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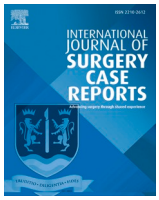

Case report

Primary breast sarcoma: Case report and literature review

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ABSTRACT

Introduction: Primary breast sarcoma (PBS), excluding phyllodes tumors, is an extremely rare and heterogeneous group of cancers, accounting for <1 % of all breast cancers. PBS is typically diagnosed in the fifth or sixth decades of life. There are no pathognomonic clinical or radiological features. Diagnosis is generally established through a microbiopsy. For young women, the diagnosis can be confused with a benign pathology.

Clinical presentation: Our patient was 27 years old, with no family or personal history of breast cancer, which was initially brought to the emergency department with a breast abscess. The clinical diagnosis of abscessed mastitis was made. The patient underwent tissue excision with evacuation of blood clots and necrotic tissue. Histopathological examination revealed a primary breast sarcoma. An MRI showed locally advanced retro-glandular tumor. An abdominal and pelvic CT scan performed showed no evidence of secondary locations. Therefore, the patient was referred for neoadjuvant radiotherapy and chemotherapy. After the third course of chemotherapy, the patient died following cardiogenic shock.

Discussion: The PBS in younger women is extremely rare. The etiopathogenesis remains undetermined. The clinical and radiological characteristics of PBS mimic breast adenocarcinoma. Mastectomy is the treatment of choice but in the case of locally advanced tumor, the use of neoadjuvant chemotherapy can be indicated. PBS presents a significantly poorer prognosis.

Conclusion: Breast sarcomas are rare malignant tumors for which treatment protocols are not well-established. Further research efforts are needed to improve the understanding and treatment of PBS.

1. Introduction

Breast sarcoma, excluding phyllodes tumors, is an extremely rare and heterogeneous group of cancers, accounting for <1 % of all breast cancers and <5 % of all soft tissue sarcomas [1]. It can be divided into two categories: de novo (primary) development or post-therapy (secondary) development. Although the clinical characteristics of primary breast sarcoma (PBS) mimic, to some extent, mammary adenocarcinoma, it presents a high risk of recurrence and a significantly poorer prognosis [1].PBS is typically diagnosed in the fifth or sixth decades of life [2]. We present the case of atypical presentation of PBS. Our patient is 27 -year-old, with no family or personal history of breast cancer, which was initially brought to the emergency department with a breast abscess.

2. Case presentation

The patient in the present study was 27 years old, nulligravida, with no family history of breast or other neoplasm and no notable personal medical history, presented with a swelling in her left breast. Upon examination, a swollen left breast measuring over 20 cm was found, occupying the two outer quadrants with necrosis and loss of skin substance in the lower outer left quadrant (Fig. 1).

A breast ultrasound showed left breast abscess mastitis without signs of malignancy.

Blood tests showed a biological inflammatory syndrome, with a white blood cell count of 26,000 and CRP level of 269. The clinical diagnosis of abscessed mastitis was made, and a bacterial culture was taken. Antibiotic treatment was initiated. Following severe sepsis with a plateau fever and tachycardia at 140 bpm, the patient underwent tissue

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Abbreviations

PBS primary breast sarcoma

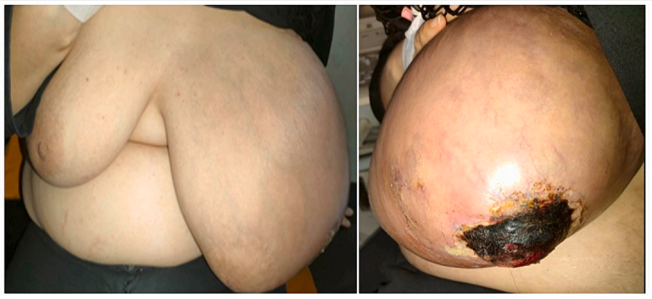

Fig. 1. Preoperative picture, in the left breast: Necrosis and loss of skin substance in the lower outer left quadrant.

excision with evacuation of blood clots and necrotic tissue. After receiving antibiotic treatment for 15 days, the patient showed good clinical and biological improvement, with gradual but incomplete healing of the lesion and a decrease in CRP to 26.

Histopathological examination revealed a malignant mesenchymal proliferation, densely cellular with several lymphatic slits arranged in diffuse sheets of spindle cells with hyperchromatic nuclei and irregular contours (Fig. 2). The mitotic figures were estimated at 38 mitoses/10CFG, with many abnormal mitoses. Immunohistochemical study showed that the tumor cells were negative for Cytokeratin, P63, EMA, Desmine, and H Caldesmone. CD34 and CK7 were still under examination.

These morphological and immunohistochemical features showed a predominant sarcomatous component that could be consistent with a sarcoma.

An MRI was performed, which showed a large retro-glandular mass with irregular lobulated contours, massive necrosis, and extensive edema-hemorrhagic changes. The mass invaded the deep muscle layer and was associated with diffuse regular skin thickening and subcutaneous fat infiltration (Fig. 3). There was also a 20 mm thick-cortex axillary lymph node. No suspicious breast lesions were found on the right side. Histopathological examination of the axillary lymph node was normal.

An abdominal and pelvic CT scan performed as part of the staging workup showed no evidence of secondary locations.

According to the 8th edition of the American Joint Committee on Cancer [3], the TNM tumor stage of our patient was T4N0M0 (T4: Tumor >15 cm in greatest dimension).

Therefore, the patient was referred for neoadjuvant radiotherapy and chemotherapy because it was a locally advanced tumor. After the third course of chemotherapy, the patient died following cardiogenic shock.

3. Discussion

Breast sarcomas as a primary site are extremely rare. They account for <1 % of all breast tumors and <5 % of all soft tissue sarcomas, with an estimated annual incidence of 4.6 new cases per million women [1].

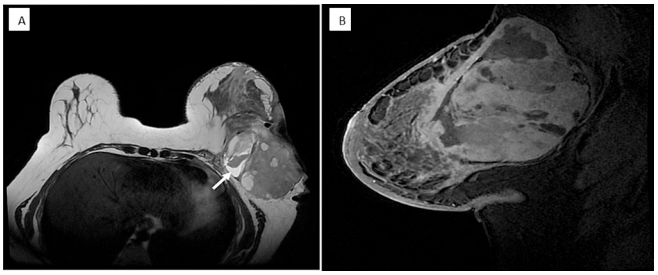

Fig. 3. MRI finding. A: Axial T2-weighted MRI image showing a large mass arising from the left breast. The shape is oval with circumscribed margins. The signal is inhomogenous with cystic areas (arrow). B**:** Sagittal T1-weighted post contrast image showing the enhacement of solid components. Heterogeneity of enhancement is due to necrosis.

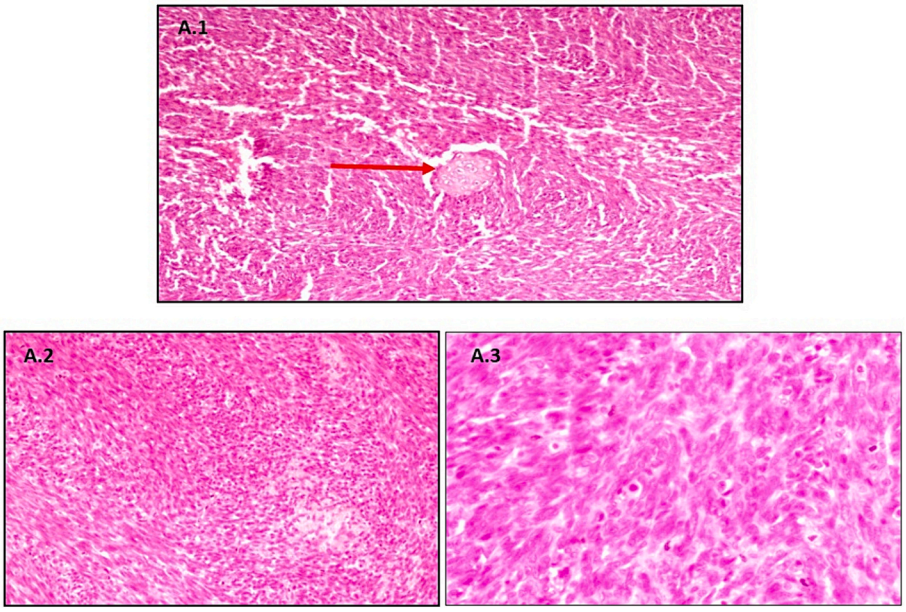

Fig. 2. Histology finding; A.1: Presence of heterologous elements: chondroid cluster (arrow), A.2: mesenchymal proliferation made of bundles of spindle cells with atypical and sometimes mitotic nuclei, A.3: obvious nuclear atypia and numerous mitoses with images of atypical mitoses (x40).

3.1. Risk factors

The etiopathogenesis of primary breast sarcoma remains undetermined; however, radiotherapy and chronic lymphedema may be associated with secondary breast sarcoma development.

The development of breast sarcomas is strongly associated with TP53 mutation in Li-Fraumeni syndrome [4]. Several environmental exposures have been suggested as possible risk factors for breast sarcomas, including previous exposure to arsenic compounds, vinyl chloride, and alkylating agents [5].

Secondary breast sarcomas most commonly occur after external radiation therapy for breast or other intrathoracic cancers. Breast cancer and non-Hodgkin lymphoma are the most common antecedents in radiation-induced sarcomas [6].

3.2. Histology

Different subtypes of breast sarcoma exist. Their cell origin type is used to name them and it includes angiosarcoma, fibrosarcoma, leiomyosarcoma, osteosarcoma, liposarcoma, chondrosarcoma, malignant histiocytoma, and Kaposi sarcoma [7]. The angiosarcoma is the most common subtype [2].

3.3. Clinical presentation and diagnosis

Breast cancer in children and adolescents aged 19 and under is rare [8].

A population-based study in the United States found that 35.1 % of all pediatric breast cancer cases were fibroepithelial tumors, while 14.2 % were sarcomas. Among the patients included in this study, 13 were 19 years old or younger, accounting for 5 % of the total patients. Two of these patients were in the age group of 0 to 4 years and both had malignant phyllodes tumors [9].

Breast sarcomas almost exclusively occur in women, although rare cases have been reported in men. In a review by Sue Zann Lim, it was found that 97.6 % of patients were women, while 2.4 % were men [10]. These findings are consistent with previously reported data by Al-Benna et al., where only 1.5 % of breast sarcomas occur in men [11].

Breast sarcomas are typically diagnosed during the fifth or sixth decade of life. The median age at diagnosis was 49.5 years, although the age range is quite wide (12 to 89 years) [10].

Patients with secondary breast sarcomas are generally older than those with primary breast sarcomas, primarily because they develop after treatment for breast carcinoma.

Skin changes and nipple alterations or the presence of axillary lymphadenopathy are not common. They do not exhibit pathognomonic radiological features, and mammographic and ultrasound findings are non-specific. Diagnosis is generally established through a microbiopsy [11].

They are typically large in size, with a median tumor size of 5.25 cm, ranging from 0.3 to 30 cm [9]. Patients usually present with a unilateral, firm, well-defined breast mass that rapidly increases in size. It is rarely associated with pain or skin changes.

In a study conducted by Ming Yin et al., a total of 787 cases were analyzed, with a median tumor size of 4.5 cm (ranging from 0.1 cm to 48.4 cm).These tumors have a high risk of recurrence and are known to have a poor prognosis [12]. Early diagnosis and appropriate treatment have an impact on survival. Delay in the diagnosis of breast cancer is associated with a negative outcome. Various imaging techniques such as mammography, ultrasound, and MRI can be used for diagnosis.

Breast sarcomas may have a non-specific appearance on radiological images. On mammography, they typically appear as an opaque mass. However, they are rarely associated with spiculations, microcalcifications or axillary lymphadenopathy [13].

Similarly, there is no specific diagnostic characteristic for breast sarcoma on ultrasound. It usually appears as an irregular mass with indistinct borders and no shadowing. MRI is increasingly used to assess the extent of the disease in breast sarcomas [13].

Indeed, the gold standard for diagnosis of the PBS is histological examination.

The staging system most frequently utilized for sarcomas is determined by the American Joint Committee on Cancer, which takes three considerations: the size of the tumor, the regional lymph node status and the presence or absence of distant metastases [3].

3.4. Treatment

The treatment of choice for primary breast sarcoma is mastectomy without axillary lymph node dissection [10]. In fact, the PBS is generally characterized by hematogenous dissemination. The probability of lymphatic spread is <5 %, and axillary lymph node dissection does not improve outcomes [10]. Therefore, in the absence of palpable axillary lymphadenopathy, lymph node dissection should not be undertaken. The standard recommendation is to obtain a 1-cm clear margin for all resected breast sarcomas, with the exception of angiosarcomas by which a 3-cm clear resection margin is recommended [14].

In high-risk cases, adjuvant and neoadjuvant chemotherapy, as well as radiotherapy, should be considered.

Adjuvant radiotherapy is recommended after a positive margin resection, in a tumor larger than 5 cm and with any high-grade sarcoma, because of the high risk of local recurrence [15].

The use of chemotherapy in PBS has remained a subject of controversy. In fact, the response of chemotherapy is very variable [11]. Adjuvant chemotherapy has been utilized in higher tumor grade, large tumors or angiosarcoma histology [16].

In patients with locally advanced tumors, the use of neoadjuvant chemotherapy added to radiotherapy increased survival and local progression free survival [17].

3.5. Prognosis

In addition to their rarity, PBS are aggressive tumors, with five-year overall survival ranging between 50 % and 66 %, and disease-free survival between 33 % and 52 %.

Prognosis factors include tumor size>5 cm, high-grade disease, positive resection margins, distant metastasis, node status, radiation history and histologic subtype of angiosarcoma [12]. The most crucial prognostic factor is achieving clear surgical margins during the procedure. This is the most important determinant of local recurrence and survival [9]. The angiosarcoma has a poor prognosis when compared to other histological subtypes [12]. However, early local recurrences are reported and an increased risk of distant metastasis is associated with breast angiosarcoma [16,18]. PBS has a poor prognosis compared to malignant phyllodes tumor [19].

4. Conclusion

Breast sarcomas are rare malignant tumors for which treatment protocols are not well-established. Surgery, particularly mastectomy with or without wide local excision, is the treatment of choice, while axillary lymph node dissection is rarely necessary. In high-risk cases, adjuvant chemotherapy and radiotherapy may be considered. However, data on the effectiveness of these treatments are limited due to the rarity of these tumors. Further research efforts are needed to improve the understanding and treatment of stromal breast sarcomas to enhance clinical outcomes.

This work has been reported in line with the SCARE 2023 criteria [20].

Patient consent

The patient's written consent was obtained to write the case report in

September 2023.

Ethical approval

Ethical approval is considered unnecessary by the ethics committee of the hospital center, because this is a unique case encountered during practice and which does not involve any experimentation on humans or animals.

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Declaration of competing interest

The authors have no conflicts of interest.

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