**CLINICAL VIGNETTE**

# Two Cases of Adenoid Cystic Carcinoma of the Breast

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***Case Report***

Case 1:
Three months after a negative mammogram revealed only dense tissue, a 49-year-old premenopausal woman palpated a right breast mass. Ultrasound revealed an 18 mm subareolar mass, corresponding to the palpable abnormality. Breast MRI showed a 30 mm highly suspicious subareolar mass. Biopsy revealed an invasive carcinoma, with features suggesting a poorly differentiated (solid) adenoid cystic carcinoma, with immunohistochemical stains revealing focal expression of CD117, Estrogen Receptor (ER) negative, Progesterone Receptor (PR) negative, ki67 intermediate (15% staining), and HER2 negative.

The patient chose breast preservation, and pathology from the segmental resection revealed a 2.8 cm grade II adenoid cystic carcinoma of the breast. Two negative sentinel nodes were removed. She then received whole breast radiation therapy, but no adjuvant systemic treatment.

After completing local therapy, this patient has remained in remission for 4 years.

Case 2:
A 71-year-old woman palpated a left subareolar breast mass 3 months after a negative mammogram. Biopsy revealed adenoid cystic carcinoma, which was ER negative, PR negative, ki67 low (9%), and HER2 negative by FISH.

This patient chose to undergo mastectomy, which revealed a 1.5 cm adenoid cystic carcinoma, and one negative sentinel node was removed. She received no postoperative therapy. She has remained in remission for 3.5 years after her mastectomy.

***Discussion***

Adenoid cystic carcinoma (ACC) of the breast is a rare subtype of malignant breast tumors, accounting for less than 0.1% of all primary breast cancers, occurring in approximately 1 out of 1 million women each year. Most of the data regarding the natural history and management of this tumor type is derived from case reports and small series. Based on a population based cohort study including 338 patients in the United States, the incidence of ACC of the breast has remained stable.[1]

The ACC histology is noted most frequently in salivary gland tumors but also can be found in tumors of the cervix, prostate, lung, skin, kidneys, and esophagus, in addition to the breast. This histology of ACC of the breast has the same characteristics as ACC of the salivary gland, and although the exact cell of origin is unknown, it is felt to arise from ductal epithelium or myoepithelium. These tumors have a "triple negative" phenotype; specifically, they are negative for ER, PR, and HER2-neu. Yet on microarray genomic analysis, ACC is distinct from triple negative breast cancer. In addition, ACC does not behave clinically like triple negative breast cancer, with a more indolent course, felt to be due to downregulation of proliferative and migrative genes[2], with proliferative markers such as ki67 generally reflecting the low proliferative rate. The epidermal growth factor receptor (EGFR) is often expressed, as can be CD117 (c-KIT) such as in the first case discussed here, and therefore these are potential therapeutic targets.

Although also reported in children and men, these tumors most often present in postmenopausal women age 50-60. The clinical presentation is frequently of a subareolar mass, as was the case for both of the patients presented here, or with pain in the breast. Only rarely is ACC identified by imaging for breast cancer screening, with a nonspecific radiographic appearance. Most often the disease is isolated to the breast with rare nodal or distant metastasis. Given the rare likelihood of a local or distant recurrence, the prognosis of ACC of the breast is excellent.

The optimal treatment of ACC of the breast has not been defined, although the mainstay of treatment is surgery. Both partial mastectomy and mastectomy have been used, and the role of adjuvant radiation therapy is not clear.

Histologic classifications based on growth pattern have been described: glandular, tubular, and solid.[3] This grading system results in a higher grade as the proportion of the solid component increases, with grade 3 including tumors with

more than 30% solid components. Varying treatment has been proposed based on the grade: local excision for grade I, simple mastectomy for grade II, and mastectomy with axillary dissection for grade 3. However, due to the rare incidence of these tumors, no consensus exists regarding management. The first patient discussed above presented with a grade II ACC with a solid component and did well with breast preservation. Recurrence rates after local excision are low, reported from 6-37%.[4,5] The role of adjuvant radiotherapy is not defined; there are no randomized trials that have addressed this question. One retrospective review[6] of 61 patients by the Rare Cancer Network found that radiotherapy after lumpectomy decreased local recurrence risk by 12% at 5 years (83% vs 95%). In another retrospective study of 376 patients of the Surveillance, Epidemiology and End Result (SEER) database, adjuvant radiation therapy improved overall and disease specific survival ,[7] but given the small numbers of patients and lack of randomized data, the role of adjuvant radiotherapy is not clear.

Regarding the pattern of spread, ACC only rarely involves axillary nodes, reported in 2% or fewer of cases.[5] In the 61 patients followed by the Rare Cancer Network,[6] 67% of the patients underwent axillary node dissection, and 16% had sentinel node evaluation, all of which were negative. After 79 months of follow up, none of the 61 patients on this study developed locoregional nodal metastasis. Although no consensus exists regarding management of a clinically negative axilla, some surgeons perform sentinel node evaluation for larger or higher grade tumors. Both of the patients presented above did have negative sentinel node evaluation, but there is no proven utility of sentinel node biopsies.

The distant spread of ACC is rare, usually occurs without axillary nodal involvement, and most commonly involves the lung, but metastases have also been reported in liver, kidneys, and brain. Although there is a small chance of distant spread, the role of adjuvant systemic therapy remains undefined. Given the hormone receptor negative nature of these tumors, adjuvant endocrine therapy does not play a role. Chemotherapy has not been shown to improve survival. The prognosis for ACC of the breast is excellent with an 88% 5 year survival[8] that exceeds that for other types of breast cancer and for ACC of the salivary gland. Given the rare number of patients with this disease, optimal local and systemic therapy is not defined with current treatment remaining mainly surgical.

**REFERENCES**


1. **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. doi: 10.1186/bcr2613. Epub 2010 Jul 23. PubMed PMID: 20653964; PubMed Central PMCID:PMC2949643.
2. **Boujelbene N, Khabir A, Boujelbene N, Jeanneret Sozzi W, Mirimanoff RO, Khanfir K**. Clinical review--breast adenoid cystic carcinoma. *Breast*. 2012 Apr;21(2):124-7. doi: 10.1016/j.breast.2011.11.006. Epub 2011 Dec 10. Review. PubMed PMID: 22154460.
3. **Ro JY, Silva EG, Gallager HS**. Adenoid cystic carcinoma of the breast. Hum Pathol. 1987 Dec;18(12):1276-81. Review. PubMed PMID: 2824330.
4. **Peters GN, Wolff M**. Adenoid cystic carcinoma of the breast. Report of 11 new cases: review of the literature and discussion of biological behavior. *Cancer*. 1983 Aug 15;52(4):680-6. Review. PubMed PMID: 6305483.
5. **Sumpio BE, Jennings TA, Merino MJ, Sullivan PD**. Adenoid cystic carcinoma of the breast. Data from the Connecticut Tumor Registry and a review of the literature. *Ann Surg*. 1987 Mar;205(3):295-301. Review. PubMed PMID: 3030200; PubMed Central PMCID: PMC1492723.
6. **Khanfir K, Kallel A, Villette S, Belkacémi Y, Vautravers C, Nguyen T, Miller R, Li YX, Taghian AG, Boersma L, Poortmans P, Goldberg H, Vees H, Senkus E, Igdem S, Ozsahin M, Jeanneret Sozzi W**. Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. *Int J Radiat Oncol Biol Phys*. 2012 Apr 1;82(5):2118-24. doi: 10.1016/j.ijrobp.2010.12.008. Epub 2011 May 11. PubMed PMID: 21570212.
7. **Coates JM, Martinez SR, Bold RJ, Chen SL**. Adjuvant radiation therapy is associated with improved survival for adenoid cystic carcinoma of the breast. *J Surg Oncol*. 2010 Sep 15;102(4):342-7. doi: 10.1002/jso.21638. PubMed PMID: 20589709.
8. **Kulkarni N, Pezzi CM, Greif JM, Suzanne Klimberg V, Bailey L, Korourian S, Zuraek M**. Rare breast cancer: 933 adenoid cystic carcinomas from the National Cancer Data Base. *Ann Surg Oncol*. 2013 Jul;20(7):2236-41. doi:10.1245/s10434-013-2911-z. Epub 2013 Mar 1. PubMed PMID: 23456318.


*Submitted October 20, 2014*