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Case Report

A Rare Case of Primary Neuroendocrine Cancer of the Breast

Dr Suraga Belakawadi[1*], Dr Jyotsana Goyal[1], Dr Bharat Bhusan Sarpathy[2], Prof(Dr) Padmalaya Devi[3]

1. MCh Resident, Department of surgical oncology, AHRCC, Cuttack.

2. Assistant Professor, Department of Surgical Oncology, AHRCC, Cuttack

3. Professor and Dean, AHRCC, Cuttack.

[*]**Correspondence to**: Dr Suraga Belakawadi; suraga.b@gmail.com.

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Abstract

Primary neuroendocrine tumors of breast previously known as argyrophilic breast carcinoma or breast carcinoid tumors first described by Cubilla and woodruff are now known as PNEC of breast. These tumors are rare accounting for less than 0.1% of all the breast cancer and less than 1% of neuroendocrine tumors. There are very few literatures available with respect to management and treatment of these tumors. We report a case of 46-year women diagnosed to have Primary neuroendocrine cancer (PNEC) of left breast of size 7×6cm involving left upper inner and lower quadrants extending to nipple areola complex. Diagnosis was confirmed by IHC. Patient received 6 cycles of Neoadjuvant chemotherapy (NACT) followed by modified radical mastectomy was done with clearance of level I, II, III axillary nodes. Postoperative period was uneventful and the patient is asymptomatic till date. The management of this case was similar to as that of other conventional types of invasive breast carcinomas.

Keywords- *PNEC Breast, Neuroendocrine tumours, Breast.*

Introduction

Neuroendocrine cells are specialized cells, that receive input from nervous system and respond by synthesizing and releasing hormones into the blood. They are widely distributed in the body. The tumors arising from the neuroendocrine cells are known as Neuroendocrine tumors (NET). They commonly arise from the bronchopulmonary system and Gastrointestinal tract. Primary Neuroendocrine cancers (PNEC) of the breast are rare, accounting for less than 0.1% of all breast cancers and less than 1% of all neuroendocrine tumors. Here we report a case of PNEC of the breast.

Case Report

A 46yr old peri-menopausal women presented with lump in the left breast since 4 months. On examination a single lump was palpated in left breast, measuring 7×6cm involving left upper inner and lower quadrants extending to nipple areola complex, hard in consistency, restricted mobility, fixed to the skin. The lump was not fixed to chest wall or pectoralis major muscle. Multiple mobile lymph nodes were palpated in left axilla.

Mammography suggested of BIRADS 4B lesion. Core needle biopsy showed poorly differentiated tumor. IHC was positive for CK (cytokeratin), Synaptophysin, Chromogranin and CD56. MIB 1 index was 80%. Tumor cells were negative for LCA, CD99 and GATA-3. Therefore, the diagnosis of primary neuroendocrine tumor was made. No distant metastatic foci found on CECT abdomen, pelvis, thorax and bone scan.

Routine laboratory investigations- complete blood counts, liver and kidney functions were normal and serological tests for HIV, Hepatitis B surface antigen and hepatitis C were negative.

In view of locally advanced disease patient was referred to medical oncology department for Neo adjuvant chemotherapy (NACT) where patient received combination of Cisplatin (40 mg/m^2) and Etoposide (150 mg/m^2). She was evaluated after 2 cycles of chemotherapy and showed complete clinical response with no palpable residual mass. Case was discussed in Institutional Tumor Board meeting and decision to complete 6 cycles of chemotherapy was taken.

Patient underwent Modified Radical Mastectomy (MRM) with clearance of level I, II and III axillary nodes two weeks after completion of NACT. On gross examination, the left MRM specimen measured 14×10×7cm. Cut section showed irregular growth of 4.5×4×3 cm, involving the inner lower quadrant. On microscopy, residual tumor was noted in small foci along with post NACT changes. Focal areas of necrosis were seen. There was no LVSI or PNI. Base, overlying skin and NAC were free of tumor. 13 lymph nodes were identified and were all free of tumor.

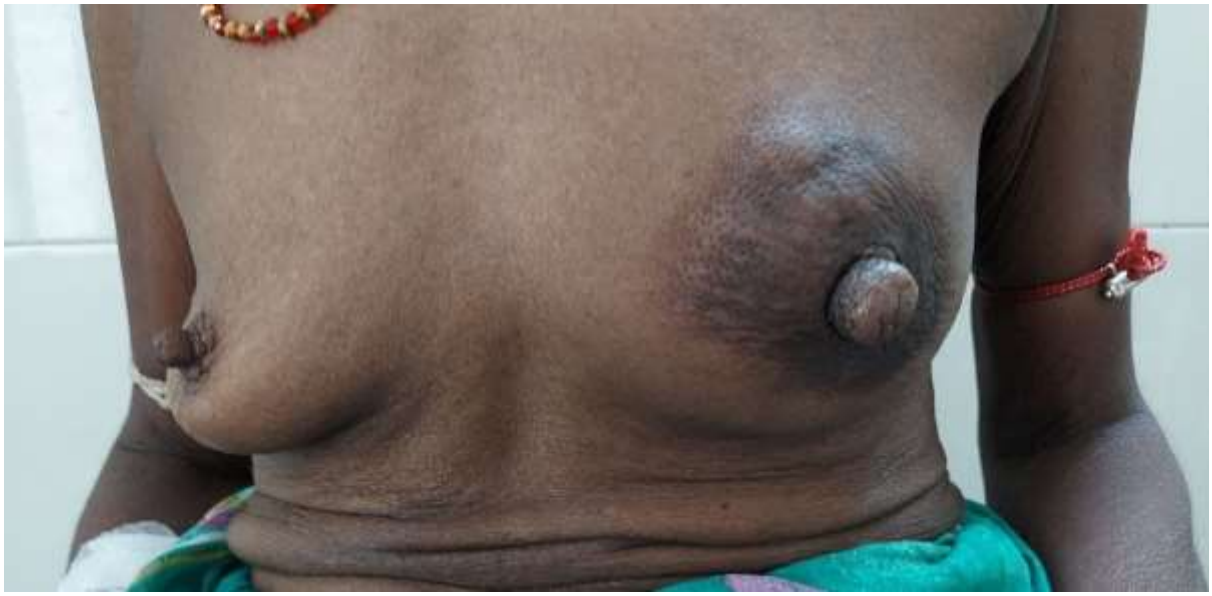

Fig 1. Tumor of size 7×6cm, involving left upper inner and lower quadrants, extending into nipple areola complex, hard in consistency, restricted mobility and fixed to skin.

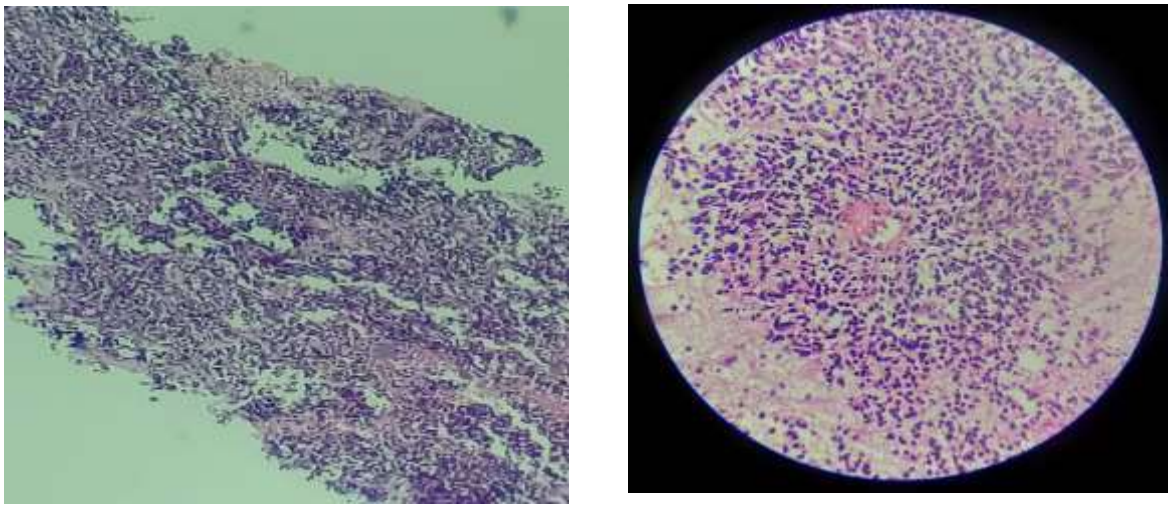

Fig 2. Microscopy

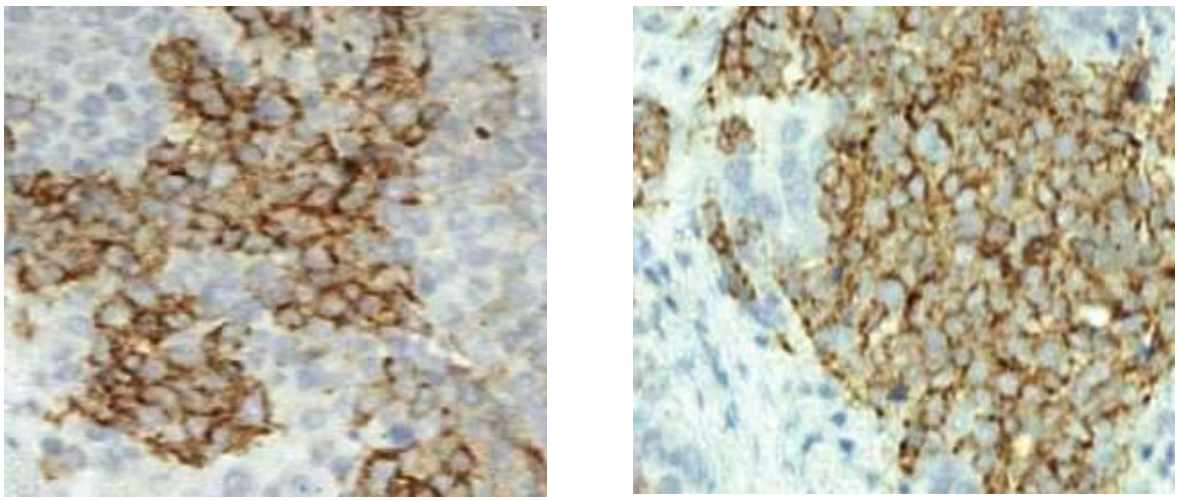

Fig 3- IHC for Synaptophysin

Discussion

Cubilla and woodruff first described the Primary Neuroendocrine tumors in the breast [1]. These tumors were initially known by various names like argyrophilic breast carcinoma, breast carcinoid tumour or endocrine carcinoma.

Following definitive criteria laid by WHO, these tumors are now known as Primary Neuroendocrine cancers (PNEC) of the breast. PNEC of the breast are rare tumors, accounting for less than 0.1% of all breast cancer and less than 1% of all neuroendocrine tumors [2].

Wang Et al in a retrospective study, reported 142 cases of PNEC of the breast out of 381,786 cases of invasive breast carcinoma recorded from 2003 to 2009 in surveillance, epidemiology and end results database (SEER). The incidence rate in their study was <0.1% of all mammary carcinomas with most patients presenting in sixth decade of life [3].

WHO, in 2012 classified breast neuroendocrine tumours into 3 categories:

- Well differentiated neuroendocrine tumour.
- poorly differentiated/small cell carcinoma.
- invasive breast carcinoma with neuroendocrine differentiation.

PNEC of breast is defined as the tumour where more than 50% of population are found to express neuroendocrine markers like synaptophysin and chromogranin.

Two more criteria required for diagnosis are:

- metastatic neuroendocrine carcinoma must be ruled out clinically and demonstration of *in situ* component histologically.
- Neuroendocrine differentiation, seen in up to 30% of invasive breast carcinomas, is most commonly associated with mucinous and solid papillary carcinomas [4].

Histologically, WHO defines PNEC of the breast as tumors consisting of cellular solid expansile nests and trabeculae.[5] Other uncommon architectural patterns include ribbons, cords and rosettes.

The tumour cells are separated by thin fibrovascular septae and cells can be spindled, plamacytoid or polygonal.[4] The cells may have abundant granular or clear vacuolated cytoplasm.[6]

The nuclear features of NETs of the breast vary from the classic smooth nuclear borders to salt and pepper chromatin seen in carcinoids of other sites. Nuclei are often pleomorphic with irregular nuclear membranes, and chromatin ranges from evenly distributed with inconspicuous nucleoli to hyperchromatic or vesicular with prominent nucleoli.[6]

Morphology might suggest neuroendocrine differentiation. For the diagnosis, expression of neuroendocrine markers is required. Synaptophysin and chromogranin A are the most sensitive and specific IHC markers [7]. Other less sensitive and specific markers include Neuron specific enolase (NSE) and CD56 [7].

Electron microscopy can also demonstrate Neuroendocrine differentiation ultra-structurally. Dense core granules correspond to chromogranin expression and clear presynaptic vesicles corresponds to synaptophysin expression under electron microscopy [5].

Very less number of cases of PNEC breast have been described in literature, hence there are no established treatment protocols. These tumours are treated similarly as that of other conventional types of invasive breast carcinoma and there is variable prognosis.[8]

In the present case, the initial presentation was a locally advanced breast carcinoma, following 2 cycles of NACT, response was assessed. The patient showed complete clinical response therefore decision of completion of 6 cycles of NACT was taken at institutional tumour board meeting. Patient underwent Modified Radical Mastectomy 2 weeks after completion of NACT. Post-operative period was uneventful and patient is symptom free till last follow-up.

Conclusion

The prognosis of primary neuroendocrine tumours of breast are similar to other invasive breast carcinomas. These are rare tumours and are classified as type of invasive breast carcinoma with distinctive histopathological features. The most important prognostic factor is grade of the tumour. Treatment of these tumours are not standardized and are treated similarly as the patients with invasive ductal carcinoma, NOS which depends on the size of the tumour, grade, clinical stage, and status of hormonal receptor.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

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