Clinical Case Report

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Adenoid cystic carcinoma of the breast in a male
A case report

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Abstract

Rationale: Adenoid cystic carcinoma (ACC) of the breast is an infrequent neoplasm, and the occurrence in males is rare. Therefore, diagnostic and therapeutic challenges are inevitable.

Patient concerns: Herein, we present a case of a 44-year-old man with a tumor on his right breast that he had known about for 6 years.

Diagnoses: The patient underwent a lumpectomy, and the histological examination confirmed a diagnosis of ACC.

Interventions: Modified radical mastectomy was subsequently conducted in the patient. No positive lymph nodes were observed in the postoperative pathological examination. Following the surgery, the patient received adjuvant chemotherapy.

Outcomes: The patient remained recurrence-free at 26 months.

Lessons: Compared to female breast ACC, male breast ACC may behave differently biologically and have a different prognosis. Our case will provide more diagnostic and treatment experience to deal with this disease.

Abbreviations: ACC = adenoid cystic carcinoma, ER = estrogen receptor, HER-2 = human epidermalgrowth factor receptor-2, MRI = magnetic resonance imaging, PR = progesterone receptor.

Keywords: adenoid cystic carcinoma, breast, magnetic resonance imaging, male, treatment

1. Introduction

Adenoid cystic carcinoma (ACC), previously called "cylindroma," is a rare malignant tumor in the breast that constitutes less than 0.1% of all breast cancers.[1,2] Although the histopathology resembles that of a salivary gland-like tumor, the prognosis of breast ACC is more favorable because metastasis to distant organs or axillary lymph nodes is less frequently observed.[3,4] The specific pathogenesis of breast ACC is still unknown as a biphasic pattern of composition, including both epithelial and basal-myoepithelial cells, is the pathological feature of breast ACC.[5] However, the correct diagnosis of breast ACC is challenging for surgical pathologists for the uncommon cases that present in clinics, especially in primary hospitals in China. With respect to the immunohistochemistry analysis, the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermalgrowth factor receptor-2 (HER-2) is always negative in breast ACC.[5,6] In contrast with the other triple-negative breast cancers with aggressive biological behavior, breast ACC has a favorable prognosis.[1,7]

Currently, optimal treatment criteria of all breast ACC are still lacking, not to mention those for male breast ACC. Due to gender differences, the occurrence of breast ACC in males is rare. Information on male breast ACC can only be found in case reports in previous articles.[8–10] Herein, we will report a case of male breast ACC to provide more clinical experience for the diagnosis and treatment of this disease. Additionally, we will review other well-documented publications to further discuss treatment strategies.

The ethics committee of the Taizhou Municipal Hospital, Taizhou University, approved the study, and informed written consent was obtained from the patient for publication of this case report and the accompanying images.

2. Case presentation

A 44-year-old man complained of a gradually enlarging and tender lump in his right breast that he had known about for 6 years. The patient had smoked for 20 years and consumed approximately 20 cigarettes a day, but he did not drink alcohol. There was no history of cancer in his family. The physical examination of the right breast showed a palpable mass measuring 1.5 cm in diameter in the subareolar area. The mass was hard, mobile, and mildly tender and was fixed to the skin of the subareolar area with a poorly differentiated boundary. The examinations of the left breast and axillary lymph nodes were unremarkable. No further metastasis was detected in the preoperative inspection, and the values of routine laboratory tests were normal.

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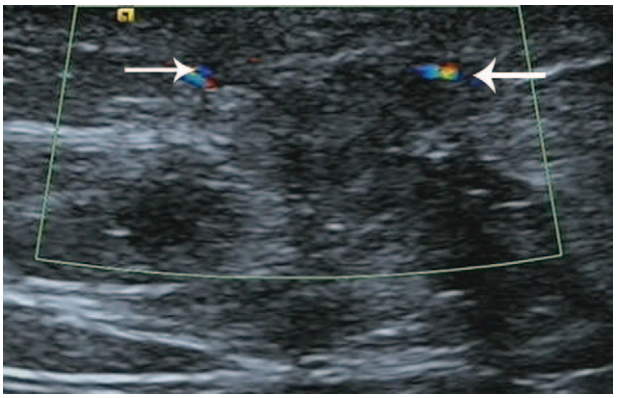

Figure 1. Ultrasonography of the tumor demonstrating an ill-defined hypoechoic lesion in the subareolar region with minimal vascularity observed on color Doppler interrogation (arrow).

Ultrasonography of the tumor revealed an irregular hypoechoic lesion (12.8 mm × 9.9 mm × 6.7 mm) with an unclear boundary (Fig. 1). No posterior acoustic shadowing or echogenic halo was observed, and the tumor was attached to the nipple. Minimal vascularity was detected on the color doppler ultrasound.

Magnetic resonance imaging (MRI) demonstrated an oval solitary nodule with a spiculated margin located in the subareolar area. The lesion (diameter 1.2 cm) had invaded the nipple, with low signal intensity on T1WI (Fig. 2A) and high signal intensity on T2WI (Fig. 2B). The diffusion-weighted image signal was high, and the apparent diffusion coefficient signal was heterogeneously low. On dynamic contrast-enhanced scanning MRI (Fig. 2C), tumor enhancement was rapid and obviously homogeneous. The time-signal intensity curve of the mass demonstrated plateau enhancement kinetics. To date, this is the first MRI information of male breast ACC, which has otherwise been well reported in the world to our knowledge. Furthermore, no abnormal axillary lymph nodes were observed on all preoperative radiographic images.

A simple lumpectomy was then performed, and the diagnosis of sclerosing adenosis with glandular epithelial hyperplasia was made by examining frozen sections. The resection specimen was measured 2.5 cm*2 cm*1.5 cm, including a hard, gray and white tumor (1.2 cm*1.0 cm*0.8 cm) inside. The final histopathologic report described breast ACC with a biphasic cell population (epithelial and myoepithelial cells). Tumor cells were arranged into a prominent solid and cribriform pattern (Fig. 3A) and a focally tubular pattern (Fig. 3B). Multiple perineural invasions were also observed in the photomicrographs (Fig. 3B). Immunohistochemically, the expression of PR, ER, and HER-2 proteins was negative in the tumor cells, which is consistent with triple-negative breast cancers. Expression of the proliferation marker Ki67 was seen in 20% of cells. The nipple margin was positive for carcinoma. Given the above pathologic diagnosis and the preferences of the patient, he was consented to undergo modified radical mastectomy with axillary lymph node dissection. All margins and lymph nodes retrieved were free of cancer metastasis in postoperative pathologic evaluation. A course of adjuvant chemotherapy (epirubicin/cyclophosphamide followed by docetaxel) was subsequently performed 10 days after the surgery. Radiotherapy and hormonal therapy were not continued in this case. The patient remains well after 26 months of follow-up.

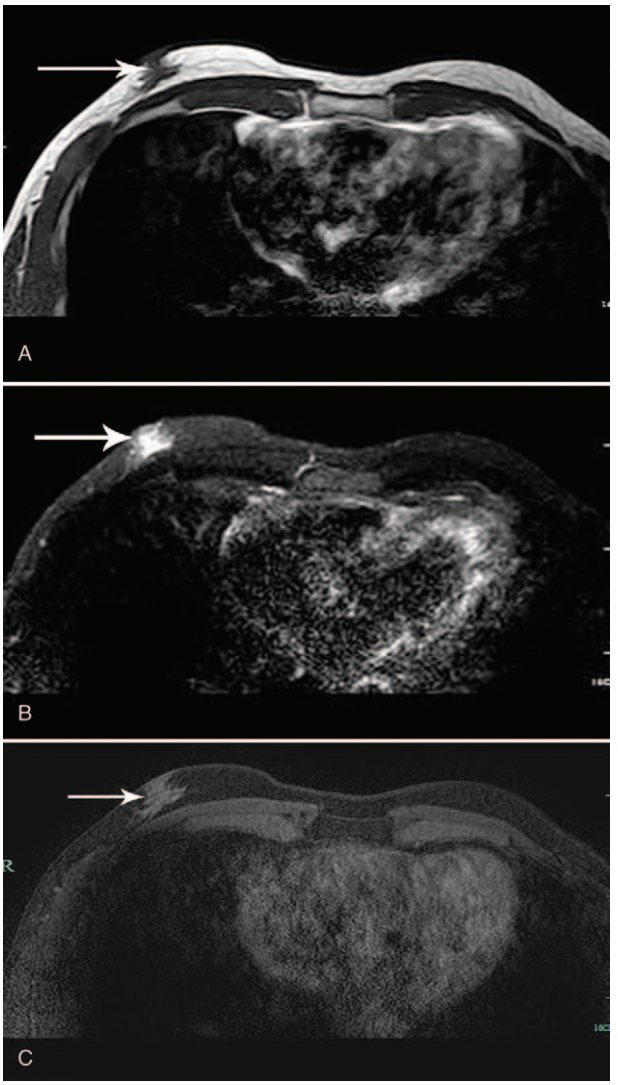

Figure 2. (A) Sagittal, TSE, T1-weighted MRI illustrating that the tumor was hypointense in T1 signal (arrow). (B) Fat-saturated, sagittal, T2-weighted MRI showing that the tumor was hyperintense in T2 signal (arrow). (C) Early-phase sagittal, dynamic, eTHRIVE, contrast-enhanced MRI showing a rapidly and homogeneously enhancing tumor (arrow). MRI = magnetic resonance imaging.

3. Discussion

ACC of the breast is a rare entity, constituting less than 0.1% of all malignant breast tumors.[11] Due to the female predominance in breast cancer, the incidence of breast ACC in men is even lower. The median age of occurrence in females with breast ACC is approximately 60,[12] but the most common age of occurrence in males is still unknown. Some authors believe it is much younger than that in female patients.[10]

Similar to other male breast cancers, the clinical presentation of male breast ACC usually includes a painless and firm nodule.[2] Only a few patients were accidentally diagnosed by radiology.[4] The presenting symptom in our patient was a tender and painful mass, which is only described in a minority of cases. Although

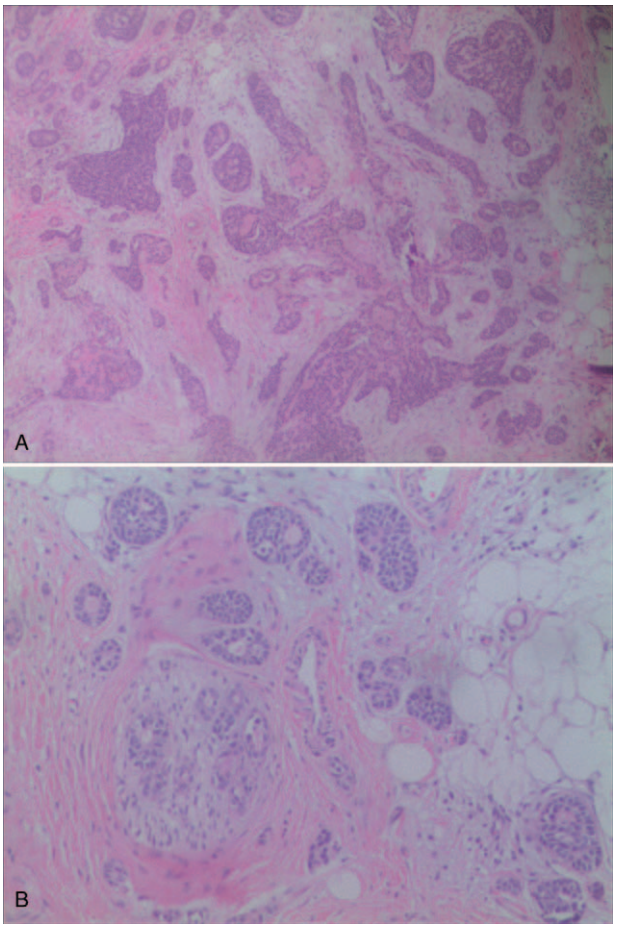

Figure 3. Characteristics of H&E photomicrographs of male breast adenoid cystic carcinoma. (A) Solid and cribriform patterns. (B) Tubular pattern with perineural invasion.

palpable axillary nodes, ulceration, and nipple retraction are frequently observed in male breast cancer,[13] they were not found in our patient, who had known about the breast mass for 6 years. Similar to the present case, the subareolar region is the preferred site of male breast ACC.[12] However, bloody nipple discharge is seldom observed in this disease.[8] The average size of breast ACC tumors ranges from 0.7 to 12 cm in females and 1.7 to 3.7 cm in males according to previous studies.[8,14] Compared with the other reported cases, the tumor in our patient was much smaller (1.2 cm).

Although several studies of the imaging manifestations of breast ACC have been published, they are inconsistent and non-specific. Mammographically, breast ACC can present as an irregular mass, a lobulated, smooth mass or an asymmetric density.[12,15] Calcification is rarely observed.[16,17] Upon ultrasonic visualization, a benign-appearing mass or an ill-defined, hypoechoic or heterogeneous mass can be observed in this subtype of breast cancer. Color Doppler imaging always shows minimal blood flow.[18,19] With regard to MRI, the imaging characteristics of breast ACC are controversial.[2,18] The tumor can appear as irregular shapes with spiculated margins or as round, oval, well-circumscribed masses. The appearance of the tumor on T2-weighted imaging is distinctive. Unlike typical breast cancers with lower T2-weighted signal intensity, the smaller instances of breast ACC show isointensity, and the larger instances show hyperintensity.[17] Moreover, Tang et al also found that the internal septations of all breast ACCs have a low T2WI signal, with delayed enhancement seen in the larger instances.[18] Contrast-enhanced scanning MRI demonstrated that the enhancement of breast ACC is quick and homogeneous or heterogeneous. On dynamic enhancement, the kinetics of the uptake curve may be related to the size of the tumor. Persistent, plateau, or washout kinetics may be observed in this carcinoma.[17,18] Therefore, in contrast with typical breast cancer and benign masses, the appearance of breast ACC on the MRI may be helpful to distinguish it from other breast tumors. Until now, all the information regarding MRI of breast ACC has been derived from females, and it may not be suitable for males. In the present case, the tumor appeared irregular in shape and showed rapid and homogeneous enhancement. In the delayed phase, the internal septations were not enhanced because the tumor was small. Dynamic enhancement revealed a time-signal intensity curve with plateau kinetics. Since the MRI findings of male breast ACC have not been reported previously, more data are needed to discuss this rare disease in the future.

The diagnosis of breast ACC is mainly based on pathologic features and a biphasic pattern of epithelial and myoepithelial cells (cribriform, tubular, and solid types).[20] According to the percentage of the tumor that is solid, it can be divided into 3 grades.[21] Tumors with a higher percentage of solid mass always have more aggressive biological behavior.[12] The diagnosis of breast ACC in the frozen section is challenging because of histological complexity. Inadequate samplings lead to an error diagnosis. Wang et al reported that the diagnosis was mistaken in 6 of 36 cases in frozen sections.[3] Although perineural invasion is commonly observed in the ACC of salivary glands, it is rarely found in the breast, and its effects on prognosis are controversial.[22–24] Immunohistochemistry can help distinguish ACC from other forms of breast cancer. ACC of the breast is usually negative for PR, ER, and HER-2. The basal cells are positive for CK 5/6 and epithelial growth factor receptor, and the epithelial cells are positive for CD117, c-kit, and carcino-embryonic antigen.[2,24,25] In our patient, the tumor was described as solid type and grade 3 (solid composition ≥30%.) Perineural invasion was observed in our case, but this has never been reported in male breast ACC before. Consistent with most studies, the tumor was triple-negative for PR, ER, and Her2 and positive for CK 5/6 and P63, and 20% of cells were positive for Ki67.

In contrast with the other triple-negative breast cancers, the prognosis of female breast ACC is more favorable because of the lack of metastasis to lymph nodes or distant organs. The incidence of axillary lymph node metastasis was less than 2% in previous reports.[21,22] Distant metastasis mostly occurred in the lung without lymph node infiltration.[20] Previous studies reported 5-year and 10-year overall survival rates of more than 95% and 90%, respectively.[3] However, all of the data are derived from female breast ACC, and these findings may not be as favorable when it comes to males. Considering that male breast ACCs are more likely to be overlooked and the difficulty in diagnosing ACC, the correct diagnosis and subsequent treatment may be delayed compared with female breast ACC. A previous study revealed that 2 of 9 patients with male breast ACC had positive axillary lymph nodes, 2 of 6 patients had local recurrence, and 1 of 6 patients had lung metastasis after surgery. Furthermore, surgery was not performed for 1 patient with

multiple lung and bone metastases who died in 1 year.[10] Millar et al reported that a male patient with breast ACC who presented with distant metastasis at the time of diagnosis died after 7 months.[26] Though our patient was well 26 months after surgery, breast ACC seems more aggressive in males than in females and is associated with a relatively worse clinical course. More studies are needed to confirm this speculation.

No optimal treatment has been determined due to the rarity of breast ACC. Surgery remains the cornerstone of multidisciplinary therapy. Some surgeons have proposed indications for different operative methods (ranging from lumpectomy to modified radical mastectomy) according to the pathologic grading system.[20] However, these have not been widely accepted by experts.[21] Simple local excision is not advised because of the unacceptably high local recurrence rate in previous experiences.[4,22,27] Mastectomy has been widely conducted by surgeons. Given that positive lymph nodes are uncommon, axillary node dissection is rarely needed. The value of sentinel lymph node excision is still unknown, and it has not been routinely recommended by some authors.[2] Although the data regarding adjuvant radiotherapy after breast-conserving treatment are insufficient, this treatment is recommended by some clinicians because of the survival benefits observed in their studies.[12,27] To date, the influences of hormonal treatment and adjuvant chemotherapy on breast ACC are still unclear. Currently, all treatment methods are derived from the experience of female breast ACC, and they may be unsuitable for male patients. We performed a modified radical mastectomy in our patient in light of the worse prognosis in male breast ACC in previous reports. However, axillary node dissection to identify a positive lymph node may not be necessary, although lymphovascular invasion was present in our case. Therefore, we propose routine sentinel lymph node excision rather than axillary node dissection in male patients.

In conclusion, breast ACC is truly rare worldwide. Unlike other triple-negative breast cancers, the prognosis of breast ACC is satisfactory. However, compared with that in female patients, the clinical behavior of this tumor in males seems more aggressive. The diagnosis in males is more often made at an advanced stage, and recurrence and metastasis are more frequently seen after surgery. Therefore, more effective treatment strategies may be required for male breast ACC. Currently, data on this rare disease are lacking. In the future, we need more research to find the optimal management strategy.

Author contributions

Conceptualization: Qiang Zhang.
Data curation: Wenyang Pang, Zhengyi Wang, Qiang Zhang.
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Writing – review and editing: Xiaoyan Jin.

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