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Case Report

Neuroendocrine Carcinoma of Breast: A Case Report

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***ABSTRACT*:**
Neuroendocrine carcinomas are rare malignant tumors located in the lungs and gastrointestinal tract. Primary location of such tumors in the breast is extremely rare, corresponding to less than 0.1% of all breast tumors. Herein, we present a case of 60 years old female diagnosed with neuroendocrine carcinoma of breast.

Key words: Neuroendocrine carcinoma, breast, tumour.

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INTRODUCTION:

Neuroendocrine carcinomas are rare malignant tumors which, in most of cases, are located in the lungs and gastrointestinal tract.[1] Primary location of such tumors in the breast is extremely rare, corresponding to less than 0.1% of all breast tumors.[2] The World Health Organization (WHO) Classification of tumors in 2003 defined neuroendocrine carcinoma (NEC) of the breast as having more than 50% neoplastic tumor cells expressing neuroendocrine (NE) markers. These tumors are usually seen in elderly women around sixth or seventh decade of life as reported in literatures.[3, 4] Herein, we present a case of 60 years old female diagnosed with neuroendocrine carcinoma of breast.

CASE REPORT:

This case was reported at the Department of General Pathology of DY Patil Medical College, Nerul, Mumbai, India. A 60 years old female presented to the department with lump in left breast from past 15 days associated with pain. A detailed medical history was taken which revealed that she does not have history of diabetes mellitus, hypertension, and tuberculosis. All the laboratory investigations were within normal ranges. Ultrasonography of the left breast was suggestive of fibroadenoma.

Fine needle aspiration cytology of the lesion suggested plenty of bizarre & atypical cells in sheets and singly scattered. Nuclear pleomorphism, increased N:C ratio, irregular nuclear margin, coarse chromatin and scanty cytoplasm was seen. Granulocytic precursors and few multinucleated and binucleated cells were also seen.Atypical mitosis was noted.

The features of left breast lump were suggestive of small round cell tumor of the breast. Cyto-morphology was indicative of Granulocytic Sarcoma. Left lumpectomy was planned and performed by the department of General Surgery. The Department of General Pathology received a left lumpectomy specimen oriented with suture on medial side and 2 sutures inferiorly. The specimen measured 7 x 5.5 x 1.5 cm. Skin flap measured 3.5 x 3 x 0.2 cm **(Fig 1)**.

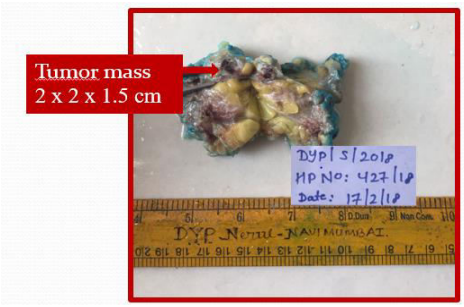


Figure 1

On serial sectioning, a grey white solid, homogenous tumor was identified measuring 2 x 2 x 1.5 cm with areas of hemorrhage and necrosis. The remaining breast parenchyma was showing elastosis **(Fig 2)**.

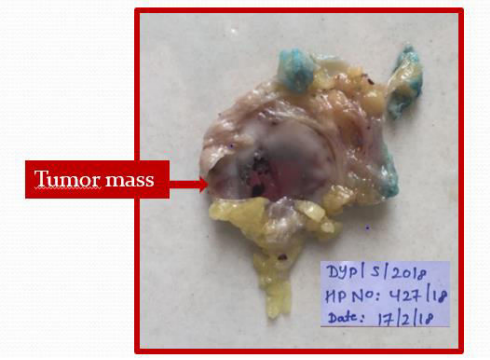


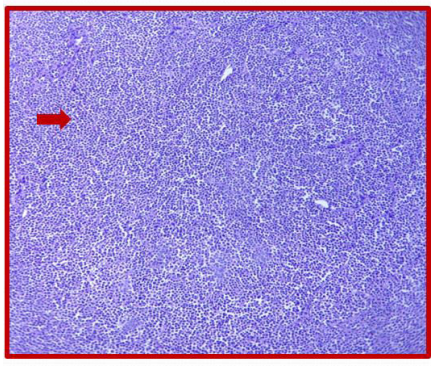
Figure 2

Distance of margins from tumor:

- Skin – 2cm
- Posterior margin – 0.2 cm
- Superior margin – 3.5 cm
- Inferior margin – 0.3 cm
- Medial margin – 3.5 cm
- Lateral margin – 3 cm

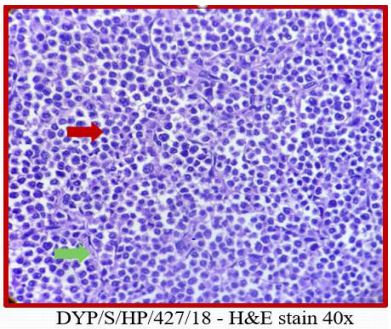
MICROSCOPY:

Multiple sections studied show a well circumscribed tumor composed of small round to oval cells (**Fig 3**). Individual cells display central nuclei with irregular nuclear membrane, coarse chromatin with indistinct nucleoli & scant cytoplasm separated by thin fibro-vascular septae (**Fig 4**). At places tumor cells were seem to be arranged in nest forming the typical Zell – Ballen pattern. Tumor cells were seen focally infiltrating the surrounding fat. Areas of hemorrhage were seen. Necrosis & mixed inflammatory cell infiltrate was seen. Atypical mitosis 3 - 4/ hpf. Lymphovascular emboli & Vascular invasion also seen. All margins including skin & base were free from tumor but tumor was close to inferior margin (0.3 cm). (**Fig 5 and 6**).



DYP/S/HP/427/18 - H&E stain 10x

Figure 3: H&E stain 10X



DYP/S/HP/427/18 - H&E stain 40x

Fig 4: H&E stain 40X

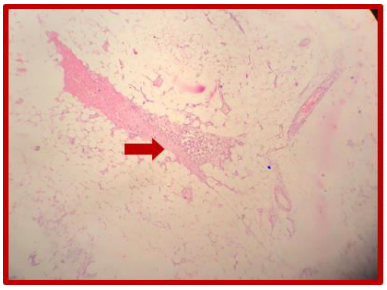


Fig 5: H&E stain 4X

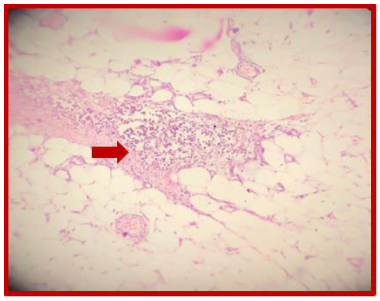


Figure 6: H&E stain 10X

Impression:

Features of high grade malignant small round cell tumor.

Differential Diagnosis:

1. Neuroendocrine Carcinoma
2. Non Hodgkins Lymphoma
3. Invasive Solid Lobular carcinoma

RB Scoring: 3 + 2 + 3 = 8

p T1c: Tumor > 10 mm but ≤ 20 mm in the greatest dimension.

Grade 3: Poorly differentiated.

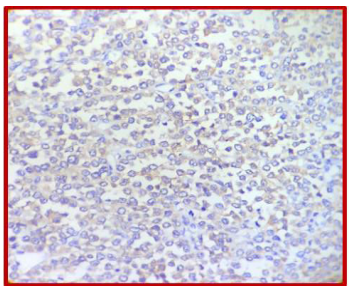


Figure 7: Synaptophysin 40X

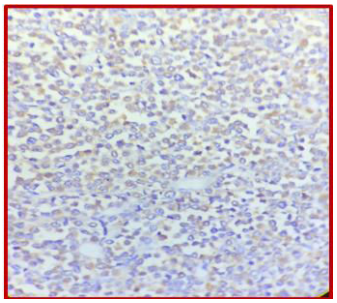


Figure 8: Chromogranin 40 X

Immunohistochemistry

- Synaptophysin & chromogranin: Positive
- ER: 70%, moderate nuclear staining intensity.
- PR: 30%, weak nuclear staining intensity.
- CK7: Negative
- LCA: Negative

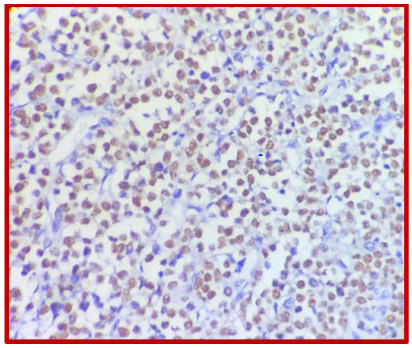


Figure 9: ER 40X

Final Diagnosis:
Neuroendocrine Carcinoma of Breast

DISCUSSION:
The gastrointestinal NEC is far more prevalent than NEBC, so WHO emphasizes the exclusion of extramammary sites before the definite diagnosis of NEBC.[5] Adams et al. recently analysed comprehensively the literature meeting the 2012 WHO criteria for primary neuroendocrine breast tumors. They found 58 published articles, generating data for 108 cases including their own. The mean size of primary tumors in their meta-analysis was 3.7 cm, compared to 2.2 cm of the current study. Lymph node involvement was recorded in 51% and distant metastases in 9% in the papers analysed by Adams et al.[6] Roininen N et al conducted retrospective study on patients with NEBC from Oulu and Helsinki University Hospitals in 2007–2015. There were 43 NEBC cases during the period. The incidence of NEBC from all breast cancers varied from 0.1% in Helsinki to 1.3% in Oulu. The mean tumor size was 2.2 cm and 23 patients (55.8%) had no lymph node metastases when diagnosed. In total, 4 patients (9.3%) had distant metastases at the time of diagnosis. High estrogen receptor (ER) expression was observed in 41 (97.7%) patients. When non-metastatic NEBC were compared to a prospective set of ductal carcinomas (n = 506), NEBC were more often HER2 negative, ER positive and the NEBC patients were older than patients with ductal carcinomas. They concluded that poor local control and worse overall survival may be linked to the more aggressive biology of the disease, despite its association with apparently indolent prognostic factors. [7] Valentim MH et al presented a case of a neuroendocrine carcinoma in an asymptomatic 75-year-old woman, detected in routine breast screening. The lesion was visible at mammography as a well circumscribed, medium density nodule, with no associated microcalcifications, and at ultrasonography as a hypoechoic nodule, with irregular shape and ill-defined margins. Magnetic resonance imaging revealed findings consistent with malignancy.[8] Murthy V et al presented a case of PNEC of breast in a middle aged lady. A 34 years lady presented with a breast lump since 1 month, who underwent modified radical mastectomy with axillary clearance. Histopathological diagnoses were infiltrating ductal carcinoma-neuroendocrine (NE) type. Immunohistochemistry showed estrogen, progesterone positivity and NE markers positivity in more than 50% of tumor cells for chromogranin, synaptophysin, neuron specific enolase. On further investigation by whole body computed tomography and magnetic resonance imaging revealed no extra mammary primary tumor.[9]

CONCLUSION:
Thus, despite the rarity of neuroendocrine carcinomas, with nonspecific imaging findings, such tumors should be included in the differential diagnosis of a nodular lesion with no associated microcalcifications on mammography and sonographically corresponding to a hypoechogenic mass with microlobulated or irregular contours.

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