CASE REPORT
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Salivary gland tumor: atypical presentation of breast cancer

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ABSTRACT

Breast cancer is a heterogeneous disease with various histological and molecular subtypes. Among them, salivary gland tumors are rare and can be divided into three groups: pure myoepithelial differentiation, pure epithelial differentiation and myoepithelial with mixed epithelial differentiation. In the last group, adenoid cystic carcinoma stands out, a rare entity with low malignant potential. It represents less than 0.1–3% of breast cancer cases and has the most frequent clinical presentation as a palpable mass. The diagnosis is confirmed by histology and immunohistochemistry. Classically, they are low-aggressive triple-negative tumors, with overall survival and specific cancer survival at five and ten years greater than 95%. However, there are rare reports of aggressive variants with a risk of distant metastasis and death. Treatment is based on surgical resection with margins. Lymphatic dissemination is rare, and there is no consensus regarding the indication of an axillary approach. Adjuvant radiotherapy is indicated in cases of conservative surgery and should be discussed in other cases. The benefit of chemotherapy remains uncertain, as most tumors are indolent. We report a case that required individualized decisions based on its peculiarities of presentation, diagnosed in an asymptomatic elderly patient during screening, in which mammography showed heterogeneous gross calcifications clustered covering 1.6 cm. Stereotactic-guided vacuum-assisted biopsy was performed, and the area was marked with a clip. The anatomopathological examination led to a diagnosis of salivary gland-type carcinoma, triple-negative. The patient underwent segmental resection of the right breast and sentinel lymph node biopsy. The final anatomopathological result was similar to that of the biopsy, with an immunohistochemical profile of the adenoid cystic type and two sentinel lymph nodes free of neoplasia. Considering age and histological subtype, adjuvant therapy was not indicated. Follow-up for three years showed no evidence of disease.

KEYWORDS: breast cancer; triple-negative breast cancer; adenoid cystic carcinoma.

INTRODUCTION

Breast cancer is the most common malignant disease in women[1], considered a heterogeneous disease with various clinical and pathological presentations[2], and among them, salivary gland tumors are rare. These can be divided into three groups: pure myoepithelial differentiation, pure epithelial differentiation and myoepithelial and mixed epithelial differentiation. In the last group, adenoid cystic carcinoma stands out, a rare entity with low malignant potential[3].

Adenoid cystic carcinoma (ACC) of the breast is a heterogeneous biphasic tumor composed of basaloid and epithelial cells. It represents approximately 0.1–3% of breast cancers[4,5]. Due to its rarity, there are few databases on this carcinoma, and most of the studies are case reports or with a small sample of patients. The management protocol remains unestablished. Therefore, to contribute to the formation of a database about the ACC, we report a case of an elderly patient diagnosed during screening, requiring individualized decisions based on their peculiarities of presentation.

CASE REPORT

A 74-year-old woman, menopausal, history of sister with breast cancer at age 58, presented to the outpatient clinic asymptomatic, and she was referred because of changes in the screening mammogram. Mammography (Figure 1) showed heterogeneous gross calcifications clustered in the superolateral quadrant of the right

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breast, measuring 1.6 cm, classified as BIRADS 4. A percutaneous vacuum-assisted biopsy guided by stereotaxis was performed, and the area was marked with a clip. The anatomopathological result showed a salivary gland-type carcinoma, histological and nuclear grade 2, with an immunohistochemical profile showing positive C-kit, CK5/6 and S-100 and negative hormone receptors and HER-2 (triple-negative).

Because of the favorable histology and extent of the disease, the patient was then submitted to segmental resection of the right breast and sentinel lymph node biopsy. The final anatomopathological result (Figure 2) confirmed that it was an invasive carcinoma of the salivary gland type, with a morphological and immunohistochemical pattern of the adenoid cystic type, histological and nuclear grade 2, measuring 2.2 x 1.5 cm, associated with flat and solid ductal carcinoma ***in situ,*** with deep and inferior margin compromised by the invasive neoplasia and two sentinel lymph nodes free of neoplasia. The patient then underwent enlargement of surgical margins, with multifocal residual invasive neoplasia, the largest focus measuring 0.81 cm, with free margins and the presence of angiolymphatic embolization. Considering age and histological subtype, adjuvant therapy was not indicated. She was followed up for three years and then had no evidence of disease.

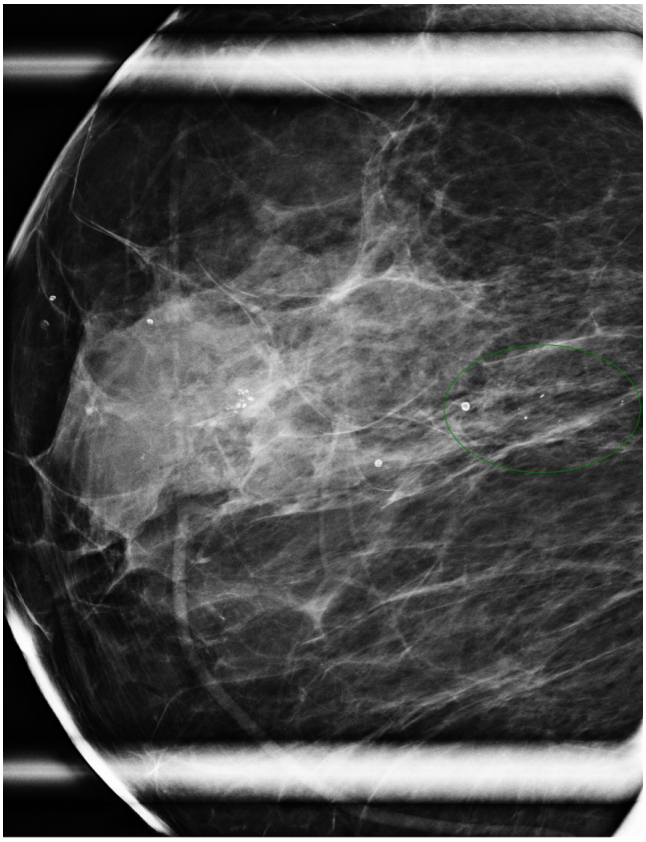

Figure 1. Calcification clustered in the superolateral quadrant of the right breast.

DISCUSSION

Clinico-pathological characteristics

ACC is a characteristically biphasic subtype of salivary gland tumor, composed of myoepithelial/basaloid and luminal/epithelial ductal cells, which can be arranged in tubular, cribriform or solid growth patterns[3,5,6]. Generally, there are these three patterns in the same tumor, present in heterogeneous proportions, the tumor being graded by the extent of the solid component[6]. Within this morphological spectrum of presentation, the basaloid predominant variants tend to have greater tumor aggressiveness[3,7].

On microscopic analysis, the cells of this tumor have scarce cytoplasm and a hyperchromic nucleus[6], but a variable spectrum of morphological aspects, similar to those seen in salivary glands, is reported, impacting the prognosis[3].

Genetically, ACC is characterized by a specific gene fusion, responsible for the development of its characteristic phenotype. The case in question had an infrequent presentation of adenoid cystic carcinoma (suspicious calcifications) on screening mammography[6].

This tumor is characterized by an insidious and continuous evolution[6], usually diagnosed in the early stages[4,5,8], as in the case of the patient in this report. The most common clinical presentation is a palpable mass/nodule, present in up to about 70% of cases[2,3,5]. The atypical presentation of the reported patient can be seen, who was asymptomatic, with a change in the screening examination.

Zhang et al. reported in a retrospective cohort and meta-analysis with a sample of 511 that more than half of diagnoses occur in patients between 50 and 69 years old[8], which is compatible with data from several other studies[2,4,5] and similar to that observed in American databases[9]. Our patient was slightly above this age range, as she was 74 years old at the time of diagnosis.

The rate of patients with a family history of breast cancer, suggesting a hereditary component, is similar to that usually described for invasive ductal carcinoma of no special type (IDC-NST).

The radiological findings are variable and may be difficult to interpret[2,3]. A suggestive sign on imaging is the presence of an isodense mass with internal septations on magnetic resonance imaging in the T2-weighted sequence[10]. The reported patient had a peculiar presentation, with a mammogram showing clustered heterogeneous coarse calcifications.

Preoperative diagnosis can be performed with fine-needle or core-needle biopsy, the latter being more accurate[3].

Immunohistochemistry helps in the diagnosis and explains the heterogeneity of the cells that make up the ACC: epithelial cells express CK7, CK8 and CD117(c-Kit); basaloids express CK14 and CK5/6; the myoepithelial ones express S-100[2-5]. As for the molecular classification, the vast majority are triple-negative[2-5,8]. However, there are controversies in the literature, with

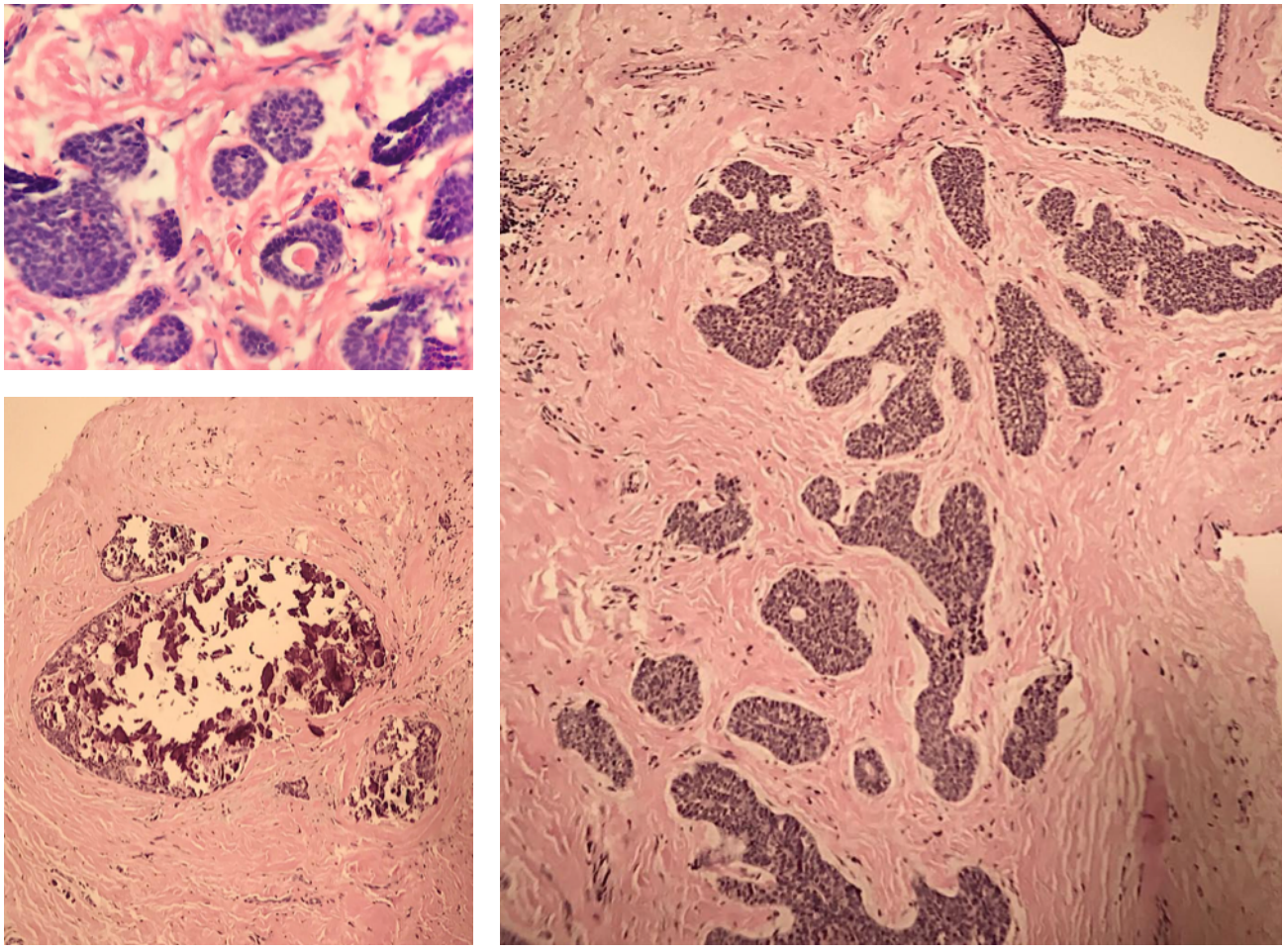

Figure 2. Histological pattern of the tumor.

the frequency of hormone receptor positive tumors ranging from 25%[11] to almost 50%[12]. The tumor in the reported case was triple-negative, fitting the most common form of molecular classification of this tumor subtype, and exhibited immunohistochemical expression of the markers mentioned in the literature, with c-Kit, CK5/6 and S-100 being positive.

Most triple-negative breast tumors are aggressive, with a high histological grade. However, ACC tends to have a favorable prognosis and low histological grade, even when it presents as triple-negative[2]. It is suggested that this is due to the lower Ki-67 rate, but there is still controversy in the literature[2]. Another study suggests that this association is due to the lower genomic instability of ACC[13].

Still, ACC may rarely undergo a process of dedifferentiation from the neoplastic clone, with the development of more aggressive high-grade carcinomas and with a greater risk of distant metastasis[3].

Treatment and prognosis

There are no well-established management protocols because of the sampling limitations of studies due to the rarity of this pathology[2,3]. Classically, treatment involves surgery with resection margins, with conservative surgery considered an adequate therapeutic option[14], always followed by adjuvant radiotherapy[2,6,14]. Zhang et al. reported a conservative surgery rate of 66%. The patient in the reported case underwent conservative surgery with assessment of intraoperative margins, which were compromised, leading to a reapproach for enlargement. Adjuvant radiotherapy followed[8].

Mastectomy may be indicated if the invasive lesion with tumor is affecting the breast in a proportion that makes an aesthetically satisfactory partial excision unfeasible[2]. In the literature, the percentage of patients undergoing mastectomy ranged from 33 to 72%[2-5,8].

An important consideration in therapeutic choice is the knowledge that there are tumor variants that can be more aggressive, such as those with a basaloid predominance. This graduation is given by the proportion of distribution of the histological components (tubular, cribriform and solid)[3]. In these aggressive basaloid variants, the rate of nodal involvement can reach 20% and that of distant metastasis, 16%[3,15].

In general, lymphatic dissemination is rare, ranging from 0 to 5% in the literature[2,4,6,8,14,16]. Khanfir et al. reported no nodal involvement in a sample of 51 patients[14]. Because of this low rate of nodal involvement, the role of axillary dissection remains

unclear[2,14]. Sentinel lymph node biopsy may be an option, with good identification rates. To decide on its use, factors such as tumor size, hormone receptor status, nuclear grade and lymphovascular invasion should be evaluated[16]. In recent studies, the rate of performance of this procedure varied between 50 and 100%[4,5]. In the present case, we opted for sentinel lymph node biopsy, whose anatomopathological examination identified two cancer-free lymph nodes.

The use of adjuvant chemotherapy is controversial but should be considered[7]. In the consensus of St. Gallen in 2011, indicating adjuvant chemotherapy was suggested for cases of high-grade tumors, tumors larger than 3 cm, lymph node involvement or distant metastasis[17]. However, this tumor is usually resistant to this therapy[6], which is why its indication is rarely described[4,8].

Wang et al. compared 36 cases of ACC with 108 cases of low-grade breast invasive ductal carcinoma, with standardized groups regarding clinical and tumor variables. These authors concluded that ACC has a lower rate of Ki-67 and tumor nodal involvement but larger-size tumor compared to low-grade IDC-NST[2].

Classically, ACC is described as being associated with a favorable prognosis, with a low rate of distant metastasis and local recurrence, with excellent survival rates[2,4,8,18]. It should be noted that some studies are controversial, perhaps because of the heterogeneity and rarity of ACC, reporting rates of local recurrence and distant metastasis varying between 8 and 14% and 8 and 21%, respectively[2,6,15]. The most common sites of distant metastasis are lung, bone and liver[2,5].

Overall survival at 10 and 15 years exceeds 90%[2], with no difference in overall or disease-free survival in relation to that described for low-grade IDC-NST[2,18]. In a study with 511 patients, Zhang et al. reported overall and cancer-specific survival at five and ten years of 95.7 and 100%, respectively[8].

Some predictive factors of recurrence-free survival are described, such as positive margin, neovascularization, basaloid variant, perineural invasion, lymphovascular invasion, >30% solid component, lymph node involvement and presence of necrosis[15].

CONCLUSIONS

ACC is a rare subtype of breast cancer, and knowledge about its peculiarities is important to guide the correct diagnosis and management. Although most triple-negative tumors are considered more aggressive, ACC is indolent and considered to have a good prognosis.

Because of its rarity, there are few and low-sample studies, subject to a higher risk of bias. Therefore, there is no consensus on the treatment to be followed, making it necessary to create management protocols. Individualized therapeutic choice is recommended, assessing the risk x benefit of each approach.

AUTHORS' CONTRIBUTIONS

MLN: Writing – original draft, Writing – review & editing. TFSD: Project administration, Supervision, Writing – original draft, Writing – review & editing. GAC: Data curation, Investigation, Methodology. FEMA: Project administration, Supervision.

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