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Case Report

Pathology Section

Acinic Cell Carcinoma of the Breast: A Rare and Diagnostically Challenging Entity

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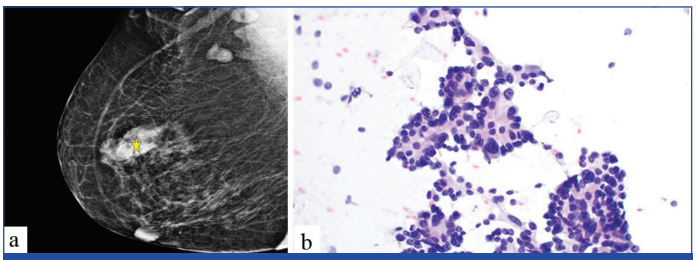
ABSTRACT

Acinic Cell Carcinoma (AcCC) of the breast is a rare subtype of invasive breast carcinoma that falls under the category of salivary gland-type tumours of the breast. Histologically, it closely resembles AcCC of the salivary gland. Here, the authors report a case of AcCC of the breast in a 51-year-old woman who presented with a palpable lump in her right breast. Radiological investigation revealed a Breast Imaging Reporting and Data System (BIRADS) score V lesion. A core biopsy was performed, and the histopathological examination revealed relatively bland cells arranged in an acinar pattern within a myxoid stroma, closely resembling adenosis rather than a neoplasm. The diagnosis posed a challenge in the core biopsy due to its close resemblance to adenosis. However, the clinical and radiological findings strongly suggested malignancy. Immunostaining with p63 was conducted, which helped demonstrate the absence of myoepithelial cells around the tumour cell nests and supported the neoplastic nature of the lesion. Despite the bland and low-grade morphology, the tumour was found to be triple negative for Oestrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal Growth Factor Receptor 2 (HER2), and it exhibited characteristic positivity for SRY-Box Transcription Factor 10 (SOX 10), S100, and CK7, which aided in making the diagnosis. The authors presented the case report to highlight the rarity of this subtype of breast carcinoma and to emphasise the importance of histomorphology and immunoprofile in reaching a diagnosis. To the best of the authors' knowledge, the present case was the second reported case of AcCC of the breast from India, adding to the novelty of this case.

Keywords: Breast, Salivary gland-type carcinoma, Triple negative

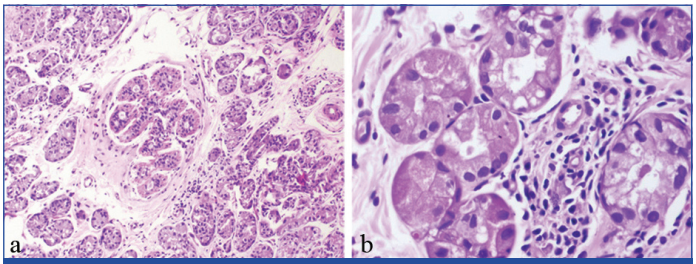
CASE REPORT

A 51-year-old woman who is a known case of invasive breast carcinoma of no special type in the left breast, diagnosed in 2018, completed treatment with neoadjuvant chemotherapy followed by left modified radical mastectomy, adjuvant radiation, and hormone treatment with tamoxifen. She completed treatment in December 2018. The patient was on regular follow-up, during which a lump was detected in her right breast on screening mammography in September 2022. Digital mammography revealed an irregular hypoechoic solid lesion with a BIRADS score of V [Table/Fig-1a]. Fine Needle Aspiration Cytology (FNAC) showed a cellular smear with atypical cells in sheets, papillaroid, and acinar patterns. The cells exhibited moderate to abundant pale cytoplasm, fine chromatin, small nucleoli, and nuclear inclusions. Occasional clusters showed cells with moderate cytoplasm and atypical nucleus, and it was reported as suggestive of carcinoma [Table/Fig-1b].



[Table/Fig-1]: a) Digital mammography showing an irregular hypoechoic solid lesion of Breast Imaging Reporting and Data System (BIRADS) score V; b) Cellular smear with atypical cells in sheets, papillaroid and acinar pattern (PAP, 20x).

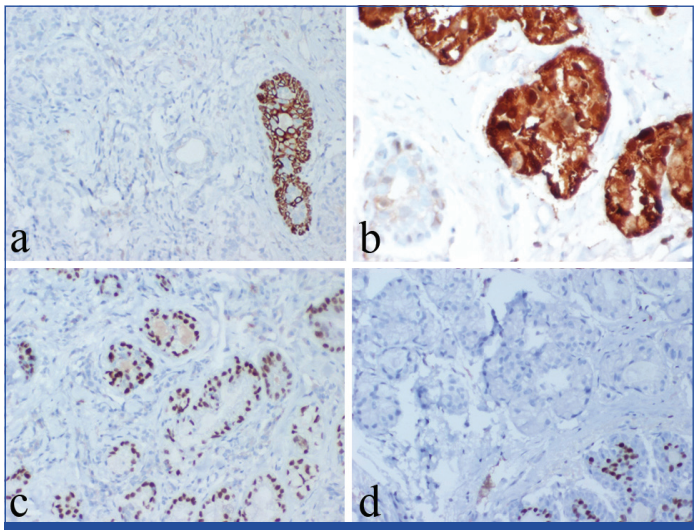
A Core Needle Biopsy (CNB) of the mass revealed a lesion composed of relatively bland cells arranged in an acinar pattern. The cells were cuboidal to columnar, with moderate to abundant clear/granular eosinophilic cytoplasm and uniform round vesicular nucleus, resembling adenosis [Table/Fig-2a,b]. However, infiltrative nature could be appreciated in some areas.



[Table/Fig-2]: a) Section from breast showing epithelial cells with abundant granular eosinophilic cytoplasm and uniform vesicular nucleus arranged in micro glandular pattern. Haematoxylin and Eosin (H&E, 10x); b) 40x showing the neoplastic cells resembling serous acini of salivary gland.

To confirm the neoplastic nature, Immunohistochemistry (IHC) was performed. CK 5/6 and Tumour Protein 63 (p63) staining highlighted the lack of myoepithelial cells around tumour cell nests, while preserved myoepithelial cells were observed around the normal breast ducts [Table/Fig-3a]. ER, PR, and HER2 were negative, and the neoplastic cells exhibited positivity for S100 protein, CK7, and SOX10 [Table/Fig-3b-d]. DOG-1 staining was negative. Periodic Acid-Schiff with Diastase (PASD) staining showed diastase-resistant cytoplasmic granules. Based on the morphology and characteristic immunoprofile, a diagnosis of salivary gland-type carcinoma, AcCC, was made. The patient underwent surgery, specifically breast-conserving surgery guided by frozen section for margin and sentinel node status. The margins were negative, and the sentinel node showed reactive changes, so axillary clearance was not performed. Gross examination revealed a tumour measuring 4.8×4.3×2.5 cm, with a grey-white appearance, firm to hard consistency, well-defined borders, and lobulated cut surface. Microscopy confirmed the presence of salivary gland-type carcinoma, AcCC, with focal higher-grade areas showing high nucleocytoplasmic ratio and nuclear pleomorphism, unlike the relatively bland appearance observed in the core biopsy. The postoperative period was uneventful. Postoperative imaging, including Computed Tomography (CT) of the thorax, abdomen, pelvis, and bone scan, showed no evidence

of metastasis. The patient was planned for adjuvant chemotherapy with six cycles of paclitaxel and carboplatin, followed by adjuvant radiation. At the time of writing the case report, the patient was undergoing adjuvant chemotherapy and has received three cycles, tolerating it well.



[Table/Fig-3]: a) Immunohistochemistry showed CK5/6 positive myoepithelial cells in normal ducts and loss of myoepithelial cells in invasive focus (10x); b) Diffuse strong positivity for S100 protein (20x); c) Diffuse strong nuclear positivity for SOX10 (10x); d) Negative for ER, while cells lining the normal ducts are positive, (10x).

DISCUSSION

The AcCC is a relatively common carcinoma of the salivary gland but rare in the breast [1]. The breast and salivary gland are tubuloacinar exocrine glands that can develop tumours with similar morphological features, but their clinical behaviour depends on whether they are primary in the breast or salivary glands [2,3]. AcCC of the breast is a rare subtype of invasive breast carcinoma listed under rare and salivary gland-type tumours in the fifth edition of the World Health Organisation (WHO) classification of breast tumours. The first case was reported by Roncaroli F et al., in 1996 [4]. Since then, less than 50 cases have been reported, including one case from India [5,6]. The breast and salivary gland share a common architecture in terms of tubulo-acinar glands with luminal epithelial and abluminal myoepithelial cells [7]. Consequently, breast tissue can develop all types of tumours encountered in the salivary gland. However, the clinical outcomes of these tumours are not always similar and depend on the primary site. Although most salivary gland-type tumours of the breast share the same molecular alterations as their salivary gland counterparts, AcCC is an exception with a different molecular profile, suggesting that they are different entities [8].

The AcCC is a malignant epithelial neoplasm composed of clear and granular epithelial cells arranged in microglandular and solid patterns. The two patterns frequently merge together. Due to the high variability in architectural patterns, the diagnosis is based on recognition of the cytological features. The neoplastic cells have abundant, variably eosinophilic and basophilic granular cytoplasm, imparting a variegated appearance. PASD staining reveals intracellular, large, coarse eosinophilic granules. In the present case report, the authors could also demonstrate diastase-resistant PAS-positive cytoplasmic granules. Intracytoplasmic granules are also clearly evident on ultrastructural examination. The neoplastic cells may occasionally have a clear cytoplasm. Atypia is usually more prominent in solid areas, and mitotic figures may be seen but are usually not marked. AcCC may be accompanied by invasive ductal carcinoma NST ("mixed" cases), as documented in some studies [9,10]. The nucleus is centrally located and atypical, with a prominent nucleolus. The neoplastic cells show various degrees of atypia. Foschini MP et al., have highlighted that the difference between AcCC with a predominant microglandular growth pattern and microglandular adenosis can be challenging [6]. The authors also experienced this difficulty in the core biopsy, where the differential diagnosis was between adenosis and carcinoma. In the present case, the initial core biopsy showed relatively bland cells, resembling adenosis, and the absence of myoepithelial cells had to be demonstrated before reaching a diagnosis of carcinoma. Cellular atypia and mitotic figures are usually more prominent in solid areas. Other differential diagnosis of AcCC include invasive carcinomas NST, apocrine carcinomas, oncocytic carcinomas, and secretory carcinoma. Secretory carcinoma lacks the intracytoplasmic granules seen in AcCC and has the characteristic ETV6-NTRK3 fusion. Apocrine carcinomas are positive for androgen receptor, while oncocytic carcinomas express ER in more than 50% of cases [2,6]. Salivary gland-type carcinomas of the breast are usually triple-negative, despite being associated with a good prognosis. Triple-Negative Breast Cancers (TNBC) as a group generally have a worse prognosis than stage-matched non-TNBC and lack the benefits of routinely available targeted therapy. However, TNBC is a heterogeneous group of neoplasms, with some special type carcinomas, including salivary gland-type carcinomas, having a relatively indolent course [9]. Ajkunic A et al., in their review article on AcCC of the breast, noted that most of the cases in the literature were triple-negative, with only seven out of 66 cases positive for ER and seven out of 62 cases positive for PR. HER2/neu status was negative for all cases [11]. The present case also showed negative ER, PR, and HER2 status. The neoplastic cells are positive for markers of serous differentiation, such as lysozyme and α1-antichymotrypsin. Additionally, they consistently exhibit positivity for S100, EMA, and low-molecular-weight cytokeratin. It also showed positivity for CK7, S100 protein, and SOX10, which is a marker for acinar cells. Most reported patients undergo chemotherapy and radiotherapy in addition to surgery [11,12]. Recurrent genomic rearrangement that upregulates the NR4A3 transcription factor has been described in salivary AcCC [13], but no study has reported on NR4A3 status for AcCC of the breast. The patient is currently undergoing adjuvant therapy following surgery.

CONCLUSION(S)

The AcCC is a rare salivary gland-type carcinoma of the breast. Due to its rarity and typically low-grade histology, it can pose a diagnostic challenge, especially in limited biopsy samples. These carcinomas are triple-negative; however, unlike other TNBCs, AcCC usually has a better prognosis. More data on this entity are needed to better understand its clinical behaviour as a salivary gland-type tumour of the breast.

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