

# Adenoid Cystic Carcinoma of the Breast: A Case Report

Aveline Marie D. Ylanan, MD<sup>1,2,3</sup> and Miriam Joy C. Calaguas, MD<sup>2,3</sup>

<sup>1</sup>University of the Philippines – Philippine General Hospital

<sup>2</sup>St Luke's Medical Center – Global City

<sup>3</sup>St Luke's Medical Center – Quezon City

## ABSTRACT

Adenoid cystic carcinoma (ACC) is a rare subtype of invasive breast cancer, occurring in <0.1% of all malignant breast tumors. Though majority are triple-negative, ACC of the breast has good prognosis with a low incidence of regional and distant metastases.

A 45-year-old premenopausal female presented with a 5-month history of a gradually enlarging mass on her left breast. After core needle biopsy and subsequent metastatic work-up, she underwent total mastectomy with sentinel lymph node biopsy. Final histopathology showed adenoid cystic carcinoma, 2.1 cm in size and no lymph nodes positive for tumor. She has completed adjuvant radiotherapy of 50 Gy to the chestwall, and is currently well after 6 years of follow-up.

Surgery with either lumpectomy or mastectomy has been established as the mainstay of treatment of adenoid cystic carcinoma of the breast, but the use of adjuvant radiotherapy (RT) and chemotherapy has not been established. While adjuvant RT has been shown to improve cause-specific and overall survival following breast-conserving surgery, its indications after a mastectomy are not as well-defined. The decision to administer adjuvant RT was based on the current evidence indicating the advantages of adjuvant treatment for breast carcinomas, lack of survival difference between invasive ductal carcinomas and adenoid cystic carcinomas, indications for post-mastectomy RT in a retrospective Rare Cancer Network study, and reported incidences of local recurrences following mastectomy alone: 21.4% and 22.2%.

Our patient with adenoid cystic carcinoma of the breast, treated with surgery and adjuvant radiation therapy, showed favorable outcomes after 6 years.

*Keywords: adenoid cystic carcinoma, breast neoplasms, postmastectomy, adjuvant radiation therapy, case report*

## INTRODUCTION

Adenoid cystic carcinoma (ACC) is the most common tumor of the minor salivary glands, but it also represents a rare type of breast cancer, accounting for <0.1% of all malignant breast tumors.<sup>1,2</sup> Though majority are triple-negative, ACC of the breast has good prognosis with a low incidence of regional and distant metastases. Diagnosis and treatment is difficult due to its low incidence. In this study, existing literature was reviewed and a case of a patient with adenoid cystic carcinoma of the breast was reported after obtaining informed consent.

## CASE PRESENTATION

A 45-year-old female presented with a 4-month history of a gradually-enlarging, movable, nontender mass on the left breast. There were no other symptoms such as nipple discharge



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Corresponding author: Aveline Marie D. Ylanan, MD  
Philippine General Hospital  
University of the Philippines Manila  
Taft Avenue, Ermita, Manila 1000, Philippines  
Email: [amdylanan@gmail.com](mailto:amdylanan@gmail.com)  
ORCID: <https://orcid.org/0000-0003-0795-4221>

or pain in other areas of the body. Her family history included her mother having ovarian cancer and her maternal aunt having breast cancer. Her past medical and social histories were not significant.

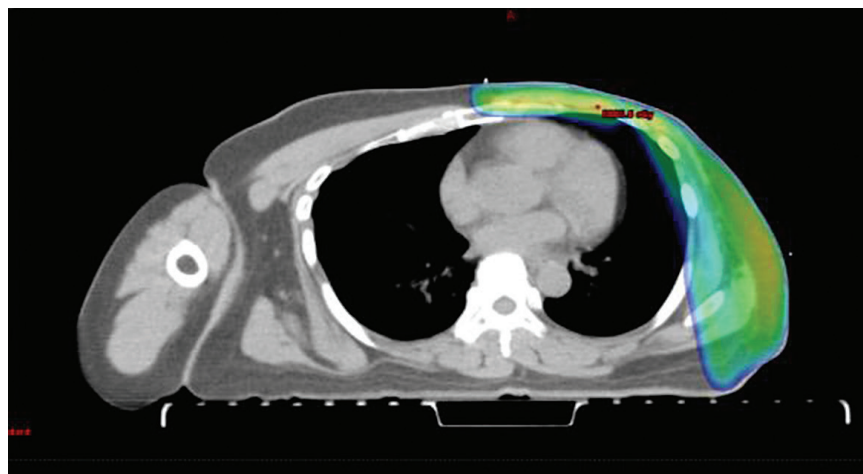
Due to persistence of the mass, she sought consult at Tseung Kwan O Hospital in Hongkong, where physical examination showed a 2-cm, nontender, movable mass on the left breast, without associated skin changes. There were no palpable axillary or supraclavicular lymph nodes. Mammography revealed a 2-cm patchy opacity in inferomedial portion of the left breast. Core needle biopsy showed features of an invasive carcinoma morphologically resembling salivary gland type tumor (adenoid cystic carcinoma). Metastatic workup including a contrast enhanced CT of the chest, abdomen and pelvis, showed no bone, lung, or liver metastases and routine blood investigations were normal. Patient consented to a total mastectomy with sentinel lymph node biopsy, which were done on January 25, 2018.

Final histopathologic diagnosis showed adenoid cystic carcinoma (ACC), stage IIA (pT2N0) (tumor size 2.1 cm). Gross examination showed a poorly-circumscribed, nodular, pink, white, solid, infiltrative tumor measuring 2.0 x 1.8 x 1.5 cm in the left lower inner quadrant, with no skin involvement and satellite nodules. Microscopic examination showed irregular clusters of basaloid tumor cells with focal microcystic and pseudoglandular differentiation, and lumina containing basement membrane material. Ductular formation was also observed. The tumor cells featured hyperchromatic nuclei with small distinct nucleoli, and mitotic activity measured 4/10 HPF (25 mm eyepiece). Solid areas accounted for less than 30% of tumor. A focal area suggestive of vascular permeation was also noted within the tumor. Immunohistochemical studies showed tumor cell reactivity with cytokeratin (MNF116), EMA, CK7, 34BE12, and c-kit; whereas chromogranin, synaptophysin, calponin, and p63 were negative. All margins and retrieved lymph nodes

were negative for malignancy. The distance from deep margin was 10 mm. There were no changes in the nipple (Paget's disease), nor peritumoral lymphovascular permeation. The intraductal carcinoma component was low grade, and the status of adjacent breast tissue was unremarkable. Hormone receptor and oncogene status was triple-negative: ER (-) PR (-) HER2neu (-).

On her last follow-up day in Hongkong, her wound was assessed to have healed well, and the JP drain was removed. She consulted at the Philippine General Hospital for continuity of care. She was first seen at the outpatient clinic of the Department of Medicine, and was referred to the Radiation Oncology clinic by the Medical Oncology team. At our clinic, physical examination was unremarkable, with no palpable axillary lymph nodes, and a dry and well-coaptated surgical scar on the left chest-wall.

Following a thorough discussion of the benefits and risks of observation versus further treatment, the patient actively participated in the decision-making process and consented to undergo adjuvant conformal radiation therapy. Three months after surgery, 50 Gy in 25 fractions was delivered to the left chest wall, daily, 5 days per week without interruptions (Figure 1). Organs at risk were properly contoured and no QUANTEC limits of organs at risk were reached. At the end of treatment, she developed grade 2 radiation dermatitis, with erythema and hyperpigmentation on the left anterior chest, and a 1 x 1 cm area of wet desquamation on the axillary fold. Appropriate creams were prescribed and this healed by 2 weeks (Figure 2). There was no other significant morbidity noted in her radiotherapy course. Throughout her radiation therapy, she reported feeling well and had no significant complaints. Her subsequent regular follow-up appointments, including complete history and physical exams, revealed no evidence of recurrence or late toxicities at six years, leading her to express satisfaction with her treatment decisions and overall outcome.



**Figure 1.** This is a dose color wash of the radiation therapy plan showing the area receiving 95% of the prescribed dose.



**Figure 2.** Taken two weeks after completion of radiotherapy. There is note of faint erythema with no areas of desquamation on the chest wall.

## DISCUSSION

### Incidence

Adenoid cystic carcinoma of the breast (bACC) is rare, accounting for <0.1% of all malignant breast tumors.<sup>1,2</sup> Predominantly diagnosed in elderly women in their fifth or sixth decade, it has been reported in women ages 38-81 years old, with a median age of 60 years old. According to Ghabach et al., in a case series of 338 patients with bACC, the age-adjusted incidence ratio (AAIR) is 0.92 per 1 million person-years.<sup>3</sup> Though most cases are seen in females, occasional cases have been reported in male patients as well.<sup>2</sup> To our knowledge, this case report represents a unique contribution to the literature, there are no other published case reports detailing the use of radiation therapy for adenoid cystic carcinoma of the breast in the Philippines.

### Clinical Features

Affecting the left and right breasts equally, it typically presents as unilateral subareolar small breast lump.<sup>1,4,5</sup> In a minority of cases, it presents with pain or tenderness, not always correlating with histologically-confirmed perineural invasion. Because radiologic findings are nonspecific, it is often misdiagnosed as benign lesions. On mammogram, bACC presents as asymmetric densities or irregular masses, and as well-defined, irregular, heterogeneous, or hypoechoic masses on ultrasound.<sup>2</sup>

### Pathology

Adenoid cystic carcinoma is most frequently seen in salivary glands. Areas that are infrequently affected include the uterine cervix, Bartholin's glands, lacrimal glands, auditory canal, skin, upper respiratory tract and lung, kidney, esophagus,

prostate, and breast.<sup>6</sup> Grossly, tumors measure a mean of 3.0 cm (0.7-12.0 cm) and are seen as well-circumscribed pink/tan/gray lesions with microcysts.<sup>2</sup> Histologically, it is characterized by a dual population of both epithelial/luminal and myoepithelial/basaloid (abluminal) cell proliferation, which may be arranged in one or more of three architectural patterns: tubular-trabecular, cribriform, and solid-basaloid.<sup>7</sup> Among which, the solid basaloid subtype is most aggressive, with higher rates of local breast recurrences and delayed metastatic disease after many years. Grading is based on the solid component, with completely glandular and cystic as grade 1, <30% solid component as grade 2; and >30% of solid components as grade 3. Although bACC is classified by the World Health Organization (WHO) as of low malignant potential, grade 3 tumors are seen to act like high-grade ductal breast cancer.<sup>1,2</sup> Immunohistochemically, bACC shows positivity for CK7, CK8/18, epithelial membrane antigen, and CD117 (c-Kit). In majority, hormone receptor (ER, PR) and human epidermal growth factor receptor 2 HER2 expression are negative.<sup>2,4</sup> In a recent study by Sun et al., 81.2% of bACC cases were triple negative, as seen in our patient.<sup>8</sup> Adenoid cystic carcinoma of the breast has distinct molecular features, notably the *MYB-NF1B* gene fusion and *MYB* overexpression, which drive tumorigenesis. Other altered genes affect cell growth, death, and metastasis control.<sup>9</sup> While these molecular details are important for diagnosis and prognosis and could inform treatment, the patient in this case did not undergo genetic testing due to logistic and financial constraints.

### Patterns of Spread

Although adenoid cystic carcinoma of the salivary glands behaves aggressively, when located in the breast, it

behaves indolently with rare nodal and distant metastases.<sup>10</sup> Ninety-two percent present with localized breast disease.<sup>11</sup> Reports of nodal metastases vary among literature, ranging from 2-15.4%.<sup>12</sup> The study by Millar et al. with the longest follow-up of 14 years showed nodal metastases in 14.3%.<sup>13</sup>

### Prognosis

When compared with other triple-negative breast cancers and adenoid cystic carcinomas in other locations, bACC has better prognosis. Five-year overall survival ranges from 88-98%, and 10-year overall survival from 75-95%.<sup>11,13,14</sup> In a recent paper by Sun et al., 5-year and 10-year cause-specific survival were 93.2% and 87.5%, respectively.<sup>8</sup> However, it was also noted in a study by Oliver et al., that though bACC has more favorable biology and lower propensity for distant and regional metastasis than invasive ductal cancer, no survival differences were noted between both histologies.<sup>5</sup>

### Treatment Plan

Due to its rarity, there are currently no established guidelines on the treatment of adenoid cystic carcinoma of the breast. Initial treatment is usually through surgery. Spiliopoulos et al. suggested that for grade 1 tumors, a simple lumpectomy is adequate.<sup>15</sup> A simple mastectomy was recommended for grade 2 tumors, and mastectomy with axillary clearance for grade 3 tumors. Most other studies did not consider grade, hence some uncertainty with this approach. On assessing locoregional control based on type of surgery, it was seen that recurrence with local excision occurred in 6-37%.<sup>10,16</sup> In a literature review of 182 patients with bACC, 7.8% (14/182) of patients experienced local recurrence, with 78.6% (11/14) developing local failure after lumpectomy and 21.4% (3/14) after mastectomy.<sup>17</sup> In a study by Millar et al., recurrence was also noted in 22.2% (2/9) of patients who underwent mastectomy without adjuvant RT.<sup>18</sup>

The optimal surgical procedure for bACC is still unclear. Five-year locoregional control is better with mastectomy compared with breast-conserving surgery.<sup>16</sup> However, recent studies show that cause-specific survival and overall survival in those who receive BCS were not inferior to those who had mastectomy.<sup>19</sup>

The dilemma with the case presented of a patient who consulted at our institution post-mastectomy was on adjuvant treatment. The role of chemotherapy is unclear, only sometimes suggested in patients with metastatic disease, tumors larger than 3 cm, and high-grade lesions. Since tumors are triple-negative, routine hormonal therapy is also not indicated. Targeted therapy, such as anti-EGFR or c-kit is still being explored.

Alternatively, the use of adjuvant radiotherapy has been seen to significantly increase overall survival. Another study showed an absolute survival benefit of 9% at 5 years and 21% at 10 years, regardless of stage, on univariate analysis. In the multivariate analysis, it continued to be a significant factor with a hazard ratio of 0.44, even after accounting for

demographic data, stage, and type of surgery (lumpectomy vs. mastectomy).<sup>20</sup>

In the retrospective study, though adjuvant RT was seen to significantly decrease locoregional recurrence, it did not influence survival since recurrences were successfully managed.<sup>16</sup> Indications for RT after mastectomy included: tumor size (T4) in 2 patients, positive margins in 1 patient, and internal quadrant tumor in 2 patients. Though univariate analysis, with median follow-up of 79 months, showed that survival was not influenced by the type of surgery or the use of postoperative RT, recurrence was noted in 2 patients underwent mastectomy without RT.

According to Sun et al., breast conserving surgery with adjuvant RT provides the best control and survival.<sup>19</sup> The noted 5-year cause-specific survivals were: lumpectomy + adjuvant RT 96.1%, lumpectomy alone 91.8%, mastectomy alone 90.2%, and mastectomy + adjuvant RT 94.1%. Local treatment strategies, as well as tumor size, nodal status, and grade were observed to be prognostic factors on cause-specific and overall survival. Lumpectomy with adjuvant RT was seen to have better survival than lumpectomy and mastectomy only. Though RT after mastectomy had better survival in the 20 patients who received the said adjuvant treatment, it was not deemed significant. However, this study was limited by the lack of indications for adjuvant RT, margin status, central pathology review, details of RT and chemotherapy, and data for local recurrence.

The decision to administer adjuvant RT was based on the current evidence indicating the advantages of adjuvant treatment for breast carcinomas (i.e. size greater than 2 cm, premenopausal status), lack of survival difference between invasive ductal carcinomas and adenoid cystic carcinomas, indications for postmastectomy RT in a retrospective Rare Cancer Network study, and reported incidences of local recurrences following mastectomy alone: 21.4% and 22.2%.<sup>5,16,18,21,22</sup>

The risks associated with adjuvant radiation therapy were little. In a series of bACC cases at Princess Margaret Hospital, 26% developed second malignancies at 15 years; however, the majority of the second cancers were not within the treated or contralateral breast, and the radiation fields did not overlie any of the sites of the second cancer. Likewise, there is also no increased risk in cardiac mortality with radiation therapy with the use of more conformal techniques since 1993.<sup>18,23</sup>

### CONCLUSION

Our patient with bACC, managed with surgery followed by adjuvant radiation therapy remains without evidence of recurrence or long-term toxicities after 6 years. Continued research and monitoring are crucial for refining therapeutic approaches for rare breast malignancies such as adenoid cystic carcinoma.

### Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

### Author Disclosure

Both authors declared no conflicts of interest.

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