CASE REPORT
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Multidisciplinary management of adenoid cystic breast carcinoma: case report and literature review

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ABSTRACT

Adenoid cystic carcinoma of the breast is a rare malignant tumor essentially classified as triple-negative for estrogen, progesterone and HER-2 protein receptors. The age range of involvement is from 30 to 90 years, and it is more common in women in the fifth and sixth decades of life. It usually presents as a slow-growing mass, often in the subareolar area, with nonspecific radiological findings. Histopathological diagnosis by puncture biopsy is essential to define the disease. This study aimed to describe the case of a 41-year-old woman with a histopathological diagnosis of breast cancer and report her follow-up and prognosis after breast-conserving surgery and adjuvant therapy. The relevance of the study was based on the rarity of the pathology described in the literature, implying diagnostic difficulties and multidisciplinary management. Thus, clinical, radiological, and histopathological aspects will be discussed in this study, highlighting the importance of multidisciplinary management for the diagnosis and treatment of adenoid cystic carcinoma of the breast, in order to promote better clinical outcomes and reduce morbidity and mortality related to this subtype of breast cancer.

KEYWORDS: adenoid cystic carcinoma; multidisciplinary care team; triple-negative breast neoplasms.

INTRODUCTION

Adenoid cystic carcinoma (ACC) of the breast is a rare malignant tumor, occurring in around 0.1% of all breast tumors and still poorly documented in the literature, making a multidisciplinary medical approach relevant, involving the specialties of mastology, pathology, clinical oncology and radiotherapy in the follow-up of the disease in order to achieve more satisfactory clinical results[1,2]. Essentially, it is classified as triple-negative for estrogen (ER), progesterone (PR) and HER-2/neu (c-erbB2) receptors, but there are reports of positive hormonal reception in one or more of these receptors, elucidating that this histological subtype cannot be summarized to just one hormonal conditioning[3].

It predominates occurs in Caucasian women between 50 and 60 years of age, although there are occasional cases in men. It has been reported that Breast ACC has an incidence 11 times higher in women aged 50 or older compared to younger women (<50 years). Factors such as exposure to ionizing radiation, low vitamin C intake, and a history of breast cancer have been considered risk factors for the development of breast ACC. Case-control studies have shown that patients who work in agricultural regions, work with nickel and rubber, and/or as hairdressers present a higher incidence of ACC.

The classic location of this tumor is subareolar or in the upper outer quadrant, in the form of a single, palpable breast mass, and may occur bilaterally[3]. Multiple nodules, breast tenderness, nipple discharge and retraction are uncommon. Its histological denomination also includes extramammary tumors, affecting the salivary glands, lungs, and prostate[1,4].

The relevance of this study is based on the rarity of the pathology described, which even implies a scarcity of the topic in breast science textbooks, although it is indeed found in indexed articles. Given its rarity, there is a lack of understanding of the onset and progression of the disease, and there is no consensus on the clinical and radiological diagnosis and optimal treatment.

The aim of this study is to describe a clinical case of breast ACC in a female patient and its multidisciplinary diagnostic and therapeutic approach.

CASE REPORT

This study was submitted to and approved by the Research Ethics Committee of the João Pessoa University Center, under CAAE 81400224.0.0000.5176, opinion number 6,951,972. Informed consent was obtained from the patient through the signing of the Free and Informed Consent Form. The entire study followed the

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standards of current resolutions (n. 510/16 and n. 466/12 of the National Health Council, an agency of the Ministry of Health), and the Code of Medical Ethics, respecting their ethical guidelines.

M.G.N., a 41-year-old female, mixed race, GIIPIIA0, single, a lunch lady, originally from Guarabira, Paraíba, and currently living in Belém, Paraíba, has had a painful, palpable lump in her right breast for approximately three years. She reports a family history of breast cancer and a history of cesarean sections and bilateral tubal ligation 14 years ago. She reports breastfeeding both daughters. She denies comorbidities and ongoing medication use. Physical examination of the breasts revealed a suspicious lesion, showing a lump with irregular edges, a stony consistency, and mobile.

A mammogram revealed BI-RADS 1 in the right breast and BI-RADS 0 in the left breast. Therefore, a complementary bilateral breast ultrasound was indicated to obtain a better breast study, since the mammogram findings were inconclusive and insufficient in relation to the patient's complaint and the physical examination findings. Breast ultrasound showed BI-RADS 3 bilaterally, identifying that the nodule on the right was solid, oval, slightly heterogeneous, with circumscribed margins, horizontal orientation, no vascular flow detected, retroareolar location, 0.6 cm from the skin and measuring 0.9 x 0.8 x 0.9 cm (Figures 1 and 2).

Despite the benign and inconclusive findings indicated by imaging studies, the biopsy was proceeded because the clinical examination indicated signs suggestive of malignancy and the patient persisted with complaints of pain in the nodule's location. Therefore, an ultrasound-guided core biopsy of a fragment of the nodule in the right breast was performed, resulting in a benign diagnosis with stromal fibrosis in the breast parenchyma.

Unconvinced by this result due to the clinical evaluation, the breast science team proceeded with a second biopsy, this time an excisional one. The newly collected material was sent for pathological analysis, which revealed invasive breast carcinoma of the adenoid cystic type without associated carcinoma in situ. The largest focus measured 1.2 cm on microscopy and was staged as pT1cN0M0. Immunohistochemistry revealed HER-2/neu (4B5) (score 0), Ki-67 (15%), Ck5/6 (positive), c-Kit (positive), p63 (positive), and a negative result for estrogen and progesterone receptor protein, resulting in a triple-negative profile.

After diagnostic confirmation, a central quadrantectomy of the right breast was performed, with removal of the nipple and areola, while a mastopexy was performed on the left breast for symmetrization, as shown in the outpatient follow-up five months after surgery (Figure 3). Intraoperative frozen section biopsy revealed a neoplasia-free right sentinel lymph node. The patient recovered well postoperatively, uneventfully, with preserved mobility and cognition.

After clinical oncology evaluation, the patient underwent radiotherapy at a dose of 50.5 Gy divided into 28 fractions, followed by an adjuvant chemotherapy protocol with docetaxel 60 mg/m^2 and cyclophosphamide 600 mg/m^2 every 21 days for four cycles. The patient is progressing well, without complications, and is undergoing outpatient clinical follow-up. Her mammograms and follow-up ultrasounds are within normal limits.

It is worth noting that the team's persistence was crucial in the assertive diagnosis of the disease, giving the patient the benefit of receiving treatment in a timely manner, since the first anatomopathological evaluation gave a benign result, and the

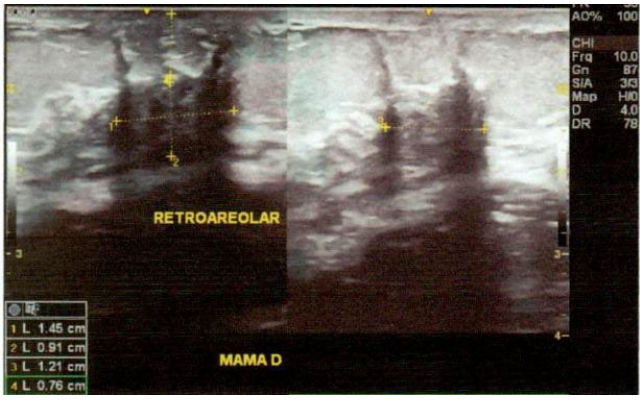


Figure 1. Retroareolar ultrasound of the right breast. Solid, oval, slightly heterogeneous nodule, circumscribed margins, horizontal orientation, no vascular flow detected, retroareolar location, 0.6 cm from the skin and measuring 0.9 x 0.8 x 0.9 cm.

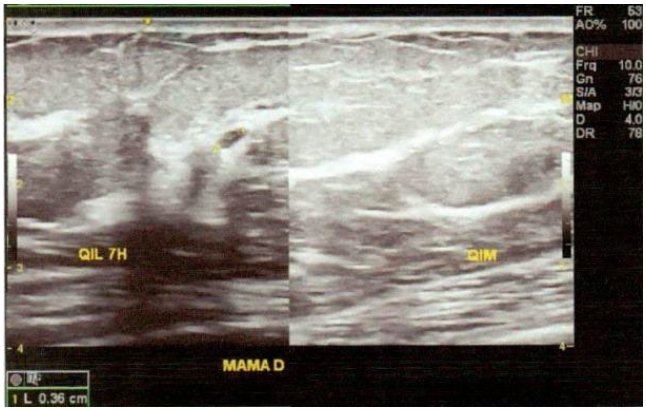


Figure 2. Ultrasound of the right juxta-areolar breast.



Figure 3. Appearance of the breasts five months after surgery.

patient could have received a different follow-up, emphasizing the importance of a well-performed history and physical examination, associated with professional expertise.

DISCUSSION

At macroscopic examination, breast ACC presents as a nodule with well-defined borders and a white cut surface. Reported sizes range from 0.6 to 2 cm and are rarely multifocal. Breast ACC includes glands lined by epithelial cells and pseudocysts lined by myoepithelial cells that secrete basophilic substances, formed by basement membrane material in the pseudoglandular lumens, and exhibits variable structural forms, including tubular, cribriform, and solid patterns. Cribriform and solid types are predominant, with tubular being less common[5,6]. The solid type has the worst prognosis, the cribriform type is intermediate, and the tubular type has the best prognosis. Solid and cribriform tumors have a higher recurrence of metastases. Classification is based on the quantity of solid components: grade I tumors have a minimal solid component, grade II tumors have less than 30%, and grade III tumors are composed of more than 30% solid components. Higher grade tumors are associated with recurrence and a higher risk of metastases[4,7,8].

Although breast cancer is usually triple-negative, its prognosis is quite favorable, with local recurrence rates of around 3 to 18%, ten-year survival rates of over 90%, five-year mortality rates of around 8.33%, and lymph node metastasis rates of around 2%[1,4]. Distant metastases are uncommon, occurring in sites such as lung, liver, kidney, and bone, and commonly only appear many years after the initial diagnosis[5].

Liu et al. point out that the good prognosis can be explained by the low expression of the Ki-67 and p63 genes[3,9]. Wang et al. demonstrated that elevated Ki67 expression and neural invasion represent significant risk factors for recurrence and metastasis in ACC, demonstrating that positive surgical margins, Nottingham histological grade, and neovascularization are reliable prognostic factors that influence outcomes in breast ACC[10]. Cima et al. reinforce that ACC requires collagenous spherulosis and invasive cribriform carcinoma as a differential diagnosis, in which both manifestations do not have double cell populations and may present positive hormonal reception and gene expressions distinct from adenoid cystic carcinoma of the breast[5,11].

Mammography reveals an irregular or lobulated mass with undifferentiated or spiculated margins, similar to benign lesions. Ultrasound reveals a solid, heterogeneous, hypoechoic mass with unclear margins and mild peripheral vascularization. Magnetic resonance imaging (MRI) findings vary, and may manifest irregular shapes with spiculated margins, round, oval, or irregular shapes with rapid enhancement from the margin to the center, and hyperintensity and isointensity on T2WI.

According to Treitl et al., the radiological diagnosis of ACC is often confused with other breast conditions, and may mimic benign findings, leading to more conservative approaches, and this highlights the importance of physical examination and clinical suspicion for further investigation[1,8,11]. Previous studies reinforce that, when a malignant lesion is suspected, a *core biopsy* and/or excisional biopsy is essential to assess the presence of malignant epithelial cells and the immunohistochemical profile of the tumor in order to guide the follow-up therapeutic strategy, even when imaging findings are benign or inconclusive[3,12].

Treatment of breast ACC involves a multimodal approach, depending on factors such as size, immunohistochemistry, and the possibility of metastasis. Breast-conserving surgery, via wide excision or quadrantectomy, is the first choice in most cases, with mastectomy reserved for high-grade and more invasive lesions. In some cases, authors postulate that breast-conserving surgery may be sufficient for treatment, without the need for adjuvant therapy, due to the small size and low lymph node spread[12]. Breast cancer rarely involves the lymphatic system surrounding the breast. It is clear that when it does occur, it is not due to lymphatic dissemination but rather to tumor expansion. Prophylactic axillary lymphadenectomy is not indicated due to the low recurrence of lymph node metastases, which is around 0.8% to 2%, and the approach should be individualized and based on the surgeon's experience[13,14].

Radiotherapy is generally administered after conservative surgery, improving overall survival by reducing the risk of tumor recurrence. Hormone therapy is not as effective because most breast cancers are triple-negative for hormone receptors. In cases of high-grade lesions with a high risk of metastasis, chemotherapy is indicated, which may include cisplatin, doxorubicin, docetaxel, and/or cyclophosphamide. If necessary, tyrosine kinase inhibitors, such as Lenvatinib, sorafenib, or axitinib, can be used as second-line agents. It is important to emphasize that, given the characteristics of this tumor, periodic outpatient clinical surveillance, including physical examination and follow-up mammography/ultrasound, are important in the follow-up of these patients to control recurrence[8,10].

CONCLUSIONS

Adenoid cystic carcinoma of the breast is essentially a triple-negative tumor and has a favorable prognosis compared to its counterparts, with indolent clinical behavior, provided it is diagnosed and treated appropriately and early. The basis for diagnosis is the combination of clinical evidence, imaging tests, and histopathological studies, including biopsy with evaluation of the immunohistochemical profile, guided by the clinical decision-making of the patient and the multidisciplinary team throughout the follow-up period.

Local conservative therapy by quadrantectomy or wide excision of the lesion followed by adjuvant radiotherapy and/

or chemotherapy has proven to be an appropriate strategy, with good outcomes in most cases. Recurrence of metastases and lymph node involvement is low. Furthermore, longitudinal follow-up of these patients is essential to reduce the risk of complications and recurrences, through scheduled outpatient follow-ups for clinical reevaluation and additional exams every 6 to 12 months, depending on the specifics of the case.

The authors of this article emphasize the importance of a multidisciplinary approach and management in the diagnosis and treatment of this cancer and suggest the regular use of vacuum-assisted biopsy, a technique that allows for larger tissue samples and can completely excise the lesion, thus reducing the risk of false-negative results, which lead to underdiagnosis of this condition. They also reinforce the importance of further studies to better elucidate the pathophysiology, diagnosis, treatment, and follow-up of breast ACC.

AUTHORS' CONTRIBUTION

PGB: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – review & editing. ARDPF: Investigation, Validation, Writing – review & editing. ATCU: Formal analysis, Investigation, Writing – original draft.

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