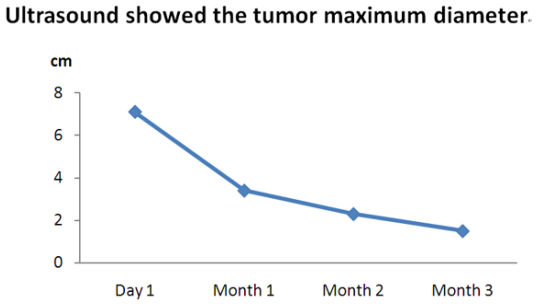

Figure 4. Breast ultrasound results showed an irregular hypoechoic substantial mass which had an irregular shape with a slightly serrated border, posterior echo attenuation and abundant blood supply. The size of the mass was 7.1 cm × 5.3 cm × 4.2 cm. Both sides of the axilla showed no abnormal lymph node. Form the chart it was clear that the tumor was significantly reduced with the neoadjuvant endocrine therapy.

Total mammectomy and breast augmentation by one-stage silicon gel filling operation and sentinel lymph node biopsy was performed after three months of neoadjuvant endocrine therapy. Gross pathology of the resected specimen showed a soft gray-white mass with a size of 2 cm × 1.6 cm in the right breast. Postoperative pathology confirmed the initial diagnosis of invasive breast carcinoma with neuroendocrine differentiation. No hemorrhage and necrosis was observed in the specimen. Moreover, no enlargedaxillary lymph node was found. The pathologicalstaging based on AJCC was pT1N0M0 IA and the patient recovered well after the operation.

Discussion

Neuroendocrine tumors can occur in various parts of the body such as the lung, gastrointestinal tract, ovary, cervix, breast, larynx, prostate, and bladder [2]. In 2003, the World Health Organization (WHO) classification of NECB defined neuroendocrine carcinoma of the breast as a subtype of invasive mammary carcinoma [3]. It is defined as 1) a tumor that is morphologically similar to neuroendocrine carcinoma of the lungs and the gastrointestinal tract and 2) a tumor where more than 50% of the tumor cells express neuroendocrine markers. In 2012, the WHO divided carcinomas with neuroendocrine features into 3 categories: 1) neuroendocrine carcinoma, well-differentiated; 2) neuroendocrine carcinoma, poorly differentiated (small cell carcinoma); and 3) invasive breast carcinoma with neuroendocrine differentiation. NECB is very rare in clinical practice, accounting for 0.3% to 5% of all breast cancer. WHO statistics show that NECB accounts for 2% to 5% of the whole breast cancer. However, Lopez et al. [4] and Gunhan et al. [5] analyzed 1368 cases and 1845 cases of breast cancer by using WHO diagnostic criteria in 2003 and NECB accounted for only 0.3% and 0.5% of breast cancer. Therefore, immunohistochemistry was used forfurther diagnosis due to its gold standard status and to be strictly in accordance with the pathological diagnostic criteria for clinical diagnosis.

Most patients with NECB are postmenopausal women, and the incidence in male and younger women is low. The median age of the patients in previous reports is 55.1 ± 1.7 years (range, 41-75) and the tumor sizeshave ranged from 10 to 180 mm (median, 45.6 ± 6.7 mm) [6]. Chieh-Sheng Lu [7] performed a review of showing that 86 patients enrolled were eligible, their mean age at diagnosis was 53.9 years (range 25-83) and 1 case was in a male.

Now there has been no uniform conclusion for the treatment of primary NECB. Mostcases reported in the treatment of NECB have been similar to that of common invasive breast carcinoma, and have been treated by surgical resection combined with radiotherapy and chemotherapy. Relatively few treatments of NECB with endocrine therapy have been reported. In the analysis of Chieh-Sheng Lu, the patients given adjuvant chemotherapy seemed to have shorter overall survival than those without chemo-

therapy. In addition, J Yao et al. [8] compared the efficacy of 74 patients with NECB who were treated with chemotherapy, endocrine therapy, and local radiotherapy and suggested that only endocrine therapy and radiotherapy have slight survival benefit, and the prognosis of chemotherapy is worse. Through these studies, further evaluation of NECB treatment was done for chemotherapy, and it was learned that endocrine therapy may be an appropriate treatment for NECB.

Endocrine therapy for breast cancer can be earliest traced back to 1896 where British surgeon Beatson reported ovariectomy in the treatment of premenopausal recurrence and metastasis of breast cancer [9]. Now neoadjuvant endocrine therapy is considered a method for patients with hormone receptor-positive breast carcinomas. Neoadjuvant endocrine therapy is a systemic endocrine therapy for breast cancer patients before the application of local treatment [10].

Neoadjuvant endocrine therapy that is similar to neoadjuvant chemotherapy can make the breast cancer sensitive to endocrine therapy to achieve the purpose of down staging the primary tumor and regional lymph node. Thus it can 1) improve the local control rate of breast cancer and provide the opportunity to preserve the breast mastectomy patients in need; 2) make some inoperable locally advanced breast cancer transformation feasible surgical treatment of tumors, and improve advanced breast cancer treatment opportunities; 3) inhibit the body which has been the presence of micrometastasis. Neoadjuvant endocrine therapy can also provide tumor of hormone sensitivity of valuable information, and effectively guide the postoperative adjuvant therapy.

In 2015 NCCN, neoadjuvant endocrine therapy was mentioned officially for the first time. A potential advantage is that it is possible to keep sustainable use in the perioperative period with fewer side effects. In addition, one of the advantages of neoadjuvant endocrine therapy in theory is to reduce the potential of cell migration with the endocrine therapy [11]. At present, adaptation of breast cancer neoadjuvant endocrine therapy is as follows: postmenopausal breast cancer patient, premenopausal breast cancer patient who unsuitable or unwilling to accept neoadjuvant chemotherapy and more than 70 years old breast cancer patient has a locally advanced breast cancer or a large breast cancer need to be reduced with ER positive and (or) PR positive tumors [12].

In the present case, the patient was young and had a large breast cancer which needed to be reduced with ER positive and (or) PR positive tumors. The patient was diagnosed histologically with poorly differentiated neuroendocrinecarcinoma. This patient was unsuitable to accept neoadjuvant chemotherapy due to the efficacy of NECB chemotherapy is not well. Neoadjuvant endocrine therapy was chosen although there has been no report on using neoadjuvant endocrine therapy to treat NECB. The patient was conscious of small changes after 1 week neoadjuvant endocrine therapy. The patient felt the mass was significantly reduced subjectively after 2 weeks neoadjuvant endocrine therapy. Finally, after 3 months of neoadjuvant endocrine therapy the signs were good.

The diagnosis of NECB is more complex. Clinical and radiologic features have no obvious specificity. The diagnosis of it is more relying on the pathological study of immunohistochemistry. For improving the diagnosis rate of the disease, it is more important for the comprehensive consideration and treatment of the disease. Neoadjuvant endocrine therapy for NECB is a good choice when we combine with individual case and flexible use of the existing medical method.

Primary NECBs are extremely rare, and the best treatment still needs to be defined. In the present case, the efficacy of neoadjuvant endocrine therapy was well demonstrated to treat breast primary neuroendocrine carcinoma with hormone receptor positive, which provided a good reference for similar cases. In this context, it is important with the long-term monitoring with multidisciplinary approaches. However, further investigations with large clinical studies of NECB are needed to confirm such preliminary results.

Disclosure of conflict of interest

None.

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