

Primary Neuroendocrine Carcinoma of Breast: An Uncommon Variant

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ABSTRACT

Neuroendocrine carcinoma of breast (NECB) is an aggressive variant of invasive mammary carcinoma. Very few cases of Primary NECB have been reported in the literature. Here we report a 50 year female presented with left breast lump measuring 15 x 12 cm. of gradual onset with left axillary lymphadenopathy. On fine needle aspiration cytology of breast and lymphnode were positive for malignant cells. On ultrasonography of abdomino- pelvis showed metastasis to liver, peri pancreatic and para aortic lymph nodes with minimal ascites. On histopathology reported as Primary NECB-Large cell type-left breast. We are presenting this case for its extreme rarity and aggressive clinical behaviour.

Keywords: – Neuroendocrine Carcinoma of Breast, Endocrine Tumor, Breast Cancer, Histopathology

Introduction

Neuroendocrine carcinoma of breast (NECB) is an aggressive variant of invasive mammary carcinoma. It is extremely rare tumor accounting for 0.27 to 0.50% of histopathologically proven breast cancers^[1,2]. Most neuroendocrine carcinomas are located in gastrointestinal tract and lung^[3]. Only a limited number of studies on neuroendocrine breast have been reported in the literature and most of them are case studies.

Case Report

A 50 year old postmenopausal female presented with a single, large, hard, non-tender, gradually increasing, lump in the left breast of 8 months duration. At that time there was no other systemic disease was evident on clinical and other investigations. Patient delayed the initial treatment and came later with retraction of nipple and left axillary lymphadenopathy. She had no history of significant systemic disease. Her obstetrics history was G4P4D0L4 with menopause six years back. Her past and family history was non contributory. Radiological examination by ultrasonography of abdomen pelvis at second visit revealed metastasis to liver, peri pancreatic and para aortic lymph nodes with minimal ascites. Mammography showed heteroechoic lesions with hypoechoic rims. Fine needle aspiration cytology left breast was positive for malignant cells. Modified radical mastectomy was performed. Histopathological examination revealed gross specimen of left breast measuring 20x18x9 cm and weighing 900gms. It was covered with skin measuring 17x15cm (Fig.1). Tumour was fixed to skin with nipple areola retraction. Peau-d-orange was also noted. On cut section

revealed a tumor measuring 15x12x6 cm (Fig.2). Tumor was grey white, firm to hard in consistency with pushing peripheral margins. On microscopy, multiple sections showed tumor composed of neoplastic cells, arranged in large sheets, alveolar pattern, solid nests separated by thin fibrous septae(Fig.3). Individual tumor cells were large, round, pleomorphic having salt and pepper chromatin and moderate eosinophilic granular cytoplasm which constituted more than 60% of tumor morphology(Fig.4). Focally invasive breast carcinoma is noted. Intervening stroma showed diffuse mononuclear cell infiltration and fibrosis. On histopathological examination diagnosed as NECB-Large cell type – left breast.

On Immunohistochemistry tumor showed > 50 % tumor population showing positivity for Synaptophysin and chromogranin. Tumor was positive for ER and PR receptors. Our patient underwent left modified radical mastectomy and received chemotherapy and radiotherapy. On follow up, the patient is doing well.

Discussion

Primary NECB is an extremely rare specific subtype of breast malignancy. Most of the neuroendocrine tumors are located in the gastrointestinal tract and lung. The morphological features of primary NECB are similar to that of other sites. Many benign and malignant lesions of various organs show neuroendocrine differentiation^[4]. Neuroendocrine differentiation in breast carcinoma shows morphological similarity to carcinoma of gastrointestinal tract, lung and other nonendocrine organs with endocrine differentiation and carcinoid tumor^[5]. In breast carcinoma,



Fig. 1: Gross specimen of left breast- modified radical mastectomy.



Fig. 2: left breast on cut open showing grey white, homogenous, firm to hard tumor with pushing borders m. 15x12x6cm.

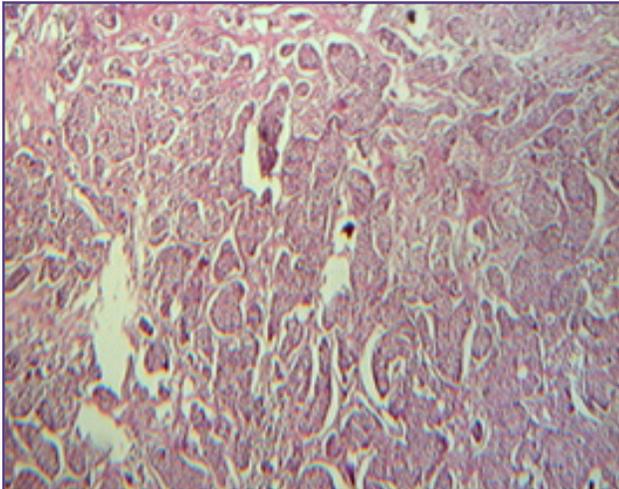


Fig. 3: photomicrograph showing breast tissue with tumor composed of neoplastic cells arranged in large sheets, alveolar pattern and solid nests separated by thin fibrovascular septa. H&E stain 100X

not otherwise specified (NOS) focal neuroendocrine differentiation can be seen scattered singly or in groups [6].

NECB used to be known as argyrophilic breast carcinoma, Carcinoid tumor or Endocrine carcinoma and now classified as breast carcinoma with neuroendocrine differentiation or Primary Neuroendocrine carcinoma [7,8].

In 50% of breast tumors, scattered neuroendocrine cells can be detected. Neuroendocrine differentiation has been reported in both in situ and invasive breast carcinoma. It is observed that mucinous carcinoma of breast has the greatest association with neuroendocrine differentiation [8]. WHO in 2003 defined NECB as breast carcinoma with

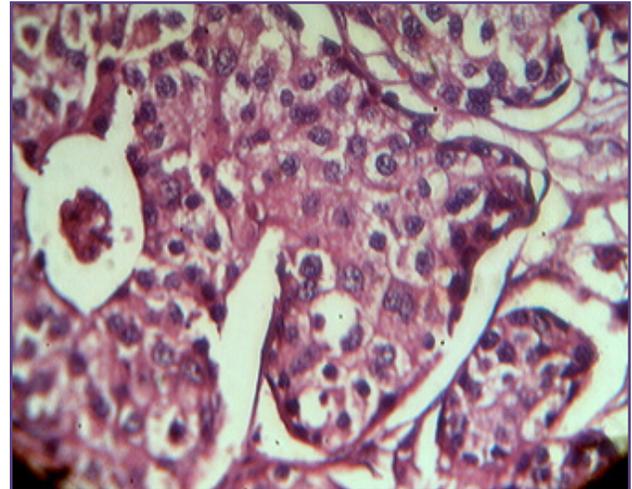


Fig. 4: Individual tumor cells are medium to large size, round to pleomorphic having salt and paper chromatin and moderate amount of eosinophilic granular cytoplasm. . H&E stain 400X

more than 50% of the population of tumor expressing immunohistochemical staining for neuroendocrine markers for diagnosing primary NECB and the extra mammary sites should be excluded [7].

Our patient was a 50 year old woman who presented with breast lump of 8 months duration which was gradually increasing in size with axillary node enlargement. Initially patient was not ready for surgical management but came at the clinic in late stage of disease. The mean age at diagnosis of the patient with NEC is 64 years. The mean tumor size is 3.2cm for NEC [6]. Whereas in our case tumor was very large size as patient presented in late stage of disease. It

is reported that about 43% of NEC cases presented with lymph node metastasis at the time of diagnosis [9]. In our case patient had significant axillary node involvement.

On histology, neuroendocrine carcinoma usually shows neoplastic cells arranged in alveolar pattern, solid sheets with tendency to produce peripheral palisidation. Depending on cell type and differentiation it is subtyped into- Solid neuroendocrine carcinoma, Oat cell carcinoma, Large cell neuroendocrine carcinoma [7, 9, 10].

In large series by Sapino et al, described tumors in 5 subtypes; solid cohesive, alveolar, small cell, solid papillary, cellular mucinous [6]. Our case shows predominant solid, alveolar and nest pattern having large cells with focal areas of mucin production. Few cases reported in literature of primary breast NEC of large cell type by Kim JW et al [2], Stita W et al [10], Hanna MY et al [11], Wei B et al. [12]. Overall survival of patients with NEC is determined significantly by tumour size, lymph node status, and proliferation rate. Clinical outcomes reported in literature showed 15% of local recurrence by 5 years, with median recurrence free time of 177 months and 34% risk for distant recurrence within 5 years [12].

Conclusion

Primary NECB is an unusual and aggressive carcinoma of breast. We are presenting this case for its extreme rarity and with advanced clinical behaviour. The treatment modality is not different from those conventional breast malignancies, however chromogranin production in neuroendocrine carcinoma has clinical and genetic implications owing to the biochemical analogy between granin and breast cancer (BRCA) protein. Hence, targeted gene therapy may be a future treatment strategy.

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