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Case Report

Pathology Section

Adenoid Cystic Carcinoma of Breast: A Rare Case Report

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ABSTRACT

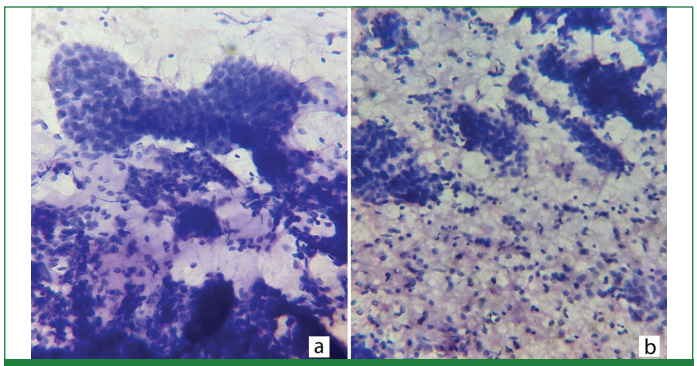
Adenoid Cystic Carcinoma (AdCC) is a neoplasm that commonly occurs in the salivary gland. It is one of the least frequent forms of primary breast carcinoma and is a special subtype of breast carcinoma that usually occurs in women during their 5th to 6th decades of life, presenting with a triple-negative phenotype. Unlike other triple-negative breast cancers, AdCC has a favourable prognosis, with long-term survival and a low incidence of metastasis. Histologically, it is characterised by a biphasic population of epithelial and myoepithelial cells exhibiting specific growth patterns. Similar to their salivary gland counterparts, these cancers demonstrate chromosomal translocation t(6;9), resulting in MYB proto-oncogene transcription factor and nuclear factor I/B (MYB-NFIB) fusion. Our case involves a 59-year-old lady who presented with a painful left breast lump of two months' duration. A mammogram showed a lobulated hypoechoic lesion with a mildly irregular border and a few cystic areas at the 3 o'clock position of the left breast, categorised as Breast Imaging Reporting and Data System IV (BIRADS IV). A Contrast-Enhanced Computerised Tomography (CECT) of the chest revealed a well-defined large soft-tissue density lesion in the lower and outer quadrant with lobulated margins. Following Fine Needle Aspiration Cytology (FNAC) diagnosis of carcinoma of the breast, the patient underwent a left Modified Radical Mastectomy (MRM) with axillary clearance, which revealed a biphasic malignant neoplasm in trabecular, cribriform, and tubular patterns. Immunohistochemistry (IHC) confirmed the dual population of neoplastic cells. We report this case owing to the rarity of the lesion, as it accounts for less than 0.1% of all breast cancers.

Keywords: Adenoid cystic carcinoma, Favourable prognosis, Rare, Triple negative breast carcinoma

CASE REPORT

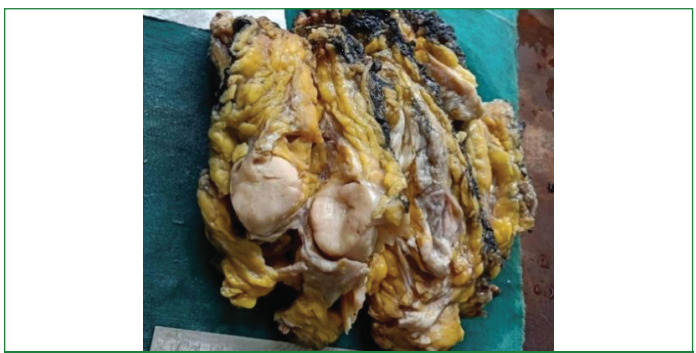
The case involves a 59-year-old post-menopausal lady who presented with complaints of a painful left breast lump of two months' duration. She did not have any past history of surgeries or any relevant family history. A mammogram showed a lobulated hypoechoic lesion with a mildly irregular border and a few cystic areas at the 3 o'clock position of the left breast, categorised as BIRADS IV [Table/Fig-1]. A CECT of the chest revealed a well-defined large soft-tissue density lesion in the lower and outer quadrant with lobulated margins. FNAC of the mass showed cohesive syncytial clusters and scattered single basaloid cells with scant cytoplasm and round/ovoid nuclei with coarse chromatin in a myxoid background [Table/Fig-2a,b]. A diagnosis of low-grade breast carcinoma was made, following which the patient underwent a left modified radical mastectomy with axillary clearance.

[Table/Fig-1]: Mammogram showing a lobulated hypoechoic lesion with mildly irregular borders.



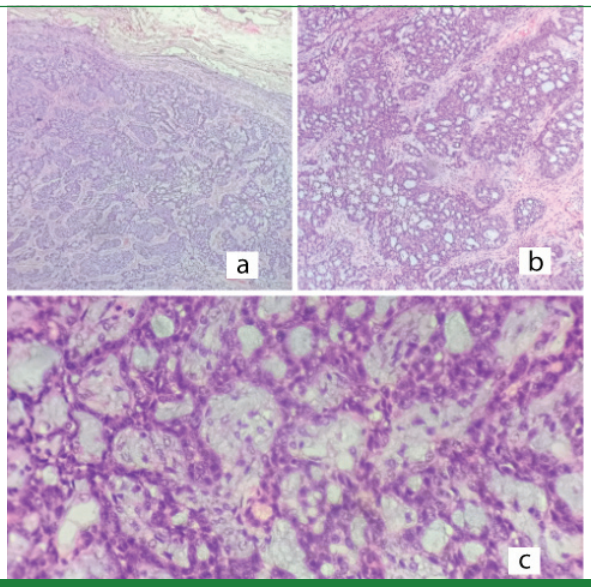
[Table/Fig-2]: a,b) FNAC showing neoplastic basaloid cells in cohesive syncytial clusters and singly in a myxoid background (PAP, 400x).

The specimen, upon sectioning, revealed a grey-white predominantly solid, fairly circumscribed nodular mass in the upper outer quadrant measuring 5×4×4 cm. The cut surface was grey-white, glistening, soft, and faintly lobulated with tiny cystic spaces [Table/Fig-3]. Axillary dissection showed 12 lymph nodes, the largest measuring 1.2 cm, with no macroscopic tumour deposits noted in any of the lymph nodes.



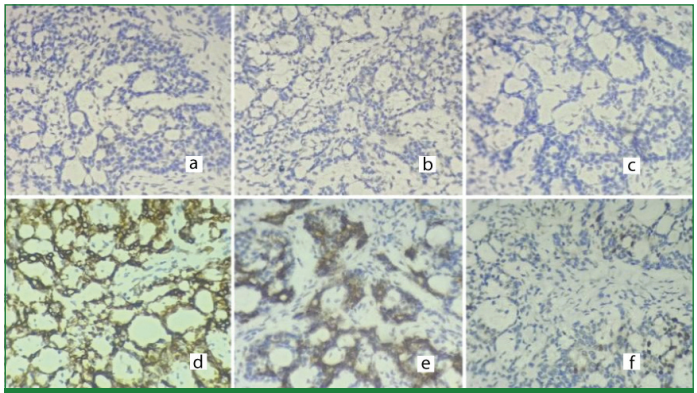
[Table/Fig-3]: Gross image of breast showing a well-circumscribed, partially encapsulated tumour with grey white, glistening cut surface.

Microscopy showed a biphasic circumscribed neoplasm with luminal and myoepithelial basal cells in cribriform, trabecular, and tubular patterns, featuring intraluminal mucin and intervening fibro-myxoid stroma. Pseudo-lumen formation lined by myoepithelial cells was present. Individual cells exhibited scant to moderate cytoplasm and hyperchromatic nuclei. Mitosis was sparse [Table/Fig-4a-c]. No perineural invasion, solid nests, or high-grade transformation was observed. All margins demonstrated good tumour clearance, and all 12 lymph nodes were negative for tumour deposits.



[Table/Fig-4]: a) Tumour cells arranged predominantly in cribriform and trabecular patterns {Haematoxylin and Eosin (H&E), 40x}; b) H&E, 100x; c) Pseudo-lumens lined by myoepithelial cells with intervening myxoid stroma (H&E, 400x).

Immunohistochemical marker studies revealed a triple-negative breast cancer with a Ki67 proliferation index of approximately 10-14%. The luminal cells were strongly positive for Cytokeratin 7 (CK7) and Cluster of Differentiation 117 (CD117), while the myoepithelial cells were positive for p63 and CK5/6, highlighting the pseudolumina [Table/Fig-5a-f]. It was reported as AdCC, left breast, classic subtype, Modified Bloom- Richardson (MBR) grade 1, with a tumour size of 5×4×4 cm and stage pT2N0Mx. The patient is doing well and is on regular follow-up post-MRM, with no further complications or additional treatment modalities.



[Table/Fig-5]: Tumour cells negative for: a) ER (IHC, 40x); b) PR (IHC, 40x); c) Her 2 neu (IHC, 40x); d) Abluminal cells showing nuclear positivity for p63 (IHC, 40x); e) Luminal cells showing expression of CD117(IHC, 40X); f) Low Ki67 index (IHC, 40x).

DISCUSSION

AdCC is a rare malignant tumour of the breast, classified under "Rare and salivary gland-type tumours" in the 5th edition of the World Health Organisation (WHO) blue book [1]. Histologically, similar to its counter parts in the salivary gland, AdCC can also occur in the nasopharynx, bronchopulmonary tree, skin, uterus, cervix, and kidneys [2]. It usually presents as a firm discrete, palpable subareolar mass or with tenderness. Pain, attributable to the perineural sensory invasion of the tumour, is very rarely observed [3]. FNAC may be a powerful tool for diagnosis when combined with mammogram or ultrasound of the breast [4]. FNAC of AdCC is described as cellular, with uniform basaloid cells in cohesive clusters and cup-like fragments, along with the presence of pink spherical globules and cores of stromal material [5,6]. Preoperative diagnosis is important as it can aid in determining the treatment strategy [7].

AdCC is a biphasic neoplasm composed of epithelial and myoepithelial cells that form ducts, cribriform patterns, and pseudolumina, as seen in the present case. Areas of squamous differentiation and sebaceous differentiation have been described in various studies, although these were not found in our case [8,9]. IHC aids in identifying the dual cell population of neoplastic cells. Epithelial cells are consistently positive for low molecular weight cytokeratins CK7 and CK8. Myoepithelial cells demonstrate positivity for CK14, CK5/6, and p63. CD117 is characteristically positive in the luminal component of AdCC, although it is not entirely specific, as focal c-KIT positivity can occur in other breast tumours, including myoepithelioma [10].

The presence of a dual cell population with characteristic cribriform architecture and spherules of acellular material can also be seen in the benign entity of Collagenous Spherulosis (CS). However, CS seldom forms a mass lesion. Immunohistochemically, the basal cell component of CS is calponin and CD10 positive, whereas the basal component of AdCC is usually calponin and CD10 negative. Additionally, the luminal cells of CS are CD117 negative, unlike AdCC, which is strongly positive for CD117 [11,12]. Another close differential diagnosis is invasive cribriform carcinoma, but it lacks the dual cell population characteristic of AdCC and is mostly Estrogen Receptor/ Progesterone Receptor (ER/PR) positive and CD1a17 negative.

Breast AdCC lacks staining for oestrogen, progesterone, and Human Epidermal Growth Factor Receptor 2 (HER-2) and has a low Ki67 index, as is the case in our study. It is classified under triple-negative breast carcinoma. Triple-negative cancers are usually aggressive, with some exhibiting a poor prognosis [13]. However, AdCC of the breast follows an indolent course and has an excellent prognosis, characterised by long-term survival and rare axillary lymph node metastasis [14]. Rare cases of metastasis to the lung have been reported, which became clinically apparent after a 9-year interval. Thus, cases require long-term follow-up. Other sites of metastasis include the liver, brain, and kidneys [15,16].

Three histological variants of AdCC have been described in the 2021 edition of the WHO breast classification: classic AdCC, solid-basaloid AdCC (SBAdCC), and AdCC with high-grade transformation, based on architectural and cytological features. Our case is of the classic variant, characterised by a low mitotic count, low to intermediate-grade nuclear atypia, and a lack of necrosis. SBAdCC is composed of solid basaloid nests with a high mitotic count, marked nuclear atypia, and frequent perineural invasion. The third subtype is rare in the breast and is the most aggressive.

In AdCC, reciprocal translocation t(6;9)(q22-23;p23-24) leads to the fusion of MYB and NFIB genes, resulting in the overexpression of the transcription factor MYB and subsequent carcinogenesis [17]. This chromosomal translocation is common to AdCC arising in various body sites. The mainstay of treatment is surgical. Breast-conserving surgery can be considered for patients with classic AdCC of the breast, with adjuvant Radiotherapy (RT) after lumpectomy showing improved survival rates [18]. For SBAdCC, axillary lymph node dissection followed by radiotherapy, based on the stage of the tumour, is recommended. All patients require long-term follow-up [19,20].

CONCLUSION(S)

AdCC of the breast differs from traditional triple-negative invasive ductal carcinoma in that it exhibits low lymphovascular and perineural invasion, negative lymph nodes, a good prognosis, and an excellent long-term survival rate. Surgical resection with axillary lymph node dissection, with or without neoadjuvant radiotherapy, is

considered curative in most cases. Long-term follow-up and regular reviews are absolutely essential.

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