CASE REPORT

Neuroendocrine Carcinoma of Breast

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ABSTRACT

Neuroendocrine tumours (NETS) are rare tumours. The commonest site of occurrence is the gastrointestinal tract. NETS in the breast are even rarer, accounting for less than 0.1% of all breast cancers and less than 1% of all NETS. We are reporting a case of primary neuroendocrine carcinoma of the breast in a 60 years old female. Investigations were done to rule out any other associated lesion. Patient was treated by modified radical mastectomy and adjuvant chemo and radiotherapy.

Key words: *NETS (Neuroendocrine tumours). Neuroendocrine markers. Breast cancer. Radical mastectomy.*

INTRODUCTION

NETS arise from neuroendocrine cells which are present throughout the body, especially in the gastrointestinal tract and the bronchopulmonary system. Breast NETS are very rare clinical entities with overall prevalence of 1-2 cases per 10,000 persons.[1] NETS of the breast account for less than 1% of all the NETS of the body. Benign NETS are even rarer than the malignant ones. So all NETS of the breast are considered as malignant. Majority NETS of breast are secondary (90-95%) while primary NETS of breast are still less (5-10%). Differentiation between primary and secondary neuroendocrine carcinoma is made on the basis of *in situ* component of NETS within the breast tissue which is highly suggestive of a primary rather than a secondary NET. Thirty eight cases of primary NETS in the breast have been reported previously. Wade *et al*. reported the first well-documented example of primary NET of the breast with extensive regional metastasis.[2] In South East Asia so far, only one case of primary NET of breast is documented from India in 2008.[3] Hereby we are reporting a case of primary solid NET in the breast.

CASE REPORT

A 60-year-old nulliparous woman, known diabetic and hypertensive, presented with painless lump in her left breast of 04 months duration with no other local or systemic manifestations. She had underwent right breast fibroadenoma excision 35 years ago and hysterectomy 12 years ago.

On examination, there was a solitary non-tender firm lump (1.5 x 2 cm) in the upper inner quadrant of the left breast. The lump was not adherent to the skin or the underlying tissue. There was no nipple retraction or discharge. There was no ipsilateral or contralateral axillary lymphadenopathy. Her systemic examination was unremarkable.

USG (ultrasonography) of the breast showed a hypoechoic, hypervascular solid nodule measuring 1.4 x 1.7 cm. Mammogram showed a low density, circumscribed, mass lesion without microcalcification in upper inner quadrant of the left breast. Mammographically, it was a benign-looking opacity (Figure 1). FNAC of the lump showed small number of moderately atypical cells. So, excisional biopsy of the lump was performed which revealed a neuroendocrine carcinoma of the breast tissue forming tumour nests and cribriform patterns. The tumour cells had a salt and pepper chromatin. Immunohistochemistry showed chromogranin-A and synaptophysin positivity (Figures 2 and 3). ER and PR Receptor status was positive. Her 2-neu receptors were negative. After histopathological confirmation of neuroendocrine carcinoma of the breast, USG abdomen, X-ray chest and contrast-enhanced CT scan of the chest and the abdomen were performed to stage the disease and to rule out any other primary site, which turned out to be negative. So the diagnosis of primary neuroendocrine carcinoma of the breast

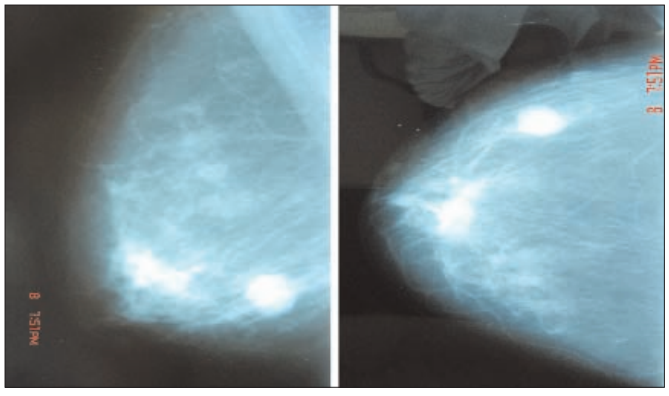

Figure 1: Mammogram of the patient showing NET.

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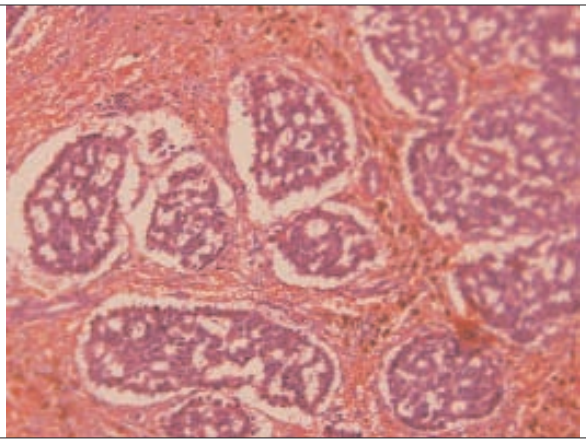

Figure 2: Histopathology slide of NET.

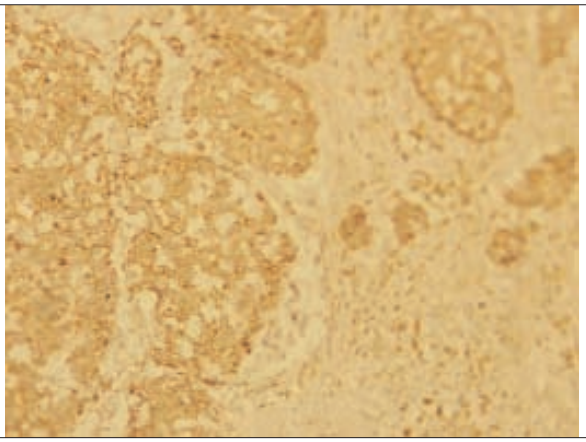

Figure 3: Immunohistochemistry slide of NET showing chromogranin A positivity.

(stage 1) was made. Left modified radical mastectomy and level-2 axillary clearance were done. Histopathology of the mastectomy specimen showed complete excision with no residual tumour or lymphovascular invasion. No metastases were detected in the axillary lymph nodes.

Postoperatively, the patient made an uneventful recovery and was referred to oncologist for adjuvant chemotherapy.

DISCUSSION

Neuroendocrine tumours (NETS) arise from the neuroendocrine cells of the body. Neuroendocrine cells belong to APUD system and secrete different types of amines and peptides. Vogler was the first to show the presence of neuroendocrine cells, lying among myoepithelial and epithelial cells of normal breast tissue.[4] NETS exhibit different types of neuroendocrine markers like chromogranin A, synaptophysin and neuron-specific enolase. Among these markers, chromogranin A is the most specific marker for neuroendocrine breast carcinoma. Diagnostic criteria for any NETS requires that 50% of the cells should be neuroendocrine marker positive, the growth of cells should be in solid sheets or insular pattern, presence of stippled chromatin and low grade cytologic features.[5] In this patient the resected specimen meets all the above immunohistochemical and histopathological criteria.

NETS of breast are graded as low grade type, NOS (not otherwise specified) and high grade (small cell). According to WHO, NET in the breast is classified as solid NETS, small cell/oat cell and large cell tumours. Only a small subset of NET (15-30%) are functionally active and produce carcinoid syndrome, so most of the cases (70-85%) presented as an isolated breast mass with or without axillary lymphadenopathy and without any systemic manifestations like cutaneous flushing, migratory erythema, watery diarrhea and palpitations. NETS are also associated with MEN syndrome type-1. This patient neither had a family history nor an abnormality of the endocrine system or the features of carcinoid syndrome. Literature search found 59 cases of NETS in the breast, 38 of which were primary breast NETS.[6] The mean age of the patients was 66 years (ranging 35-97) and none had reported symptoms of carcinoid syndrome.[6]

It is difficult to diagnose NETS in the breast on CT, MRI or USG. The radiological features of NETS are non-specific. On mammogram these tumours may lack the typical features of carcinoma breast like micro-calcification, irregular margins and so may be labelled as benign lesion. FNA or core needle biopsy examination is necessary for the diagnosis.

As NETS of breast are rare and very few cases had been reported, so standard therapy remains controversial. It is important to differentiate primary breast NETS from metastatic disease to breast because of difference in treatment and to avoid unnecessary radical intervention in case of metastatic tumour. Surgery is still the mainstay in the management of breast NETS according to stage of disease (lumpectomy with sentinel node biopsy to modified radical mastectomy). Adjuvant hormone therapy should be given since the tumour is frequently immunohistochemically receptor positive (ER 80% PR 35%). Due to the presence of specific cellular receptors in NETS of the breast, somatostatin and interferon has been claimed as a useful tool both for diagnosis (octreoscan) and therapy (for metastatic disease). As for therapy, radio-labelled synthetic analogs of somatostatin show advantages as compared to native somatostatin because of longer half life in cases who had positive octereotide scan.[7] As MIBG is absorbed and concentrated in neuroendocrine breast cells, therapeutic use of meta-iodobenzylguanidine (MIBG) has been tested in metastatic cases in few centres.[8]

NEC has vastly different outcome if compared to more common tumours of the same anatomic site.[9] A prognosis is difficult to make owing to the lack of long-

term survival data among such patients. Size is an important prognostic factor in this tumour, as in breast carcinoma of the usual type. The stage of the disease at the time of diagnosis is a determinant factor in its evolution.[10] ER and PR are important markers for directing therapy and determining prognosis. Low grade NETS with low proliferation rate and ER expression are to be considered to have a better prognosis.[11] NETS generally are more indolent than adenocarcinoma of the same site.

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