

Case Report

Primary Male Breast Adenoid Cystic Carcinoma - A Case Report and Review of the Literature

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Abstract

Adenoid Cystic Carcinoma (AdCC) of the breast is a rare subtype of breast cancer, accounting for less than 0.1% of all breast carcinomas. In contrast to the aggressive nature of AdCC of salivary glands, AdCC of the breast has a favorable prognosis, low rate of lymph node involvement and uncommon distant metastases. Many cases of adenoid cystic carcinoma are successfully treated with breast conserving surgery and sentinel lymph node biopsy. Chemotherapy, radiation and hormonal treatment are infrequently used. We report a rare case of primary adenoid cystic carcinoma of breast in a 75 year-old male with a subareolar, well-defined, 2.2 cm mass. The core-biopsy was diagnosed as AdCC with a basal-like phenotype (negative for ER-, PR-, and HER-2/neu) and was positive for c-Kit, p63, SM myosin, and e-cadherin. The Ki-67 labeling index was 28%. The patient underwent total mastectomy, with subsequent AJCC pathological staging pT2 pN0 pM0. He was treated with post-op methotrexate and 5-fluorouracil chemotherapy. We report this rare primary breast AdCC with in this 75-year-old male patient.

Keywords: Adenoid cystic carcinoma; Breast; Male

Introduction

Adenoid Cystic Carcinoma (AdCC) is most commonly seen as a tumor of salivary glands, but is also a rare subtype of breast cancer, with an overall incidence of 0.1% (of all breast malignancies) [1-4]. AdCC is characterized by the presence of a dual cell population of

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luminal and basaloid cells. Breast AdCC generally affects older female patients (range 40-96 years) [1,5]. Primary AdCC of male breast is extremely rare and its' clinical pathological features have not been completely characterized. We report this primary male breast AdCC due to its' rarity.

Case Report

General clinical appearance

A 75 year-old male with a past medical history of melanoma presented with a palpable, sub-areolar, right breast mass of 5 weeks duration. The mass was located at the 12:00 o'clock position, 1 cm from the nipple. There was no nipple discharge, pain, inverted nipple, tenderness or skin change. No significant axillary lymphadenopathy was noted on either side. The patient also self-reported a history of melanoma, of which, the histopathologic type, AJCC pathological staging and treatment of his melanoma were unknown. The patient was a non-smoker with past medical history significant for hypertension, prostate hyperplasia and degenerative joint disease. He did not have family history of breast carcinoma. Routine laboratory studies, serum PSA level, and the tumor marker, CA27-29 (29.1 U/mL, reference range: 0-38.6 U/mL) were within normal limits.

Radiological images' studies

Mammography revealed an asymmetrical, 2.3 cm lesion in the subareolar region of the right breast, classified as BI-RADS 4. Ultrasonographic findings showed a 2.4×2.4×1.6 cm heterogenous, mostly hypoechoic mass at 12:00 o'clock position, 1 cm superior to the nipple within the right breast.

Right breast core biopsy

An ultrasound guided core biopsy of the right breast mass was performed and revealed an invasive tumor comprised of a biphasic population of epithelial and myoepithelial cells. There were also islands of basaloid cells surrounding variably sized cysts (Figure 1A and C). Immunohistochemical studies were performed were positive for p63, c-Kit (Figure 1D), smooth muscle myosin, and e-cadherin. The overall features were consistent with adenoid cystic carcinoma. Breast cancer biomarkers, Estrogen Receptor (ER), Progesterone Receptor (PR) were negative and HER2/neu was equivocal. A Ki-67 showed a proliferation index of 28%. Reflex HER2/neu FISH studies were negative for amplification (Figure 1F), the HER2/CEN-17 ratio was 1.25 and the average HER2 copy number was 2.0.

Total mastectomy and sentinel lymph node dissection of right breast

After biopsy, the patient underwent total mastectomy and axillary sentinel node evaluation. The mastectomy revealed a mid-areolar. 2.2×2.2×2.1 cm well circumscribed, firm, gray-tan mass (Figure 1B), which abutted the nipple. The margins of resection were negative for tumor. The AJCC pathology staging was pT2 pN0 pMx.

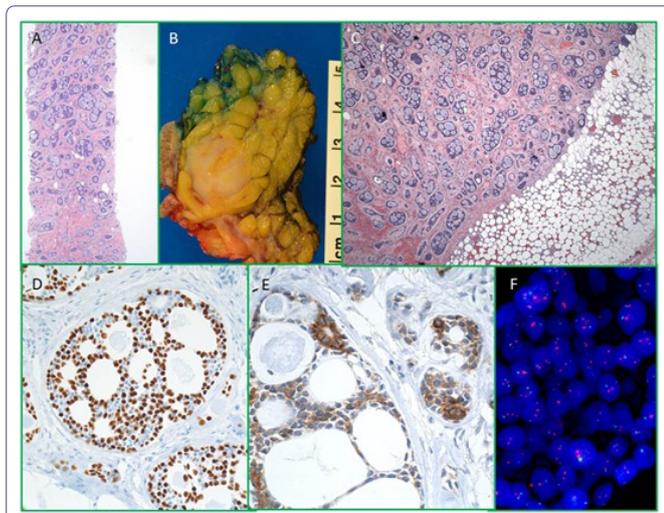


Figure 1: Right breast core biopsy reveals AdCC, H & E, (A) There is a well-defined mass in mastectomy specimen grossly, (B) and microscopically, (C) Carcinoma cells are positive for p63, (D) and c-Kit, (E) by immunohistochemical studies, and (F) HER2/neu FISH studies are negative for amplification.

Post-op management

After mastectomy, the patient was treated with methotrexate and 5-fluorouracil chemotherapy, and at the time of this publication, has been clinically stable for 21 month without recurrence of AdCC. However, six weeks post-mastectomy, the patient complained of gross hematuria. His urine was collected for cytologic examination and revealed urothelial carcinoma. Subsequently, he underwent cystoscopy transurethral resection and was diagnosed with invasive, high-grade papillary urothelial carcinoma involving the lamina propria. After resection, he underwent local BCG therapy. Three months later, his repeat urine cytology was positive for high grade urothelial carcinoma, which was then treated with bladder fulguration.

Discussion

We report a rare case of primary AdCC of the breast in a 75 year old male, with basal-like phenotype (negative for ER, PR, and Her-2) and pathological staging pT2 pN0pMX.

Most reported breast AdCC cases are in females. Breast AdCC has an excellent prognosis with a low incidence of lymph node metastasis and distant metastases uncommon [4-7]. Histologically, AdCC is composed of two cell populations, epithelial and myoepithelial cells, which are similar to that of their salivary gland counter parts. Similar to AdCCs of the salivary gland, breast AdCCs are characterized by the t (6;9) (q22-23; p23-24) chromosomal translocation, which generates fusion transcripts MYB-NFIB [8]. It is important to distinguish this from other types of breast cancer as breast AdCC has an excellent prognosis.

Male breast carcinoma is an uncommon malignancy, accounting for 1% of all breast carcinomas. Male AdCC is extremely rare. Few cases of male AdCC have been reported, thus its causes and clinical pathological features have not been completely characterized [9-11]. The clinical features of published male AdCC cases are summarized in table 1 [12-18]. Among these, AdCC of the male breast occurs in wide age distribution, which ranges from 13 to 82 years. AdCC usually presents as a firm mass, ranging from 1.7 cm to 6 cm, occurring equally on the left and right sides. It usually locates in the subareolar region. Nipple discharge is uncommon. AdCC of the male breast shows histopathological findings similar to AdCC of the salivary gland. Perineural invasion and axillary node metastasis are rare. The resection margin is virtually never involved by carcinoma. Immunohistochemically, the majority of male breast ACCs are immune phenotypically triple-negative (i.e., ER-, PR- and HER2-negative). However, in contrast to triple-negative breast carcinomas, AdCC of the breast usually has an excellent prognosis. Cytogenetically, breast AdCC is similar to AdCCs of the salivary gland, which characterized by the t (6;9) (q22-23; p23-24) chromosomal translocation, generating a fusion transcripts involving the oncogene MYB and the transcription factor gene NFIB. It has been reported that this chromosomal translocation is present in majority of breast AdCC cases. In these reported male breast cases as summarized in table 1, most patients are treated with mastectomy (simple, radical or total mastectomy) with excellent. However, one patient, reported by Kshirsaga, had a large 6 cm ulcerative AdCC. A modified radical mastectomy was done and found had three of the five axillary lymph nodes excised were positive for carcinoma. The patient refused postoperative radiotherapy. After 2 years, the patient

Cases	Age	Clinical finding	Side	Size	PNI	Margin	Axillary node	Treatment	Outcomes
Tang et al.,	19 Yr	Painless mass	Right	2 cm	Absent	Negative	Negative	Radical mastectomy	No recurrence
Ferlito et al.,	60 Yr	Body nipple discharge	Left	"pea-like"	N/A	N/A	N/A	Radical mastectomy	N/A
Hjorth et al.,	21 Yr	Tender lump under nipple	Left	2 cm	Present	N/A	Negative	Simple mastectomy	No recurrence
Miliauska et al.,	13 Yr	Tender and enlarged mass	Right	3.8 cm	Absent	Negative	Negative	Subcutaneous mastectomy	No recurrence
kshirsaga, et al.,	82 Yr	Ulcer	Left	6 cm	Absent	Negative	Positive	Radical mastectomy	Local recurrence after 2 years
Liu et al.,	20 Yr	Tender mass	Right	2 cm	N/A	N/A	Negative	Simple mastectomy	N/A
Yoo et al.,	41 Yr	Cervical back pain (bone metastasis)	Left	1.7 cm	N/A	N/A	Positive	N/A	Bone and lung metastasis
Present study	75 Yr	Painless mass	Right	2.2 cm	Absent	Negative	Negative	Total mastectomy	No recurrence

Table1: Summary of reported male breast AdCC cases.

had local recurrence at anterior chest wall, which then underwent wide excision and postoperative radiation therapy. There was no evidence of recurrence for at least 9 months duration after wide excision [15]. The case reported by Yoo et al., had a small 1.7 cm AdCC with bone and lung metastasis at the time of diagnosis [17]. Although guidelines for diagnosis and treatment of male breast AdCC are not clear due to the extremely low numbers of reported cases; surgical management, such as mastectomy, is the main stay of treatment. Our reported case of primary male AdCC was treated with total mastectomy, which had negative resection margins and negative axillary lymph nodes. There was no evidence of recurrence or distant metastasis of AdCC at a follow up interval of 21 months.

In addition, this patient had two other neoplasms: one is a self-reported previous melanoma and the other a subsequently diagnosed urothelial carcinoma (six weeks later after mastectomy). Prior melanoma is very likely an independent event in relation to the AdCC. The later diagnosed urothelial carcinoma is also less likely associated with AdCC at the pathogenesis point. Multiple exogenous risk factors have been linked to bladder cancer, such as tobacco smoking, occupational risk, and lifestyle exposure to carcinogens, which are believed to take years for development of bladder cancer. However, this is the 1st case report of male breast AdCC with co-existing bladder urothelial carcinoma. Further investigation will potentially elucidate the pathogenesis of male adenoid cystic breast carcinoma.

In conclusion, although rare, adenoid cystic carcinoma of male breast is a well-known entity. It is important to recognize this lesion as it has relatively excellent prognosis.

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