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A Rare Tumor Of The Breast: Solid Neuroendocrine Carcinoma

Corresponding Author:
Dr. Samia S Ghanem,
Oncologist, Department of Medical Oncology, National Institute of Oncology , Avenue Allal-el-Fassi, BP 6213, 00212 - Morocco

Submitting Author:
Dr. Samia S Ghanem,
Oncologist, Department of Medical Oncology, National Institute of Oncology , Avenue Allal-el-Fassi, BP 6213, 00212 - Morocco

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Author(s): Ghanem S S, Glaoui M , Naciri S , Khoyaali S , Kabbaj M , Khanoussi B , Errihani H

Abstract

Background:
Solid neuroendocine carcinoma of breast (NECB) is extremely rare. In this paper, we present a case of inflammatory primary solid neuroendocrine carcinoma of breast managed by surgery and chemotherapy and a brief review of the epidemiology, clinical features, diagnosis, pathologic features, treatment, and prognosis of solid NECB.
Methods:
A 63-year-old woman was admitted in our institution with inflammatory primary solid neuroendocrine carcinoma of breast. A bulky mass of 8.0 cm tumor was located in the upper-outer and intern quadrant of her right breast. The patient inderwent neoadjuvant chemotherapy, Lumpectomy and subsequent radical mastectomy with axillary lymph node dissection . Microscopically, the tumor was classified as solid cohesive, the tumor cells were positive for neuroendocrine markers chromogranin A and synaptophysin. 16 lymph nodes of 27 were metastatic.
Results:
Local recurrence and metastatic progression was noted only one month after the surgery, the patient was managed by chemotherapy and hormonotherapy. She is still alive, 18 months after diagnosis.
Conclusions:
Solid neuroendocrine carcinoma is a subtype of mammary carcinoma with several distinctive features. Because of the rarity of this disease, there is no standard treatment, they are caracterised by a higher propensity for local and distant recurrence, This case reinforces the importance to explore the novels therapeutics regimen and one of ways to explore is the use of VP16-cisplatine as treatment as it was partially efficacy for this kind of tumor.

Introduction

Primary neuroendocrine carcinoma (NEC) of the breast is extremely rare and accounts for less than 5% of all cancers arising from the breast [1]. The first case was described in 1963 by Feyrter and al [2] and sporadically reported in the literature since then [3, 4]. Solid neuroendocrine carcinoma is one of types of NEC, the others types are: small cell carcinoma, and large cell NE carcinoma.
The diagnosis of NEC of breast is based on the criteria established recently en 2003 by the WHO classification system, who has clarified the confusing interpretation of the phenomenon of neuroendocrine differentiation in breast cancer disease. WHO's classification clearly establish that the immunohistochemical expression of NE markers in more than 50% of the tumor cell population is the unique requisite for the diagnosis of primary pure neuroendocrine breast carcinomas (NECB) [1]. NEC of the breast is associated with more aggressive behavior than ductal carcinoma, with a higher propensity for local and distant recurrence and poorer OS.
Because of the rarity of this disease, and in the absence of randomized controlled trials, there is no standard treatment. We present a case of inflammatory primary solid neuroendocrine carcinoma of breast managed by surgery chemotherapy and hormonotherapy and a brief review of the epidemiology, clinical features, diagnosis, pathologic features, treatment, and prognosis of solid NECB.

Case report

A 64-year-old woman developed a palpable inflammatory mass in her right breast in June 2008. The patient noticed this mass two months before and it was rapidly growing. She was a non smoker and she had 10 children. There was 7 years history of oral contraceptive use. She had no remarkable past medical history, no family history of breast, colon or ovarian cancer, and was not using any medicine.
On examination, the right breast showed a bulky inflammatory mass of 8 cm of in the upper-outer and intern quadrant of her right breast. She has one ipsilateral mobile axillary lymphadenopathy. The left breast examination and other clinical examinations were within normal limits. Mammography and echography revealed the nodule to have suspicious characteristics. The biopsy of the lump revealed a solid neuroendocrine carcinoma of the breast. CT scan of the lung, abdomen and bone scan was normal. At the time of evaluation, our patient was in good general condition, The performance status (PS) was

equal to 1, the Patient completed four cycles of neo-adjuvant chemotherapy consisting of carboplatin and etoposide , The chemotherapy consisted of intravenous carboplatin AUC5 on day 1 plus intravenous etoposide at 120 mg/m 2 on day 1, 2, and 3, repeated every 3 weeks the clinical evaluation showed complete resolution of inflammatory sign and partial resolution of right breast mass, The performance status was 0.These drugs were chosen for their described efficacy both in breast carcinoma as in lung cancer , subsequently the patient underwent a right radical mastectomy with axillary lymph node resection. Macroscopically, the tumor was 8 cm in maximum diameter (pT3). It was yellowish-white indurated and irregular. Widespread vascular invasion was present. 16 lymph nodes of 23 were metastatic. Microscopically, the tumor was characterized by Atypical cells relatively monomorph and homogeneous organized in solid and trabecular arrangements, with fine granular eosinophil cytoplasm and hyperchromatic nuclei (illustrations 1 and 2). Widespread necrosis was present. Mitoses were rare. A minima ductal carcinoma in situ was observed grade intermediate.

The tumor cells were highly positive for neuron specific enolase (NSE), chromogranin (illustration3) and negative for c-erb-B2 and cytokeratin 20 (Figure 1). Estrogen receptors were positive in 80% of the tumor cells, progesterone receptors were positive in 90%, Ki-67 at 10%.

Local recurrence with multiple pleural and liver metastases developed only 5 weeks after surgery, the metastasis was confirmed by biopsy

Our patient was treated by chemotherapy, doxorubicin 60 mg/m2 and cyclophosphamide 600 mg/m2 with six cycles every 21 days. The tumor response was in favor of stabilization. In consideration of the positive hormonal status and of the negative c-erb-B2, and after chemotherapy, our patient received anastrozole 20 mg daily for six months. After 6 months, the hormonotherapy was discontinued for pleural metastasis progression, and the patient was treated by chemotherapy etoposid and carboplatin ,our patient has progressed after 2cycles , and actually she is in bad health with a Performance Status equal to 3 (ECOG).

Discussion:

Primary SNEC is a rare disease that accounts for less than 5% of all cancers arising from the breast [1]. Their prevalence is about 0.5% in a series of 1368 histopathologically proven breast cancers [5] . The first case was described in 1963 by Feyrter et al [2], since then, 166 cases of SCCB have been diagnosed.

The World Health Organization defines them as tumours that exhibit morphologic features similar to those of neuroendocrine tumours of both the gastrointestinal tract and lung, and that express neuroendocrine markers in more than 50% of the cell population. This criterion distinguishes NEC of the breast from other mammary carcinomas that show only NE morphological features or focal (

The importance of this definition is highlighted by 2 studies that showed that focal NE differentiation had no prognostic significance as compared with breast carcinoma NOS [6, 7].

The histogenesis of neuroendocrine breast tumors is unclear, but they are thought to arise from endocrine differentiation of a breast carcinoma rather than from pre-existing endocrine cells in the breast [8].

Morphologically, neuroendocrine carcinomas of the breast include solid neuroendocrine carcinoma, small cell or oat cell carcinoma and large cell neuroenocrine carcinoma. The most helpful features are cellular monotony, nuclear palisading and pseudorosette formation. Positive neuroendocrine markers must be found in order to make the diagnosis. The presence of an intraductal component is a helpful criterion to confirm the breast as the origin of a neuroendocrine carcinoma. Moreover, immunostaining for progesterone and estrogen receptor can provide additional evidence for the primary origin of a tumour in the breast. Sapino et al [4] have recently described five subtypes of neuroendocrine breast carcinoma. These subtypes are solid cohesive, alveolar, small-cell/Merkel cell-like, solid papillary and cellular mucinous carcinomas. The two latter subtypes are associated with a favorable prognosis. In the present case, the patient had solid cohesive neuroendocrine carcinoma.

NEC is rare and newly defined entity, to date there have been only 6 retrospective series reported using the diagnostic criteria of the recent WHO classification; they had relatively small numbers of patients. Three studies with 13, 12, and 7 patients, respectively, showed better prognosis in NEC [9, 10, 5], two studies with 35 and 10 patients showed no prognostic significance. [4, 11] and one study with 74 patients [12] showed that NEC has a more aggressive course than ductal carcinoma, with a higher propensity for local and distant recurrence and poorer OS.

The mean age at diagnosis was 61 (29-82) years [12]. a mass of the breast was the most common presenting symptom in SNEC of the breast, Nipple blood discharge was reported in few cases. The clinical and imaging features of NEC mimic those of breast carcinomas without any specificity [13]. Our

patient had an irregular lump of 8 cm, with erythematous skin, and its mammography revealed an irregular bulky mass with mastit carcinomatois.

Diagnosis of SCCB was most often accomplished via biopsy or extemporané. The morphological features of the neuroendocrine carcinomas of the breast should be confirmed by immunohistochemical means . A CT scan of the abdomen and pelvis, bone scan, and chest radiograph at the time of diagnosis of SNECB, and CT scan of the brain in the presence of neurologic signs or symptoms were warranted. .

most of patients with NEC reviewed in the literature were grade 2 tumors ER/PR positive and HER-2 negative , like our patient, it's the particularity of the primary NEC of the breast [3-5].

Because SCCB is rare, and in the absence of randomized controlled trials, there is no standard treatment. SCCB tends to behave aggressively, 15% risk for local recurrence by 5 years, 34% risk for distant recurrence within 5 years, with up to 25% of patients presenting metastatic disease and up to two-thirds developing distant recurrence [12]. Our patient relapsed only 5weeks after the mastectomy which is consistent with the literature data.

Histologic grade is the most important predictor of prognosis. Solid neuroendocrine carcinoma is considered to be well-differentiated tumors. However, small cell or oat cell carcinoma and large cell neuroendocrine carcinoma are poorly differentiated. Hence, we can assert that patients with a solid neuroendocrine carcinoma or have a better prognosis than those with small cell or oat cell carcinoma and with large cell neuroendocrine carcinoma. Regional lymph node metastasis and high nuclear grade is a poor prognostic predictor for both disease free survival and overall survival as demonstrated in a retrospective study of MD Anderson of 74 patients [12].

Most patients are treated like adenocarcinoma of the breast; there is no standard treatment protocol and a large variety of chemotherapy protocols have been employed in treating this disease. Systemic therapy principles have been derived from small retrospective case reviews of primary neuroendocrine breast carcinomas and extrapolated from studies of non breast neuroendocrine carcinomas, since the clinical behavior and histology are similar. Our patient was treated by neoadjuvant chemotherapy type VP16+cisplatine, we notice a partial response, and then she was treated using anthracyclin and cyclophosphamide as first line of palliative chemotherapy with no efficacity. So we can conclude that VP16-cisplatine is probably more appropriated in the NEC and can be a start of more depth research.

Conclusion

It seems to be very important to identify the mammary primary sarcomas as entity separated from the carcinomas of the breast. This case reinforces the importance to explore the novels therapeutics regimen for this very rare tumor, and one of ways to explore is the use of VP16-cisplatine as treatment as it was partially efficacy for this kind of tumor.

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Illustrations

Illustration 1

Atypical cells relatively organized in solid and trabecular arrangements, with hyperchromatic nuclei(x 40).

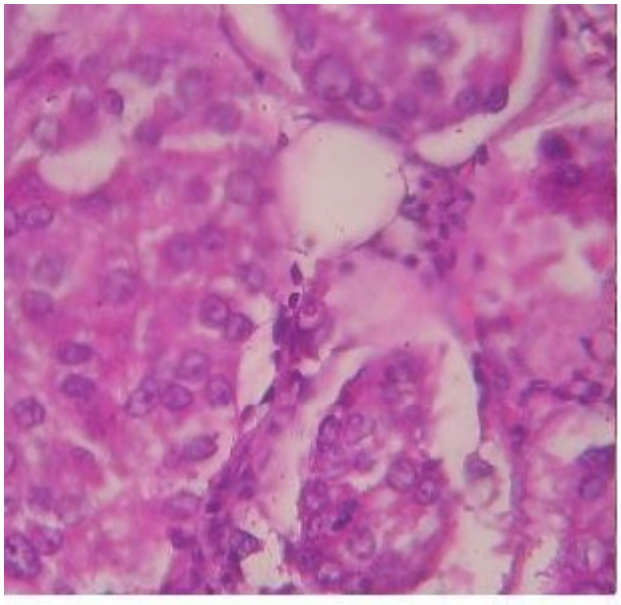


Illustration 2

Tumoral proliferation organized in solid and trabecular arrangements (x 20).

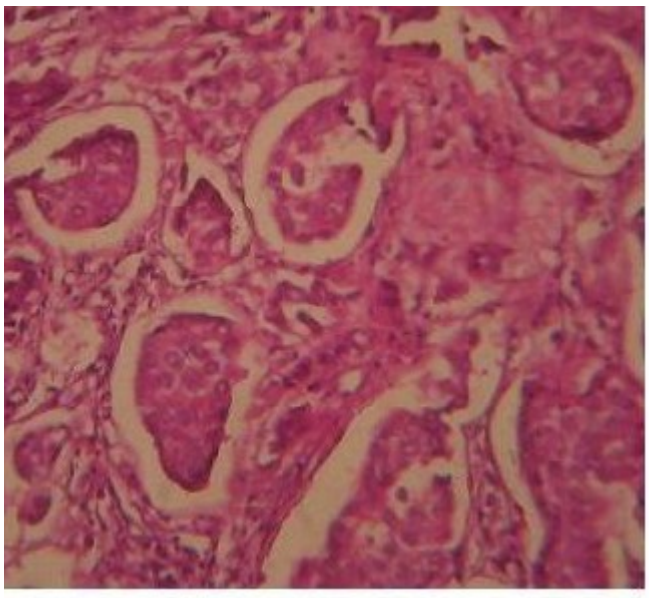
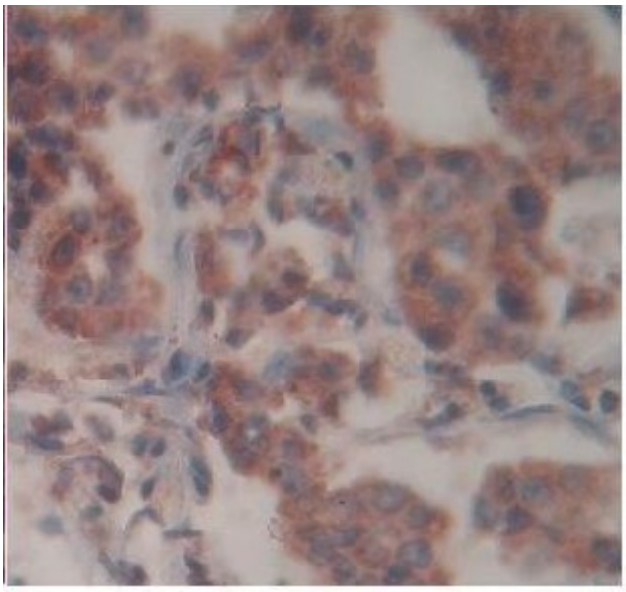


Illustration 3

Chromogranin A immunostaining positive in solid neuroendocrine carcinoma (x 20).



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