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Case Report

Oncology Section

A Case Report of Adenoid Cystic Carcinoma of Breast– So Close Yet So Far from Triple Negative Breast Cancer

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ABSTRACT

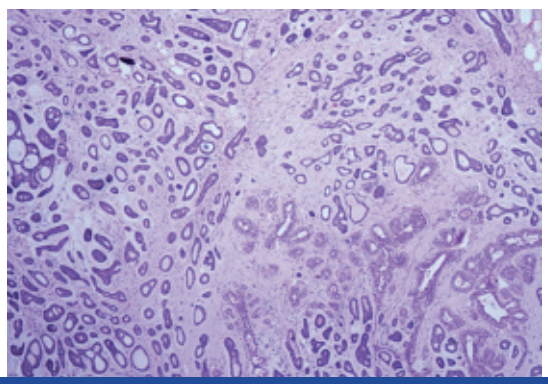
Adenoid cystic carcinoma (ACC) of breast is a rare tumour with a low malignant potential. Though negative for oestrogen (ER), progesterone (PR) and human epidermal growth factor receptor 2 (Her2/neu), it is different from triple negative breast cancer (TNBC); ACC has an indolent course with a good prognosis.We present a case of a 40 year old premenopausal female initially diagnosed with ductal carcinoma in situ (DCIS) on core needle biopsy. She underwent breast-conserving surgery (BCS) and her final histopathological diagnosis was ACC. She subsequently underwent adjuvant external beam radiotherapy. The patient is on follow-up for more than a year with no recurrence till date.

Keywords: Breast-conserving surgery, Ductal carcinoma in situ, Molecular profiling

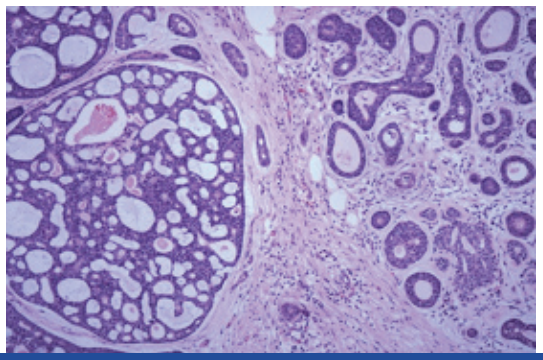
CASE REPORT

A 40-year-old female presented to our outpatient department a year and a half back with a history of a painless lump in her left breast of one year duration. Other tumour related history was unremarkable. She had one child 18 years ago who was breast fed for one year. Her menstrual and family histories were not significant. Examination of the left breast showed a 2 cm x 2 cm firm painless mobile mass in the upper outer quadrant 7 cm away from the nipple areola complex with no skin fixity. Her axilla was clinically negative.

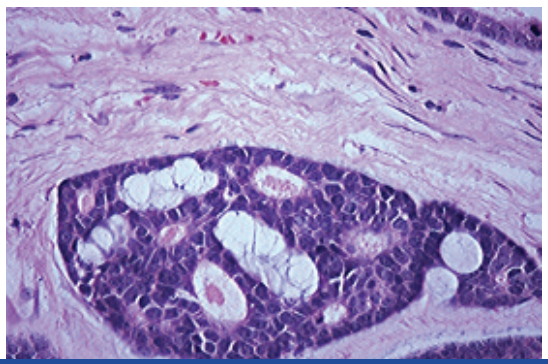
Mammogram revealed an ill defined lesion with minimal architectural distortion and specks of calcification. Core needle biopsy showed focal DCIS with possibility of microinvasion. Metastatic workup and routine blood investigations were normal. After discussing the treatment options for DCIS with a possibility of early stage invasive ductal carcinoma (IDC), patient consented for BCS with an axillary lymph node dissection (ALND).The procedure was performed and the final histopathology report was adenoid cystic carcinoma (ACC) (tumour size 1.7 cm), with predominantly basaloid cells and some cribriform and tubular growth pattern, having hyperchromatic nuclei and scanty cytoplasm [Table/Fig-1-3]. There was no perineural invasion. All margins and retrieved lymph nodes were negative for malignancy. Immunohistochemistry (IHC) was negative for ER, PR and Her2/neu. Proliferation marker Ki67 was low [Table/Fig-4]. She was given adjuvant external beam radiotherapy to the entire breast (50Gy in 25 fractions with a 10Gy boost). Patient is on follow-up for the past one year without any evidence of recurrence.



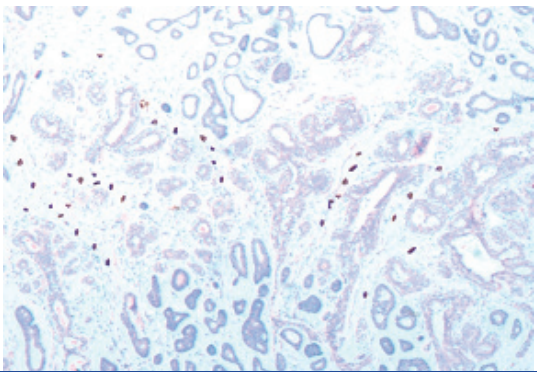
[Table/Fig-1]: H&E stain (4x magnification) showing tubular and solid growth patterns



[Table/Fig-2]: H&E stain (10X magnification) showing cribriform and solid growth patterns



[Table/Fig-3]: H&E stain (40X magnification) focussing predominantly on the cribriform architecture



[Table/Fig-4]: Immunohistochemistry showing Low Ki 67

DISCUSSION

ACC of the breast is one of the special types of breast cancer that has <1% overall incidence [1]. It can be histologically mistaken for DCIS and its IHC profile overlaps with TNBC; but ACC has a very good prognosis. It occurs more commonly in the postmenopausal age group with the median age being the late 5th or 6th decade [2,3]. Rare cases occurring in younger women have been reported just as in our patient.

ACC is a localised disease, presenting as a well defined palpable lump. Other presenting symptoms are breast pain and nipple retraction. Both lymph node (<2%) [1] and distant metastasis are rare [2]. Local recurrences occur late with some even 10 years after treatment [4].This is in contradistinction to TNBC where recurrences more commonly occur in the first three years. Perineural invasion, a feature commonly seen in ACC of salivary glands, is rare in the breast. Khanfir et al., reviewed data from Rare Cancer Network between 1980 and 2007 and observed that only 5 out of 61 patients had perineural spread and even this was not a prognostic factor [4]. Occasionally, ACC can occur with DCIS or IDC and shows a more aggressive behaviour than ACC alone [5].

Imaging studies can have benign appearances and hence be misleading. Mammogram shows a lobulated lesion with regular or irregular margins and rare microcalcifications. Ultrasound reveals a hypoechoic solid/heterogeneous mass. MRI shows a well circumscribed benign looking lesion though in some cases they may be spiculated.

ACC is a histological diagnosis. They have a dual cell composition – luminal epithelial and basal myoepithelial cells; hence the alternate term epi-myoepithelial carcinoma. The epithelial cells stain positive for periodic acid schiff and diastase. On H&E staining, the epithelial cells show round nuclei and eosinophilic cytoplasm. They have low mitotic activity with no atypia. Morphologically they form three architectural patterns – tubular, cribriform and solid. The architectural pattern is of prognostic importance because the solid (basaloid) variant has a more aggressive course with increased propensity for lymph node metastasis [6]. Tumour cells in this variant are also larger with hyperchromatic nuclei showing pleomorphism and increased mitotic activity. TNBC on the other hand exhibit geographic necrosis, a pushing border of invasion, and stromal lymphocytic response.

Diagnosis can be elusive as Invasive cribriform carcinoma and DCIS of cribriform type have a similar histological appearance. IHC can further help in the diagnosis. Both the cell types in ACC are ER, PR and Her2/neu negative. Basal cells also express CK 5/6, vimentin and EGFR, while epithelial cells express c-kit and CEA [7]; they are also expressed in TNBC. But Androgen receptors (AR) are absent in ACC [8] while positive in TNBC and DCIS. The salient features of ACC, TNBC and DCIS are compared in [Table/Fig-5] [8-11].

Treatment is mainly surgical with both mastectomy and BCS being the options. There has been no prospective trial to compare their efficacy, but in most cohort studies, local recurrence after mastectomy and BCS were 0% and 6% respectively [2]. Local recurrence after BCS did not affect overall survival (OS) [4].

The benefit of adjuvant radiotherapy after BCS was recently confirmed by a large study conducted by California Cancer Registry. The study concluded that RT was a positive prognostic factor for OS and disease specific survival [12]. Axillary staging is not necessary as less than 2% of patients have lymph node metastasis [4]. Exceptions to this rule would be concomitant presence of invasive carcinoma and the solid variant of ACC. Shin and Rosen reported two positive cases of nodal metastases among six ALND performed among this variant [6]. In retrospect our patient having undergone ALND may be beneficial to her given the moderately aggressive nature of the solid variant and its increased tendency for nodal spread.

Systemic therapy is recommended only for high grade lesions or tumours >3 cm [13]. Hormonal therapy is not indicated as they are ER/PR negative. Over expression of EGFR and c-kit in ACC could theoretically open doors for targeted therapies though no such treatment has been reported as of now [8].

SALIENT FEATURES	ADENOID CYSTIC CARCINOMA	TNBC	DCIS
Cell types	Dual cell population – Epithelial and myoepithelial (basal)	Single cell population (>50% basal like cells)	Single Cell Population
Lymph node involvement	<2%	60% at presentation	2%
Distant metastasis	Rare	Common; occurs within 3 years	Rare
Recurrence	Peak Recurrene late (sometimes >10 years)	Recurrence within 3 years from diagnosis	50% develop invasive cancer
ER,PR & Her2/neu	Negative	Negative	80% ER positive
AR	Negative	Positive	33% AR Positive
Ki67	Low	High	47.5% have high Ki67
Ploidy	Diploid	Aneuploid	Non-diploid
BRCA	Negative	Positive	37% of BRCA carriers have DCIS
p53	Normal	Mutated	Mutated in 30%-67%
Survival rate	>95% 10 year survival rate	Among poorest survival rates in breast cancer	>95% 5 year survival rate

[Table/Fig-5]: Salient features of ACC, TNBC& DCIS [8-11]

Prognosis of ACC of breast is excellent with rare nodal or distant metastasis. In Surveillance, Epidemiology and End Results (SEER) Program, Ghabach B et al., reported the 5 year, 10 year and 15 year survival rates to be 98%, 95% and 91% respectively [3]. Veeratterapillay R et al., reported similar survival rate with a 100% 5 year disease free survival rate [14]. Our patient has been in follow-up for more than a year without any recurrence; nevertheless the surveillance period should be long as ACC has a tendency for late recurrence.

CONCLUSION

ACC of breast has uniformly been described as a rare malignancy with favourable tumour biology. It has a triple negative phenotype, but is different from TNBC and can often be mistaken for DCIS. It has an excellent prognosis and survival and this reinforces the importance to differentiate it from other TNBC and DCIS. That said, the solid variant of ACC must be treated more aggressively. Recurrence can occur though curiously late and patients are to be in follow-up for periods longer than 10 years. Tailoring the right treatment for ACC would be difficult on count of its rarity.

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