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Adenoid cystic carcinoma of the breast from a single-center cohort

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ABSTRACT

Adenoid cystic carcinoma (ACC) of the breast is a rare breast tumor, comprising less than 1% of breast adenocarcinomas. Histopathologically, it is estrogen receptor (ER), progesterone receptor (PR), and HER2-negative (i.e., triple negative) but has a more indolent course than typical triple negative breast cancers. Most of what is known regarding ACC of the breast's treatment and prognosis is from case reports and case series. This case series reports a single institution's experience with ACC. Between 2003 and 2014, seven patients were found to have ACC of the breast. Most (6 of 7 cases) presented as a mammogram abnormality on routine screening. One patient was lost to follow up after initial diagnosis. All six patients underwent lumpectomy, sentinel lymph node biopsy (SLNB), and adjuvant radiation. None received systemic endocrine therapy or chemotherapy. All of the patients are without disease recurrence at median follow up of 6.2 years (range 0.4–10). Given the generally excellent prognosis of ACC of the breast and low tumor metastatic potential, it is reasonable to withhold adjuvant chemotherapy in the treatment of ACC and instead manage this malignancy with local therapy.

1. Introduction

Adenoid cystic carcinoma (ACC) is a rare form of well differentiated adenocarcinoma that is most commonly seen in head and neck region, in particular, the salivary glands. Although it can be seen in any site of the body, ACC comprises less than 1% of breast adenocarcinomas [1–5]. Histopathologically, it is characterized by the presence of both luminal and myoepithelial components irrespective of site of origin, however, similarities in morphology often do not correspond to the aggressiveness of the tumor, with ACC of the breast often presenting with a more indolent course than its salivary counterpart [6–8]. Immunophenotypically, ACC of the breast is estrogen receptor (ER) progesterone receptor (PR) and human epidermal growth factor 2 (HER2) negative, fitting into the triple-negative subtype of breast cancer with the major distinction being the high grade, clinically aggressive nature of most triple negative breast cancers as compared to the low grade indolent course of ACC [9,10]. Given this great difference in clinicopathologic features despite immunophenotypic similarity between ACC of the breast and triple negative invasive breast cancer, a deep understanding of ACC of the breast is essential. This report presents a single institution's experience and literature review of ACC of the breast.

2. Results

Patients of age ≥ 18 years carrying a diagnosis of ACC of the breast between 2003 and 2014 were included in the analysis. Cases were identified from the Northwestern University Electronic Pathology Database using the keywords Adenoid cystic carcinoma and breast. The diagnoses were rendered based on the histomorphology of the tumor and wherever necessary, appropriate immunohistochemical stains were utilized to confirm the diagnosis (Figs. 1–3). The most common immunostains utilized were C-kit (CD117) and p63 (Fig. 2). Relevant clinical data was abstracted, including demographics, imaging, staging, and treatment history.

Seven patients were identified with the diagnosis of ACC of the breast (Table 1). Detailed treatment plan and follow up was available in six of the seven patients, with the seventh patient presenting only for initial diagnosis. All seven patients were postmenopausal females with a median age of 61 years old (range 56–75). Four were African American (57.1%), two Caucasian (28.6%), and one unknown race (14.3%). A majority of the patients (six of seven patients, 85.7%) presented by routine screening mammography while one presented with breast pain with subsequent palpable mass. Mammographic appearance (Table 2, Fig. 4) varied among patients – two tumors appeared as a focal asymmetric density, two as an isodense mass with indistinct margins, one as a mass with spiculated margins, one as an ill defined mass, and one partially obscured round mass. All six patients that received treatment at Northwestern University underwent

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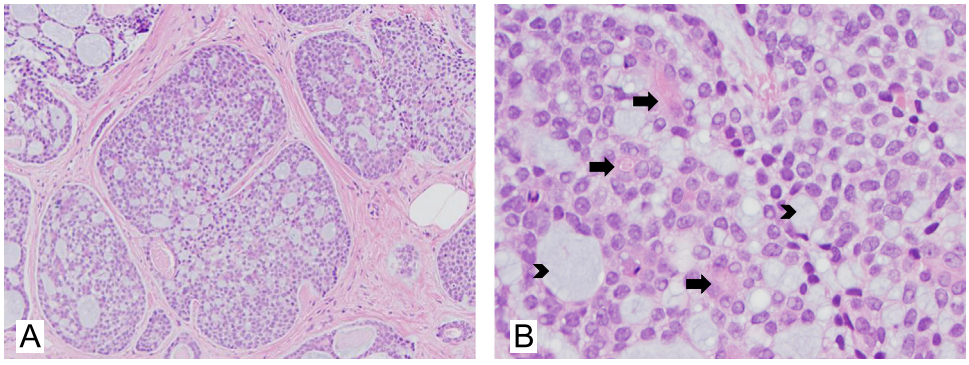

Fig. 1. Adenoid cystic carcinoma of the breast. (A) H & E stained section from adenoid cystic carcinoma (Case 6) showing a cribriform architecture (200 ×) and (B) higher power highlighting the presence of true lumens (arrow) and false lumens (arrow heads) containing myxoid material (400 ×).

lumpectomy with sentinel lymph node biopsy and all six had uninvolved axillary lymph nodes despite a mean tumor size of 3.1 cm (range 0.9–5). Three of the seven (42.9%) cases presented as grade 1 lesions, four (57.1%) were classified as grade 2, while none were grade 3 (Table 1). Estrogen and progesterone receptor expression were negative in all seven cases (100%). HER2 expression by IHC was negative (0 or 1+) in all cases (100%). Ki-67 was reported in two cases, with both being < 10%. Of the six patients whose treatment was known, all six received lumpectomy, sentinel lymph node biopsy (SLNB), and standard adjuvant radiation, but none received adjuvant endocrine therapy, chemotherapy, or targeted therapy. At a median follow up of 6.2 years (range 0.4–10), all six patients remain free of local and distant recurrence (Table 1).

3. Case presentations

3.1. Case #1

A 60-year-old African American postmenopausal female presented to an outside facility for a routine screening mammogram. The mammogram revealed a 1.7 cm mass in the right upper outer quadrant with spiculated margins which was confirmed as a shadowing mass on ultrasonography (Table 2). Image guided core biopsy revealed invasive ductal carcinoma grade 1 with adenoid cystic features. She underwent a right breast lumpectomy and SLNB. Final tumor size was 2.6 cm wide with widely free margins and uninvolved sentinel lymph nodes (0/2). Initial pathological diagnosis was reported as invasive ductal carcinoma with adenoid cystic features, grade 1. Upon further immunohistochemical (IHC) staining, tumor was found to be ER, PR, and HER2 negative with Ki-67 < 10%. Given the discordant grade and IHC staining, additional IHC was performed including p63 and CD117, both were found to be strongly positive, and diagnosis was changed to ACC of the breast, stage 2 (pT2N0M0) [11]. The patient received adjuvant radiation treatment without any chemotherapy and currently remains without evidence of recurrence at 0.4 years.

3.2. Case #2

A 75-year-old postmenopausal African American female presented with an ill defined nodular mass in the left breast on screening mammography that was confirmed by diagnostic imaging to be a 2.5 cm mass without calcification and by ultrasonography as a lobulated heterogeneous solid mass (Table 2). Core biopsy demonstrated grade 2 adenoid cystic carcinoma, cribiform type, ER/PR/HER2 negative. She underwent a lumpectomy and SLNB which revealed a 5 cm mass with positive margins for carcinoma and 2 negative sentinel lymph nodes. Re-excision of the margins showed no residual cancer. She completed radiation therapy and remains disease free for over 10 years.

3.3. Case #3

A 67-year-old Caucasian postmenopausal female presented for a second opinion after a screening mammography found a focal 1.5 cm asymmetric density in the outer right breast. Ultrasound revealed a 9 × 8 × 8 mm irregular ovoid mass corresponding to the mammographic asymmetry along with a 9 × 5 × 5 mm vague area of shadowing 1 cm anterior to the mass. Core biopsy of the first mentioned mammographic abnormality (the area of shadowing could not be demonstrated at time of biopsy) revealed ACC, grade 1 with an organoid and focally tubular pattern (Table 2). The carcinoma was ER/PR/HER2 negative, p63/CD10/CD117/AE1/AE3 focally positive, and Laminin/collagen IV positive in hyaline

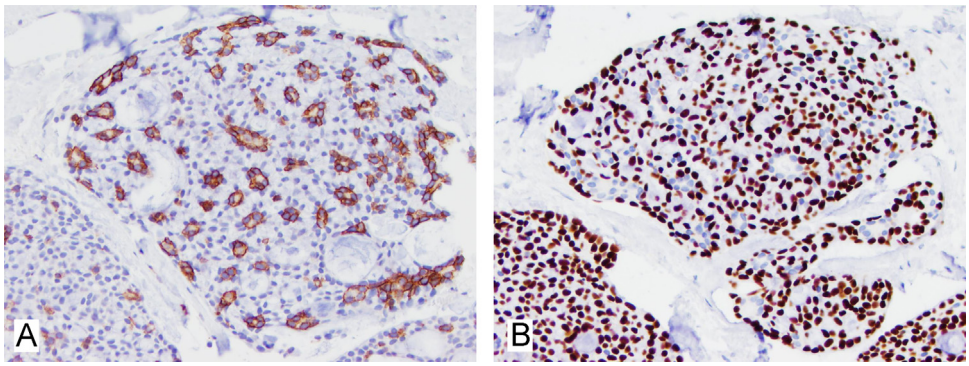

Fig. 2. Immunoreactivity of adenoid cystic carcinoma of the breast. (A) A positive CD117 immunostain (Case 6) highlighting the epithelial cells (200 ×), (B) Myoepithelial cells show strong nuclear positivity for p63 immunostain in adenoid cystic carcinoma.