

**NEUROENDOCRINE CARCINOMA OF THE BREAST, UNUSUAL BREAST TUMOR : A
CASE REPORT AND LITERATURE REVIEW**

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ABSTRACT

Background: The neuroendocrine carcinoma of the breast (NECB) is a very rare type of breast cancer, defined by a common phenotype characterized by the expression of general neuroendocrine markers and sometimes by cell specific hormonal products. Due to the rare nature of this tumor, there are no data from prospective clinical trials on its optimal management. A Early stage tumors are usually treated with the same strategy used for the other types of invasive breast cancer, For metastatic disease, a multimodality therapeutic strategy can be considered on an individual basis. **Presentation Of Case:** A 59-year-old female who presented a left breast mass. After biopsy, she was diagnosed with a primary NECB with regional lymph node involvement. She was treated by surgery, adjuvant chemotherapy and radiation therapy with a good clinical response. **Conclusion:** NECB is a heterogeneous group of tumors with different biologic behavior and prognosis. Further research is needed to better understand the behavior of this rare tumor in order to develop a standard approach to treatment.

INTRODUCTION

Neuroendocrine carcinoma of the breast is a very uncommon type of breast cancer. In 2003 it was recognized by World Health Organization (WHO) as a separate entity of breast cancer. Thus, it was defined as tumors of epithelial origin, with morphology similar to gastrointestinal and pulmonary neuroendocrine tumors, expressing a neuroendocrine marker in at least 50% of the total cell population.^[1] According to the 2012 WHO classification, based on morphology, breast tumors with neuroendocrine features are divided into three groups: neuroendocrine tumor, well-differentiated (carcinoid-like); neuroendocrine carcinoma, poorly differentiated/small-cell carcinoma; and invasive carcinoma with neuroendocrine differentiation.^[2] This report summarizes a case of primary NCB and presents a review of the literature

CASE REPORT

A 59-year-old G1P1 menopausal female, with 15-year history of oral contraception use, she presented to her gynecologist with complaints of a left breast mass noticed during six months ago, gradually, increasing in volume. She was referred to our institute for consultation with a surgical breast oncologist. Clinical examination revealed a small breasts, and 03 cm palpable mass in the left one, with homolateral axillary adenopathy. She proceeded to have a diagnostic mammogram and ultrasound which demonstrated an irregular mass, highly

suggestive of malignancy. Biopsies revealed a neuroendocrine tumor, well-differentiated, ER/PR positive, HER2 negative. Immunohistochemical staining was positive for synaptophysin and chromogranin, suggesting a primary small cell carcinoma of the breast.

Radiologic workup included a CT of the chest, abdomen and pelvis as well as an MRI of the brain to exclude a primary tumor outside of the breast and complete a staging workup of the breast lesion. There were no lung, pancreatic, adrenal, or pelvic masses identified. The patient had a left mastectomy with lymph node dissection. Based on the regional lymph node involvement, the patient was started on a chemotherapy regimen of carboplatin and etoposide followed by radiation therapy and hormonal therapy. She tolerated this treatment well and clinical follow up showed a good clinical response during four years after treatment.

DISCUSSION**Etiology and Demographics**

Neuroendocrine carcinoma of the breast is a distinct entity of breast cancer, it is a very rare, with a reported incidence of <0.1% to 1-5% of all breast cancers.^[3] The histogenesis of NECB is not clearly defined yet. One theory suggests the development of NECB from neuroendocrine cells constitutively present in the breast, but these cells have not been consistently found in normal breast tissue.^[4] According to another theory, NECB would rather result from an early divergent

differentiation of breast cancer stem cells into both neuroendocrine and epithelial lines.^[5]

Clinical Presentation and Diagnosticwork-Up

The NECB is generally presents, in women over 60 years old, as a palpable breast lump with or without axillary lymphadenopathy, lymph node involvement at the time of presentation is 50-67%.^[6] The radiological features of primary NECB are non specific.^[2] However, some authors reported that NECB often appears on mammography as a round, sharply circumscribed, hyperdense mass and on breast ultrasound as a hypoechoic solid mass with ill-defined margins, increased vascularity, enhanced posterior echo, and a cystic component. Magnetic resonance imaging shows homogeneous low signal intensity with heterogeneous rapid initial enhancement on the T1-weighted image.^[7] diagnosis is made with core needle biopsy or with surgical specimen. The presence of an associated ductal carcinoma in situ component is a valid proof of the primary nature of the tumor.^[8] Other useful diagnostic tools to determine the site of origin, include the expression of neuroendocrine markers on immunohistochemical staining. They are inconsistently expressed and only support the diagnosis rather than exclude it.^[9] NECB is often positive for hormone receptors, whereas HER2 is almost always negative.^[2] However, when a NECB is diagnosed, a breast metastasis from other primary sites should be ruled out by appropriate imaging, such as a chest and abdomen computed tomography (CT) scan. Somatostatin receptor scintigraphy (SRS) or positron emission tomography (PET)-CT with 68Gallium-labeled somatostatin analogs also may be useful to exclude a different primary site in the case of well-differentiated neuroendocrine carcinomas, whereas 18-fluorodeoxyglucose PET-CT could be used with the same purpose in the case of poorly differentiated neuroendocrine carcinoma with a high proliferation rate.^[10] Metastatic sites include liver, bones, lung, pancreas, soft tissues, and brain.^[11]

Treatment and Prognosis

There is no standard approach to treatment. Treatment regimens discussed in the literature include various combinations of surgery, chemotherapy, radiation therapy, and endocrine therapy. Recent reports have described treatment with breast conservation therapy combined with either neoadjuvant or adjuvant chemotherapy depending on the clinical scenario.^[12]

Surgery is the mainstay of the treatment for early NECB, and the choice of surgical procedure depends on the location of the tumor and on the clinical stage.^[13] Anthracycline-andtaxane-based regimens represent the most frequently administered chemotherapy in neoadjuvant and adjuvant setting, as well as for metastatic disease. There are no specific studies with adjuvant radiation therapy for NECB, but radiotherapy should be considered according to the recommendations given for the other types of invasive breast cancer.^[2]

Patients with hormone receptor-positive NECB are candidates to receive adjuvant endocrine therapy.^[14]

Prognosis

Primary neuroendocrine carcinoma of the breast (NECB) includes a heterogeneous group of tumors with different biologic behavior and prognosis.^[15] When the specific histologic subgroup was taken into account, small-cell carcinoma was significantly associated with worse prognosis in comparison with all the other neuroendocrine tumors of the breast. Moreover,^[2] other known prognosis factors such as age, tumor size, nodal status, histologic grade, hormone receptor status, and therapy, neuroendocrine differentiation are an independent adverse prognostic factor.^[16]

CONCLUSION

Primary neuroendocrine carcinoma of the breast is a very rare type of breast cancer, thus, there is no standard approach to treatment and several treatment strategies have been described based on current guidelines for breast cancer treatment. Further research is needed to better understand the behavior of this rare tumor in order to develop a standard approach to treatment

Figure Captions

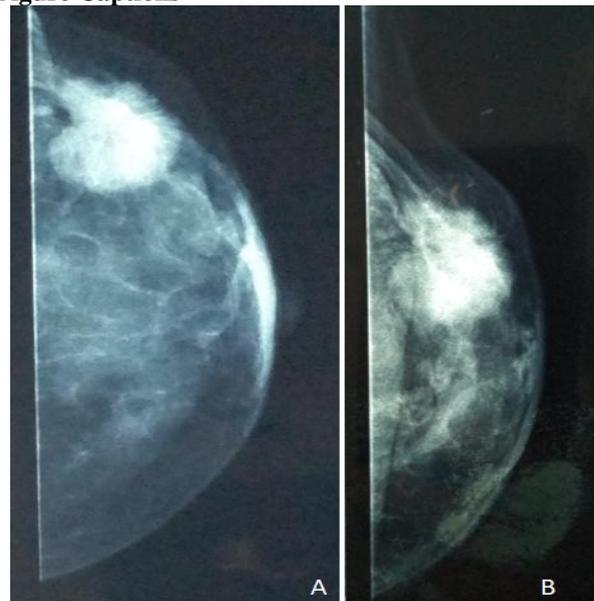


Figure 1: Diagnostic mammogram: A.left cranial-caudal view, B.mediolateral-oblique view showing an irregular high density mass in the left breast.

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