Case Report:

Small Cell Neuroendocrine Carcinoma of the Breast: Report of a Case

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Abstract

Small cell neuroendocrine tumor of the breast is a rare clinical condition. Although there's limited information about this entity, it is considered to have a poor prognosis. A 44-year-old woman presented with a 5 cm mass in the lower-outer quadrant of the right breast and its tru-cut biopsy results revealed a neuroendocrine tumor. She underwent a modified radical mastectomy followed by neoadjuvant chemotherapy and radiotherapy. She remains disease-free at the end of her 6-months follow-up period.

Keywords: Neuroendocrine tumors; breast; general surgery

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Introduction

Small cell neuroendocrine carcinoma (SCNEC) constitutes a subgroup of neuroendocrine tumors. SCNEC has generally been documented to be encountered in the pulmonary sites. On the other hand, these tumours have also been rarely reported in the breast, trachea, stomach, larynx, small intestine, bladder, prostate, cervix, and ovaries.¹ SCNEC of the breast is very rare and is known to have a more aggressive nature.^{1,2} There is no consensus for the management of primary SCNECs of the breast because of their rare incidence.² In this study, we aimed to present a 44-year-old female patient with the diagnosis of primary SCNEC.

Case Report

A 44-year-old woman with a palpable mass in the right breast was admitted to the hospital. She was premenopausal and had no family history of breast cancer. On physical examination, a 5-cm mass in the lower-outer quadrant of the right breast and palpable right axillary lymph nodes were identified. Mammography revealed a spiculated, 4.5×4.0 cm strongly enhancing lesion in the right breast (**Figure 1**). Magnetic resonance imaging (MRI)

revealed a 4.6×4.7 cm hyperintense lesion in the right breast (**Figures 2A, 2B**). A core biopsy was performed and on histopathological examination it was determined to have the features of a SCNET. In order to rule out a possible extramammary location of the neuroendocrine tumor, a positron emission tomography - computed tomography scan (PET-CT) was performed, but no other lesions were detected. The lesion was diagnosed as a primary neuroendocrine tumor of the breast. The patient received three courses of neoadjuvant (NA) chemotherapy. However, there was no sign of regression, and in fact, the tumor showed progression (**Figures 3A, 3B**). For this reason, a surgical intervention was decided on, and the patient underwent a modified radical mastectomy. On pathological examination, the tumor cells were consisted of atypical epithelial cells with scanty cytoplasm, and pleomorphic with hyperchromatic nuclei (**Figure 4**). The tumor cells were stained positively for, synaptophysin, chromogranin A, and CD56, while the Ki67 proliferative index was 60% and the mitotic count was 25/10 high power fields (HPF) (**Figure 5**). Estrogen and progesterone receptors were negative. The tumor

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Figure 1. Mammography of the right breast, revealing a 4.0×4.5 cm lesion.

Figure 3A. PET-CT scan image (before neoadjuvant therapy) showing a 2.01 cm lesion in the right breast.

Figure 2A. MRI image (T1) showing a 4.6×4.7 cm lesion in the right breast.

Figure 3B. PET-CT scan image (after neoadjuvant therapy) showing a 3.58 cm lesion in the right breast indicating a progression of the lesion.

Figure 2B. MRI image (T2) showing a 4.6×4.7 cm lesion in the right breast.

Figure 4. Micrograph revealing densely packed hyperchromatic small cells with scant cytoplasm (H&E, A:×40 B:×600).

Figure 5. Tumor cells expressing synaptophysin (A:×100), chromogranin A (B: ×100) and CD56 (C: ×100). The Ki67 proliferation index was 60% (D: ×200).

cells were stained negatively for GATA-3 (**Figure 6**). Among all dissected axillary lymph nodes, four were detected as positive for metastasis, and the remaining 20 showed reactive lymphoid hyperplasia.

Discussion

Most commonly neuroendocrine tumors occur in various sites; pulmonary sites and extra-pulmonary sites such as the pancreas, larynx, trachea, small intestine, stomach, prostate, uterus, cervix and breast.⁴

The term “neuroendocrine carcinoma of the breast” was first defined by Cubilla and Woodruff in 1977. After that, breast tumors in which more than %50 of the total cell population express neuroendocrine markers immunohistochemically can be recognized as neuroendocrine carcinomas.³ Primary neuroendocrine carcinoma of the breast (PNCB) is extremely rare, accounting for less than 0.1% of all breast cancers, and less than 1% of all neuroendocrine tumors.⁵ PNCB shows a wide spectrum of severity from non-aggressive carcinoid tumors to highly aggressive small cell carcinomas.⁶ It usually occurs in the 7th or 8th decades of life, and there are no remarkable differences in the clinical presentation from other breast carcinomas. Moreover, paraneoplastic syndromes due to hormone production are extremely rare.³ The number of cases with radiology findings has been too small to allow generalization of the imaging features.

There is no distinct clinical findings that would reliably differentiate PNCB from other types of breast cancer.⁶ It is also difficult to distinguish PNCB from metastasis histologically because of the similarities in morphologic features and immunohistochemical expressions.⁶ Therefore, a definitive diagnosis of PNCB can only be made by biopsy because of the aforementioned similarities. Distinguishing between primary or metastatic neuroendocrine carcinoma of the breast is significantly important for the decision of mastectomy with or without axillary lymph node dissection as well as the decision of the treatment protocol.⁵ Most cases are treated with modified

radical mastectomy and axillary clearance with adjuvant chemotherapy like adenocarcinomas of the breast.⁵

According to the 2012 WHO classification, carcinomas with neuroendocrine features are classified as neuroendocrine tumor, well-differentiated; neuroendocrine tumor, poorly differentiated / small cell carcinoma, and invasive breast carcinoma with neuroendocrine differentiation.⁸ The histopathologic features and mitotic count of our case were consistent with “neuroendocrine carcinoma poorly differentiated/ small cell carcinoma”.

Because of the rare incidence and limited reports of this tumor, the standard treatment strategy of primary SCNET of the breast remains controversial.⁴ Treatment options (including chemotherapy, radiotherapy, surgery and anti-hormonal therapy) have been discussed in the literature in concern of their efficacy, and their results when used in various combinations. Modified radical mastectomy with adjuvant chemotherapy or radiation therapy was common in the earlier reports. Currently, the most applicable treatment in the recent years is breast conservation therapy combined with neoadjuvant or adjuvant chemotherapy.² Endocrine therapy is also an option for adjuvant treatment in patients with receptor-positive SCNETs of the breast.⁷ The choice of treatment should be tailored on an individual basis, considering the features of the tumors depending on the particular clinical scenarios. Besides the anthracycline and taxane based regimens which are the most current chemotherapy agents, platinum compounds and etoposide have also been widely used for tumors with a high proliferation index.⁷

In the conclusion, surgical resection is the main option in treatment of SCNETs when these tumors can be discovered in early stages.⁹ Anthracycline-based adjuvant chemotherapy and endocrine therapy may play a limited role in these patients and can be used either in cases with a high risk of recurrence, or locally advanced, inoperable SCNETs.^{7,9}

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