Acta Biomed 2025; Vol. 96, N. 1: 15735 DOI: 10.23750/abm.v96i1.15735

Case report

An aggressive and recurrent bilateral breast angiosarcoma in a young woman

Marina Balbino[1], Manuela Montatore[1], Federica Masino[1], Daniela Erriquez[2], Francesca Anna Carpagnano[2], Giuseppe Guglielmi[1,3,4]

[1]Department of Clinical and Experimental Medicine, Foggia University School of Medicine, Foggia, Italy; [2]Breast Unit, "Dimiccoli" Hospital, Barletta, Italy; [3]Radiology Unit, "Dimiccoli" Hospital, Barletta, Italy; [4]Radiology Unit, "IRCCS Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo, Foggia, Italy

Abstract. *Background and Purpose:* Breast sarcoma is an uncommon kind of cancer that starts in the breast's connective tissues, which include the muscles, fat, blood vessels, and other tissues that support the breast. Breast sarcomas are not the same as more prevalent forms of breast cancer, which usually originate from glandular tissue (ducts or lobules). Breast sarcoma has several subtypes, one of which is angiosarcoma. It is characterized by aggression and originates from blood vessels. Less than 1% of all breast malignancies are breast angiosarcomas, making them extremely uncommon. When compared to other more prevalent types of breast cancer, it frequently affects younger women. *Methods:* To better identify and distinguish breast angiosarcoma from other lesions, it is critical to assess and optimize currently available imaging modalities, such as mammography, ultrasound, and magnetic resonance imaging (MRI). *Results:* Since angiosarcoma is an uncommon kind of cancer, there is a shortage of precise information on its course. Nonetheless, in comparison to more prevalent forms of breast cancer, angiosarcoma of the breast typically has a poorer prognosis. This is mostly because it is frequently detected at a later stage, and it may have a higher propensity to spread quickly to other body areas. *Conclusions:* Breast angiosarcoma is a rare cancer that can be treated with surgery, radiation therapy, and chemotherapy. However, its aggressive nature may not always lead to effective treatment. The prognosis depends on factors like disease stage, tumor size, treatment response, and personal factors. Understanding angiosarcoma can help prevent misdiagnoses and prompt early medical attention. Medical professionals with extensive knowledge can offer specialized treatment and management approaches to patients with this rare cancer. (www.actabiomedica.it)

Key words: angiosarcoma, breast cancer, cancer recurrence, breast angiosarcoma, sarcomas

Introduction

Breast angiosarcoma is rare, accounting for fewer than 1% of all breast malignancies. It primarily affects women, but it can also occur in men, albeit infrequently (1-2). Breast angiosarcoma is often diagnosed with a combination of imaging tests (such as mammography, ultrasound, or MRI) and a Tru-Cut core needle biopsy to evaluate tissue samples under a microscope for malignant cells (Table 1).

Breast angiosarcoma is commonly treated with surgery, radiation therapy, and chemotherapy (3-5).

Because of its rarity, research into breast angiosarcoma is restricted, and treatment techniques are continuously improving. Patients diagnosed with this ailment frequently benefit from multidisciplinary care that includes oncologists, surgeons, and other healthcare specialists who specialize in handling rare cancers (6).

Table 1. Summary table on the characteristics of angiosarcoma in each imaging technique.

Imaging Modality	Characteristics of Angiosarcoma
Mammography	• May show a dense mass or focal asymmetry • Calcifications may be present, typically linear or branching • Margins may be ill-defined or spiculated • Associated features may include skin thickening and/or architectural distortion • Limited sensitivity for detecting angiosarcoma
Ultrasound	• Limited sensitivity for detecting angiosarcoma • Hypoechoic mass with irregular or indistinct margins • Increased vascularity within the lesion may be observed • Heterogeneous internal echotexture
MRI	• T1-weighted imaging may show heterogeneous enhancement • T2-weighted imaging may show hyperintensity • Irregular or spiculated margins may be seen • Dynamic contrast enhancement may demonstrate rapid washout • Presence of areas of necrosis or hemorrhage • High sensitivity for detecting breast lesions

Case Presentation

Anamnesis

A 40-year-old woman arrived at the hospital with pain and discomfort. During the clinical examination, a palpable tumor in the breast was discovered, along with swelling and redness of the skin. The patient also complained about breast soreness for several weeks. Given the presence of a lump in the breast, a battery of imaging procedures, including mammography and breast ultrasound, were performed to further assess the lump and identify its nature. Differential diagnosis was considered, taking into account various possibilities such as benign masses, cysts, or more common malignancies like breast carcinoma.

Diagnostic evaluation

The patient received a mammography followed by an ultrasonography examination. Breast angiosarcoma exhibited on the mammography as an aberrant lump with uneven borders and a unique pattern of calcifications; the lesion distorted the surrounding tissue architecture. However, because angiosarcoma is a rare illness with variable imaging characteristics, diagnosing it with mammography can be difficult and not always definitive. Additional imaging tests were required for a more thorough examination. An ultrasonography examination was undertaken. The lesion seemed to be an inhomogeneous hypoechoic mass with posterior acoustic shadowing and irregular boundaries that were unclear and spiculated on ultrasonography; additionally, ultrasound exam showed an increased blood flow within the lesion, highlighted through the visualization of color Doppler signals (Table 2).

Although ultrasound imaging offered useful information for detecting and defining angiosarcomas, a Tru-Cut biopsy guided by ultrasound was required for a final diagnosis.

After a few days, the histological examination revealed the following findings: “Mesenchymal proliferation of angiomatous type with papillary structures with tufting and atypia. It is consistent with a malignant vascular lesion (angiosarcoma).” The patient then had an MRI to determine the extent of the lesion and to stage it (Figure 1).

The 3T MRI revealed a solid nodular mass-like development with lobules, significant contrast enhancement, and maximum axial dimensions of 77mm (3, 4). The extensive size of the lesion resulted in infiltration of the skin, with spicules reaching the nipple-areola complex. The surprising finding was that the MRI revealed two additional lesions on the right side, with the largest located at the upper inner quadrant. These solid formations exhibited similar characteristics to the main lesion on the left, being mass-like and showing early and intense contrast enhancement with type IIII intensity-time curve. Then the patient underwent an ultrasound second look and a further biopsy

Table 2. Summary table of ultrasound features with their explanation.

Ultrasound Features	Description
Hypoechoic Mass	Appears darker than surrounding tissue on ultrasound due to increased density or decreased reflection of sound waves.
Irregular Margins	Borders of the mass are irregular or poorly defined, often suggesting invasive or malignant growth.
Vascularity	Increased blood flow within the lesion, often visualized as color Doppler signals or power Doppler enhancement.
Heterogeneous Texture	Uneven internal structure of the mass, reflecting variations in tissue composition, necrosis, or hemorrhage.
Posterior Acoustic Shadowing	Dark area beyond the mass on ultrasound due to attenuation of sound waves, commonly seen in lesions with dense or calcified components.

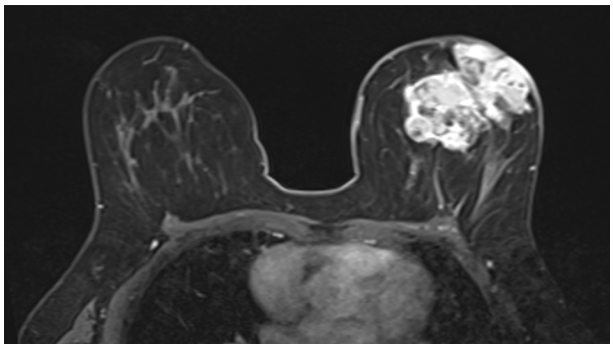

Figure 1. 3T MRI. The image on the axial plane of a T1-weighted 3D acquisition of the first post-contrast dynamic frame: poly-lobed, irregular lesion with alternating heterogeneous enhancement and relatively hypovascularized central areas in the left retro-areolar region.

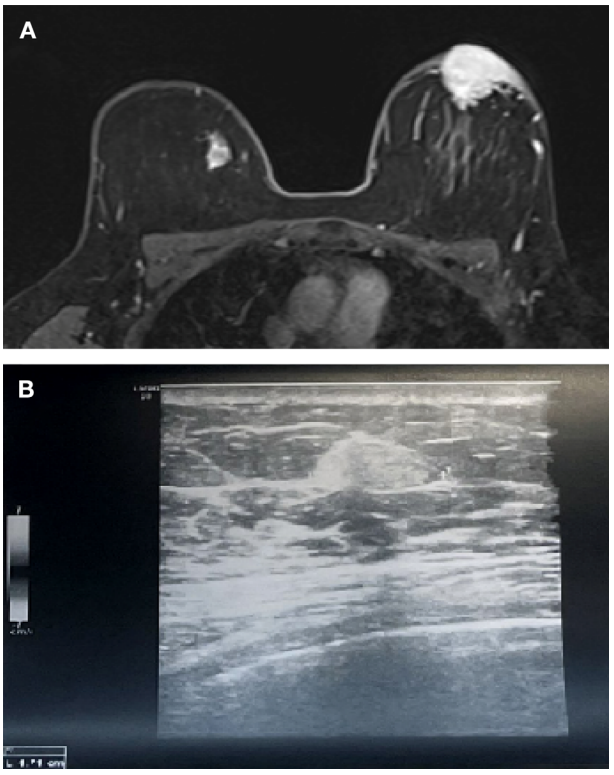

Figure 2 (A, B). (A) 3T MRI. The image on the axial plane of a T1-weighted 3D acquisition of the first post-contrast dynamic frame: evidence of a similar lesion, with irregular margins and marked contrast enhancement, is also revealed in the upper inner quadrant of the right breast. (B) Ultrasound. Irregularly oval-shaped formation with heterogeneous hyper-echogenicity (measured about 1.70 cm)

examination on the right side, which confirmed the malignant nature of the lesions and the same histological outcome (Figure 2).

The differential diagnosis

Radiographic findings can be non-specific and may be hard to differentiate from other lesions (5). Differential diagnosis for breast angiosarcoma involves distinguishing it from other breast lesions or conditions that may present with similar symptoms or imaging findings. Some potential considerations include hemangioma, phyllodes tumor, metastatic lesions, and of course other primary breast cancers. Hemangioma is a benign vascular tumor that can sometimes mimic the appearance of angiosarcoma on imaging. However, hemangiomas typically have well-defined margins and lack aggressive features seen in angiosarcoma. Phyllodes tumor is a rare fibroepithelial tumor of the breast that can have vascular features on imaging.

Phyllodes tumors often present as a rapidly growing breast mass and may show areas of hemorrhage or necrosis, which can mimic angiosarcoma (Table 3).

To differentiate breast angiosarcoma from these other conditions, a combination of imaging studies along with histopathological examination through biopsy is necessarily required.

Table 3. Summary table with the differential diagnoses and their features on US and MRI.

Differential Diagnosis	US Features	MRI Features
Angiosarcoma	Hypoechoic mass with irregular margins	Heterogeneous enhancement, irregular margins
Hemangioma	Hyperechoic mass with well-defined margins	T1 hyperintense, T2 hyperintense
Phyllodes Tumour	Heterogeneous hypoechoic mass with leaf-like projections	Heterogeneous enhancement, rapid washout
Metastatic Lesions	Variable echogenicity, irregular margins	Variable enhancement, often multiple lesions
Other Breast Cancers	Irregular hypoechoic mass with microcalcifications	Irregular enhancement, spiculated margins

Abbreviations: US: Ultrasound; MRI: Magnetic Resonance Imaging.

Interventions

The patient was subsequently evaluated by multiple specialist figures during the Breast Unit meeting. The patient was able to speak with the breast specialist, oncologist, surgeon, psychologist, radiation oncologist, gynecologist, and other physicians. Only after this meeting and multidisciplinary evaluation, it was decided that the best course of action would be a neoadjuvant chemotherapy followed by a post-MRI checkup 5 months later. In fact, in agreement with the literature, neoadjuvant chemotherapy followed by surgery and adjuvant therapy is a commonly utilized treatment strategy for large breast angiosarcoma. The MRI showed a slight reduction in the mass on the left, which remained substantial in size, while the lesion on the right exhibited a fainter contrast enhancement. Therefore, the conclusion was a partial response to neoadjuvant therapy (Figure 3).

The patient and the breast specialists agreed to proceed with total surgery with bilateral mastectomy without reconstruction. These treatments were only the first part of a broader therapeutic plan, followed by intensive chemotherapy with targeted therapies to reduce the risk of recurrence and improve survival prospects.

Follow-up and outcomes

The patient underwent close monitoring thereafter with a clinical examination and ultrasound every

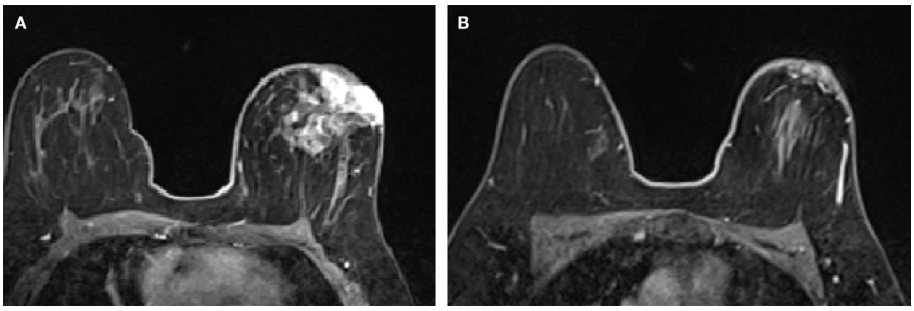

Figure 3 (A, B). 3T MRI. The image on the axial plane of a T1-weighted 3D acquisition of the first post-contrast dynamic frame: evidence of a substantial irregular mass, slightly reduced in size is still visible in the left retro-areolar region (A), and in the upper inner quadrant of the right breast, a faint and irregular formation with a weaker contrast enhancement compared to the previous examination is noticeable (B).

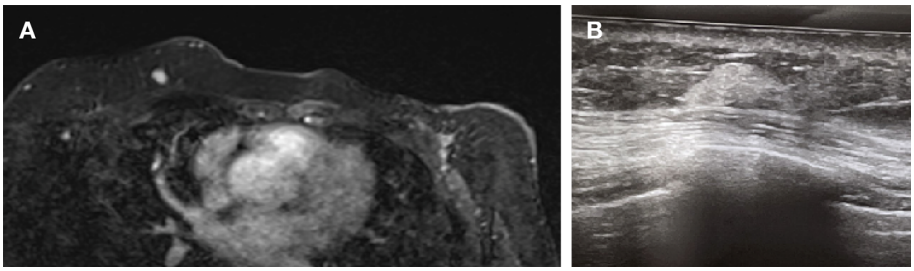

Figure 4 (A, B). (A) 3T MRI. The image on the axial plane of a T1-weighted 3D acquisition of the first post-contrast dynamic frame: the disease recurrence in a patient who underwent bilateral radical mastectomy reveals a small nodular formation with significant contrast enhancement in the soft breast tissues remaining on the right side. (B) Ultrasound: irregularly oval-shaped formation with heterogeneous hyper-echogenicity.

6 months, alternating with MRI, to ensure the absence of recurrence of an aggressive and often fatal pathology like angiosarcoma. Just one year later, during a routine MRI, a solid, slightly lobulated nodular formation with contrast enhancement measuring 15 mm was observed in the residual soft tissues on the right side in the superomedial/super-internal mammary region. This formation was further examined during a targeted second-look ultrasound, revealing a hyperechoic area suggestive of disease recurrence (Figure 4).

The patient was inevitably led to undergo further guided biopsy examination, which unfortunately confirmed the ominous diagnosis. The patient is currently being followed by an expert team of oncologists who have modified the ongoing therapy, making it as aggressive and responsive as possible towards a condition as little understood and as forceful and recurrent as angiosarcoma.

Discussion

Angiosarcoma is a rare and aggressive form of cancer that arises from the endothelial cells lining blood vessels or lymphatic vessels. While it can occur in various body parts, including the skin, soft tissues, and internal organs, breast angiosarcoma specifically refers to angiosarcoma originating in the breast tissue (7, 8). Angiosarcomas develop from endothelial cells that line blood and lymphatic arteries. These tumors can overgrow and spread (metastasize) throughout the body. While the specific etiology of breast angiosarcoma is rarely understood, some risk factors may increase the likelihood of acquiring the disease (9, 10). These factors may include prior breast radiation therapy, particularly for the treatment of other tumors such as breast cancer. Breast angiosarcoma symptoms can include a palpable breast tumor, swelling, skin changes (such as redness or coloring), and pain. However, these symptoms are not exclusive to angiosarcoma and can also be found in other breast disorders.

One of the challenges in managing breast angiosarcoma is its rarity, which can lead to delayed diagnosis and limited treatment options. Additionally, its aggressive nature and tendency to metastasize make it difficult to treat successfully. In fact, recurrence rates can range from approximately 30% to 50%, depending on the study and patient population. Similarly, mortality rates vary, but overall survival rates for breast angiosarcoma tend to be lower compared to more common types of breast cancer. However, advancements in imaging techniques, such as MRI and ultrasound, along with multidisciplinary approaches involving surgery, chemotherapy, and radiation therapy, have improved outcomes for some patients (11).

Conclusions

Angiosarcoma is a rare and aggressive form of cancer that poses significant challenges in diagnosis and treatment. Its rarity often leads to delayed diagnosis and limited treatment options, while its aggressive nature and tendency to metastasize make successful treatment

difficult. However, advancements in imaging techniques and multidisciplinary approaches have improved outcomes for some patients. Early detection of a solid lump through regular screenings and close monitoring is crucial for timely intervention as well for improving prognosis generally in breast cancer and also in the case of an unexpected histological outcome of angiosarcoma. Collaboration among healthcare professionals from various specialties is essential to develop personalized treatment plans tailored to each patient's specific needs. Despite these challenges, ongoing research and advancements in treatment strategies offer hope for better outcomes for patients with angiosarcoma. Raising awareness about this rare condition among healthcare professionals and the public is also crucial for facilitating early diagnosis and prompt management, ultimately improving patient outcomes and quality of life.

Ethics and Patient's Informed Consent: Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: The authors confirm contribution to the paper as follows: study conception and design: M.B. Author M.M. Author; data collection: M.M., Author, F. M. Author; analysis and interpretation of results: M.B. Author, F.M. Author, D.E. Author, F.A.C Author; draft manuscript preparation: M.B. Author, M.M. Author. G.G. Author. All authors reviewed the results and approved the final version of the manuscript.

References

1. Terrier P, Terrier-Lacombe MJ, Mouriesse H, Friedman S, Spielmann M, Contesso G. Primary breast sarcoma: a review of 33 cases with immunohistochemistry and prognostic factors. Breast Cancer Res Treat. 1989;13(1): 39-48. doi:10.1007/BF01806549
2. Arora TK, Terracina KP, Soong J, Idowu MO, Takabe K. Primary and secondary angiosarcoma of the breast. Gland Surg. 2014;3(1):28-34. doi:10.3978/j.issn.2227-684X.2013.12.03
3. Bentley H, Roberts J, Hayes M, et al. The Role of Imaging in the Diagnosis of Primary and Secondary Breast Angiosarcoma: Twenty-Five-Year Experience of a Provincial Cancer Institution. Clin Breast Cancer. 2023;23(2): e45-e53. doi:10.1016/j.clbc.2022.11.003
4. Wu WH, Ji QL, Li ZZ, Wang QN, Liu SY, Yu JF. Mammography and MRI manifestations of breast angiosarcoma. BMC Womens Health. 2019;19(1):73. Published 2019 Jun 10. doi:10.1186/s12905-019-0769-3
5. Scow JS, Reynolds CA, Degnim AC, Petersen IA, Jakub JW, Boughey JC. Primary and secondary angiosarcoma of the breast: the Mayo Clinic experience. J Surg Oncol. 2010;101(5):401-407. doi:10.1002/jso.21497
6. Gutkin PM, Ganjoo KN, Lohman M, et al. Angiosarcoma of the Breast: Management and Outcomes. Am J Clin Oncol. 2020;43(11):820-825. doi:10.1097/COC.0000000000000753
7. Kunkiel M, Maczkiewicz M, Jagiełło-Gruszfeld A, Nowecki Z. Primary angiosarcoma of the breast-series of 11 consecutive cases-a single-centre experience. Curr Oncol. 2018;25(1):e50-e53. doi:10.3747/co.25.3816
8. Dogan A, Kern P, Schultheis B, Häusler G, Rezniczek GA, Tempfer CB. Radiogenic angiosarcoma of the breast: case report and systematic review of the literature. BMC Cancer. 2018;18(1):463. Published 2018 Apr 24. doi:10.1186/s12885-018-4369-7
9. Darre T, Djiwa T, N'Timon B, Simgban P, Tchaou M, Napo-Koura G. Breast Primary Angiosarcoma: A Clinicopathologic and Imaging Study of a Series Cases. Breast Cancer (Auckl). 2022;16:11782234221086726. Published 2022 Mar 29. doi:10.1177/11782234221086726
10. Fraga-Guedes C, André S, Mastropasqua MG, et al. Angiosarcoma and atypical vascular lesions of the breast: diagnostic and prognostic role of MYC gene amplification and protein expression. Breast Cancer Res Treat. 2015;151(1):131-140. doi:10.1007/s10549-015-3379-2
11. Esposito E, Avino F, di Giacomo R, et al. Angiosarcoma of the breast, the unknown-a review of the current literature. Transl Cancer Res. 2019;8(Suppl 5):S510-S517. doi:10.21037/tcr.2019.07.38

Corresponding Author:
Received: 16 February 2024
Accepted: 19 March 2024
Giuseppe Guglielmi, MD and Professor of Radiology, Department of Clinical and Experimental Medicine, Foggia University School of Medicine, Viale L. Pinto 1, 71122, Foggia, Italy;
E-mail: giuseppe.guglielmi@unifg.it
ORCID: 0000-0002-4325-8330