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Primary Breast Carcinoma with Neuroendocrine Differentiation: A Rare and Challenging Entity

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ABSTRACT

Primary neuroendocrine carcinoma of the breast is a distinct subtype, first recognized by the World Health Organization (WHO) in 2003 [1]. In 2012, the WHO revised the category renaming it as Breast Carcinoma With Neuroendocrine Features (BCNF) [2]. However, in 2019 WHO classification recommended defining the tumours with invasive breast carcinoma having nonspecific and specific morphology types (mucinous carcinoma, solid papillary carcinoma, etc) and non-uniform neuroendocrine morphology and neuroendocrine marker expression as "Invasive carcinoma of the breast with neuroendocrine differentiation" [3].

These tumours are exceedingly rare and under-recognized subtype of breast carcinoma representing only 2-5 % of all invasive breast cancer. We hereby report a case diagnosed as invasive ductal carcinoma with neuroendocrine differentiation in a 60-year old female patient who presented with a painless left breast lump.

Keywords: Breast carcinoma; Invasive; Ductal carcinoma; Neuroendocrine differentiation

CASE REPORT

A 60-year old female patient presented with a painless left breast lump for a duration of 4 months. On local examination of the breast, the mass measured 5 cm x 4 cm located at 2 o'clock position. There was no history of any nipple discharge and overlying skin and nipple- areolar complex were normal. No axillary lymphadenopathy was noted. Initial mammographic evaluation showed a dense lobulated mass measuring 44 mm x 35 mm situated at upper outer quadrant of left breast (BI-RADS category 4a). Subsequent evaluation with ultrasound-guided tru-cut biopsy confirmed Infiltrating ductal carcinoma. The patient underwent Left Modified radical mastectomy. Histopathological examination revealed two foci of invasive breast carcinoma – No special type with focal mucin production, focal micropapillary pattern and focal solid papillary carcinoma pattern with neuroendocrine differentiation. One axillary lymph node showed evidence of macro-metastasis with Grade-3 extranodal extension. The Bloom-Richardson (BR) Score was 3+2+3 = 8/ Grade 3.

Furthur, immunohistochemistry performed showed tumour cells positive for CD56, Cytokeratin, insulinoma-associated protein 1(INSM-1), Estrogen Receptor (ER), Progesterone Receptor (PR), Human Epidermal Growth Factor 2 (Her2Neu) and negative for transcription factor (GATA3). The pathological stage of tumour is pT2pN1.

DISCUSSION

Neuroendocrine tumours are most commonly found in gastro-intestinal tract, pancreas and bronchopulmonary system but rarely found in the breast [4]. There are three categories of neuroendocrine breast tumours as mentioned by WHO in 4th revised edition:-

1. Well differentiated
2. Poorly differentiated neuroendocrine/small cell carcinoma and
3. Invasive breast carcinoma with neuroendocrine differentiation

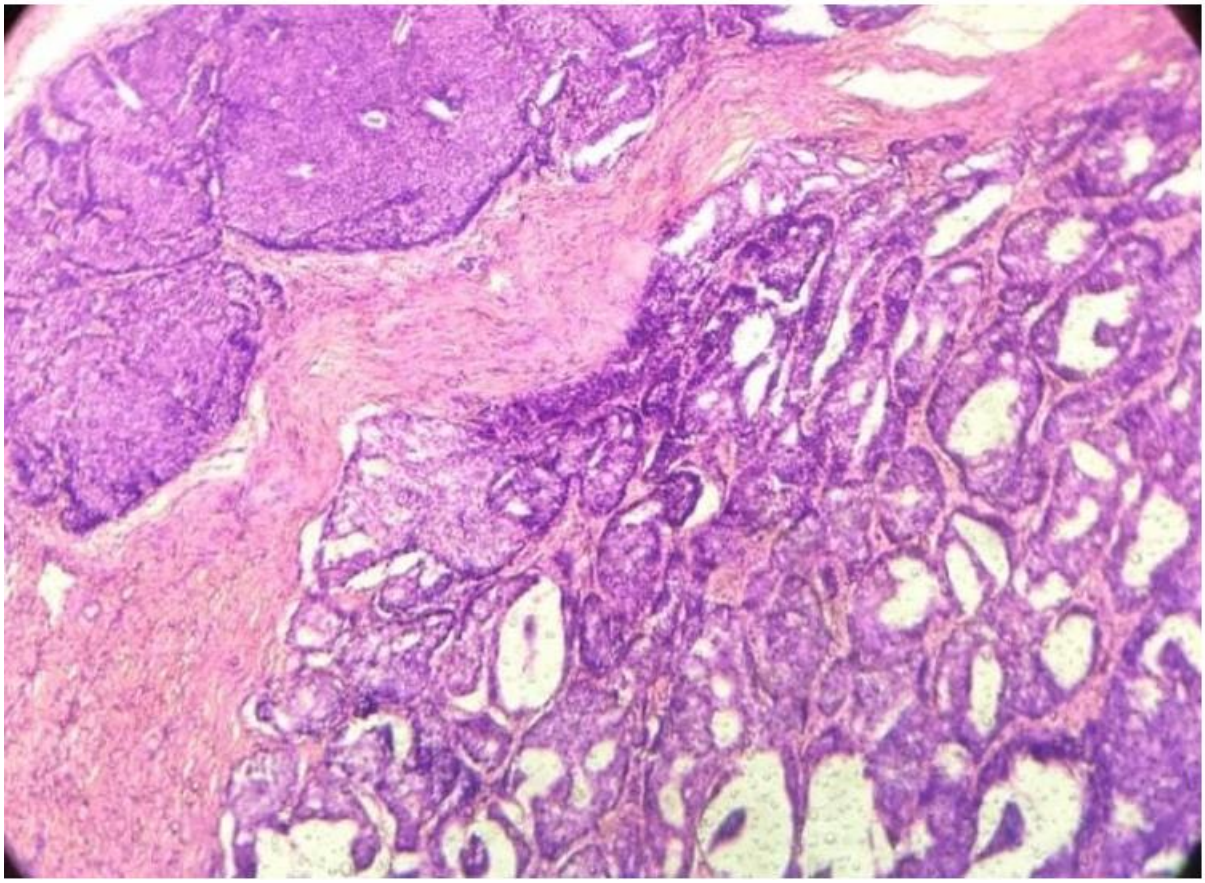
In presence of variable microscopic features, immunohistochemistry markers such as synaptophysin, chromogranin A or B, CD56, INSM-1, neuron-specific enolase, Leu 7 (CD-57), Ki-67 are necessary for diagnosis. Histologically, these tumours show features of neuroendocrine tumours of gastrointestinal tract with nuclear palisading, cellular monotony, loss of cell cohesion, pseudorosette formation, nuclei with stippled chromatin and abundant eosinophilic cytoplasm [5]. Additionally, these tumours have to be differentiated from metastatic neuroendocrine tumours from extramammary sites. For example, neuroendocrine breast carcinoma are positive for CK-7 and negative for CDX-2, whereas in gastrointestinal neuroendocrine tumours, CK-7 is negative and CDX-2 is positive [6].

Radiologically, neuroendocrine breast tumours may present on ultrasonography as hypoechogenic mass with irregular morphology and ill-defined margins, with or without cystic component. Mammography typically shows well circumscribed lesion with no associated microcalcifications. On magnetic resonance imaging, neuroendocrine breast tumours might sometime present as hypointense irregular lesion on T1-weighted sequences with early and intense enhancement [7].

The treatment of these tumours are essentially same as other invasive breast carcinomas. Surgery involves mastectomy with axillary lymph node dissection followed by mostly platinum/etoposide based regimen or chemo-radiotherapy depending on histopathological features of neuroendocrine breast carcinoma. Neuroendocrine breast tumour mostly exhibit luminal phenotype and considering the promising role of endocrine therapy in treatment of HR-positive breast cancer, it could be useful tool in management of breast tumours with neuroendocrine differentiation [8]. Also, the combination of Palbociclib and fulvestrant has been used in the treatment of patients affected from neuroendocrine breast carcinoma with encouraging results [9]. Neuroendocrine differentiation is considered as an independent adverse prognostic factor according to the multi-variant analysis based on SEER database (Surveillance, Epidemiology and End Results programme) [10]. Breast carcinoma with neuroendocrine features showed a poor survival rate, high rate of distant metastasis and an overall lower recurrence-free survival rate [11].

CONCLUSION

In cases of breast carcinoma with neuroendocrine differentiation, a combined approach of clinical assessment, radiological imaging along with histomorphology and immunohistochemistry aids in diagnosis and plan treatment for improved outcome. Considering that this cohort of breast tumours have poorer prognosis and variable biological behaviour, early diagnosis and treatment as an invasive breast carcinoma is of paramount importance.



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