

Case Report

**STUDY ON APOCRINE CARCINOMA OF BREAST:
HISTOMORPHOLOGIC FEATURES AND IMMUNOHISTOCHEMICAL
BEHAVIOR**

***Gayatri Gogoi, Mondita Borgohain, Asha Borah and Vishal Agarwal**

**Department of Pathology, Assam Medical College*

**Author for correspondence*

ABSTRACT

Apocrine carcinoma of breast is a very rare morphologic entity with an incidence of less than 1% of female invasive breast carcinoma. Historically it was called as apocrine metaplasia or sweat gland carcinoma. Apocrine carcinoma cells are characterized by abundant eosinophilic cytoplasm, large round nuclei and sharp cell borders. We have studied 128 cases of invasive carcinoma of breast for a period of 17 months from histomorphology and immunohistochemistry perspective in a tertiary care hospital where two cases were labeled as apocrine type carcinoma. Here, we report these two cases of invasive apocrine type of breast carcinoma in females and its co-relation with various prognostic and predictive parameters. One case was of 51 years and the other case was 46 years and both were post menopausal women. After Modified radical mastectomy, specimens were histologically diagnosed as apocrine carcinoma and graded histologically with Modified Bloom Richardson Grade (BRG). Then the tumors were studied for Immunohistochemistry profiles and it showed negativity for Estrogen Receptor (ER), Progesterone receptor and her2/neu, also called as triple negative breast cancer (TNBC). Most of the studies show no difference in survival in apocrine carcinoma than usual infiltrating ductal carcinoma (IDC-NOS) but few newer points are emerging in diagnostic and prognostic perspective of apocrine carcinoma. Also few recent studies suggest a better prognosis in cases of pure invasive apocrine carcinoma.

Key Words: *Apocrine Carcinoma, Immunohistochemistry, Prognosis and Triple-Negative*

INTRODUCTION

Apocrine carcinoma of breast is a very rare morphologic entity with an incidence of less than 1% of female invasive breast carcinoma. Historically it was called as apocrine metaplasia or sweat gland carcinoma. Apocrine carcinoma cells are characterized by abundant eosinophilic cytoplasm, large round nuclei and sharp cell borders. We have studied 128 cases of invasive carcinoma of breast for a period of 17 months from histomorphology and immunohistochemistry perspective in a tertiary care hospital where two cases were labeled as apocrine type.

CASES

Case 1

A 46 years old lady presented with a breast lump in upper central area size 2.6X 3 cm², which was gradual in onset for 8 months, nipple or skin was unaffected and there was no history of nipple discharge. Axillary nodes were not palpable. Fine Needle aspiration Cytology (FNAC) report was Fibroadenoma with apocrine change and atypia. Lumpectomy was performed and lump was sent for histopathological examination. Formalin fixed paraffin embedded (FFPE) blocks and haematoxylin and Eosin (H&E) stained sections were examined under light microscope. It showed sheets of large round tumor cells having abundant eosinophilic cytoplasm, with sharp borders, round nuclei, vesicular chromatin pattern, and prominent nucleoli in most of it (Figure 2). There were two foci of in situ component with similar

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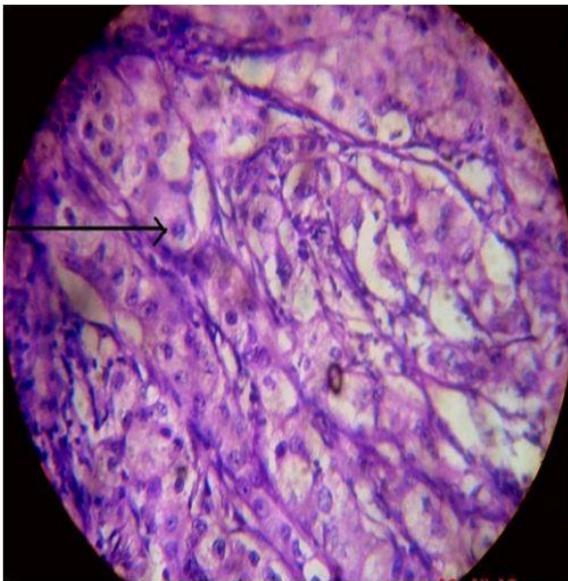


Figure 1: INVASIVE APOCRINE



Figure 2: APOCRINE DCIS (Case 1)

cellular picture. Modified Bloom Richardson (BRG) grading was done on basis of tubule formation, nuclear pleomorphism and count of mitotic figures. The case was labeled as apocrine carcinoma of breast, BRG grade II. Further FFPE blocks were processed and immunohistochemistry was performed for detection of ER, PR, Her2/neu and proliferative marker Ki67. The tumor cells were not immunoreactive for ER, PR, Her2neu, so it can be categorized as TNBC. Ki67 nuclear staining was low (<9/10 high power field). Later case was subjected to modified radical mastectomy and finding was similar to previous lumpectomy specimen.

Case2

A 51 year lady presented with a breast lump in lower and outer quadrant 4X4 cm², irregular margin, firm in consistency and adherent to underlying structure, which was gradual in onset for 8 months with peau d orange in the overlying skin. Axillary nodes were palpable.

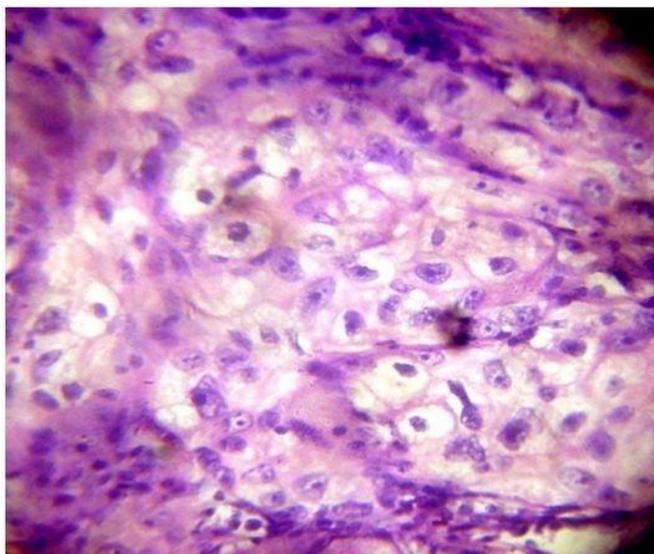


Figure 3: (Case 2)

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Fine Needle aspiration Cytology (FNAC) report was infiltrating duct carcinoma (NOS). Modified Radical mastectomy with axillary node dissection was performed and entire specimen was sent for histopathological examination. Formalin fixed paraffin embedded (FFPE) blocks and haematoxylin and Eosin (H&E) stained sections were examined under light microscope. It showed sheets of large moderately pleomorphic tumor cells having abundant eosinophilic cytoplasm, with sharp borders, round nuclei, vesicular chromatin pattern, prominent nucleoli in most of it (Figure 3).

Case No.	Age (in yrs)	Location in the breast	Size (in cm ²)	Histological diagnosis	BRG	ER/PR & Her2/Neu	Ki67 staining
1	46	Upper central area	2.6 x 3	Apocrine carcinoma	2	Not immunoreactive	Low (<9/10 HPF)
2	51	Lower & Outer quadrant	4 x 4	IDC with areas of apocrine differentiation	3	Not immunoreactive	Moderate (16/10 HPF)

Modified Bloom Richardson (BRG) grading was done on basis of tubule formation, nuclear pleomorphism and count of mitotic figures. The case was labeled as IDC with areas of apocrine differentiation of breast, BRG grade III. Five axillary lymph nodes were infiltrated by tumor cells. Further FFPE blocks were processed and performed immunohistochemistry for detection of ER, PR, Her2 neu and proliferative marker Ki67 expression profile. The tumor cells were not immunoreactive for ER, PR, Her2neu, so it can be categorized as TNBC. Ki67 nuclear staining was moderate (16/10 high power field).

DISCUSSION

As apocrine carcinoma is rarer category of carcinoma, very less frequently encountered and so less often studied. The definition and consequently the reported incidence of these tumors varies considerably (Eusebi *et al.*, 1984 and McDivitt *et al.*, 1968) included this entity under the group of "relatively rare carcinomas." Frable and Kay (1968) in a survey which covered a 16-year period stated that apocrine carcinoma accounts for 1% of mammary carcinomas. A lower incidence (0.3-0.4% of cancers) was suggested by Azzopard *et al.*, (1979) that carcinomas of the breast are considered "apocrine" only if they are composed largely of easily recognizable apocrine-type epithelium. Apocrine carcinomas are mostly variants of ductal carcinoma, while lobular carcinomas more rarely exhibit apocrine differentiation (Japaze *et al.*, 2005) proposed criteria are (1) Apocrine feature should consist of 75% of cells (2) Large cells with eosinophilic granular cytoplasm (3) Nucleus to cytoplasm ratio of 1:2 or more (4) Nucleus large round and vesicular, may be pleomorphic (5) Sharply defined borders. Minor and non mandatory criteria includes, prominent nucleoli in >50% of fields and apical cytoplasmic snouts into luminal spaces.

In our first case, Japaze 2005 criteria 1-5 were fulfilled and diagnosis was apocrine carcinoma histologically. In second case, apocrine features did not comprise of 75% of tumor cells though other criteria for cell features were consistent. So we had labeled that case as IDC with apocrine features.

Apocrine carcinoma should be differentiated from other histologic types of breast cancer i.e oncocytic type, secretory type, lipid rich type, histiocytoid type and which we have done in our study. From our observation it can be said that Japaze criteria could be reasonably helpful in differential diagnosis.

Eusebi *et al.*, (1986) used an immunocytochemical method for the detection of GCDFP-15, a protein present in apocrine epithelium and in the fluid of tension cyst of the breast; the presence of apocrine differentiation was confirmed in 4 cases initially diagnosed as apocrine carcinoma. But we could not perform same in our cases but cytokeratin was positive in our cases.

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Mossler *et al.*, (1980) found an absence of ER activity in their apocrine carcinomas which was similar to our both the cases. These cases also showed negativity for Her2/neu and we included them in TNBC category. Though, TNBC are regarded as very high grade tumor which are chemotherapy resistant with overall worst survival, but small percentage of TNBC such as pure apocrine type likely to show better outcome due to low grade features. From the clinicopathological viewpoint, including the prognosis, pathogenesis and therapy, it seems reasonable that the apocrine-type TNBC should be distinguished from the non-apocrine-type TNBC, as viewed by Tsutsumi *et al.*, (2012). But IDC with apocrine features according to (Japaze *et al.*, 2005) has same prognosis as IDC NOS.

CONCLUSION

Japaze *et al.*, (2005) commented that Pure Invasive Apocrine Carcinoma may be a distinct clinicopathological entity with a less aggressive behavior than high-grade IDC-NOS and might be regarded as an independent prognostic factor in early breast cancer. Our first case can be considered pure invasive carcinoma, low grade histologic features, axillary lymph node negative and likely to have prolonged survival. So, the recognition of apocrine morphologic type may add to the understanding of disease pathogenesis and predict a better prognosis of breast cancer.

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