

Primary Neuroendocrine Carcinoma of the Breast: A Rare Case Report

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Abstract: Primary neuroendocrine carcinoma of the breast [NEC] is a rare variant of breast carcinomas which most of the times is under diagnosed and treated. Only 30 cases have been reported in the literature including male breast. Age incidence varies from 40-70 years. Here we present a rare case of primary neuroendocrine carcinoma of right breast with right axillary lymph node metastases in a 60 years female. Clinical and radiological parameters were analyzed to rule out metastatic deposit from other primary sites or involvement and distant metastasis to other organs ruling out possibility of invasiveness. Special stains and immunohistochemistry helped us to confirm the diagnosis the diagnosis of this rare variant of breast carcinoma.

Keywords: Enterochromaffin cells, Neuroendocrine tumor, Chromogranin, bad prognosis

INTRODUCTION

Neuroendocrine tumor of the breast is most frequently used generic term to describe duct cell carcinoma with predominant neuroendocrine differentiation. It was first reported in the year 1963[1]. Neuroendocrine tumors of the breast arises from the enterochromaffin cells identified by Kulchitskyin 1897. Neuroendocrine cells are known to be present normally in the mammary tissue, these are argyrophilic in nature and are seen between basal myoepithelial cells and luminal epithelial cells [2].

Primary NEC of the breast accounts for <1% of breast carcinomas. To call NEC atleast 50% of tumor cells must be positive for neuroendocrine markers. Primary breast origin shows endocrine elements only in the invasive portion along with presence of intraductal components. Immunohistochemistry for neuroendocrine markers like Chromogranin and Synaptophysin is important to confirm the diagnosis and for planning treatment modalities, as the prognosis seems worse than for the conventional ductal cell carcinoma NOS type [3].

CASE REPORT

A female of 60 years presented with lump in the right breast since 3 months which had recent increase in size for the past few weeks. Past history of child births revealed first pregnancy at the age of 19 years. Obstetric history –P3, L0, D2, A1, two still births and no live children. Routine laboratory investigations were within normal limits. Computerized Tomography study of chest, abdomen and pelvis showed no organomegaly or any focal lesion ruling out the

possibility of involvement of lung or ovary. Local examination revealed a spherical swelling of size 4x4 cms in the upper outer quadrant of right breast with smooth surface. Margins were ill defined. Nipple retraction was present along with bulging of the nipple areola complex. Consistency of the swelling was firm to hard. Lymphnode examination revealed three nodes in the right axilla, central group which were firm to hard in consistency, size ranged from 0.8-2.0cms with restricted mobility. Clinical diagnosis offered was carcinoma of right breast with axillary node metastasis and clinical staging of T3N1M0. Fine needle aspiration cytology was done, suggested diagnosis of Duct cell carcinoma of right breast with metastatic deposits (Fig. 1). For which patient underwent modified radical mastectomy (MRM) with axillary clearance.

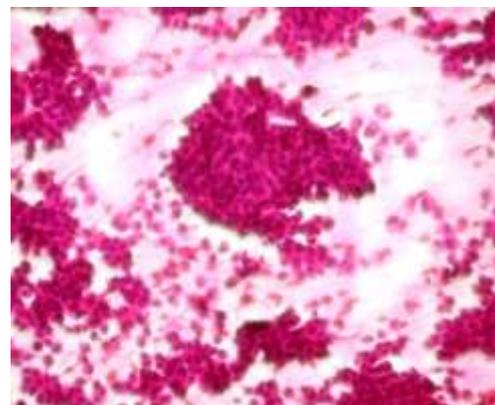


Fig. 1: Hematoxylin and eosin stained (10x) cytosmear with sheets of pleomorphic ductal epithelial cells with high N/C ratio-Cellular monotony

Gross

We received right mastectomy specimen (MRM) with nipple and areola measuring 11x9x4 cms along with skin flap measuring 10x8 cms. Nipple was found to be pushed to one side. Grossly nipple and areola appeared involved. Cut section showed grey

white tumor tissue measuring 5x4x4cms with grey brown areas close to the nipple area. Three lymphnodes were resected of sizes 1.8 to 0.8cms. Cut surface of the lymphnodes showed grey white areas (Fig. 2 and Fig. 3).



Fig-2



Fig-3

Fig. 2 and 3: Gross picture-mastectomy, cut surface with gray white tumor mass of size 5x4x4cms, close to nipple and areola

Microscopy

Multiple sections studied showed tumor tissue arranged in nests, solid sheets and alveolar like patterns separated by fibrous septae in >50% of the tumor area. Individual tumor cells were, round to oval monomorphic, scant to moderate eosinophilic cytoplasm, round nuclei, evenly distributed chromatin (salt and pepper appearance) prominent nucleoli in some of them. Mitotic activity was 1-2 per/ 10 HPF. Focal areas showed tubule and acinar formation, tumor emboli in lymphatics and hemorrhages were also noted (Fig. 4, 5, 6). Nipple and areola however was free from tumor infiltration. Deep resected margin and other margins were also free from tumor infiltration. All the three lymphnodes showed metastatic deposits of the same tumor (Fig. 7). Diagnosis of duct cell carcinoma with neuroendocrine differentiation/ neuroendocrine carcinoma with lymph node metastasis was provisionally offered.

Further help with Immunohistochemistry showed estrogen receptor negativity, progesterone receptor negativity, HER-2neu negativity and diffuse cytoplasmic positivity for synaptophysin, neuron specific enolase and chromogranin neuroendocrine markers (EP-1, Pg R636, C-erb-2, BBS/NC/V1-H14 and polyclonal rabbit clones respectively). The Final diagnosis of Primary Neuroendocrine carcinoma – invasive variant was confirmed (Fig. 8, 9 and 10).

DISCUSSION

Primary NEC of the breast is a rare entity newly defined in the 2003 WHO classification of tumors of the breast. It is a distinct histologic type of

aggressive mammary carcinoma first recognized in 1963 and sporadically reported in the literature since then. Incidence of this variant is 2-5%. It comprises several different histologic types. One type is solid papillary variant and is mainly considered as an in situ carcinoma associated with better prognosis. Other type is cellular mucinous type and also has a better prognosis. Third type is the invasive variant of NEC which spreads to distant organs and has worst prognosis. Poor prognostic are factors being higher nuclear grade and spread to regional lymphnodes [5]. Other terminology used in the past were Oat cell carcinoma; High grade NEC; Small cell undifferentiated carcinoma.

These tumors can secrete hormones and can rarely cause any particular clinical manifestation. They are immunohistochemically more likely to be ER/PR negative and HER-2 negative with higher tendency to have local and distant recurrences [6].

In 2003 WHO classification included three histologic sub types of neuro endocrine tumors; solid NEC, small cell NEC and large cell NEC. Small cell variant is indistinguishable from its counter part in the lung [7]. Exclusion of extra mammary primary site and/or demonstration of an insitu component within the breast should be confirmed to diagnose the primary small cell NEC of the breast. Most tumors are reactive for Neuron-Specific Enolase, Cytokeratin, Neuro endocrine indicators like Grimelius stain, Synaptophysin, Leu 7, Serotonin, Chromogranin A and Chromogranin B. Pulmonary small cell NEC are negative for CK7 and CK 20, whereas NEC of breast

will show positivity for these markers [8]. Suggested histogenesis being from multi potential stem cell capable of divergent differentiation [9]. Older age of presentation, absence of estrogen, progesterone

receptors expression and expression of ki 67 are prognostically of poorer overall survival and distant recurrence free survival.

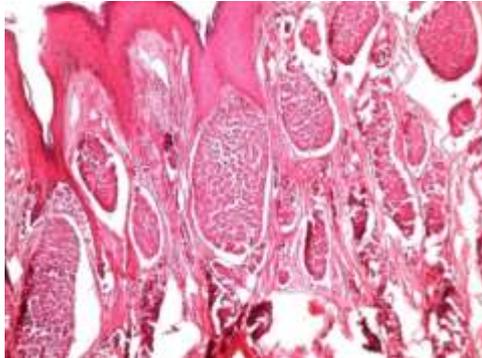


Fig. 4

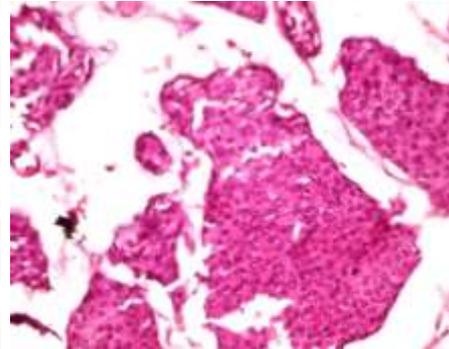


Fig. 5

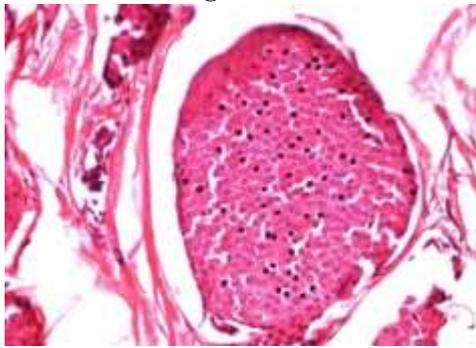


Fig. 6

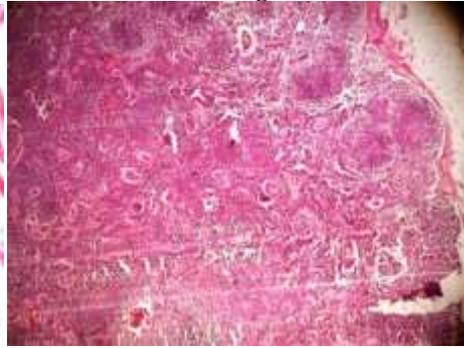


Fig-7

Fig. 4, 5, 6: Hematoxylin and eosin stained (10x) sections from nipple and areola and tumor tissue showed tumor arranged in nests and alveolar pattern, tumor cells with monotony and nuclei with salt and pepper chromatin
Fig. 7: Hematoxylin and eosin stained (10x) section of axillary lymph node with metastatic deposits

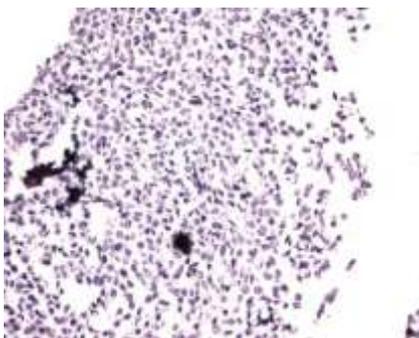


Fig. 8

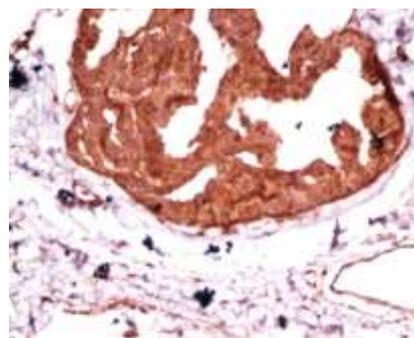


Fig. 9

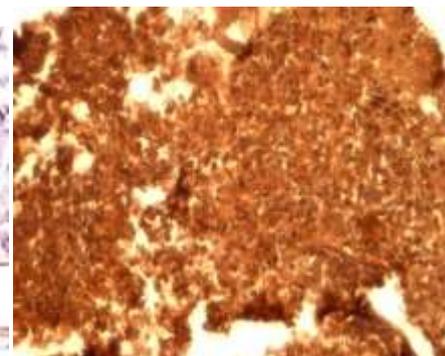


Fig. 10

Fig. 8, 9, 10: Immunohistochemistry-estrogen receptor negativity, diffuse chromogranin positivity and neuron specific enolase positivity respectively

CONCLUSION

NEC of the breast is a distinct type of neoplasm with higher malignancy, that exhibits morphological features similar to those of the neuroendocrine tumors of the gastrointestinal tract and lung. They are known to have aggressive behavior and a higher propensity for local and distant recurrences.

Hence we present this case for its extreme rarity, however awareness of this variant helps in early recognition. Treatment modalities like endocrine therapy should be studied, but for which larger case studies are needed.

REFERENCES

1. Ogawa H, Nishio A, Satake H, Naganawa S, Imai T, Sawaki M *et al.*; Neuroendocrine tumor in the breast. *Radiat Med.*, 2008; 26(1): 28-32.
2. Maluf HM, Koerner FC; Carcinoma of the breast with endocrine differentiation: a review. *Virchow Arch.*, 1994; 425(5): 449-457.
3. Samli A, Righi L, Casoni P, Papotti M, Gugliotta P, Bussolati G; Expression of apocrine differentiation markers in neuroendocrine breast carcinoma. *Mod Pathol.*, 2001; 14(8): 768-776.
4. Aggarwal G, Duhan A, Kalra R, Kataria SP, Sen R, Singh S; Primary neuroendocrine carcinoma of breast. *Journal of Cytology*, 2011; 28(2): 91-92.
5. Feyrter F, Hartmann G; On the carcinoid growth form of the carcinoma mammae, especially the carcinoma solidum (gelatinosum) mammae. *Frankfz Pathol.*, 1963; 73: 24-39.
6. Shin SJ, DeLellis RA, Ying L, Rosen PP; Small cell carcinoma of the breast; a clinicopathologic and Imuunohistochemical study of nine patients. *AMJ Surgpathol.*, 2000; 24(9): 1231-1238.
7. Tavassoli FA, Devilee P; Pathology and genetics in: tumors of the breast and female genital organs; WHO Classification of tumor series. Lyonfrance: IARC Press, 2003: 32-34.
8. Nesland JM, Holm R, Johannessen JV, Gould VE; Neurone specific enolase immunostaining in the differentiation of breast carcinomas with neuroendocrine differentiation. Its usefulness and limitations. *J Pathol.*, 1986; 148(1): 35-43.
9. Rosen PP; Mammary carcinoma with endocrine features In Rosen PP editor; *Rosen`s Breast Pathology*. 2ndedition, Philadelphia. Lippincott Williams & Wilkins, 2001: 503-508.