Small cell carcinoma of the breast: case report

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Summary

Background: Small cell neuroendocrine carcinoma of the breast is a rare tumor with fewer than 30 cases reported in the literature. The reported age of incidence of mammary small cell carcinoma is similar to that of breast carcinoma of the usual types. *Case:* The clinicopathologic findings of a primary mammary small cell neuroendocrine carcinoma occurring in a 28-year-old female are presented with a review of pertinent literature. She was treated with lumpectomy and sentinel node biopsy as well as chemotherapy and radiotherapy. *Conclusions:* To the best of our knowledge, this is the youngest patient with primary small cell carcinoma of the breast reported in the English literature, indicating that these tumors occur in a wide age range.

Key words: Small cell carcinoma; Neuroendocrine; Breast.

Introduction

Small cell carcinoma, although most commonly encountered in the lung, has been reported in many other sites, including the gastrointestinal tract, upper respiratory tract, salivary glands, thymus, genitourinary system, and skin [1]. Thus, extrapulmonary small cell carcinoma is a distinct entity which can occur in many sites, and is pathologically similar to small cell lung cancer. In contrast to pulmonary small cell carcinomas, extrapulmonary tumors of this type are very uncommon. Few examples of mammary small cell carcinoma have been described in the literature, most of them as case reports [2-5] and several in three small series [6-8]. We report a case of a 28-year-old woman with a primary neuroendocrine small cell carcinoma of the breast, confirmed by immunohistochemical and ultrastructural studies. This is the youngest patient of all reported cases, indicating that primary small cell carcinoma of the breast occurs in a wide age range.

Case Report

A 28-year-old healthy female presented to the breast health center with a palpable left breast mass, which she had felt one week previously. She denied any previous breast pathology and reported one maternal aunt with breast cancer. Clinical breast exam demonstrated a 3 cm well demarcated mass in the medial left breast without palpable axillary lymph nodes. On mammographic and ultrasound examination the mass was noted to be a 2.4 cm lobular solid mass lesion. A percutaneous core needle biopsy was performed, which was suggestive of small cell carcinoma.

Imaging studies including bone scan and FDG-PET scan did not reveal any evidence of extra-mammary disease; therefore a lumpectomy and axillary sentinel lymph node biopsy were performed.

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Pathological findings

Grossly the tumor consisted of a well-circumscribed 2.5 cm mass with a firm consistency and a solid white cut surface.

Microscopic examination demonstrated patternless sheets of undifferentiated small round to ovoid cells with hyperchromatic nuclei, inconspicuous nucleoli and scant cytoplasm, with extensive areas of necrosis (Figure 1). Numerous mitotic figures and apoptotic bodies were identified. No in-situ component was identified.

Immunohistochemical studies revealed that the tumor cells were diffusely and strongly immunoreactive for total cytokeratin (Biomeda, Foster City, CA, dilution 1:100), cytokeratin-7 (Bio-Genex, San-Ramon, CA, dilution 1:20), EMA (Dako, Glostrup, Denmark, dilution 1:100), e-cadherin (Zymed, San-Francisco, CA, dilution 1:20), BCL-2 (Dako, dilution 1:50), synaptophysin (Zymed, ready to use), and NSE (Dako, dilution 1:100), focally immunoreactive for chromogranin (Dako, dilution 1:100), Leu-7 (Zymed, ready to use), vimentin (Zymed, dilution 1:100), and O-13 (Signet Pathology Systems, Dedham, MA, dilution 1:40), and negative for CD-56 (Signet Pathology Systems, dilution 1:40), estrogen receptors (Novocastra, New Castle, UK, dilution 1:25), progesterone receptors (Novocastra, dilution 1:25), HER-2/Neu (Zymed, dilution 1:200), leukocyte common antigen (LCA) (Dako, dilution 1:100), and thyroid-transcription-factor-1 (TTF-1) (Zymed, dilution 1:50). P53 (Zymed, ready to use), and Ki-67 (Novocastra, dilution 1:50) were positive in approximately 90% and 70% of the tumor cells, respectively.

Electron microscopic investigation demonstrated one or more small (150 nm) dense core neurosecretory granules with a distinct halo in the cytoplasm of many tumor cells (Figure 2). Poorly formed cell junctions and rare desmosomal attachments were present, as well as sporadic primitive luminas.

This histologic, immunohistochemical and ultrastructural profile was consistent with that of a primary mammary small cell carcinoma.

Discussion

Primary small cell carcinoma of the breast is a very uncommon tumor, with less than 30 cases documented in the literature [8]. The histological features of breast and

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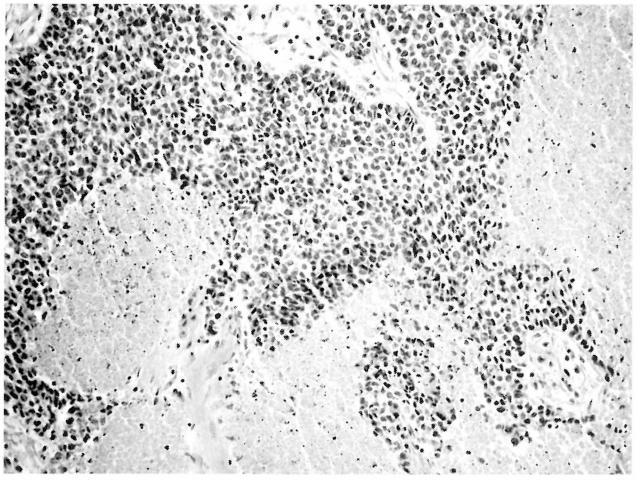

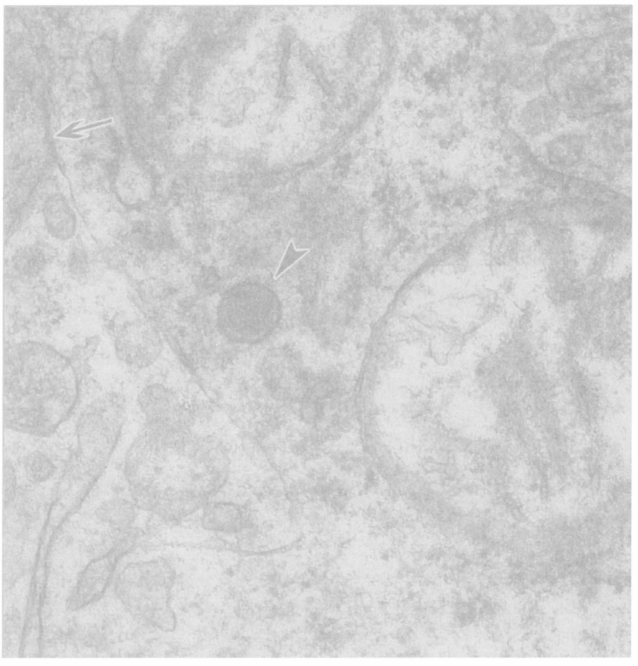

Fig. 2

Figure 1. — Solid sheets and irregular nests of small cell carcinoma cells with darkly staining nuclei and scanty cytoplasm separated by areas of necrosis. (hematoxylin & eosin stain, original magnification x 200).
Figure 2. — Electron micrograph showing two tumor cells with a primitive cell junction (arrow), and one round neurosecretory granule (arrowhead) with a distinct halo (bar = 500 nm).

other extrapulmonary small cell carcinomas are indistinguishable from bronchogenic oat cell carcinoma [1].

The first reported cases of mammary small cell carcinoma had a relatively poor prognosis [2, 3, 5, 6], but it probably reflects an advanced stage at diagnosis. Shin *et al.* [7] suggested that the prognosis could be better if the tumors were detected earlier and without lymph-node metastasis, since in their series the disease was identified at an earlier stage and their patients had a better outcome. The results of the study by Papotti *et al.* [6] support this statement, because the only patient who survived a relatively long period with no evidence of disease in their four cases series had a small tumor and negative axillary lymph nodes.

The reported age of incidence of mammary small cell carcinoma varies from 40 to 71 years [2, 3, 5, 7-10], with a higher incidence in women older than 60 years [8] and a mean of 56 years. Our patient, only 28 years old, is the youngest, thus expanding the age range of mammary small cell carcinoma significantly. All clinical, radiological and computerized tomography examinations performed suggest that the breast tumor was a primary one, since the possibility of a tumor in another site was excluded by all follow-up studies.

The tumor in our case measured 2.5 cm, within the range of tumor size of previously reported cases, which is 1.0 cm to 10.0 cm [2, 5, 7-9]. The tumor in our case was remarkably well-circumscribed, mimicking radiographically the appearance of fibroadenoma. Thus, mammary small cell carcinoma may present in young patients with a mammographic appearance of a benign lesion, emphasizing the importance of performing a biopsy in solid breast lesions.

Electron microscopy of our case demonstrated occasional neuroendocrine granules and tiny intercellular junctions as well as intermediate cytoplasmic filaments, findings similar to those of oat cell carcinomas of the lungs and other sites [1].

The immunohistochemical profile of the tumor was that of a neuroendocrine carcinoma; the tumor cells were positive for total cytokeratin, vimentin and various neuroendocrine markers. CK7 was positive in the tumor cells, as seen in most mammary small cell cancers, in contrast to pulmonary small cell carcinoma, which is usually negative for this marker [7]. In further contrast to pulmonary small cell carcinoma, which is positive for TTF-1 in the vast majority of cases [11], the tumor in our case was negative for this marker.

Mammary small cell carcinoma is almost always positive for BCL-2 and negative for HER-2/Neu [7, 8, 10], and the same results were obtained in our case.

The estrogen and progesterone receptor expression in mammary small cell carcinoma is diverse, with negative [8] and positive [7, 10] cases; the tumor presented herein was completely negative.

E-cadherin expression has been documented in many previously reported cases of primary small cell carcinoma of the breast [12], as well as in our case, suggesting that this tumor is a form of ductal carcinoma with neuroendocrine differentiation. Only one case of E-cadherin negative small cell carcinoma of the breast is reported in the literature [13], raising the possibility of lobular histogenesis in some of these tumors.

Hoang *et al.* [14] performed molecular analysis on two cases of mammary small cell carcinoma, and confirmed that the invasive small cell carcinoma is clonally related

to the intraductal component. They postulated that mammary small cell carcinoma arises from differentiation along a neuroendocrine phenotype from a multipotential neoplastic stem cell.

There is no standard therapy for small cell carcinomas of the breast, due to their rarity. However, it seems reasonable that the treatment of extrapulmonary small cell carcinomas should be similar to their pulmonary counterpart, with cisplatin-based chemotherapy and radiation therapy [15]. In the present report the patient underwent a lumpectomy with axillary sentinel lymph-node biopsy. She subsequently received etoposide and cisplatin followed by radiation therapy, 5000 cGy in 200 cGy fractions to the breast. The sentinel lymph node was negative, therefore axillary lymph-node dissection was not performed. The patient is alive and well with no evidence of disease ten months following diagnosis.

Conclusion

This report documents a rare case of primary small cell neuroendocrine carcinoma of the breast in a 28-years-old woman, indicating that this distinct type of breast tumor occurs in a relatively wide age range. Primary mammary breast carcinoma does not essentially differ from the much more common breast carcinomas of the usual types with regard to clinical presentation but the oncologic treatment is similar to primary pulmonary small cell cancer [7, 8].

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