

Case report

A rare case presentation of Adenoid Cystic Carcinoma of the Breast in a 36-Year-Old Female

Abstract

Background: Primary adenoid cystic carcinoma (ACC) of breast is rarely seen clinically. It is a special subtype of triple-negative breast cancer characterized by low expression of Ki-67, low malignant potential, slow progression and favourable prognosis. To date, treatment for this disease is controversial and no consensus is reached. We analyzed clinical manifestations and pathological characteristics of a primary breast ACC and reported in combination with literature review to promote understanding, diagnosis and treatment of this disease.

Case presentation: We reviewed a case of 36-year-old female with pathologically diagnosed breast ACC and treated at our department. Molecular type was triple negative and Ki-67 expression was low (5/7). Patient underwent Modified Radical Mastectomy with Axillary Lymph node Dissection. She received both adjuvant chemotherapy and adjuvant radiation. At the follow-up of 36 months patient was disease free and was on regular follow up.

Conclusion: Breast ACC is accompanied with favourable prognosis, which is different from typical triple-negative breast cancer. Accurate diagnosis of ACC is particularly important. Multidisciplinary approach should be considered in the management.

Keywords: Breast, Adenoid cystic carcinoma, Treatment, Prognosis, Chemotherapy, Radiotherapy.

Introduction

“Adenoid cystic carcinoma (ACC) of the breast is rare, accounting for less than 0.1% of all breast cancers” [1]. “This variant is typically seen in the salivary glands but has been reported in other organs including the breast, skin, lung, cervix, larynx, and Bartholin gland” [2]. “It is made up of a mix of epithelial and myoepithelial neoplastic cells that grow in cribriform, tubular, and/or solid patterns” [3]. Unlike ACC in the salivary gland, ACC of the breast has a good prognosis, with axillary metastases being rare. Given the rarity of this tumor, diagnosis remains a challenge.

“Mammographically, ACCs have been reported as smooth or irregular masses or asymmetric densities” [4]. “Distant metastases, usually to the lung, can occur without positive axillary nodes, and local recurrences are more likely if radiotherapy was not administered” [5]. “It is a good-prognosis subtype of triple-negative breast cancer (i.e., tumors that are devoid of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 expression, and express basal cell markers) characterized by low expression of Ki-67, low malignant potential, slow progression and favorable prognosis” [6]. “Treatment may consist of either lumpectomy with radiotherapy, or mastectomy; with both surgical options associated with equivalent survival” [7]. “There is no clear evidence on the literature on the efficacy of adjuvant systemic therapy for the treatment of ACC of the breast. The 5-year and 10-year survival rates are greater than 95% and 90%, respectively, and lymph node metastasis, as well as distant metastases, which primarily affect visceral organs, are uncommon” [8,33,34].

Hence, we report this rare variant of Breast Cancer in a 36-year-old female who presented to our oncology department.

Case Presentation

A 36-year-old female with no personal or family history of breast cancer, presented to our department with complaints of palpable non-painful lump in the lower quadrant of left breast. The patient has past history of benign breast disease in left breast 2 years back and underwent lump excision. The biopsy showed features favoring lymphocytic maculopathy.

She was evaluated and diagnosed as a case of carcinoma of left breast cT3N0M0. Bilateral ultrasonomammogram showed ill-defined irregular hypoechoic lesion taller than wide measuring 3.3 x 3 cm angular margins retro areolar region of left breast 5- 8 o'clock region. The lesion shows internal vascularity. No evidence of calcification. Another few hypoechoic lesions are seen adjacent to the lesion measuring 5 mm. Left axilla shows few benign lymph nodes largest measuring 14 x 9 mm. BIRADS (Breast imaging reporting and data system) scoring was found to be 4. A true cut biopsy was taken which was suggestive of Adenoid Cystic Carcinoma.

She underwent Modified radical mastectomy of left breast with axillary lymph node dissection.

Post-operative period was uneventful. On Post-Operative Histopathological examination:

Microscopically, tumor shows an invasive neoplasm composed of basaloid cells with scanty cytoplasm, with high nuclear to cytoplasmic ratio and mild pleomorphism. The tumor cells are seen invading in solid nests, in a desmoplastic and myxoid stroma, Mitosis are few. Cribriform pattern with luminal basement membrane like material noted in some foci. Lymphovascular and perineural invasion noted. 15 Axillary lymph nodes were dissected and are free of tumor. Her pathological staging was pT3N0Mx. Photomicrograph of histopathologic specimen shows cribriform architecture (Figure 1)

Immunohistochemistry (IHC) demonstrated diffuse expression of cytokeratin 7 (CK7). The tumor lacked estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2) expression. The Ki67 proliferation index was approximately 10%. A medical oncology consultation was obtained. Given the triple negative phenotype and biopsy proven negative lymph node status, adjuvant chemotherapy was recommended. Patient was given Dose dense Adriamycin, Cyclophosphamide (AC) for four cycles and Paclitaxel for four cycles, which she tolerated well.

The patient was referred to radiation oncology and adjuvant radiation was planned in view of large tumor size and advanced disease. She received adjuvant radiation therapy to 40 Gray in 15 fractions to left chest wall by 3DCRT (3-Dimensional Conformal Radiation Therapy). She tolerated the treatment well. She was on regular 3 monthly follow-up. She has remained clinically disease free at one year follow up.

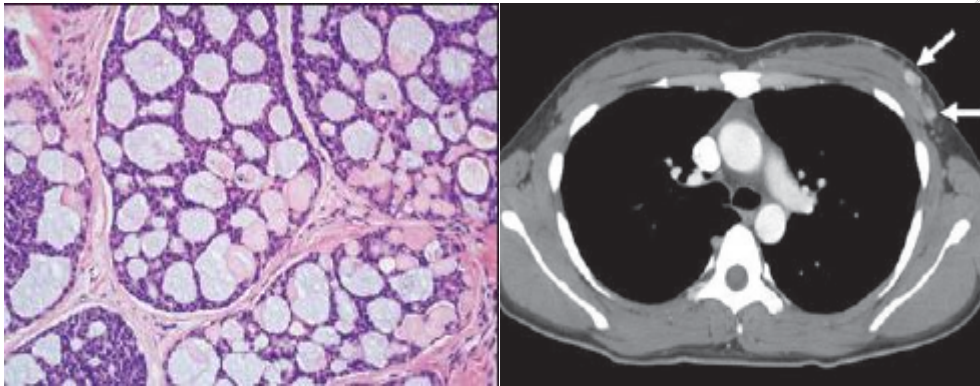


Figure 1: Photomicrograph of histopathologic specimen shows cribriform architecture, with predominantly glandular spaces with basophilic secretions and focal cylindromatous nodules.

Figure 2: Contrast-enhanced CT image of chest shows nodular areas (*arrows*) of rapid contrast enhancement in left breast, corresponding to ACC.

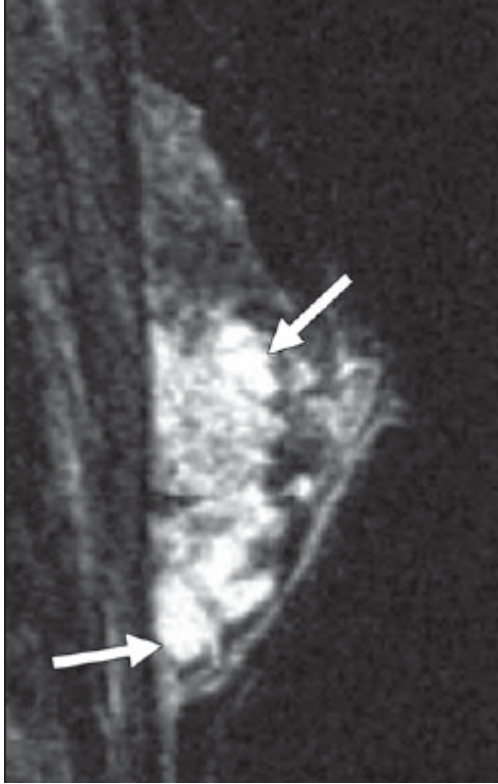


Figure 3: Fat-saturated, sagittal, T2-weighted MR image of left breast shows areas of hyperintense T2 signal within mass (*arrows*).

Discussion

“ACC accounts for only 0.1% to 1% of all breast tumors”.^[9] There have been case reports on ACC in salivary glands, digestive tract, external auditory canal, skin, uterus, and breast cancer. ^[10,11] Breast ACC mostly affects women in their fifth and sixth decades of life”.^[12] “Breast ACC can occur in men even though it is primarily seen in females”.^[13]

“ACC is most commonly found in the superior lateral quadrant or beneath the areola of the breast. The most common chief complaints are palpable masses”. ^[15,16] “The mass is often solitary, and reports of multiple masses are rare. On palpation, tender is seen if tumor is located adjacent to the peripheral neural network. Rarely it can involve nipple and breast skin retractions, as well as pectoralis muscle invasion. For early detection fine needle biopsy plays an important role”.^[17]

“There is no significant specificity in the imaging presentation of primary breast ACC based on imaging of previous cases. It has been reported that the X-ray appearance of breast ACC can be irregular and high-density mass with fuzzy edge, containing slightly low-density or lipoid density lesions, with less calcification. Ultrasound appearance of breast ACC is non-mass like lesion with high echo and no distribution along direction of catheters. Likewise, there are some valuable findings on MRI. Most lesions of breast ACC are clear. On T2WI, large breast ACC can show extensive internal septum of high and low signal, which can be enhanced in delayed phase” [18,19]. “Therefore, Katrina et al. concluded that combination of multiple imaging examinations could increase diagnostic efficiency, despite final diagnosis still depended on pathology” [20].

“MYB is the first discovered proto-oncogene located in 6q22-23, which has strong carcinogenic effect and is known to be expressed in a variety of malignant tumours. Nuclear factor IB (NFIB) is a member of the NFI family and serves as a protein coding gene located in 9p23-24. It plays an important role in cell proliferation, apoptosis and development. ACC repetitive translocation t (6; 9) (q22-23; p23-24) leads to the fusion of MYB and NFIB, which is the main molecular mechanism of the disease. A large number of studies have shown that the fusion of MYB and NFIB is closely related to the occurrence and development of breast ACC”. [21,22].

“The pathological grading of ACC is disputed. According to the cell structure, tumours composed of tubular or cribriform structures alone are classified into histological grade I; those with solid component < 30% are classified into histological grade II and those with solid component \geq 30% are classified into histological grade III. The higher the percentage of solid components, the worse the prognosis of the patients” [23]. “There is also another classification system: classic ACC is classified into low grade and solid adenoid cystic carcinoma with basal cell like features is classified into high grade” [24].

“Surgery is now recognized as the primary treatment for breast ACC patients. However, due to the rarity of this pathological type, there is no clear guidance in the selection of detailed surgical method for this disease, resulting in differences in treatment. Ro et al. suggested that the operation method should be selected according to the ACC grade. Tumour lumpectomy should be used for grade I tumours, mastectomy should be used for grade II tumours, and mastectomy plus

lymph node dissection should be used for grade III tumours” [25]. “The axillary lymph node metastasis of classic breast ACC is rare, generally 0–2%. Axillary lymph node dissection (ALND) is not necessary if there is no preoperative definite clinical evidence of axillary lymph node metastasis. Thompson et al. investigated 244 patients with confirmed breast ACC, discovering that patients with unknown lymph node status have the same favourable 10-year relative cumulative survival rate as known non-lymph node metastasis patients. Therefore, the author believed that ALND was not necessary for patients with breast ACC, especially for patients with T1 stage” [26]. “Kulkarni et al. designed a clinical study and included 933 patients with breast ACC, among whom 6% received axillary lymph node assessment and only 5% were axillary lymph node positive. He came to the same conclusion that ALND was not necessary for breast ACC patients” [27].

There are literatures on postoperative adjuvant RT, showing that postoperative adjuvant RT can improve the overall survival (OS) and disease-specific survival of patients after receiving local surgery [28]. Khanfir et al. retrospectively analysed 61 breast ACC patients undergoing BCS. The result indicated that 5-year local area control rate of patients with adjuvant RT was higher than those without RT. The author suggested that BCS should be the preferred treatment for patients with breast ACC and adjuvant RT could bring more benefits to patients [29].

“At present, there are still controversies about adjuvant CT after operation and no consensus is reached. Arpino G et al. suggested that postoperative adjuvant CT did not improve disease free survival or OS in breast cancer patients [30]. Treitl et al. investigated six patients with breast ACC, and none of them were found accompanied with lymph node metastasis. The researcher assumed that patients with breast ACC did not need adjuvant CT after operation”[31]. “Coincidentally, there is another study in which only 11.3% of all patients receive adjuvant CT after surgery. However, for patients with axillary lymph node metastasis, some experts claim that systematic adjuvant CT is necessary and for patients with high grade or large tumour with diameter larger than 3 cm, adjuvant CT should be considered” [31]

“ACC of breast is often regarded as a subtype of TNBC. Therefore, endocrine therapy is unnecessary. Yigit retrospectively reviewed seven patients diagnosed with breast ACC. IHC showed

that expression of progesterone receptor (PR) and HER2 was absent in all patients. Only one patient showed weak positive expression of estrogen receptor (ER). Besides, six of them showed positive expression of androgen receptor. Therefore, the author presented that hormone therapy could be applied in androgen receptor positive patients in the future” [32]. However, more in-depth studies are needed to confirm this viewpoint.

Conclusions

Breast ACC differs from traditional TNBC. It is characterized by slower clinical process and lower invasiveness. It is necessary to diagnosis breast ACC clearly. At present, BCS and mastectomy are widely used and ALND is evitable. Adjuvant RT should be considered in Locally advanced and also in patients undergoing BCS. Regular review and long-term follow-up for patients are absolutely necessary.

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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Details of the AI usage are given below:

- 1.
- 2.
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