Content available at: https://www.ipinnovative.com/open-access-journals

IP Archives of Cytology and Histopathology Research

Journal homepage: https://www.achr.co.in/

Review Article

Update on adenoid cystic carcinoma breast: A rare, special subtype of breast cancer: Review

Sunil Vitthalrao Jagtap[1]*, Shubham S Jagtap[2], Anshuli M Vispute[1], Abhilasha S Jadhav[3], Shivani V Khillare[1], Ipsita Singh[1]

[1]Dept. of Pathology, KVV, Krishna Institute of Medical Sciences Deemed University, Karad, Maharashtra, India
[2]Dept. of Medicine, KVV, Krishna Institute of Medical Sciences Deemed University, Karad, Maharashtra, India
[3]Dept. of Pharmacology, KVV, Krishna Institute of Medical Sciences Deemed University, Karad, Maharashtra, India

Abstract

Introduction: Adenoid cystic carcinoma (ACC) of the breast is a rare special subtype of breast cancer. It is characterized by its slow-growing tumor and low rate of recurrence. A 49 -year-old female presented with history of a gradually increasing, firm palpable, painless mass in right breast of six months duration. On physical examination, the single, mobile, firm mass measuring 3.0 x2.5x 1.5 cm was noted in right upper outer quadrant of breast. FNAC was positive for low grade carcinoma cells. The mammogram was graded as per (Breast Imaging Reporting and Data System category (BI-RADS): 4, suspicious for malignantneoplasm. Patient underwent surgical treatment of wide excision of right breast lump with clear margins and right axillary nodal resections. On gross examination showed well circumscribed, firm, solid and microcystic tumor measuring 2.0 x1.2x 1.0 cm. Cut section showed single pink-grey, firm to soft tumor with microcysts formation. Microscopic examination reported as Adenoid cystic carcinoma, histologic classic variant, sub-type-tubular, cribriform, with solid areas (20%) of right breast. Immunohistochemical staining were negative for Estrogen receptor (ER), Progesterone receptor (PR), and Human Epidermal Growth Factor Receptor 2 new (HER-2) and positive for CK5, CK7, P63, and PAS. Tumor showed Ki-67 proliferation index of 10%. Patient underwent surgical treatment and advised regular follow-up, which showed a favourable prognosis with no evidence of recurrence or any metastasis.
Conclusion: Adenoid cystic carcinoma of the breast is a rare special subtype of breast cancer. ACC is characterized by slow tumor progression, low malignant potential, rare axillary lymph node metastasis, usually triple negative, low expression of Ki-67, and overall favorable prognosis. Herewith emphasis on the recent update and review on ACC breast.

Keywords: Breast cancer, Adenoid cystic carcinoma, Immunohistochemistry, Rare special subtype of breast cancer

Received: 18-10-2025; **Accepted:** 31-10-2025; **Available Online**: 01-11-2025

1. Introduction

ACC is rare subtype of breast cancer, histomorphologically identical to salivary gland counterpart. ACC is characterized by its biphasic ductal and myoepithelial differentiation having tubular/cribriform/solid architecture pattern on histological features.[1] It is characterized by its slow-growing nature, low local recurrence, and rare for the distant metastasis.[2] Most breast ACCs are triple-negative as noted on phenotypically, both luminal and myoepithelial-basaloid cells in ACC of the breast are generally negative for ER, PR, and Her2 proteins. Recently the molecular and genetic features of the ACC are specific chromosomal translocation t(6;9) that results in a *MYB-NFIB* fusion gene, have been made.

2. Case Report

A 49 -year-old female presented with history of a gradually increasing, firm palpable, painless mass in right breast of nine months duration. On physical examination, the single, mobile, firm mass measuring 3.0 x2.5x 1.5 cm was noted in right upper outer quadrant of breast. The right axillary lymphadenopathy was present. The left breast was normal. Her past medical history was unremarkable, and there was no family history of breast or ovarian cancer. FNAC was positive for carcinoma cells. The mammographic appearance

Corresponding author: Sunil Vitthalrao Jagtap
Email: drsvjagtap@gmail.com

https://doi.org/10.18231/j.achr.67799.1761996762

of right breast showed asymmetric dense breast with irregular, ill-defined, lobular mass with coarse internal calcifications. On Sonography showed an irregular, heterogeneous, hypoechoic mass. In the retro-areolar. The axillary regions were of normal morphology. The mammogram was graded as per (Breast Imaging Reporting and Data System category (BI-RADS):4, suspicious for malignant neoplasm. Ultrasound demonstrated an irregular, not parallel, solid, hypoechoic mass with microlobulated margins, echogenic rim, posterior acoustic shadowing, and peripheral vascularity. In this case, patient underwent surgical treatment of wide excision of right breast lump with clear margins and right axillary nodal resections. We received specimen right breast lump, on gross-well circumscribed, firm, solid and cystic measuring 2.0 x1.2x 1.0 cm. Cut section showed single pink-grey, firm to soft solid tumor with microcysts formation. Microscopic examination showed shows a biphasic tumor composed of basaloid and luminal epithelial cells. Areas of pseudoglandular spaces with mucin was noted (**Figure 1**-**3**). The tumor cells are distributed around small cysts, forming both true glands and pseudoglandular spaces. The lumen is filled with eosinophilic or basophilic mucin. The histologic sub-type were predominantly tubular, cribriform, with solid areas (20%).The surgical margins were clear. There was no evidence of neuronal or lymphovascular invasion. On histopathology reported as Adenoid cystic carcinoma, histologic classic variant right breast. Immunohistochemical staining were negative for Estrogen receptor (ER), Progesterone receptor (PR), and Human Epidermal Growth Factor Receptor 2 new (HER-2) There was no axillary lymph node metastases. Tumor showed Ki-67 proliferation index of 10%. Immunohistochemical stain p63 positive for basal cells. Immunohistochemical staining were positive for CK5, CK7, P63, and PAS.

The patient underwent surgical treatment and advised regular follow-up, which showed a favourable prognosis with no evidence of recurrence or any metastasis.

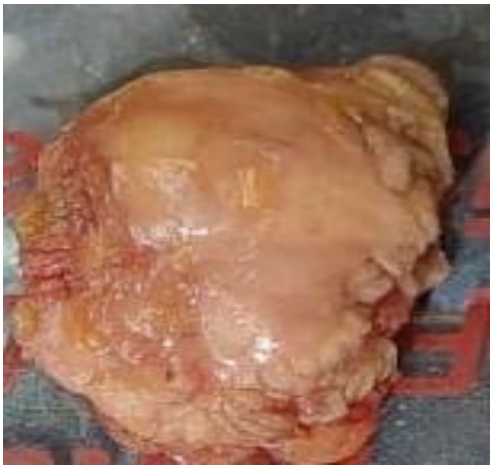

Figure 1: Right breast lump on gross-well circumscribed, firm, cystic.

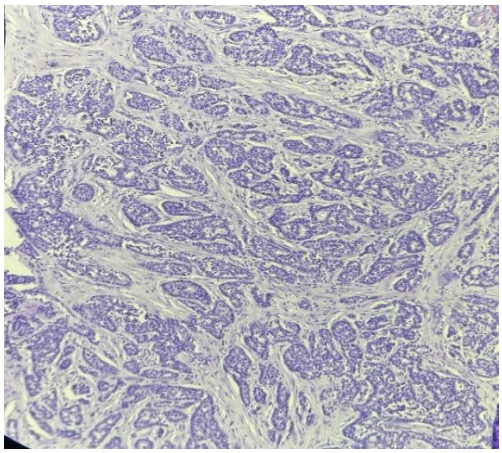

Figure 2: Microscopic features showing- ACC classic variant composed of tubular, cribriform and solid architectural patterns. (H&E stain, 40x)

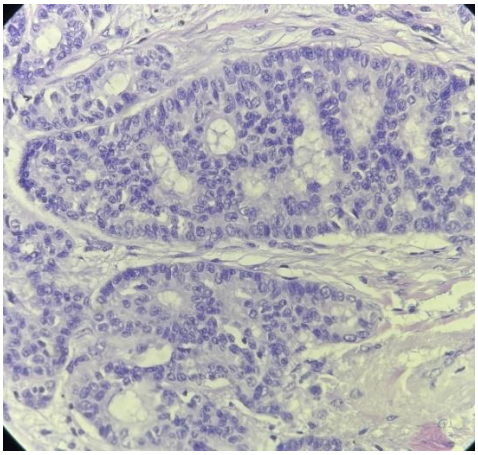

Figure 3: Microscopic features showing- ACC classic variant, tumor with low to intermediate nuclear grade, composed of tubular, cribriform patterns.(H&E stain,100x)

3. Discussion

Adenoid cystic carcinoma of the breast is a rare breast tumor accounting < 0.1% of all breast cancer.[4] ACC of the breast may be associate with various benign lesions like tubular adenosis, adenomyoepithelioma, microglandular adenosis and fibroadenoma.[5]

3.1. Clinical and radioimaging features of ACC breast

Clinically ACC tumors, mostly present as well circumscribed, solitary, painful, palpable breast mass. The localization of tumor is frequently below the areola. Rarely present with nipple discharge. He size varies from with the mean size of 3.0 cm. on gross examination tumor is pink, tan, or gray. On cut surface firm with microcysts formation. It occurs mostly in female patients and rarely in male patients. A rare case of synchronous bilateral breast cancer of ACC was reported in male patient.[6] In ACC the axillary lymph node metastasis is rare having incidence about 0–2% in cases.

1. On radio imaging breast mammography shows asymmetric densities or irregular tumors masses. On sonography these tumors appear as well-defined, irregular, heterogeneous, or hypoechoic masses. On MRI breast ACC on T2WI, may show extensive internal septum of high and low signal in large ACC masses.[7]

3.2. Pathological features of ACC Breast

It is known to have a dual cell population of both luminal and basal cells making it indistinguishable from ACC arising in salivary tissue. In our case Breast ACC shows a biphasic tumor composed of basaloid and luminal epithelial cells. Diagnostic criteria for ACC requires a biphasic cellular pattern comprised of myoepithelial and epithelial cells having luminal and basaloid cells.[8]

As per recent WHO Classification of Breast Tumors, 5th edition, breast ACC are classified on architectural patterns as tubular-trabecular, cribriform, and solid-basaloid and ACC with high-grade transformation.[9] In tubular pattern true glandular spaces or pseudolumina are noted. The luminal cells are round having nuclei and moderate amount of eosinophilic cytoplasm. The lumina shows periodic acid-Schiff-positive neutral mucin. In areas squamous cell metaplasia and sebaceous cell differentiation can be seen. The histological grade of tumors are grade I; grade II -those with solid component < 30% and grade III -solid component ≥ 30%.[10] Histologic variants are a) Classic variant which is most common which shows, tumor with low to intermediate nuclear grade, composed of mixture of 3 different architectural patterns (tubular, cribriform and solid), (b) Solid - basaloid variant: solid nests, increased mitotic rate, presence of necrosis, Ki67 > 30%, prominent basaloid features with more aggressive clinical course and c) Adenoid cystic carcinoma with high grade transformation: associated with different higher grade component subtypes such as invasive breast cancer of NST type. It is observed that solid variant of ACC were associated with an aggressive clinical course.[11]

3.3. Differential diagnosis ACC Breast

The differential diagnosis for ACC are cribiform breast carcinoma. On histopathology, the cribriform cell nest is more irregular. The cribriform lining cells of invasive cribriform carcinoma lack expression of basal like cells and myoepithelium. Infiltrative glands lack circumscription by myoepithelial cells. Also these tumor lacks dual cell population. These tumor shows immunoreactive for Estrogen receptor, Progesterone receptor, and CD117 / KIT.[12]

Another differential is, collagenous spherulosis.[13] In these collagenous spherules are irregular, mostly observed at the periphery of the lesions, and no mucosubstance is detected within lumina. Noninfiltrative proliferation of myoepithelial cells enclosing basement membrane material confined within preexisting ducts or lobules. These are positive for calponin and smooth muscle myosin. The differential diagnosis for the solid (basaloid) variant of ACC includes small cell carcinoma (neuroendocrine carcinoma), solid papillary carcinoma.[14]

3.4. Immunohistochemistry and molecular features of ACC breast

ACC typically triple-negative, basal-like phenotype. These are negative immunohistochemical staining for estrogen receptor, progesterone receptor, and Human Epidermal Growth Factor Receptor 2 (HER-2). The majority of ACC are triple-negative as per the National Cancer Data Base review of mammary ACC.[15]

ACCs are usually low-grade and exhibit an indolent clinical behavior. Wetterskog D, et al, observed that ,triple-negative breast cancers usually have high proliferative activity, while ACC of the breast exhibits a low proliferation rate using standard Ki-67 labeling index.[16] The ACC luminal cells are positive for CK7,CK8/18, epithelial membrane antigen, and CD117(c-Kit).The myoepithelial-basal cells are immunoreactive for basal cytokeratins (CK5, CK5/6, CK14, CK17) and myoepithelial markers p63, actin, calponin, S-100 protein, vimentin, and epidermal growth factor receptor are positive. The molecular and genetic features of the ACC, including a specific chromosomal translocation t(6;9) that results in a *MYB-NFIB* fusion gene, have been made in recent years.[16] The study on microRNA expression profiling, Kiss et al, reported that the let-7b was overexpressed in ACC of the salivary gland, while decreased in ACC of the breast.[17]

3.5. Prognosis and treatment of ACC breast

ACC of the breast, contrast with other triple-negative, basal-like breast cancers is its excellent prognosis. In our case showed triple-negative tumor and showed a favorable prognosis with no evidence of recurrence or any metastasis. The evidence of presence and percentage of solid architecture reflects clinical outcome and should be reported in the pathology report.

The primary management of breast ACC patients is surgery. Khanfir K, et al noted that, the ACC of the breast is generally cured by breast-conserving surgery, such as wide excision or quadrantectomy with or without radiotherapy.[18] In cases of breast-conserving surgery, adjuvant radiation therapy is generally recommended.

However, due to the rarity of this pathological type, there is no clear guidance in the selection of detailed surgical protocol for ACC, resulting in differences in treatment. Tumor lumpectomy should be used for grade I tumors, mastectomy should be used for grade II tumors, and mastectomy plus lymph node dissection should be used for grade III tumors.[18]

The newer advances in detecting the circulating tumor DNA(ctDNA) analysis holds promise for monitoring tumor

management. The reported survival rates in study from B. Ghabach et al for ACC at 5 years, 10 years, and 15 years are 95.5%, 93.5%, and 91%, respectively.[8] Arpino G, et al observed that, ACC of the breast have very favorable biologic characteristics and an excellent prognosis with no recurrence.[19]

4. Conclusion

Adenoid cystic carcinoma of the breast is a rare special subtype of breast cancer. ACC is characterized by slow tumor progression, low malignant potential, rare axillary lymph node metastasis, usually triple negative, low expression of Ki-67, and overall favorable prognosis.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Miyai K, Schwartz MR, Divatia MK, Anton RC, Park YW, Ayala AG, et al. Adenoid cystic carcinoma of breast: Recent advances. *World J Clin Cases*. 2014;2(12):732–41. https://doi.org/10.12998/wjcc.v2.i12.732.
2. Sapino A, Sneige N, Eusebi V. Adenoid cystic carcinoma. In: Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, eds. WHO Classification of Tumours of the Breast. Lyon: IARC Press; 2012:56–57.
3. Fusco N, Geyer FC, De Filippo MR, Martelotto LG, Ng CKY, Piscuoglio S, et al. Genetic events in theprogression of adenoid cystic carcinoma of the breast to high-grade triple-negative breast cancer. *Mod Pathol*. 2016;29(11):1292–305. https://doi.org/10.1038/modpathol.2016.134.
4. Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, et al. Schwart'z Principles of Surgery. New York: McGraw Hill, 2015;556.
5. Da Silva L, Buck L, Simpson PT, Reid L, McCallum N, Madigan BJ, Lakhani SR. Molecular and morphological analysis of adenoid cystic carcinoma of the breast with synchronous tubular adenosis. *Virchows Arch*. 2009;454(1):107–14. https://doi.org/10.1007/s00428-008-0700-z.
6. SV Jagtap, SS Jagtap, N Goswami, N Desai, M Tamberi. Adenoid cystic carcinoma of the male breast: Case report and review of literature. *Indian J Pathol Oncol*. 2024;11(1):47–51. Https://doi.org/10.18231/j.ijpo.2024.010
7. Sperber F, Blank A, Metser U. Adenoid cystic carcinoma of the breast: mammographic, sonographic, and pathological correlation. *Breast J*. 2002;8(1):53–4. https://doi.org/10.1046/j.1524-4741.2002.08012.x.
8. Ghabach B, Anderson WF, Curtis RE, Huycke MM, Lavigne JA, Dores GM. Adenoid cystic carcinoma of the breast in the United States (1977 to 2006): A population-based cohort study. *Breast Cancer Res*. 2010;12(4):R54. https://doi.org/10.1186/bcr2613.
9. MP Foschini, FC Geyer, MM Hayes, C. Marchio R. Nishimura. (5th ed), Breast Tumours, 2, Lyon: IARC Press,2019:142-5.
10. Kleer CG, Oberman HA. Adenoid cystic carcinoma of the breast: value of histologic grading and proliferative activity. *Am J Surg Pathol*. 1998;22(5):569–75. https://doi.org/10.1097/00000478-199805000-00008.
11. Foschini MP, Rizzo A, De Leo A, Laurino L, Sironi M, Rucco V. Solid Variant of Adenoid Cystic Carcinoma of the Breast: A case series with proposal of a New Grading System. *Int J Surg Pathol*. 2016;24(2):97–102. https://doi.org/10.1177/1066896915606973.
12. Mastropasqua MG, Maiorano E, Pruneri G, Orvieto E, Mazzarol G, Vento AR, et al. Immunoreactivity for c-kit and p63 as an adjunct in the diagnosis of adenoid cystic carcinoma of the breast. *Mod Pathol*. 2005;18(10):1277–82. https://doi.org/10.1038/modpathol.3800423.
13. Rabban JT, Swain RS, Zaloudek CJ, Chase DR, Chen YY. Immunophenotypic overlap between adenoid cystic carcinoma and collagenous spherulosis of the breast: potential diagnostic pitfalls using myoepithelial markers. *Mod Pathol*. 2006;19(10):1351–7. https://doi.org/10.1038/modpathol.3800658.
14. Jagtap SV, Aher VC, Bhosale SJ, Hulwan A, Gosavi AN. Primary neuroendocrine carcinoma of breast: An uncommon variant. *Ann Pathol Lab Med*. 2017;4(2):C50–2.
15. Kulkarni N, Pezzi CM, Greif JM, Klimberg VS, Bailey L, Korourian S, et al. Rare breast cancer: 933 adenoid cystic carcinomas from the National Cancer Data Base. *Ann Surg Oncol*. 2013;20(7):2236–41. https://doi.org/10.1245/s10434-013-2911-z.
16. Wetterskog D, Lopez-Garcia MA, Lambros MB, A'Hern R, Geyer FC, Milanezi F, et al. Adenoid cystic carcinomas constitute a genomically distinct subgroup of triple-negative and basal-like breast cancers. *J Pathol*. 2012;226(1):84–96. https://doi.org/10.1002/path.2974.
17. Kiss O, Tőkés AM, Spisák S, Szilágyi A, Lippai N, Székely B, et al. Breast- and salivary gland-derived adenoid cystic carcinomas: potential post-transcriptional divergencies. A pilot study based on miRNA expression profiling of four cases and review of the potential relevance of the findings. *Pathol Oncol Res.* 2015;21(1):29-44. https://doi.org/10.1007/s12253-014-9770-1.
18. Khanfir K, Kallel A, Villette S, Belkacémi Y, Vautravers C, Nguyen T, et al. Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. *Int J Radiat Oncol Biol Phys*. 2012;82(5):2118–24. https://doi.org/10.1016/j.ijrobp.2010.12.008.
19. Arpino G, Clark GM, Mohsin S, Bardou VJ, Elledge RM. Adenoid cystic carcinoma of the breast: molecular markers, treatment, and clinical outcome. *Cancer.* 2002;94(8):2119–27. https://doi.org/10.1002/cncr.10455.

Cite this article: Jagtap SV, Jagtap SS, Vispute AM, Jadhav AS, Khillare SV, Singh I. Update on adenoid cystic carcinoma breast: A rare, special subtype of breast cancer: Review. *IP Arch Cytol Histopathol Res*. 2025;10(3):89-92.