Neuroendocrine Carcinoma of the Breast: Case Report and Literature Review

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Key Words
Neuroendocrine tumor · Synaptophysin · Breast

Summary
Background: Neuroendocrine carcinoma of the breast is a rare disease. Case Report: We present a 65-year-old female patient with an enlarged breast mass within 2 months. Solid neuroendocrine carcinoma of the breast was diagnosed by excision biopsy and histopathological analysis. A lumpectomy with the right axillary sentinel lymph node biopsy was performed, and the mass was completely resected. The literature on neuroendocrine carcinoma of the breast is reviewed. Conclusion: Due to the diversity of imaging findings from primary breast neuroendocrine carcinomas, the diagnosis is based on immunohistochemical staining of neuroendocrine markers. Surgery has turned out to be the first-line treatment and subsequently radiation may play a role in palliative treatment.

Background
Primary neuroendocrine carcinoma of the breast is a rare entity. Reports of a breast tumor showing features of carcinoids date back to 1963 [1]. Since the first description by Cubilla and Woodruff in 1977 [2], less than 150 cases have been reported. These carcinomas mostly occur in elderly women. The diagnostic investigation commonly involves fine needle aspiration and histopathological analysis [3]. The tumor cells of mammary neuroendocrine carcinomas are argyrophilic but not argentaffin and are found to contain dense-core secretory granules of various types ultrastructurally [4]. Here, we report a case of primary neuroendocrine carcinoma of the breast and review the literature.

Case Report
The 65-year-old woman had been in her usual state of health until 5 months previously, when she underwent a mammography screening. There was no family history of breast cancer. The mammography screen-
ing (fig. 1) showed a 1.7 × 1.2 cm ovoid, isodense, circumscribed, opaque nodule in the mid-portion of the right upper quadrant without microcalcification. Physical examination revealed a coarse, firm, fixed tumor above the right breast in the 12 o’clock position 2 cm from the nipple. Ultrasoundography (fig. 2) revealed one ovoid, microlobulated, hypoechoic mass with posterior acoustic enhancement at the same site by palpation. Core needle biopsy showed only some atrophic mammary glands, and there was no evidence of malignancy. 2 months later, she came to our clinic because of the enlargement of the same mass. Ultrasonography (fig. 2) revealed a 2.5 × 2.0 cm hypoechoic mass with daughter nodules and hypervascularity. Excisional biopsy was performed under local anesthesia. Neuroendocrine carcinoma was diagnosed by histological examination. Lumpectomy was done following sentinel lymph node biopsy (SLNB). Macroscopically, the tumor was pale yellow, measuring 1.6 × 1.5 cm in dimension. Microscopically (fig. 3), the tumor cells were solid and rosette in pattern. Immunohistochemical staining (fig. 4) revealed positive for synaptophysin. The tumor cells were strongly estrogen receptor-positive (ER+), while progesterone receptor and HER-2 were negative. The sentinel lymph nodes were negative. The whole-body positron emission tomography (PET) scan showed no evidence of other primary sites or metastatic lesions.

Discussion

In 1963, Feyrter and Hartmann [1] were the first to demonstrate argyrophilia to describe 2 breast carcinomas with a neuroendocrine nature of mucoid carcinoid patterns. However, it was not until 1977 when Cubilla and Woodruff [5] announced that the granules in the tumor cells were of the neurosecretory type and classified a subset of breast carcinomas as ‘carcinoid’. In 1982, Azzopardi [6] presented 14 cases among which the argyrophilic breast tumors appeared to be a wide range of morphological and histochemical forms.

It is well known that neuroendocrine elements can be found in ductal and lobular carcinoma. Unlike those in lungs...
primary mammary neuroendocrine tumors show neuroendocrine markers in more than 50% of the tumor cells and thus can be distinctly separated from breast carcinoma with the focal endocrine differentiation method. Among the different types of neuroendocrine tumors, i.e. solid neuroendocrine carcinoma, atypical carcinoid tumors, small cell/oat cell carcinoma, large cell neuroendocrine carcinoma, our case was specifically the solid neuroendocrine carcinoma. This type of carcinoma consists of dense and solid nests or trabeculae of cells separated by delicate fibrovascular stroma. They occur mainly in older women around the age of 70. Zekioğlu et al. [10] reported a series of 12 cases with only 2 cases under 60 years old, and more than half of these patients were over 70 years old. Our case was a 65-year-old postmenopausal woman.

In neuroendocrine carcinomas, immunohistochemical studies for neuroendocrine markers have been recorded. Neuron-specific enolase (NSE), cytokeratins (AE1/AE3, CAM 5.2, or CK7), and neuroendocrine differentiation indicators, such as Grimelius stain, synaptophysin, Leu 7, serotonin, bombesin, and chromogranin A or B, are most commonly used [11]. The result in our case was evident with synaptophysin stain. Sapino and Bussolati [12] proposed that only tumors that express chromogranin A, or chromogranin B, or synaptophysin in more than 50% of their cells be recognized as endocrine breast tumors. Miremadi et al. [8] compared 3 markers, NSE, chromogranin A, and/or synaptophysin, and found them to have no relationship with established prognostic factors or patient outcome.

The imaging features of mammary neuroendocrine carcinomas can be very diverse. Wade et al. [13] reported the first case in 1983, in which the mammography showed a 10-cm multilobulated soft tissue mass with numerous ill-defined margins, while the sonography demonstrated both solid and cystic components of the mass. In 2000, Rubini et al. [14] described their case in mammography as a 5-cm high-density mass with irregular margin, however, in sonography as cystic with intracyctic tracts. In 2003, Günhan-Bilgen et al. [3] reported the first mammographic and sonographic series (5 cases) of this rare tumor with pathological correlation. In most cases, mammography showed dense round masses with predominantly spiculated or lobulated margins correlating with the pathological margins. Most of the tumors were hypoechoic and of homogeneous echo texture with normal sound transmission. Mammographically, our case was an isodense, circumscribed, opaque nodule, and sonographically, it was a hypoechoic mass with microlobulated margin, posterior acoustic enhancement, and hypervascularity. The mass did not contain any cystic components.

Treatment for neuroendocrine carcinomas is limited to surgery. Most reported cases involved lumpectomy or mastectomy with axillary lymph node dissection. In our case, lumpectomy was performed with axillary SLNB. The frozen section for SLNB was negative for malignancy. Radiotherapy is not effective for carcinoid tumors and no reports of adjuvant radiation for primary mammary neuroendocrine carcinomas have been recorded. However, chemotherapy can be effective for this type of tumor [15]. The tumor was ER+ and the patient has been taking tamoxifen after the surgery. Our patient did not receive any chemotherapy due to the small size of the tumor and negative axillary node status.

Finally, primary breast neuroendocrine carcinomas are rarely found and mainly in older women over 60 years old. Due to the diversity of imaging findings, the diagnosis is based on immunohistochemical stain in neuroendocrine markers. Surgery has turned out to be the first-line treatment and subsequently radiation may play a role in palliative treatment.

**Conflict of Interest**

The authors declare that they have no competing interests.
Solid Neuroendocrine Carcinoma of the Breast

References


