



## ADENOID CYSTIC CARCINOMA OF THE BREAST: A TRIPLE NEGATIVE BREAST TUMOUR WITH PARADOXICAL FEATURES – A CASE REPORT WITH IMMUNO-HISTO CORRELATION.

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### ABSTRACT

Adenoid cystic carcinoma (ACC) of the breast is a very rare and indolent tumour with a favourable prognosis, despite its triple-negative status. They are uncommon tumours that are not well characterized and have seemingly paradoxical features. Immunohistochemical studies revealed an estrogen receptor (ER), progesterone receptor (PR), Human epidermal growth factor receptor 2 (HER2/neu) negative tumour (triple negative tumour) with immunoreactivity for C-kit and Cytokeratin 7 (CK 7) along with Smooth muscle actin (SMA). The unique and paradoxical features of this tumour are presented along with a review of the literature.

**KEYWORDS:** Adenoid cystic carcinoma, Breast neoplasms, Triple negative Breast carcinoma.

### INTRODUCTION

Adenoid cystic carcinoma (ACC) of the breast is a rare type of primary breast cancer accounting for less than 0.1% of all primary breast cancers.<sup>[1]</sup> A characteristic histologic pattern of ACC of the breast includes both epithelial and myoepithelial components and resembles a well-known tumour of the salivary gland known by the same name. However, patients diagnosed with ACC of the breast have better prognosis than those who are diagnosed with ACC of the salivary gland.<sup>[2]</sup> ACC of the breast belongs to the basal like subgroup of breast cancers.<sup>[3]</sup> Based on extensive molecular and genetic profiling studies, basal-like tumours are more often hormone receptor negative [estrogen receptor (ER), progesterone receptor (PR)], do not express human epidermal growth factor receptor 2 (Her2), but express one or more basal/myoepithelial cell markers [e.g., cytokeratins (CKs) 5, 5/6, 14 and 17].<sup>[4]</sup> Due to its rarity and paucity of literature, we are presenting this case by highlighting the histopathological correlation with immunohistochemistry (IHC) and differential diagnosis.

### CASE REPORT

A 37 year old female presented with lump in right breast since 3 years. On examination there was a hard, mobile, non-tender irregular lump in upper outer quadrant of right breast 2x1.5 cm. Mammography and breast ultrasonography (US) showed an irregular mass measuring 2.4x1.4cm with a speculated margin in the upper outer quadrant of right breast. Haematological and biochemical parameters were normal. Patient underwent

quadrantectomy. Grossly, specimen is of 4.3x 3.1cm in size with tumour size is 2.4x1.4cm. Tumour is well defined with a firm, pale, cut surface appearance. No lymph node identified. Microscopy shows two cell types as follows.

- (i) Small basaloid myoepithelial cells arranged in cribriform growth patterns and surrounding pseudo glandular spaces containing basement membrane material.

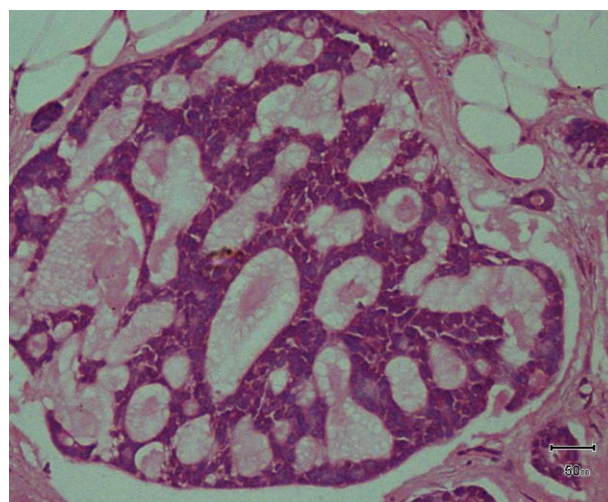
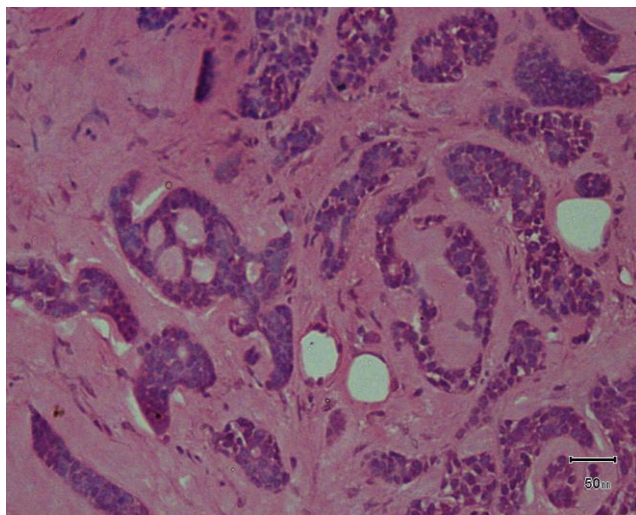


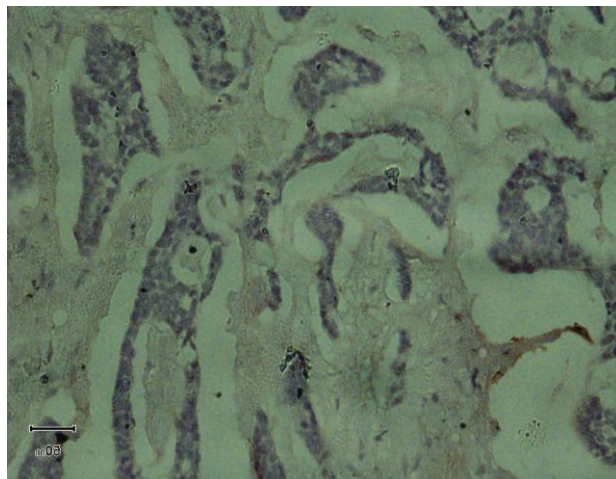
Fig. 1.

- (ii) Epithelial cells arranged around true glandular lumina.

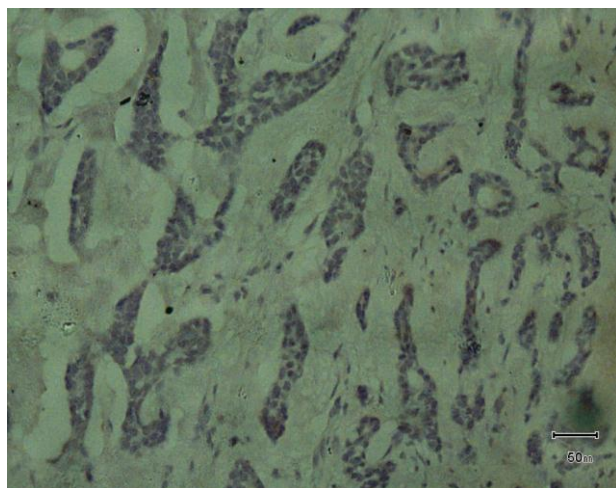


**Fig. 2:** Vascular invasion was not identified, and all margins were free of tumour. There was no involvement of the breast by Paget's disease or dermal lymphatic infiltration.

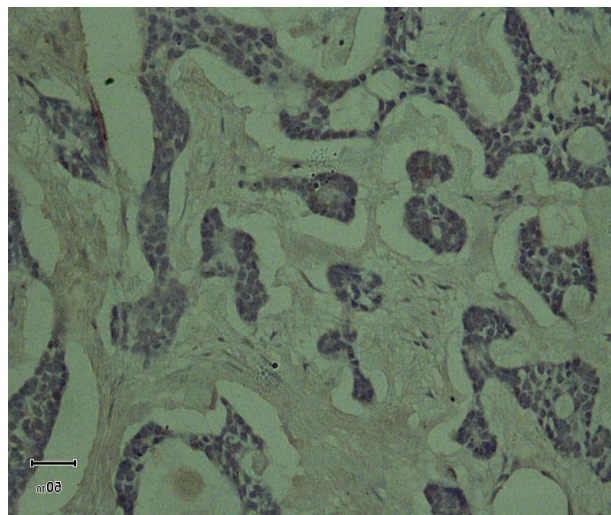
Immunohistochemistry for ER, PR and HER2/neu were negative (i.e. Triple negative). C-kit protein (CD 117) did show overexpression.



**Fig.3-ER Negative.**

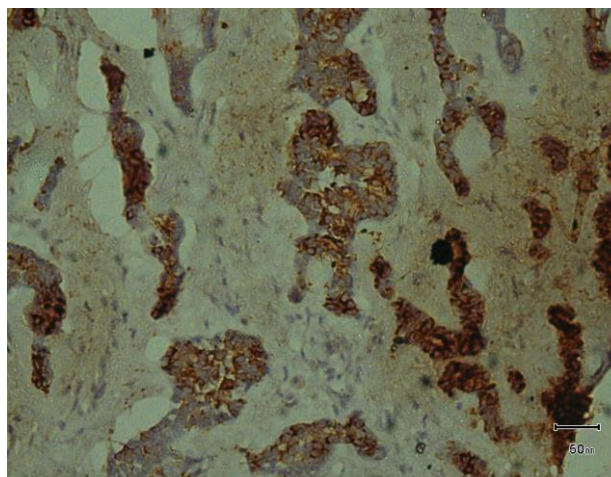


**Fig. 4-PR Negative.**

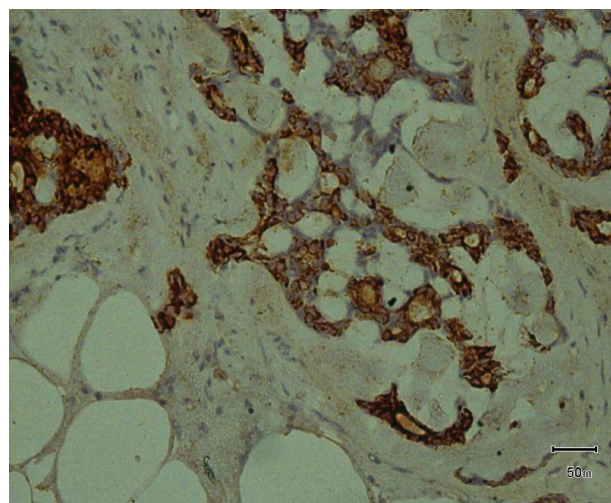


**Fig. 5-Her2 neu Negative.**

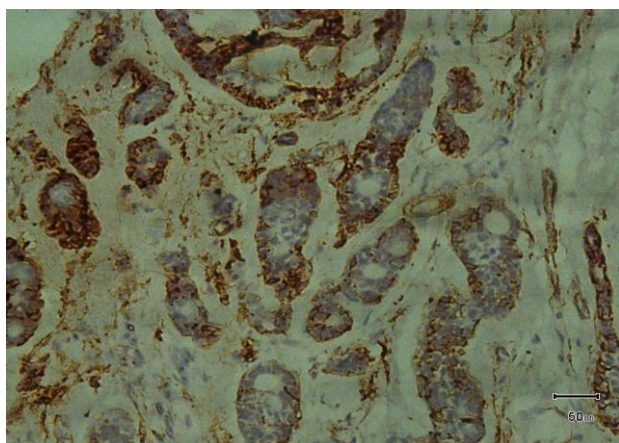
Epithelial cells were stained by Cytokeratin 7(CK 7) whereas myoepithelial cells were stained by Smooth muscle actin (SMA).



**Fig. 6-CK 7 expressed by epithelial cells.**



**Fig.7- More epithelial cells with CK7.**



**Fig. 8: SMA by Myoepithelial cells**

Thus diagnosis of Adenoid cystic carcinoma was made.

## DISCUSSION

Adenoid cystic carcinomas are relatively uncommon primary breast tumours accounting for less than 0.1% of all primary breast cancers. Breast ACCs typically present as a mass, while some ACCs have been associated with breast tenderness and pain. The etiology behind the clinical presentation in these cases remains unclear.

Histologically, ACCs of the breast, like their counterparts in other locations, are composed of glandular elements (adenoid component) and basement-membrane material (the cylindromatous component).<sup>[5]</sup> Ro and colleagues divide ACCs into 3 grades based on the percent solid growth pattern: grade 1=no solid growth, grade 2=less than 30% and grade 3=greater than 30%. The authors found that Grade 2 and Grade 3 tumours were more likely to be larger compared to Grade 1 ACCs.<sup>[6]</sup>

Immunohistochemical staining has become invaluable in the diagnosis of unusual variants of invasive breast carcinoma. Triple negative breast carcinomas are a group of carcinomas that show negative staining for ER, PR, and HER2/*neu* receptors. This is a histologically and molecularly heterogeneous group of tumours.<sup>[7]</sup> The epithelial cells stain with antibodies to cytokeratin, such as CAM5.2 and CK7, whereas the myoepithelial cells stain with the antibodies to smooth muscle actin, calponin, and p63. In addition, basement membrane material, both around the periphery of the tumour nests and in the pseudocysts, may be demonstrated with antibodies to laminin and collagen IV. The tumours typically express c-kit and basal cytokeratins. A characteristic translocation t (6; 9) is seen, resulting in fusion of MYB and NFIB genes.

The differential diagnoses of breast ACCs include both benign and malignant entities, such as collagenous spherulosis and invasive cribriform carcinoma. Collagenous spherulosis also has a cribriform architecture and central eosinophilic material composed of acellular spherules, thereby creating an adenoid cystic-like pattern. The lumens in collagenous spherulosis may be irregular compared to that in ACC.

Although myoepithelial cells around the spherules may not be readily identified on H&E stained sections, these are highlighted by IHC stains for myoepithelial cells.<sup>[8]</sup> Cribriform carcinoma and ACC share some features such as low nuclear grade and a cribriform pattern. Cribriform carcinoma is differentiated from ACC by positivity for ER and PR and a negative PAS/Alcian blue stain. In addition, a desmoplastic stromal reaction may be identified in invasive cribriform carcinoma, but this is absent in ACC.<sup>[9]</sup> No stromal response was identified in the case we report here. To summarize, ACCs are breast tumours with a unique histology, Immunohistochemical profile, and a paradoxically good prognosis. Studies to date have been unable to identify the molecular mechanisms or precursor lesion for ACC. This information is critical to enhance our understanding of this triple negative tumour and add to our insight into the more aggressive basal type breast carcinomas, ultimately identifying possible therapeutic targets.

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