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Review Article

Rare case of bilateral primary breast angiosarcoma and review of literature

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ABSTRACT

Primary angiosarcoma of the breast is very rare, accounting for 0.05% of all malignant breast tumors, and it usually occurs in younger individuals. To the best of our knowledge, bilateral primary angiosarcoma is extremely rare, with only 16 cases reported in the published literature. The imaging features might give a false impression of a benign lesion, delaying diagnosis.

We report a case of a 34-year-old woman with a left breast lump. Her initial core needle biopsy was negative, and she was briefly lost to follow-up. However, when she returned with worsening symptoms, a vacuum-assisted biopsy revealed angiosarcoma. After undergoing surgery, she received radiation therapy but subsequently developed angiosarcoma in the contralateral breast. Our case is unique because we present the variable imaging appearances of angiosarcoma using imaging modalities such as mammography, ultrasound, MRI, and PET-CT, at the time of initial presentation, final diagnosis, and recurrence.

We also report the successful use of a vacuum-assisted breast biopsy following a non-diagnostic core needle biopsy without experiencing overt bleeding during the procedure in a case of angiosarcoma. There have been very few reported cases in which vacuum-assisted biopsy has been performed in cases of angiosarcoma, indicating that it can be used in hypervascular masses without the risk of excessive bleeding, especially when an initial core biopsy is discordant.

Keywords: Bilateral breast angiosarcoma, Breast sarcoma, Hypervascular breast mass, Hyperechoic breast mass, VABB

INTRODUCTION

Angiosarcoma of the breast is an extremely rare type of cancer that can either develop as a primary neoplasm or as a result of previous radiation therapy after breast-conserving surgery. About 20% of angiosarcomas are of primary type. The incidence of primary breast angiosarcoma is approximately 17 new cases per million women.[1] Primary lesions typically affect younger individuals, usually in their thirties or forties.[2] On ultrasound, they may appear as a hyperechoic lesion, and on T2-weighted (T2W) imaging, they may appear hyperintense, misleadingly resembling benign lesions. Management of angiosarcoma involves surgery, sometimes followed by chemotherapy. Since most of the angiosarcomas are caused by prior radiation treatments, whether radiotherapy might be used for treatment remains an issue. The prognosis is usually poor.[3,4]

CASE REPORT

We present a case of a 34-year-old woman, who came to our hospital with a painful lump in her left breast. She had no personal or family history of breast or ovarian cancer and was otherwise in good health. A physical exam revealed a lump in her left breast. No axillary lymphadenopathy was palpated. The mammogram [Figure 1] revealed a focal asymmetry in the upper-outer quadrant of the left breast, with no signs of microcalcification or distortion. An ultrasound of the breast [Figure 2] revealed a hyperechoic mass with indistinct margins in the area where palpable abnormality was felt, between the 12 and 1 o'clock position in the left breast. The etiology of this lesion was unclear, but due to its hyperechoic appearance on ultrasound, a benign etiology was considered. A breast MRI [Figure 3] revealed an area of non-mass enhancement (NME) in the upper-outer quadrant of the left breast. A core biopsy of the lesion was performed with a 14-gauge needle, which revealed fibromuscular tissue with a few vessels and no signs of malignancy, ductal carcinoma in situ, or inflammatory cells. However, the regional NME seen on the breast MRI in this area could not be explained by normal histopathology. Hence, the histopathology was considered discordant, and a repeat biopsy was recommended.

An incidental finding of a radial scar in the upper-outer quadrant of the right breast was also confirmed through a core needle biopsy. It appeared as a stellate lesion with a lucent center on the mammogram [Figure 1], a hypoechoic area with marked shadowing on ultrasound (images not included), and a spiculated lesion with central enhancement on the MRI [Figures 3]. During a subsequent surgery for the left breast lesion, a wire-guided lumpectomy was performed for the radial scar. The final histopathology revealed a radial scar with a small area of apocrine atypical ductal hyperplasia with clear margins.

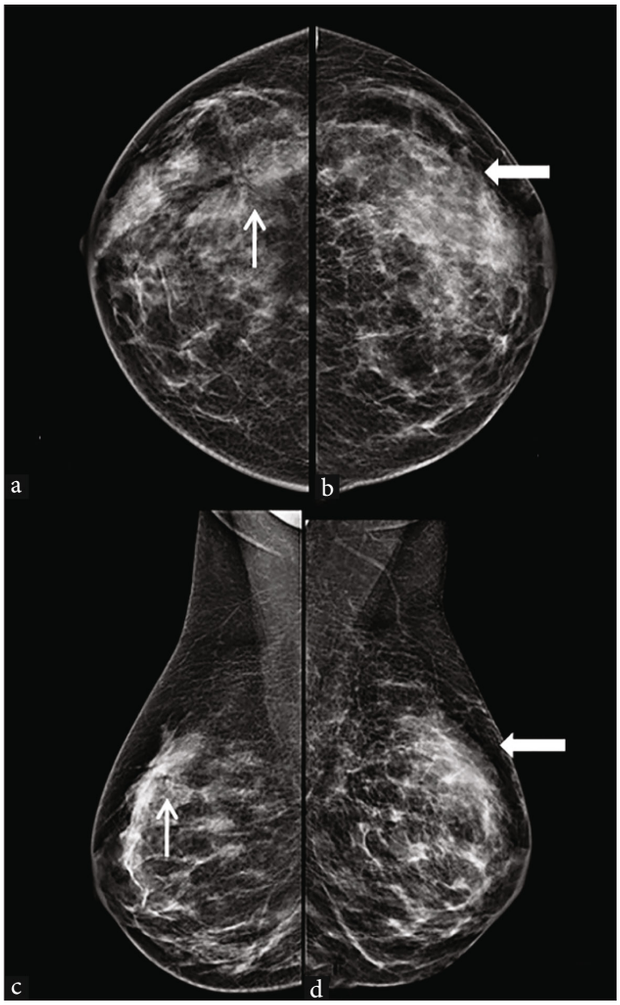

Figure 1: Mammogram in (a-b) craniocaudal and (c-d) mediolateral oblique views showed a stellate lesion with lucent center in the upper-outer quadrant of right breast (thin white arrows). Focal asymmetry was seen in the upper-outer quadrant of the left breast in the area of palpable abnormality with no microcalcification or distortion (thick white arrows).

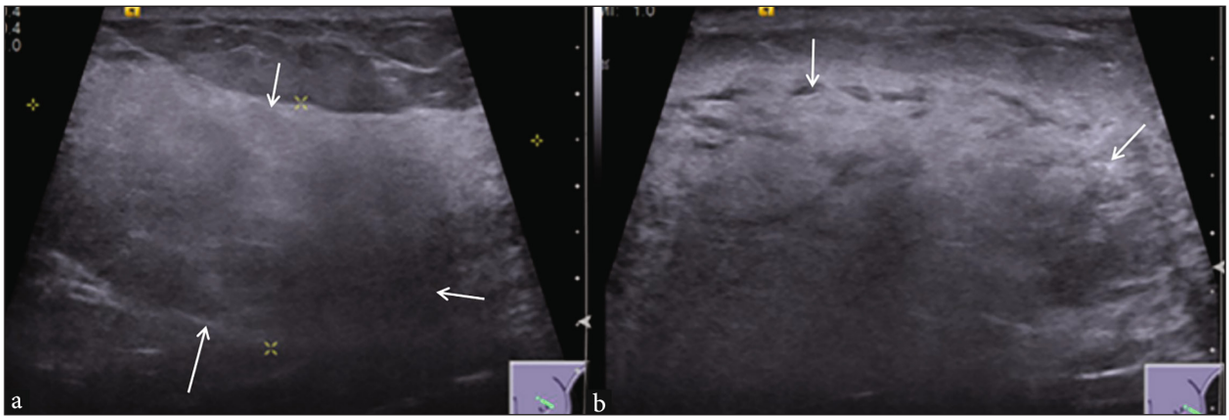

Figure 2: (a-b) Ultrasound breast revealed a hyperechoic mass (white arrows) with indistinct margins from 12 to 1 o'clock position in the left breast.

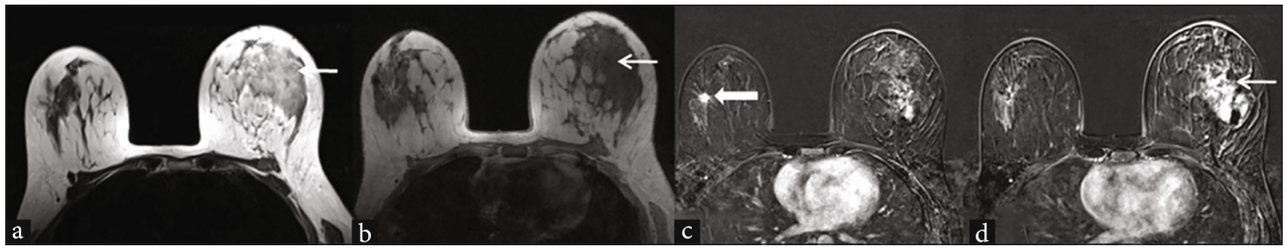

Figure 3: Contrast-enhanced MRI revealed (a) ill-defined T2W hyperintensity (white arrow) and (b) T1W hypointensity (white arrow) with indistinct margins in the upper-outer quadrant on the left side. (c-d) Post-contrast images revealed a small spiculated enhancing lesion in the right breast (thick white arrow) at 10 o'clock position (biopsy-proven radial scar) and segmental non-mass enhancement (thin white arrow) in the area of abnormality in the left breast. MRI: magnetic resonance imaging.

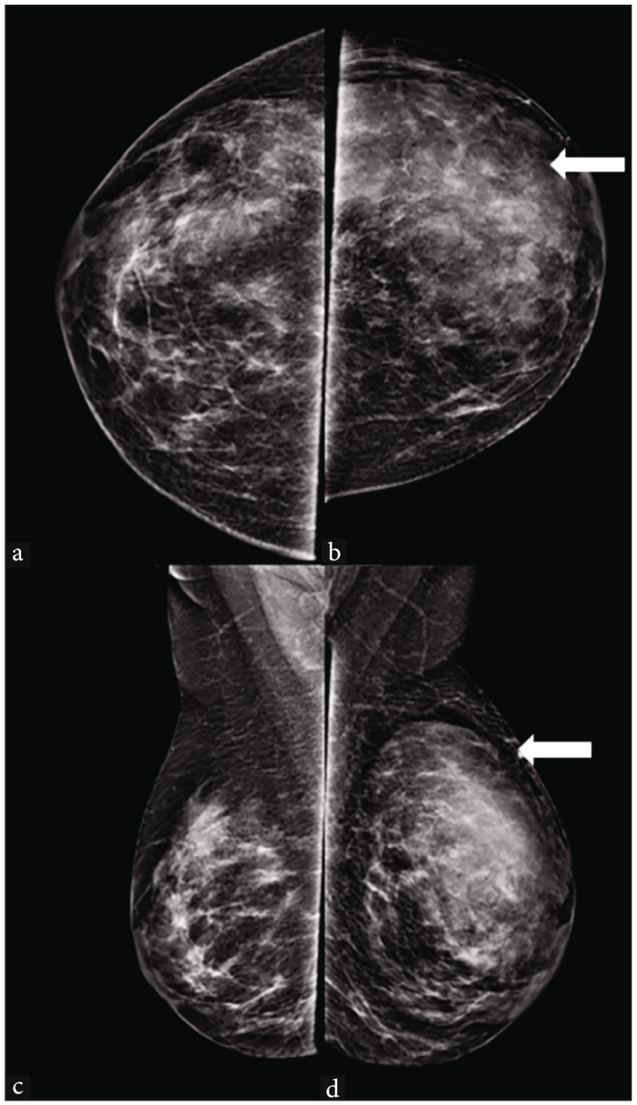

Figure 4: Mammogram in (a-b) craniocaudal and (c-d) mediolateral oblique views after six months, revealed no significant change on the right side and an interval increase in the area of abnormality in the upper-outer quadrant of the left breast (thick white arrows).

The patient returned after six months due to the COVID-19 pandemic, with a significant increase in size and bluish discoloration of the overlying skin of the left breast. Repeat imaging revealed a partially obscured mass in the upper-outer quadrant of the left breast on the mammogram [Figure 4]. On ultrasound [Figure 5] examination, a large non-mass lesion nearly occupying the whole of the upper and outer half of the left breast, having heterogenous echotexture with predominant echogenic areas and mixed hypoechoic areas with mild vascularity was observed. The abnormality had significantly increased in size compared to the previous scan, and atypical malignancy was suspected. A repeat CEMRI breast [Figure 6] revealed left breast enlargement due to a large, ill-defined T2 hyperintense and T1 hypointense lesion with indistinct margins and areas of normal fat trapped within. It revealed intense persistent enhancement with few susceptibility artifacts as well as few hyperintense foci on T1 fat-saturated sequences, suggestive of hemorrhagic products. At the posterior aspect of the lesion, there was a non-enhancing, well-circumscribed component with marked T2 hypointensity likely chronic hemorrhagic products. Furthermore, there was mild restricted diffusion and low ADC values. Edematous changes were seen around the lesion. Mild skin thickening was also seen on the left side. No evidence of any large feeding vessels or early draining veins was seen. No evidence of any abnormally draining lymph node was seen. Although the lesion was hyperechoic on ultrasound and hyperintense on the MRI breast, due to its rapid growth and intense contrast enhancement, the possibility of an atypical sinister etiology was kept. To ensure a representative sample, since the previous core biopsy was negative from the lesion, an ultrasound-guided vacuum-assisted biopsy was performed with a ten-gauge needle, and high-grade angiosarcoma was confirmed on histopathology, which had rapidly increased in size due to internal bleeding. There was no excessive bleeding at the

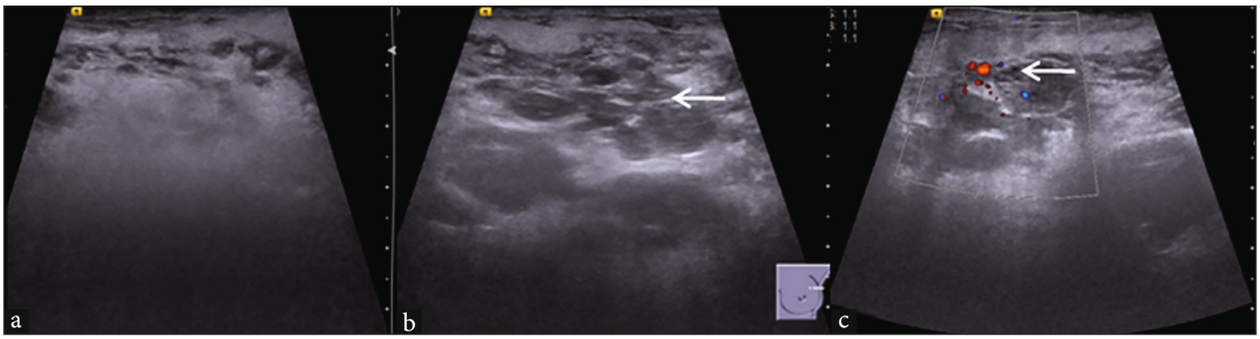

Figure 5: Ultrasound breast showed (a) a large non-mass lesion nearly occupying the whole of the upper and outer half of the left breast, having heterogenous echotexture with (b) predominant echogenic areas and mixed hypoechoic (white arrow) areas with (c) mild vascularity (white arrow). The area of abnormality had significantly increased as compared to the previous scan.

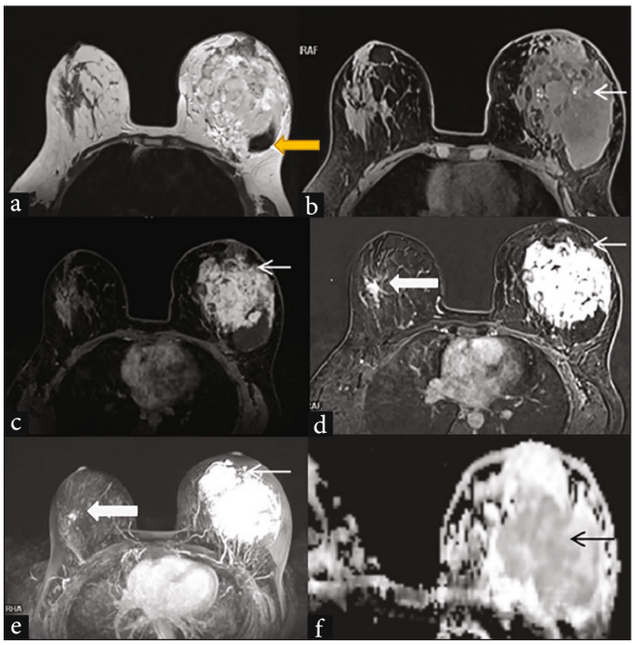

Figure 6: Repeat Contrast-enhanced MRI breast showed (a-b) enlargement of the left breast due to a large T2 hyperintense and T1 hypointense lesion with indistinct margins and areas of normal fat trapped within, few hyperintense foci on T1 fat-saturated sequences (white arrow), few susceptibility artifacts, and a non-enhancing, well-circumscribed component with marked T2 hypointensity on the posterior aspect likely chronic hemorrhagic products (thick yellow arrow). (c-e) It revealed intense persistent enhancement (thin white arrows). Radial scar was seen as before (thick white arrows). (f) Diffusion weighted imaging showed mild restricted diffusion in the left breast mass with low apparent diffusion coefficient (ADC) values (black arrow). MRI: Magnetic resonance imaging.

time of biopsy. A total body PET-CT scan didn't show any metastasis. The patient underwent a left-sided mastectomy and a sentinel node biopsy. Histologically [Figure 7], the tumor showed papillary formations and vascular structures lined by atypical cells with hyperchromatic nuclei and eosinophilic cytoplasm. Extensive areas of hemorrhage, or "blood lakes," and necrosis were also seen, which led to a rapid increase in size. Dissected axillary lymph nodes were free of tumor [pT3N0 (sn)]. The immunohistochemical studies show positivity for CD31 and Factor VIII, while D2-40 was negative. The proliferative index Ki-67 was 35–50%. Adjuvant chemotherapy and radiotherapy were also prescribed to our patient in anticipation of high rates of recurrence and metastasis. However, the patient was not keen on taking chemotherapy. Therefore, after a multidisciplinary tumor board discussion, the decision to administer localized radiation therapy was made, and she received 30 fractions of adjuvant radiation (60Gy) to the left chest wall. She was lost to follow-up for about one year after radiation therapy and then presented with pain in the left thigh and gluteal region. Evaluation with PET-CT [Figure 8] revealed an inconsistent appearance of a mildly hypermetabolic heterogeneously enhancing mass in the lower outer quadrant of the right breast along with moderately hypermetabolic lesions in the left hemipelvis and left femur and multiple tiny bilateral lung nodules. This was deemed to be a progressive disease (M1; Oss, Lungs).

Mammography and ultrasound were performed to further characterize the mass in the right breast. The mammography [Figure 9] revealed an irregular, dense mass in the lower inner quadrant of the right breast. The ultrasonography [Figure 10] revealed an avascular irregular hypoechoic mass with long tubular extensions within a large area of hyperechogenicity at the 5 o'clock position in the area of PET-CT concern, with prominent ducts seen adjacent to it. An ultrasound-guided biopsy was performed for the right breast lesion, and angiosarcoma was confirmed on histopathology.

In light of the metastatic nature of the disease, local breast surgery was deferred, and the patient received palliative

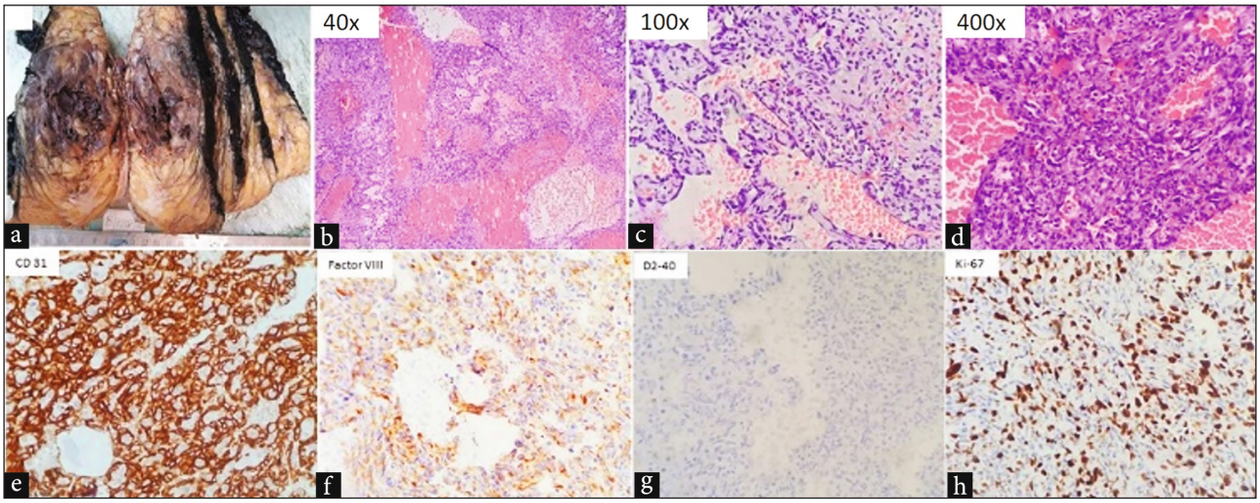

Figure 7: (a) Gross image of left mastectomy specimen showed a large, ill-defined gray-brown mass measuring 110 mm. (b–d) Hematoxylin and eosin (H&E) stained sections at (b) 40x, (c) 100x and (d) 400x magnification showed anastomosing vascular channels lined by moderately pleomorphic hyperchromatic spindle cells with oval to elongated nuclei. Mitosis was brisk, and foci of solid areas were seen. The immunohistochemical studies showed positivity for (e) CD31 and (f) Factor VIII, while (g) D2-40 was negative. (h) The proliferative index Ki-67 was 35–50%.

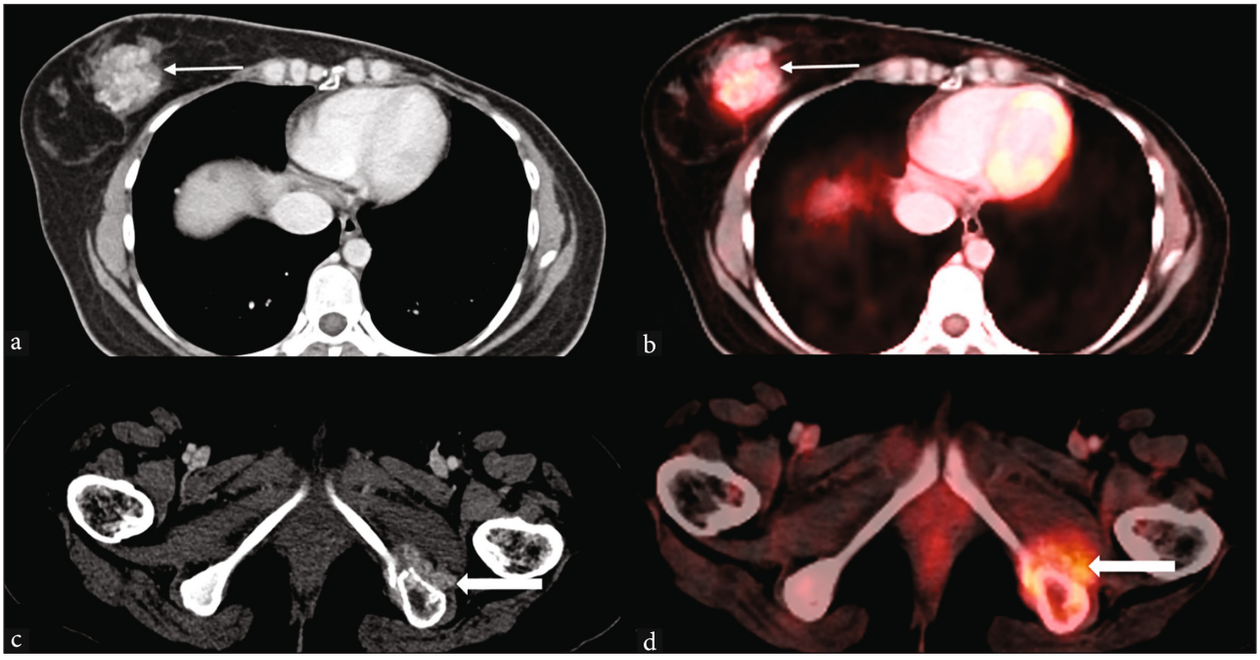

Figure 8: Follow-up PET-CT, one year after completion of adjuvant radiotherapy revealed (a-b) interval appearance of an FDG avid (SUV max 7.89) heterogeneously enhancing mass (white arrows) in the lower inner quadrant of the right breast and (c-d) an FDG avid (SUV max 13.14) lytic lesion with an enhancing soft tissue component associated with pathological fracture (thick white arrows) in the left inferior ischiopubic ramus. A few other hypermetabolic lesions in the femur, acetabulum, and multiple tiny random lung nodules were also noted (not shown). PET-CT: Positron emission tomography-Computed tomography, FDG: 18-fluorodeoxyglucose, SUV: Standardized uptake value.

radiotherapy at the symptomatic site. Subsequently, the patient underwent multiple lines of systemic chemotherapy for multiple recurrences observed on serial PET-CT scans over a period of five years since the initial diagnosis. The last PET-CT revealed stable disease, and the patient is otherwise doing well.

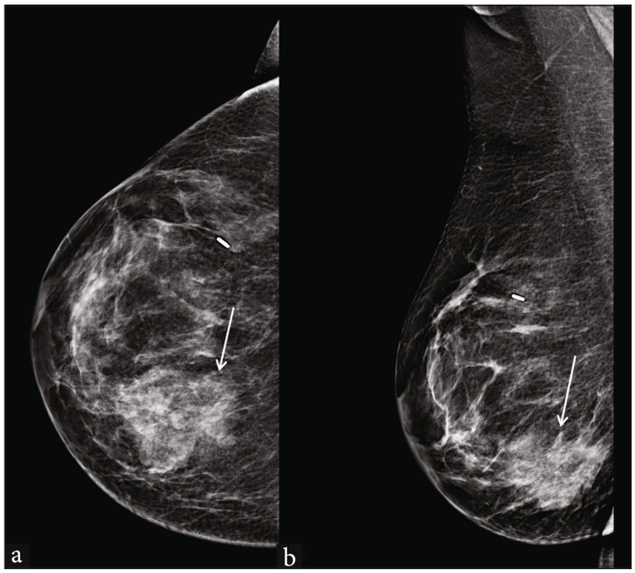

Figure 9: (a-b) Right mammogram (craniocaudal and mediolateral oblique views) revealed an irregular, dense mass in the lower inner quadrant of the right breast (white arrows).

DISCUSSION AND REVIEW OF LITERATURE

Breast is one of the common organs affected by angiosarcoma.[5] Breast angiosarcoma was first described by Schmidt in 1887.[6] It is classified into primary, i.e., arising de novo, or secondary, to chronic lymphoedema or breast irradiation after breast-conserving surgery.[2,7] Over a period of ten years from 1997 to 2007, Wang *et al.* reported more than 5,000 cases of breast tumors, which included only 11 cases of breast angiosarcomas, out of which only one was a primary breast angiosarcoma.[8] It represents less than 0.05% of all malignant breast tumors.[9] To the best of our knowledge, till now, there are only 16 case reports of bilateral primary breast angiosarcoma in the literature. Primary angiosarcomas of the breast usually develop during the third and fourth decades of life (with a median age of 35 years), although few cases have been reported in postmenopausal women.[10] Primary angiosarcoma usually arises in the non-irradiated breast parenchyma, and patients usually present with a rapidly growing palpable painless lump (≥4 cm), rarely associated with purple-blue skin discoloration as in our case. In the series by Yang *et al.*,[11] the mean tumor size of the mass at presentation was 5.9 cm. Mammographically, the appearance is nonspecific. An ill-defined, non-calcified mass or focal asymmetry is the most common finding.[11] Liberman *et al.*[12] reported that 33% of angiosarcomas in their series were not detectable mammographically. In the study by Yang *et al.*[11] 19% of patients had tumors that were not visible mammographically but were visible with sonography and MRI thereafter. Various studies have shown that angiosarcomas reveal both hyperechogenicity

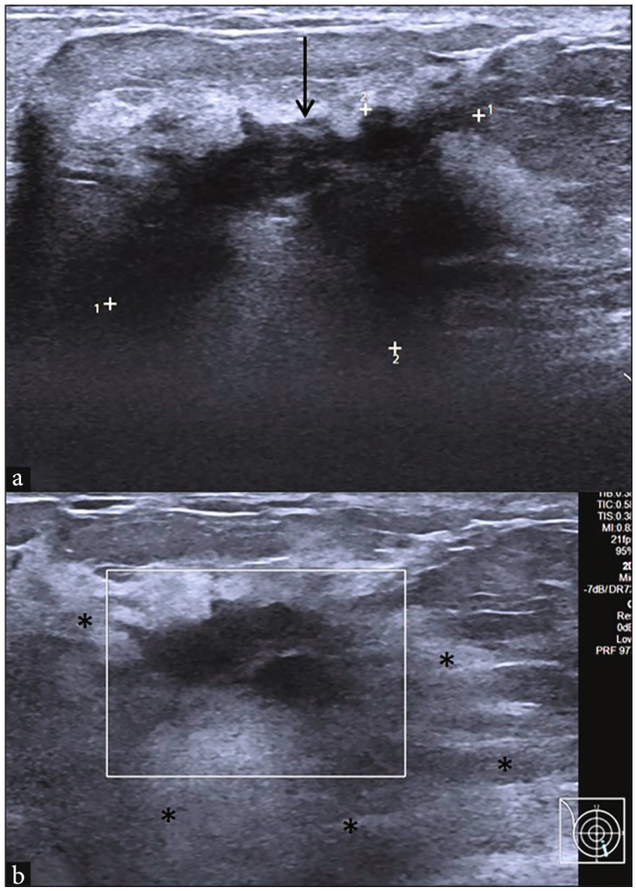

Figure 10: (a-b) Ultrasound showed an irregular ill-defined hypoechoic mass (black arrow) with long tubular extensions, (+) at 5 o'clock position. Surrounding marked hyperechogenicity (black asterisks) was seen increasing the overall area of abnormality. No significant vascularity was seen in the lesion on color doppler imaging (white rectangle).

as well as mixed hyper- and hypoechogenicity. Even in our case, the lesion was hyperechoic on the first ultrasound and had developed hypoechoic areas on the second interval ultrasound. The hypoechoic areas are due to bleeds, which explains the rapid increase in the size of the lesion in our case. The hyperechoic appearance of the lesion can provide false reassurance, so features like NME in MRI should be viewed as suspicious for a sinister etiology.[12] Internal vascularity is usually reported[13] aligning with our case. However, the right breast lesion showed a lack of vascularity, but its other characteristics were more typical of malignancy, seen as an irregular and ill-defined hypoechoic mass with long tubular extensions within a large area of hyperechogenicity. Thus, our case is unique as it showcases all the varied imaging appearances of angiosarcoma, also highlighting the temporal changes possible and emphasizing the importance of keeping a low threshold for doing an MRI and/or biopsy.

MRI is thought to be the best modality for diagnosing angiosarcoma.[13] Our case also highlights the diverse MR appearance, with NME being the only feature seen initially. However, the latter MRI showed a heterogeneously enhancing mass with areas of hemorrhage. T2 hyperintensity should not be used as an exclusion criterion for malignancy, as angiosarcomas are often hyperintense on heavily weighted T2 images.[2] Low-grade angiosarcomas show progressive enhancement on dynamic MRI imaging, while high-grade angiosarcomas show rapid enhancement and washout, and large draining vessels may be visualized.[2] We observed rapid early enhancement with persistence in a dynamic study. Diffusion-weighted imaging can help to some degree, with low ADC values being in more favor of malignant etiology. Previous published reports lack data about diffusion-weighted imaging, and this should be further studied.

PET with 18-FDG can be used in staging angiosarcoma. Case reports have shown focal, intense accumulation of FDG in angiosarcomas.[2] However, FDG uptake can also be relatively low, possibly due to blood products. In our case, the SUV maximums were 8.84 and 7.89 for the left and right breast lesions, respectively.

A fine needle biopsy may give false negative results in a quite high percentage of cases.[5,14] Therefore, a core biopsy is recommended. In cases of worsening clinical features or radio-pathological discordance, a repeat biopsy can be considered, as we proceeded with, in our case.

The prognosis in primary breast angiosarcoma is usually poor due to the high risk of recurrence and metastasis. High tumor grade and positive margins are mainly associated with local recurrence. The average survival is between 25 and 48 months.[15] However, with improved treatment, the survival rates are also improving. In our case, despite recurrence, the patient is doing well on chemotherapy.

The treatment of primary breast angiosarcoma usually involves surgery in the form of a simple mastectomy, although breast-conserving surgery can be considered in selected cases. Axillary clearance is generally not performed, as tumors do not usually follow lymphatic dissemination. Only large tumors invading the axilla necessitate an axillary node dissection.[4,16] Adjuvant chemotherapy and/or radiotherapy seem to improve survival.[16] Primary breast angiosarcoma is a rare entity, and literature contains only a few data regarding adjuvant treatment, and there is no generally agreed standard course of action. A multidisciplinary discussion should always be held to decide the best course of action. Hormonal treatment doesn't seem to be appropriate since these tumors usually do not express estrogen receptors.[17]

Dynamic contrast-enhanced MRI with diffusion-weighted imaging and histologic examination should be performed at the earliest for a suspected angiosarcoma of the breast.[13] Early and precise diagnosis remains the most important prognostic factor. Randomized, controlled, prospective studies should ideally be undertaken to have a better understanding of the role of adjuvant treatment in breast angiosarcoma. However, the rarity of the disease is an obstacle to these studies. It is thus important to report these cases and to present treatments and the patient's evolution.[17]

CONCLUSION

The diagnosis of breast angiosarcoma is challenging for the radiologist. The young patient population, nonspecific radiological findings, and ordinary symptoms pose challenges for the radiologist. Hyperechogenecity or T2 hyperintensity can give a false reassurance of benignity. Hence, radiologists should be aware of the variable imaging appearances of angiosarcoma on different imaging modalities to avoid a misdiagnosis. Further, a repeat biopsy should be considered where the initial biopsy is discordant and a vacuum-assisted biopsy can be an alternative for the same to acquire a better representative sample.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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