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## Adenoid Cystic Carcinoma of Breast: A Rare Case Report

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### ABSTRACT

**Background:** Adenoid cystic carcinoma (AdCC) of the breast is a rare type of invasive breast cancer, accounting for less than 1% of all breast cancer cases. It is usually a low-grade tumor that rarely metastasizes to the axillary lymph nodes and distant organs. AdCC of the breast is mostly negative for estrogen receptor, progesterone receptor, and HER2-neu. However, despite being triple-negative, it has favorable outcome, and patients with AdCC of the breast generally have a good to excellent long-term survival.

**Case presentation:** Here we report a case of a 51-year-old female presenting with left breast mastalgia who was finally diagnosed with AdCC of the left breast. The patient underwent breast-conserving surgery and axillary staging followed by adjuvant chemoradiation.

**Conclusion:** Because of the rarity of AdCC of the breast, it has been difficult to conduct prospective trials to determine the best treatment option. Different types of therapy, including BCS and mastectomy with or without axillary staging with or without adjuvant chemoradiation have been reported, all with overall good to excellent long-term results. Prospective controlled trials will help in determining the best treatment.

### Introduction

Adenoid cystic carcinoma (AdCC) of the breast is a rare type of invasive breast cancer, accounting for less than 1% of all breast cancer cases. It is mostly seen in the 5th and 6th decades of life and affects both genders, although females are affected more frequently.<sup>1-5</sup>

Breast AdCC is a low-grade tumor that rarely metastasizes to the axillary lymph nodes and distant organs.<sup>1-4, 6-10</sup> Distant metastasis generally occurs in

the absence of axillary lymph node involvement<sup>2,8,10</sup> and lungs are the most commonly involved organs.<sup>10</sup>

Breast AdCC is usually negative for estrogen receptor, progesterone receptor, and HER2/neu (triple-negative).<sup>1-4,6,11</sup> However, unlike other triple-negative invasive breast cancers, breast AdCC has a favorable prognosis, and 5-, 10-, and 15-year survival rates have been reported to be 94–98.1%, 85–100%, and 91.4%, respectively.<sup>1-10,12</sup>

Because of the rarity of breast AdCC, it has been difficult to conduct prospective trials to compare different types of local and systemic treatments; therefore, there is currently no standard treatment recommendations.<sup>1, 3, 7, 8</sup> Different types of surgery including breast-conserving surgery (BCS) and mastectomy, with or without axillary staging, with or without adjuvant chemoradiation or hormone therapy, have been used in different studies, with overall similar good results.

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Here, we report a case of a 51-year-old female presenting with left breast mastalgia who was finally diagnosed with AdCC of the left breast.

### Case Presentation

A 51-year-old woman referred to our breast clinic with bilateral breast pain, especially in her left breast. She had no history of previous medical or surgical diseases and was taking no medications. Her age at menarche was 13; she was 21 at her first live birth and had two children. She had an abortion and had reached menopause 3 years before. There was no family history of breast or ovarian cancers. On her physical examination, an area of tissue thickening, measuring 30 mm, was palpated in the upper central portion of her left breast. Examination of the right breast and bilateral axillary regions was unremarkable.

Bilateral digital mammography and breast ultrasound were requested. Mammography revealed an asymmetry with irregular borders in the left breast in medial and deep retroareolar area. This finding was reported to be highly suspicious for malignancy. Also, an asymmetry was detected in axillary tail of the right breast which was stable in comparison with the last year's mammography. Ultrasonography showed an irregular mass (18 × 12 mm) at 10 o'clock position in the left breast, and a hypoechoic lesion (7 × 4 mm) without blood flow in the axillary tail of the right breast. Ultrasound-guided core-needle biopsies (CNB) of both lesions were performed. Pathologic examination reported the left breast lesion as invasive carcinoma. Immunohistochemistry (IHC) staining of the lesion was negative for estrogen receptor, progesterone receptor, HER2/neu, CK20, GCDFP-15, mammaglobin, synaptophysin, and chromogranin, and positive for Ki-67 (10–20% of tumor cells) and CK7. Pathologic examination of the right breast lesion showed no evidence of malignancy.

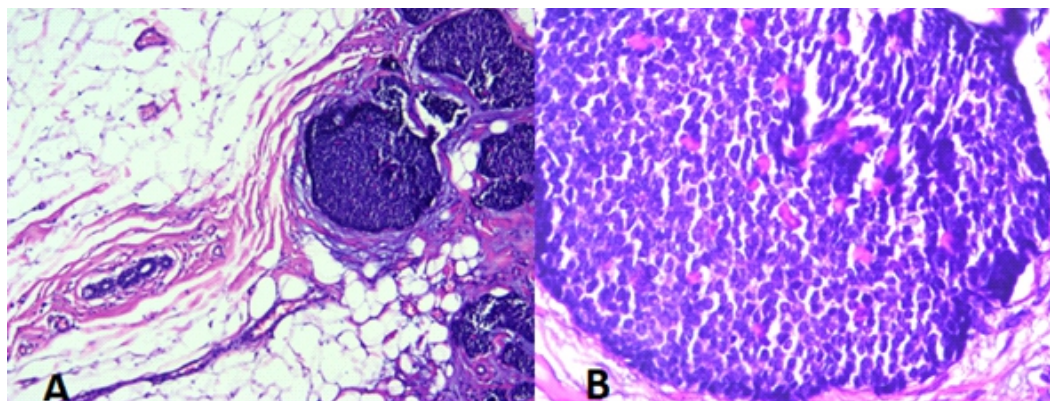
According to pathology report of the left breast mass, and considering the patient's clinical stage, breast conserving surgery and sentinel node biopsy with the use of technetium 99 (<sup>99</sup>Tc) injection was

planned. After excision of the breast specimen, surgical margins were evaluated using frozen-section analysis and were declared clear. However, despite the injection of <sup>99</sup>Tc at the standard dosage in the periphery of the lesion before the surgery, sentinel lymph nodes were not identified. Therefore, limited axillary dissection was done for the axillary staging.

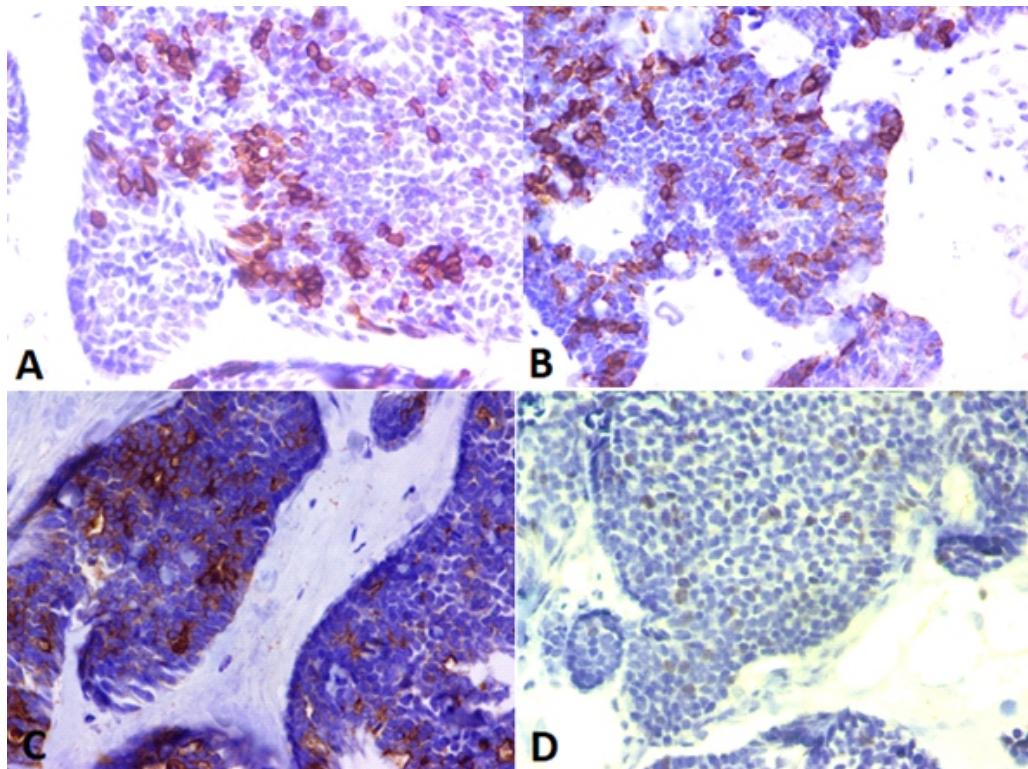
Gross examination showed an infiltrative tumor measuring 18mm. Microscopic examination showed solid and cribriform nests of basaloid cells consistent with adenoid cystic carcinoma. (Figure 1) Immunostaining confirmed the dual epithelial and modified myoepithelial differentiation of tumor cells. (patchy staining for CK5/6, CK7, EMA and P63) The solid component constituted more than 30% of tumor, consistent with grade 3. No tumor calcification, perineural and vascular invasion were reported; clear surgical margins was confirmed. There were six lymph nodes in the axillary specimen which all showed reactive changes. (Figure 2)

According to the pathology report, which confirmed high-grade breast AdCC, and after multidisciplinary review, metastatic workup was pursued; whole-body bone scan and thoracic CT scan were normal. Abdominal ultrasound showed an echogenic mass in the posterior segment of the right lobe of the liver, followed by abdominal CT scan showing a 27 mm low attenuation mass in the right hepatic lobe in favor of metastatic lesion. For further clarification of the lesion, abdominal MRI was done which showed a 38 mm round mass with low signal intensity on T1 and high signal intensity on T2 images at the 6th segment of the right hepatic lobe, which was suggestive of a metastatic lesion. Ultrasound-guided percutaneous needle biopsy of the lesion was decided, but the patient refused to undergo biopsy. Therefore, for deciding on the best management, we had an expert radiologist repeat the ultrasound and review the MRI images. He strongly suggested the possibility of a liver hemangioma, so <sup>99</sup>mTc-RBC scanning of the liver was performed.

The scan demonstrated a hemangioma in the right



**Figure 1.** A: Photomicrograph shows breast tissue (arrow) infiltrated with cribriform and solid nests of basaloid cells morphologically consistent with adenoid cystic carcinoma, x100, H&E. B: Higher magnification of tumor, x400, H&E



**Figure 2.** Immunostainings for CK5/6 (A), CK7 (B), EMA (C) and P63(D) confirm the presence of dual population of epithelial and modified myoepithelial cells in tumor.

hepatic lobe, and we did not pursue further workup after that.

Following the completion of metastatic workup, 4 sessions of adjuvant chemotherapy with 3-week intervals, and 30 sessions of adjuvant radiotherapy were performed. The patient has been visited twice since completion of the therapy. On the last visit, 8 months after surgery, she was symptom-free, and her physical examination was normal.

### Discussion

Breast AdCC is a rare type of invasive breast cancer accounting for less than 1% of all breast cancers.<sup>1,4,7,9</sup> It is mostly seen in the 5th–6th decades of life, although there are reports of patients with younger and older ages at the time of diagnosis.<sup>3,4,9</sup> Although breast AdCC predominantly occurs in women, there have been reports of men with breast AdCC.<sup>4,6,11</sup> Signs and symptoms of breast AdCC are usually similar to those of other types of breast cancer, including breast mass and breast pain. It mostly involves subareolar region, as in our patient;<sup>2-4, 9, 11</sup> although, in a retrospective study on 338 women, the most involved quadrant was the upper, outer quadrant.<sup>6</sup> Despite the preference of the malignancy for areolar region, nipple discharge is not a common symptom.<sup>2</sup>

Unlike AdCCs of other organs like head and neck, breast AdCCs are low-grade tumors with a good to excellent prognosis and long-term survival that rarely metastasizes to regional lymph nodes and distant sites.<sup>1, 3, 6, 8, 11</sup> In our patient, axillary lymph nodes were not involved, although the tumor was of

high grade. Distant metastasis usually occurs in the absence of lymph node involvement.<sup>2, 8, 10</sup> The most common sites of distant involvement are lungs, although metastasis to brain, bone (vertebrae), liver, or kidneys has also been reported.<sup>5,10,11</sup>

In a review by Miyai *et al.* of seven studies on patients with breast AdCC, lymph node involvement was reported to be 0–6.1%, distant metastasis (including bone, liver, lung, and kidney) 1–20%. Also, 5- and 10 year survival rates were reported to be 88–94% and 90–94.9%, respectively.<sup>11</sup> In another study by Chen *et al.* on 86 breast AdCC patients, 88.4% of patients had grade 1 or 2 tumors; 100% had stage 1–2 cancer; and the rate of lymph node involvement was 2.3%.<sup>1</sup> A retrospective study of 244 women with invasive breast AdCC found that 92.2% of the patients had localized disease, 4.9% had regional disease, and only 7 patients had distant metastasis. The 5-year and 10-year relative cumulative survival rates were 95.5% and 93.5%, respectively, and lymph node involvement ratio was 5.5%.<sup>2</sup> In a retrospective study by Ghabach *et al.* on 338 women with breast AdCC, regional and distant disease was reported in less than 5% of case. The ratio of lymph node involvement was 2.5%, and the overall 5-, 10-, and 15-year relative survival rates were 98.1%, 94.9%, and 91.4%, respectively. Women aged <50 years and ≥50 years had an excellent 5-year relative survival of 94.4% and 99.0%, respectively. Ten-year relative survival was similar for both age groups (94.4%), although 15-year survival rate was slightly lower for older patients compared with the younger ones (88.9% vs



94.3%).<sup>6</sup>

Breast AdCCs are usually triple-negative,<sup>1,3,4,7-9, 11</sup> as was the case for our patient, although hormone receptor-positive breast AdCCs have also been reported.<sup>1</sup> Unlike other triple-negative invasive breast cancers, which have worse outcomes than their positive counterparts, all breast AdCC tumors, including triple-negative ones, have good prognosis overall.<sup>1,2</sup> In Chen *et al.*,<sup>1</sup> the rate of triple-negative tumors was 77.9%, and Kim *et al.* reported that all of their 6 patients were triple-negative.<sup>7</sup>

Different types of treatment including BCS and mastectomy with or without axillary staging, with or without adjuvant chemotherapy, radiation therapy or hormone therapy have been used for breast AdCC, mostly with no significant difference in outcomes.<sup>2,3</sup> In our case, with the initial diagnosis of invasive carcinoma, the patient underwent BCS with sentinel lymph node biopsy followed by adjuvant radiation and chemotherapy, because of the high grade of the tumor. Because of the rarity of these tumors, it has been difficult to conduct prospective randomized trials to compare different treatment options and elucidate the best option. Existing data are mostly the results case series and retrospective studies; therefore, there is no universal guideline for treatment of breast AdCC.

The surgical approach for local breast disease control ranges from BCS to mastectomy. Regarding BCS, however, there is no consensus about the adequate surgical margin. Ro *et al.* suggested a grading system for breast AdCC based on the proportion of solid growth of the tumor: no solid element (grade 1), < 30% solid element (grade 2), and >30% solid element (grade 3). Consequently, they proposed local excision, simple mastectomy, and mastectomy with axillary node dissection for grade 1, 2, and 3 tumors, respectively.<sup>13</sup> Another issue is the role of adjuvant treatments, as there is no strong evidence for determining the type of adjuvant therapy (i.e., radiation vs chemotherapy) and identifying the patients who will benefit most from these therapeutic modalities.

According to some studies, mastectomy is the preferred local surgical treatment. In one study, recurrence rate following local excision was reported to be 6–37%.<sup>3</sup> This lower rate of recurrence may explain why mastectomy is the preferred choice of clinicians, despite the fact that there is no randomized controlled trial comparing BCS to mastectomy. A meta-analysis found that recurrence-free 10-year survival rates following mastectomy and BCS were 85.1% and 45.7%, respectively ( $p < 0.05$ ). Six of 10 local recurrences and 7 of 8 distant metastases had occurred 5 years or later after initial treatment. It concluded that patients with breast AdCC should be treated using mastectomy followed by extended follow-up.<sup>14</sup>

Most reports favor BCS as the preferred local

treatment, especially along with adjuvant radiation. In a case report by Ichikawa *et al.*, a patient with breast AdCC underwent BCS with axillary lymph node dissection. After a 5-year follow-up, without adjuvant therapy, they reported that the patient had no clinical recurrence of the disease.<sup>15</sup> In another study, women with breast AdCC were treated with lumpectomy (41 patients) or mastectomy (20 patients), and 40 of them received adjuvant radiotherapy (35 after lumpectomy, 5 after mastectomy). The median follow-up was 79 months, and 5-year overall survival (OS), disease-free survival (DFS), and 5-year locoregional control (LRC) rates were 94%, 82%, and 95%, respectively. Univariate analysis revealed that neither the type of surgery nor the use of postoperative radiotherapy affected survival. The 5-year LRC rate was not different between the mastectomy and BCS groups (100% vs 93%,  $P = 0.16$ ). A significant correlation was observed between the use of radiotherapy and LRC for the BCS group ( $P = 0.03$ ). The 5-year LRC rate was 95% for the radiotherapy arm compared with 83% (95% CI: 54%–100%) for the no-radiotherapy arm. In patients with positive margins, all of whom received postoperative radiotherapy, no local failure occurred. The authors concluded that BCS should be considered the preferred treatment for patients with breast AdCC and that postoperative radiotherapy should be proposed in the case of BCS.<sup>12</sup>

In another study, patients with breast AdCC underwent simple or modified radical mastectomy ( $n = 22$ ) or lumpectomy ( $n = 6$ ). Of the 6 patients who had lumpectomy, 5 also received postoperative radiation therapy. No local recurrence occurred in either group. The 5-year DFS and OS rates were 100% and 85%, respectively. The authors concluded that breast AdCC has very favorable biologic characteristics and that both lumpectomy with radiation and simple mastectomy result in good local control.<sup>16</sup>

In a retrospective study, Sun *et al.* followed up 478 patients with breast AdCC for a median of 59 months and reported 10-year cause-specific survival (CSS) and OS rates of 87.5% and 75.3%, respectively. The 5-year CSS rates for different treatment modalities were as follows: lumpectomy + adjuvant RT = 96.1%, lumpectomy alone = 91.8%, mastectomy alone = 90.2%, and mastectomy + adjuvant RT = 94.1% ( $P = 0.026$ ). Multivariate Cox analyses revealed that lumpectomy + adjuvant RT could be an independent prognostic factor for CSS and OS. Patients who underwent lumpectomy + adjuvant RT had better survival rates than patients who had lumpectomy only (CSS:  $P = 0.018$ ; OS:  $P = 0.031$ ) or mastectomy only (CSS:  $P = 0.010$ ; OS:  $P = 0.004$ ). They concluded that breast AdCC had an excellent prognosis and suggested that BCS be used as the treatment of choice for patients with breast AdCC, along with adjuvant RT to improve survival rates.<sup>17</sup>



In another study on 376 patients who underwent surgery with or without postoperative adjuvant RT, 10-year absolute OS and CSS benefits were 21% and 7%, respectively ( $P=0.005$  and  $0.12$ , respectively). Multivariate analysis revealed RT to be a significant predictor of overall and cause-specific survival with hazard ratios of 0.44 (95% CI: 0.22–0.88) and 0.1 (95% CI: 0.01–0.88), respectively. They concluded that RT after local surgical therapy for breast AdCC resulted in better cause-specific and overall survival rates and that “use of RT in this rare tumor should be considered in patients otherwise eligible for RT.”<sup>18</sup>

Boujelbene *et al.* contend that BCS with postoperative radiotherapy is comparable to mastectomy alone in terms of survival, although they also acknowledged that the value of adjuvant systemic therapies is not established. They suggested that patients with breast AdCC should be under long-term follow-ups as late relapses are possible.<sup>19</sup>

Considering very low involvement of regional lymph nodes in breast AdCC and the inherent complications associated with axillary staging, another dilemma is whether to pursue axillary lymph node staging or dissection in patients with clinically negative axillary lymph nodes or not.

In a study on 20 patients with breast AdCC, preoperative axillary ultrasound was normal in 10 and suspicious in 3 of 13 women who had a subsequent negative lymph node fine-needle aspiration (FNA). Fifteen patients (75%) had sentinel lymph node surgery and were pathologically node-negative, while the remaining 5 had no axillary surgery. After a median follow-up of 3.6 years (range: 0.2–38.6 years), three patients experienced an in-breast recurrence. They observed no cases of nodal metastasis in 20 patients and concluded that preoperative axillary ultrasound with FNA of suspicious nodes could accurately predicted pathologic nodal stage, and that surgery might be omitted safely in patients with pure breast AdCC and a clinically negative axilla.<sup>20</sup> In the study of Khanfir *et al.*, which was previously mentioned, 84% of the 61 node-negative women with breast AdCC had axillary lymph node dissection or sentinel node biopsy, concluding that axillary lymph node dissection or sentinel node biopsy might not be recommended.<sup>12</sup> In Arpino *et al.*, axillary lymph node dissection was performed in 23 patients with breast AdCC, only one of whom (4%) had histologic positive lymph nodes (2 of 10), and no recurrence was detected for the patient. They concluded that axillary lymph node dissection is not helpful in clinical management of patients with breast AdCC.<sup>16</sup>

Considering all these reports and reviews, mastectomy as well as BCS with adjuvant radiation appear to be reasonable surgical approaches for local treatment of breast AdCC, with equivalent oncologic outcomes. The need for axillary staging in clinically negative axillary lymph nodes, as well as the need for

adjuvant chemotherapy, is still unclear. The importance of prospective randomized trials to elucidate the best treatment option cannot be overemphasized.

Breast AdCC is a rare type of invasive breast cancer with good prognosis and low rate of regional lymph node and distant organ involvement. Although there is currently no universal agreement on the best treatment, different types of therapy, including BCS and mastectomy—with or without axillary staging, with or without adjuvant chemoradiation have been used, all with overall good to excellent long-term results. Prospective controlled trials will help in determining the best treatment options.

The decision to report this case was completely explained to the patient and her informed consent was obtained.

#### Conflict of Interest

None to declare.

#### References

1. Chen QX, Li JJ, Wang XX, Lin PY, Zhang J, Song CG, *et al.* Similar outcomes between adenoid cystic carcinoma of the breast and invasive ductal carcinoma: a population-based study from the SEER 18 database. *Oncotarget*. 2017;8(4):6206-15.
2. Thompson K, Grabowski J, Saltzstein SL, Sadler GR, Blair SL. Adenoid cystic breast carcinoma: is axillary staging necessary in all cases? Results from the California Cancer Registry. *Breast J*. 2011;17(5):485-9.
3. Canyilmaz E, Uslu GH, Memis Y, Bahat Z, Yildiz K, Yoney A. Adenoid cystic carcinoma of the breast: A case report and literature review. *Oncol Lett*. 2014;7(5):1599-601.
4. Kocaay AF, Celik SU, Hesimov I, Eker T, Percinel S, Demirer S. Adenoid Cystic Carcinoma of the Breast: A Clinical Case Report. *Med Arch*. 2016;70(5):392-4.
5. Yoo SJ, Lee DS, Oh HS, Kim HJ, Kim MH, Ahn YC, *et al.* Male breast adenoid cystic carcinoma. *Case Rep Oncol*. 2013;6(3):514-9.
6. Ghabach B, Anderson WF, Curtis RE, Huycke MM, Lavigne JA, Dores GM. Adenoid cystic carcinoma of the breast in the United States (1977 to 2006): a population-based cohort study. *Breast Cancer Res*. 2010;12(4):R54.
7. Kim M, Lee DW, Im J, Suh KJ, Keam B, Moon HG, *et al.* Adenoid cystic carcinoma of the breast: a case series of six patients and literature review. *Cancer Res Treat*. 2014;46(1):93-7.
8. Muslimani AA, Ahluwalia MS, Clark CT, Daw HA. Primary adenoid cystic carcinoma of the breast: case report and review of the literature. *Int Semin Surg Oncol*. 2006;3:17.
9. Alis H, Yigitbas H, Kapan S, Kalayci M, Kilic G,



- Aygun E. Multifocal adenoid cystic carcinoma of the breast: an unusual presentation. *Can J Surg.* 2008;51(2):E36-7.
10. Silva I, Tome V, Oliveira J. Adenoid cystic carcinoma of the breast with cerebral metastatisation: a clinical novelty. *BMJ Case Rep.* 2011;2011.
  11. Miyai K, Schwartz MR, Divatia MK, Anton RC, Park YW, Ayala AG, *et al.* Adenoid cystic carcinoma of breast: Recent advances. *World J Clin Cases.* 2014;2(12):732-41.
  12. Khanfir K, Kallel A, Villette S, Belkacemi Y, Vautravers C, Nguyen T, *et al.* Management of adenoid cystic carcinoma of the breast: a Rare Cancer Network study. *Int J Radiat Oncol Biol Phys.* 2012;82(5):2118-24.
  13. Ro JY, Silva EG, Gallager HS. Adenoid cystic carcinoma of the breast. *Hum Pathol.* 1987;18(12):1276-81.
  14. Sinn HP, Lehnert T, Otto HF. [Adenoid cystic cancer of the breast. Case report and meta-analysis of the literature]. *Chirurg.* 1993;64(3):198-202.
  15. Ichikawa K, Mizukami Y, Takayama T, Takemura A, Miyati T, Taniya T. A case of adenoid cystic carcinoma of the breast. *J Med Ultrason(2001).* 2007;34(4):193-6.
  16. Arpino G, Clark GM, Mohsin S, Bardou VJ, Elledge RM. Adenoid cystic carcinoma of the breast: molecular markers, treatment, and clinical outcome. *Cancer.* 2002;94(8):2119-27.
  17. Sun JY, Wu SG, Chen SY, Li FY, Lin HX, Chen YX, *et al.* Adjuvant radiation therapy and survival for adenoid cystic carcinoma of the breast. *Breast.* 2017;31:214-8.
  18. Coates JM, Martinez SR, Bold RJ, Chen SL. Adjuvant radiation therapy is associated with improved survival for adenoid cystic carcinoma of the breast. *J Surg Oncol.* 2010;102(4):342-7.
  19. Boujelbene N, Khabir A, Boujelbene N, Jeanneret Sozzi W, Mirimanoff RO, Khanfir K. Clinical review--breast adenoid cystic carcinoma. *Breast.* 2012;21(2):124-7.
  20. Welsh JL, Keeney MG, Hoskin TL, Glazebrook KN, Boughhey JC, Shah SS, *et al.* Is axillary surgery beneficial for patients with adenoid cystic carcinoma of the breast? *J Surg Oncol.* 2017;116(6):690-5.