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Neuroendocrine Carcinoma of the Breast: Report of A Case

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ABSTRACT

Objective: Breast cancer is the most prevalent malignant disease among women and ranks among the top three most common cancers globally, alongside lung and colon cancer. Various subtypes of breast cancer have been identified. Primary neuroendocrine breast cancer, a rare and distinct type of breast carcinoma, lacks specific radiological findings. The definitive diagnosis is achieved through the expression of Synaptophysin and Chromogranin A on tumor biopsy, and it necessitates the absence of tumor detection in other regions. Staging and treatment are recommended to follow a similar approach as that of conventional breast cancer. It is believed that the prognosis of neuroendocrine breast tumors is generally poorer compared to invasive cancers.

Keywords: Breast, malignancy, neuroendocrine cancer

INTRODUCTION

Breast cancer is the most common type of cancer in women and ranks among the top three most prevalent cancers, along with lung and colon cancer (1). Primary neuroendocrine cancer is a relatively uncommon subtype that differs from other types of breast tumors. It represents approximately 0.27% to 0.5% of all breast malignancies (2) and less than 1% of neuroendocrine tumors overall (3).

This particular subtype does not exhibit specific clinical or imaging features (4). The definitive diagnosis relies on the detection of Synaptophysin and Chromogranin A expression using tumor-specific dyes in a biopsy, while ensuring the absence of concurrent neuroendocrine carcinoma outside the breast.

Treatment and staging of this type of cancer are generally approached similarly to other forms of breast cancer. The prognosis of primary neuroendocrine breast cancer is not universally agreed upon. However, large-scale studies have suggested that it carries a worse prognosis compared to invasive breast carcinomas (2).

In this study, we present the case of a 52-year-old woman who presented with a palpable mass in her right breast and subsequently underwent segmental mastectomy and axillary lymph node sampling after being diagnosed with neuroendocrine carcinoma. The patient received postoperative chemoradiotherapy, and her disease-free follow-up is still ongoing.

CASE

Our patient was a 52-year-old female who presented with a palpable mass in her right breast that she had noticed approximately two months ago. Upon physical examination, a 2 cm diameter mass was palpated at the 10 o'clock position of the right breast, along with a lymph node in the right axilla. The mediolateral oblique (MLO) mammogram of the right breast revealed a 20 mm round mass with spiculated edges in the upper outer quadrant, classified as BI-RADS 4 (Figure 1a).

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Further evaluation with MRI showed rapid contrast enhancement of the mass in the early stages. Lymphadenomegaly was observed in the ipsilateral axilla without a fatty hilum, measuring 16x5 mm. Ultrasonographic examination revealed a hypoechoic solid lesion with irregular borders measuring 20 x 13 mm and axillary lymphadenomegaly. To confirm the diagnosis in conjunction with the radiological findings, a tru-cut biopsy was performed on the breast lesion and a fine needle aspiration biopsy on the axillary lymph node. Histopathological examination revealed a tumor with neuroendocrine differentiation and a high proliferative index.

The patient subsequently underwent lumpectomy and sentinel lymph node sampling. The surgical margins were tumor-free, and no lymphatic metastasis was detected in the frozen-section examination. The patient had an uneventful postoperative course and was discharged on the second day after surgery.

The histopathological examination of the 16 mm diameter lesion revealed a large cell neuroendocrine carcinoma diagnosis. The tumor showed strong positivity for Synaptophysin and Chromogranin A. Additionally, the tumor was found to be estrogen receptor (ER) and progesterone receptor (PR) positive with a 100% staining. The CERB B2 marker was negative, and the Ki-67 proliferation index was 30% in the hottest area. The pathological stage was determined as pT1c N0(s) (Figure 2).

Following the diagnosis, the patient received oncological treatment. At the end of twenty months of follow-up, she remains disease-free, indicating a favorable disease-free survival outcome.

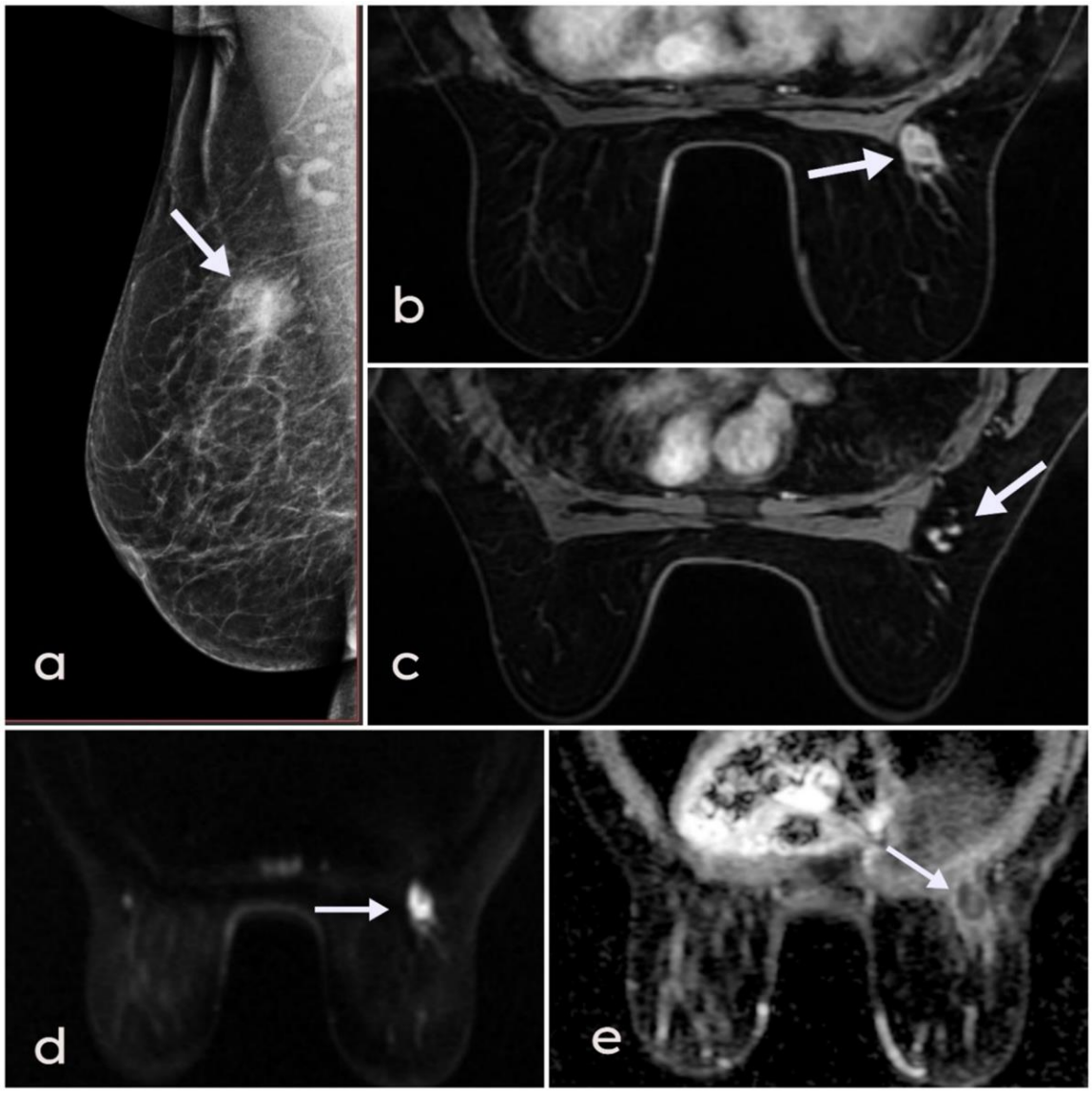

Figure 1. (a) Mediolateral oblique (MLO) mammogram of the right breast shows a 20 mm round mass with spiculated edges in the upper outer quadrant. This lesion is classified as BI-RADS 4. **(b)** On MRI, In dynamic studies, the mass showed a fast enhancement in the early phase. **(c)** Lymphadenomegaly was detected in the ipsilateral axilla. **(d)** Diffusion weighted and **(e)** ADC maps shows that the lesion demonstrated restricted diffusion.

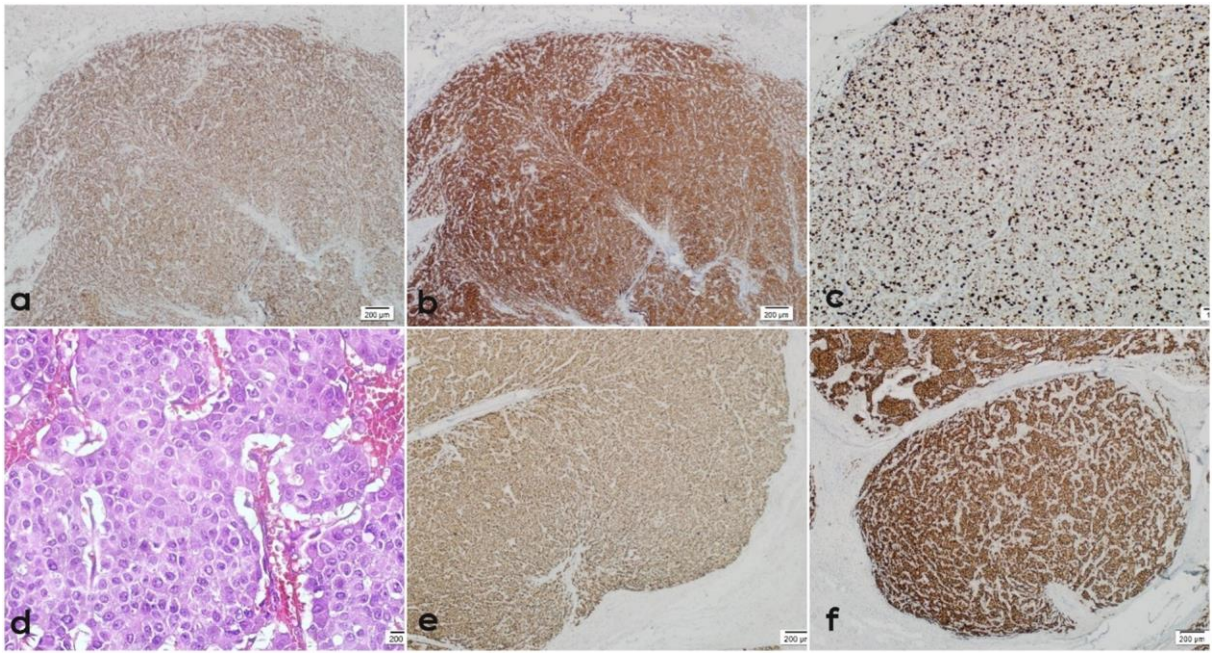

Figure 2. Tumor shows diffuse positivity with chromogranin **(a)** and synaptophysin **(b)** (x100). Ki-67: Tumor shows 30% positivity with Ki-67 immunohistochemical staining **(c)** which supports the diagnosis of neuroendocrine carcinoma. (x100). Histological appearance showing monomorphic tumor cells, a little atypical with rounded nuclei and scant cytoplasm **(d)** (hematoxylin&eosin,× 200). 100% immunoreactivity is seen in tumor cells with estrogen receptor **(e)** and progesterone receptor **(f)** which is concordant with neuroendocrine carcinoma diagnosis (x100)

DISCUSSION

The widespread use of breast screening, increased awareness of breast cancer, increased patient awareness, and easy access to imaging methods have been effective factors in early detection of breast cancer (5). Neuroendocrine neoplasms are a large heterogeneous group of epithelial neoplastic proliferations. Neuroendocrine tumors can exhibit a wide spectrum of differentiation, ranging from well-differentiated neuroendocrine tumors to aggressive, poorly differentiated neuroendocrine carcinomas (6).

The most recent classification of neuroendocrine breast cancers is the WHO classification made in 2019. Breast neuroendocrine neoplasms are classified into three categories in this classification: neuroendocrine tumors, small cell neuroendocrine cancers, and large cell neuroendocrine cancers (7). Primary neuroendocrine carcinomas of the breast have morphological features similar to neuroendocrine tumors of the gastrointestinal tract and lung (4). The disease is mostly seen in postmenopausal women in their sixth and seventh decades. However, rare male cases have also been reported.

Markers that help in the diagnosis of neuroendocrine breast cancer are not routinely used, so the true incidence of the disease is difficult to determine (8). The most common neuroendocrine breast carcinoma symptoms are a palpable breast mass and spontaneous nipple discharge (9, 10). There are limited studies describing the imaging features of neuroendocrine breast carcinomas. Calcification was a rare finding in cases In the reported case series, calcification is a rare finding in neuroendocrine carcinomas, unlike typical invasive ductal carcinomas (IDCs), with mammographic findings in neuroendocrine carcinomas. The lesion is revealed with a mass on mammography (10).

It is frequently detected as an irregular hypoechoic mass on ultrasonography (9, 10). MRI is used to define breast masses as irregular and poorly defined lesions, which are highly suspicious for malignancy. In many cases, the washout kinetics of the lesions are observed, leading to their classification as BI-RADS category 5, indicating a high likelihood of malignancy (9, 10).

In the differential diagnosis, benign or malignant lesions are considered. The possibility of neuroendocrine tumor metastasis from a non-mammary region to the breast was a possibility that needed to be kept in mind and clarified. Among breast tumors, the rate of metastasizing tumors of the breast is less than 1%. It may be due to a tumor originating from the opposite breast or a malignancy of hematological origin. The rate of neuroendocrine tumors among metastatic breast tumors is approximately 1-2%. Primary or metastatic neuroendocrine carcinomas in the breast may also be morphologically similar. If the patient's history or any other concomitant neuroendocrine tumor is unknown, this also complicates the diagnosis (11).

The confirmation of a detected lesion as a primary breast neuroendocrine tumor can be established through various criteria. These include the expression of neuroendocrine markers in more than 50% of the malignant cells, the absence of another primary focus to rule out the possibility of metastasis, and the presence of an in situ component observed during the histopathological examination (12). After histopathological confirmation, options for disease management are evaluated (13). No guidelines have yet been issued for staging or treatment in primary neuroendocrine breast cancers, it is recommended that the disease be staged and treated similarly to conventional breast cancer (10).

CONCLUSION

Neuroendocrine breast cancer is an uncommon type of breast cancer. Clinical and radiological findings are similar to invasive breast cancers. No specific radiological identification feature of the disease is known. It is diagnosed by the presence of neuroendocrine markers Synaptophysin and Chromogranin A expression in breast biopsy samples to confirm the diagnosis, and by demonstrating the absence of concurrent neuroendocrine carcinoma in the extramammary regions. Large-scale population studies have shown that neuroendocrine tumors of the breast have worse prognosis outcomes than invasive breast carcinomas.

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Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions.

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