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Case report

Breaking the odds: A rare case of bilateral breast angiosarcoma

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Abstract. Breast angiosarcoma is an extremely rare and aggressive tumor, presenting several challenges in diagnosis and treatment. Imaging techniques play a crucial role in the early diagnostic assessment, initially allowing for a differential diagnosis with other breast tumors (using ultrasound and MRI techniques) and subsequently for patient follow-up through CT and MRI examinations. Currently, there is no standardized or unified treatment protocol, especially regarding metastatic forms, where the use of chemotherapy or radiotherapy remains subject of debate. The rarity of this tumor entity suggests the need for future research and multidisciplinary collaboration in order to further optimize diagnostic accuracy and treatment options. (www.actabiomedica.it)

Key words: breast angiosarcoma, breast MRI, radiation therapy, soft tissues, breast oncology, diagnostic challenges

Introduction

Breast angiosarcoma is an extremely rare tumor, accounting for approximately 0.4% of all malignant breast neoplasms. It may appear as a primary form, which is more typical in women aged 30 to 50, or in a secondary form (following radical mastectomy or radiotherapy), typically observed in women aged 67 to 71 (1). Tumor cells develop from the endothelium of small vessels surrounding or infiltrating the glandular lobules of the breast (2). This cancer is highly aggressive, with an overall 5-year survival rate of about 33% (3). Diagnosis is often misleading and complicated by a wide variety of non-specific symptoms and inconclusive radiological findings. Consequently, diagnosis often occurs when the tumor has already spread to other organs, particularly to the liver. The gold standard for treating this condition remains surgical excision, while the roles of chemotherapy and radiotherapy are still under discussion.

Case Presentation

The patient is a 55-year-old Caucasian woman with a family history of breast carcinoma (father, mother, and maternal uncle). She appears to be in good general health and does not present additional risk factors such as smoking, alcohol abuse, or drug use. She underwent surgery for fibroadenomas at the ages of 20 and 30. As part of her routine breast cancer screening, she underwent two breast biopsies in 2020 for suspicious nodules: a B2 fibroadenoma on the right and a capillary hemangioma on the left, both of which were completely excised. Two years later, a mammogram revealed an oval lesion measuring approximately

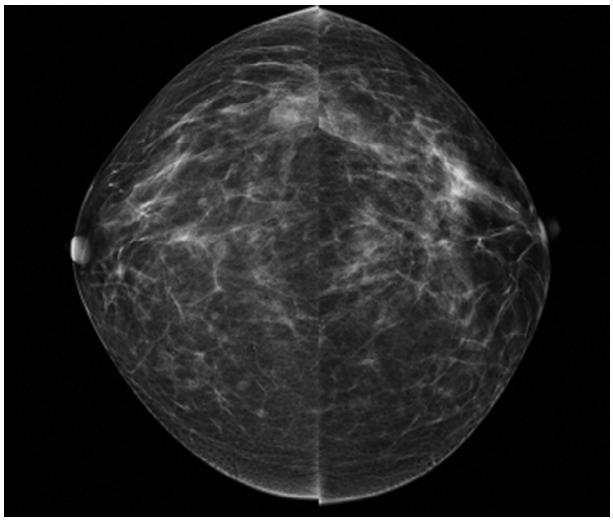

Figure 1. Bilateral mammography: on the right side an oval lesion measuring 1 cm with regular margins; on the left side several hypoechoic lacunae with edematous thickening of glandular tissue measuring a total diameter of 4 cm.

1 cm with regular margins on the right side and several hypoechoic lacunae with edematous thickening of glandular tissue measuring a total diameter of 4 cm on the left side (Figure 1).

This prompted another biopsy. Histological examination confirmed breast angiosarcoma with a Ki-67 index of 25%. A whole-body CT scan identified a heterogeneous lesion in the left breast measuring 5.5 cm, with no evidence of metastasis elsewhere. An MRI of the breasts was subsequently performed before and after intravenous administration of a paramagnetic contrast medium. The imaging revealed a solid, nodular mass in the left breast and another solid mass in the right breast. Based on the size, shape, and enhancement patterns of these lesions, histological analysis was conducted, confirming breast angiosarcoma with a Ki-67 index of 25%. Neoadjuvant therapy was initiated but yielded a poor response. The patient underwent bilateral mastectomy; histological examination revealed two fibroadenomas measuring 14 mm and 5 mm on the right and an angiosarcoma measuring 6 cm on the left. She was subsequently enrolled in an adjuvant radiotherapy preparation protocol. During radiotherapy preparation, simulation CT revealed the persistence of a nodule in the upper right quadrant. Consequently, radiotherapy was postponed. Two months later, follow-up imaging indicated disease recurrence. A new nodule was excised, and bilateral radiotherapy was initiated. The most recent imaging follow-up revealed metastases at multiple sites: multiple nodular formations at the thoracic level, space-occupying lesions in subcutaneous adipose tissue, and bone-level lesions.

Discussion

Currently, there are no specific diagnostic imaging tests for breast angiosarcoma. Due to its rarity and the broad range of non-specific symptoms, diagnosis can be challenging (4). Mammography is not specific for this carcinoma; studies describe oval or lobulated masses without associated calcifications and with heterogeneous density alterations in glandular structures. Often, changes in adjacent subcutaneous tissue are noted, including thickening of local vessels and altered adipose tissue density. Ultrasound (US) offers greater diagnostic power for detecting breast carcinomas in younger women with dense breast tissue (5). These lesions may appear hypoechoic, hyperechoic, or mixed. Hyperechoic forms are typically associated with benign lesions; however, additional criteria such as necrotic or haemorrhagic components or hypervascularization on Doppler signal must always be evaluated (6). While CT is not primarily used for diagnosing breast carcinomas, it was requested for staging purposes due to the aggressive nature of angiosarcoma and its tendency to metastasize rapidly. MRI is currently considered the most sensitive technique for differential diagnosis of angiosarcoma (7). Literature describes most breast angiosarcoma lesions as nonspecific thickening and enhancement of the skin with or without nodularity or underlying masses. In our case, MRI examination was performed before and after intravenous administration of a paramagnetic contrast medium. This included morphological and dynamic imaging sequences, along with multiplanar reconstruction (MPR) image processing and quantitative analysis of the areas exhibiting the greatest enhancement. The breast was then classified as fibro-glandular type, with a background parenchymal enhancement (BPE) rated as type 1. A solid, mass-type nodular

formation (measuring approximately 77 x 76 mm), described as polylobulated, was detected at the supero-median-retroareolar site of the left breast. The mass exhibited early, and intense contrast enhancement noted in dynamic post-contrast sequences. The lesion showed non-homogeneous enhancement attributed to necrotic-colliquated components. Skin infiltration corresponding to the lesion was observed, with spicules appearing to infiltrate the nipple. Another solid mass-type area was documented in the right breast, measuring approximately 20 x 13 mm with early and intense contrast enhancement in post-contrast dynamic sequences (type III IS/T curves) (Figure 2).

This area was recommended for a second-look ultrasound. The characteristics of the lesions-particularly their size, shape, and enhancement patterns-are critical for assessing potential malignancy. The histological analysis verified the diagnosis of breast angiosarcoma, showing a Ki-67 index of 25%. Given the histological results and the patient's clinical history along with probable familiar predisposition, genetic tests for BRCA1/BRCA2 mutations were performed, yielding negative results. Additional tests for other possible mutations related to breast neoplasia are still ongoing (8-9). Neoadjuvant therapy was initiated with Epirubicin (120 mg/m²) and Ifosfamide (9000 mg/m²) for three cycles followed by Gemcitabine-Docetaxel (1.8q21). The patient responded minimally to the treatment, especially on the left side, with only a slight reduction of the lesion. The patient underwent bilateral mastectomy; histological examination revealed two fibroadenomas measuring 14 mm and 5 mm on the right and an angiosarcoma measuring 6 cm on the left. The patient was subsequently initiated to a protocol for adjuvant radiotherapy preparation. During the preparatory phase of radiotherapy, simulation CT revealed the persistence of a nodule in the right upper quadrant. For this reason, it was decided not to proceed with radiotherapy. After two months, imaging follow-up indicated disease recurrence. CT detected a new lobulated formation (measuring 14x13 mm) in soft tissues anterior to the right pectoralis major. Breast MRI described that in the residual soft tissues of the right breast region—specifically in the superinternal area—a lobulated, inhomogeneous solid nodular formation was observed measuring 11 x 11 x 20 mm (APXLLXCC). Upon second ultrasound evaluation, a hyperechoic nodular formation with 15 mm hypoechoic areolas was confirmed, indicating recurrence of underlying disease. Additionally, in the lower quadrants of the right breast, there is a fluid collection measuring 42 x 18 x 14 mm (APXLLXCC), attributed to recent surgical procedures. After diagnosing recurrence, the nodule was excised and after surgery it was decided to proceed with bilateral radiotherapy. A new total body CT scan was performed to stage the disease after treatment. At thoracic level, multiple nodular formations of repetitive significance have been documented. In subcutaneous adipose tissue, several space-occupying lesions exhibited uneven density and enhancement pattern after administration of contrast medium; this is compatible with additional repetitive lesions. A new breast MRI was performed. At the level of the inferior third of the left body of the sternum, a small oval area (maximum size approximately 7 mm) was documented characterized by restriction in DWI and enhancement after contrast medium; this alteration was not previously documentable in previous MRI examinations. Between the seventh and eighth anterior ribs on the right side, a hyperintense signal alteration was documented in STIR and hypointense in T1-weighted sequences showing heterogeneous enhancement after contrast medium. These findings were not unequivocally interpretable and require further diagnostic investigation. The last follow-up CT scan, performed nine months after radiotherapy, confirmed the metastatic condition at the pulmonary level and in the subcutaneous soft tissues, also demonstrating the appearance of repetitive lesions at the bone level, as evident in the left transverse process of the L1 vertebra.

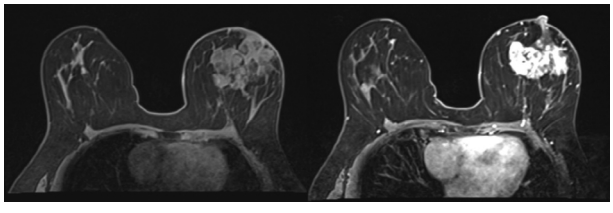

Figure 2. Breast MRI Axial Scan with T1 sequence: a solid, mass-type nodular formation at the supero-median-retroareolar site of the left breast: with early and intense contrast enhancement in post-contrast dynamic sequences; another smaller solid lesion of the right breast.

Conclusion

Breast angiosarcoma is an extremely rare tumor that has been described in only a few clinical studies, and its treatment has yet to reach a definitive consensus (10). In localized forms, surgical excision remains the gold standard therapeutic approach, with particular attention to resection margins (wide negative margins are associated with a better prognosis). In metastatic forms, surgical treatment is often combined with chemotherapy—both adjuvant and neoadjuvant—though the actual prognostic benefit remains controversial (11). The role of radiotherapy is even more debated, particularly in secondary forms (12); some studies suggest that radiation may accelerate progression in secondary angiosarcoma, while others provide hope for controlling localized malignant forms.

Consent to Participate and for Publication: Written informed consent for publication was obtained from the patient.

Ethic Approval: Code Of Ethics And Conduct Of The University Of Foggia. (https://www.unifg.it/sites/default/files/normative/2023-08/302EN-Codice_etico_e_di_comport_ott.2018.pdf).

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Declaration on the Use of AI: Perplexity chatbot has been used to check English grammar.

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