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Case Report

Radiology Section

Primary Angiosarcoma of the Breast: A Case Report with Multimodality Imaging Workup

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ABSTRACT

Angiosarcomas of the breast are rare and aggressive malignant tumours. They are further divided into primary and secondary angiosarcomas. Primary angiosarcomas occur sporadically in young women; whereas secondary angiosarcomas are seen post radiation therapy. We hereby report a case of a biopsy proven primary angiosarcoma of the breast in a young female patient; highlighting the role of imaging in its diagnosis. On mammographic evaluation the angiosarcoma appeared as a large, ill-defined, high density, lobulated breast mass, raising suspicion of a malignant Breast Imaging-Reporting and Data System (BI-RADS) 4 lesion. Breast Ultrasound (US) and colour Doppler findings of this mass demonstrated features of a malignant vascular tumour. This was further confirmed by the contrast enhanced breast MRI findings of an intensely enhancing mass with type II contrast kinetics. Thus, adequate knowledge of the imaging features of primary angiosarcoma of the breast, on various imaging modalities is imperative for making an accurate and timely diagnosis of this rare malignancy with a poor prognosis.

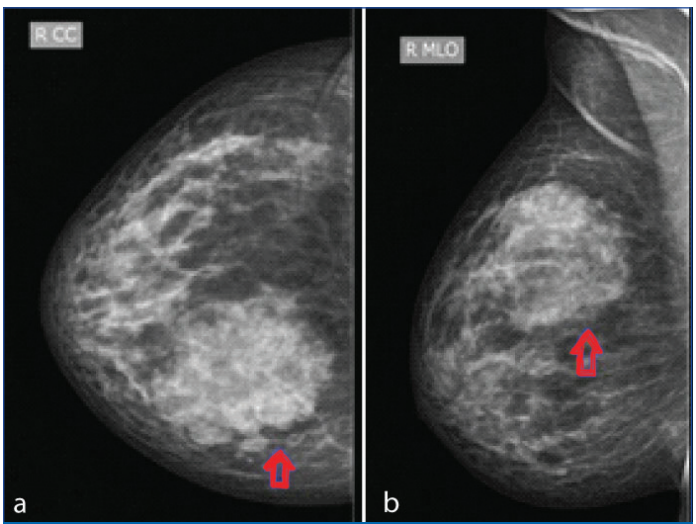
Keywords: Breast neoplasms, Diagnostic imaging, Mammography

CASE REPORT

A 34-year-old female patient presented with chief complaint of lump in the right breast associated with bluish discoloration of the overlying skin since one month. She also gave history of accidental injury to the right breast caused by her pet dog one month ago. She did not have any family history of breast cancer. There was no history of nipple discharge also.

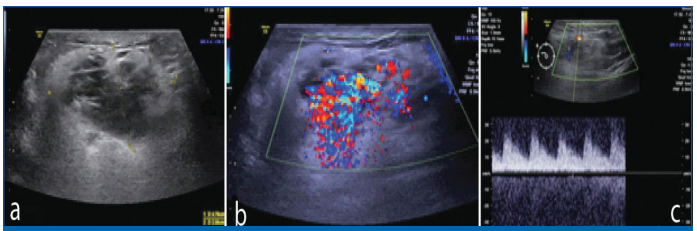
On examination, a slightly tender, immobile palpable lump with firm to hard consistency was identified in the upper inner quadrant of the right breast. It was associated with mild bluish discoloration of the overlying skin. No axillary swelling or lymphadenopathy was evident.

A mammogram and breast US were requested for further evaluation of the lump. Mammography was performed on a Mammomat Analogue Mammography system (Siemens Healthcare, Erlangen, Germany). The medio-lateral oblique and cranio-caudal views of right breast showed a large, ill defined, high density, lobulated mass in the upper inner quadrant [Table/Fig-1a,b]. No intralesional calcifications were noted. No obvious skin thickening, nipple retraction or axillary lymphadenopathy was appreciated. BI-RADS 4 category was assigned to the right breast mass, on mammography.



[Table/Fig-1]: Mammogram of right breast. (a) The craniocaudal (CC); and (b) mediolateral oblique (MLO) views showing a large, ill defined, high density, lobulated mass (red arrows) in the upper inner quadrant of the right breast.

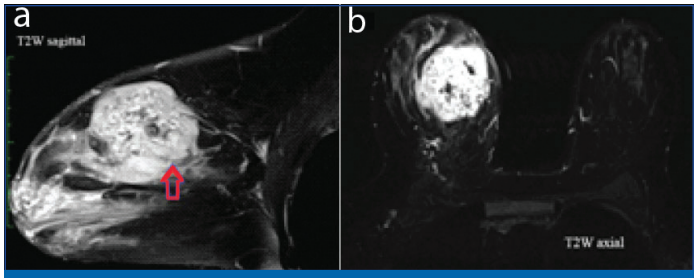
Breast US performed on an EPIQ 7G Ultrasound Colour Doppler system (Philips Healthcare, the Netherlands) using linear transducer of 18-5 MHz frequency; revealed a hypoechoic, solid mass with ill-defined margins, in the right breast (12-3 o' clock position) [Table/Fig-2a]. The mass measured approximately 4.7cm x 2.5 cm in dimensions and showed subtle posterior acoustic enhancement. No intralesional calcifications were seen. On colour Doppler evaluation the mass was found to be hypervascular with significant intralesional vascularity, predominantly observed in the centre of the lesion [Table/Fig-2b]. The spectral trace within these intralesional vessels showed a low velocity and low resistance flow pattern with Resistive Index (RI) of 0.4 [Table/Fig-2c]. No axillary lymphadenopathy was identified on US. In view of its large size, ill-defined lobulated margins and presence of hypervascularity, a diagnosis of malignant vascular tumour was made for the breast mass on US.



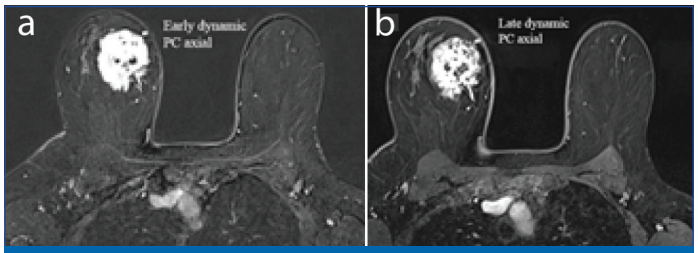
[Table/Fig-2]: Ultrasound (US) and Colour Doppler of the right breast mass. (a) Grey scale US image showing an ill-defined hypoechoic solid mass with a hyperechoic rim in the upper inner quadrant of the right breast. It measures approximately 4.7x2.5 cm in transverse antero-posterior dimensions; (b) Colour Doppler image showing hypervascular nature of this breast mass with significant central vascularity; (c) Spectral trace showing presence of low velocity and low resistance flow in the vessels within the breast mass (Resistive Index=0.4).

Magnetic Resonance Imaging (MRI) was advised for further assessment of the characteristics as well as extent of this mass. Plain and contrast enhanced MRI of the breast was performed on a 1.5 Tesla MR system, (Siemens Healthcare, Erlangen, Germany), using a dedicated 15-channel breast coil. The MR images demonstrated a large, ill-defined right breast mass with irregular, lobulated margins. The mass appeared hypointense on T1-Weighted (TIW) images. On T2-Weighted (T2W) and Short Tau Inversion Recovery (STIR) images, it appeared hyperintense with few hypointense foci within [Table/Fig-3a,b]. On post contrast MR images, intense enhancement was seen with few non-enhancing areas within (representing necrosis) [Table/Fig-4a,b]. On dynamic post-contrast evaluation, the breast mass showed early rapid uptake of contrast with delayed persistent

enhancement, indicating type II (plateau curve) contrast kinetics. No obvious invasion of the underlying pectoral fascia or muscles or



[Table/Fig-3]: MRI of the breasts. (a) T2W sagittal and (b) T2W axial fat-suppressed MR images showing an ill-defined hyperintense mass (red arrow) with few hypointense foci within; in the upper inner quadrant of the right breast. This mass shows irregular lobulated margins.



[Table/Fig-4]: Contrast-enhanced breast MRI. (a) Early dynamic (2 min), fat- suppressed, contrast enhanced T1 axial image of the breasts demonstrating early rapid uptake of contrast with intense enhancement of the right breast mass, interspersed with few non-enhancing areas representing necrosis. (b) Late dynamic (8 min), fat- suppressed, contrast enhanced T1 axial image showing delayed persistent enhancement within the right breast mass

of the overlying skin was seen. No axillary lymphadenopathy was identified.

Correlating the MRI features of intense post contrast enhancement with US feature of hypervascularity and considering the absence of axillary lymphadenopathy and skin changes; an imaging diagnosis of angiosarcoma of the breast was made. In the absence of any history of exposure to radiation therapy, a diagnosis of primary angiosarcoma of the breast was considered.

US guided core biopsy obtained from breast mass, revealed vascular structures with vessel walls showing cell atypia and hyperchromatic nuclei. Solid areas of the mass also showed atypical cells interspersed with the vascular structures. A diagnosis of Grade 3 Angiosarcoma was given on histopathology. The patient further underwent total mastectomy of the right breast, followed by adjuvant chemotherapy. She expired six months after the initial diagnosis.

DISCUSSION

Angiosarcomas are rare malignant tumours that arise from endothelial cells [1,2]. Primary angiosarcomas of the breast occur sporadically in young women and usually present as palpable breast masses. Secondary angiosarcomas of breast occur most frequently following radiation therapy; the average latency period being 5-6 years [3]. Primary angiosarcomas are rare and constitute 0.04% of all malignant breast tumours [4].

Histologically angiosarcomas of breast have been classified into low-grade (Type I), intermediate grade (Type II) and high-grade (Type III) tumours [5]. High-grade angiosarcomas have poorest prognosis [5]. Multiple grades may exist in the same tumour, so grading from a core biopsy specimen may not be possible. Complete excision and careful histologic evaluation are needed to accurately determine the tumour grade [6]. Primary angiosarcomas arise in younger women, usually during the third and fourth decades of life. These patients usually present either with a rapidly growing palpable mass or skin discoloration or rarely skin plaques or nodules, or a combination of these signs. Bluish discoloration of the overlying skin occurs in around one third of patients and is thought to be attributable to the vascular nature of the tumour.

On mammography, angiosarcoma usually presents as an ill-defined, non-calcified, radio-dense mass or as a focal asymmetry. In the series by Yang WT et al., the mean size of the breast mass at presentation was 5.9 cm [4]. Sometimes dense breast parenchyma in young women may obscure visualisation of the mass. On US, the mass may show circumscribed or ill-defined margins and may appear either hypoechoic or of mixed echogenicity. Colour Doppler US demonstrates hyper vascularity [3].

MRI of angiosarcoma shows a heterogeneous mass with low signal intensity on T1W images and high signal intensity on T2W images; as was seen in the index patient [4]. Irregular areas of high T1 signal may be seen in the higher-grade lesions; these represent areas of haemorrhage or venous lakes. Enhancement of the mass depends on tumour grade. Low-grade angiosarcomas show progressive enhancement. High-grade angiosarcomas present as heterogeneous masses with areas of necrosis and haemorrhage and show rapid post contrast enhancement with washout. MRI is useful in determining tumour extent and in pre-surgical evaluation of the patient.

Positron Emission Tomography (PET) with 18F-FDG (Fluorodexyglucose) may be used for staging of angiosarcoma. PET CT shows focal, intense accumulation of FDG in the angiosarcoma with standard uptake values up to 7.5 [7-9]. Regions with spread of angiosarcoma also show avid FDG uptake thus helping in tumour staging.

[Table/Fig-5] compares the clinical and imaging findings described in the index patient of primary angiosarcoma of breast to those described in earlier comparable case reports [10-12].

Secondary angiosarcomas usually are found in older women who have undergone breast cancer treatment. The mean age at presentation is the late 60s [3]. These are of two types -lymphedema-associated cutaneous angiosarcoma and post-irradiation angiosarcoma.

On mammograms changes due to breast conservation therapy and prior radiation therapy such as skin thickening are visible. The subgroup of cases with parenchymal involvement may present with ill-defined, asymmetric masses. On breast US, skin thickening is noted. Intra parenchymal masses are seen as heterogeneous echogenicity areas. MRI shows rapid gadolinium enhancement and plateau or washout with delayed imaging features similar to primary angiosarcoma [4].

Surgical resection with mastectomy is the mainstay of treatment for both primary as well as secondary forms of angiosarcoma. For small and grade 1 primary angiosarcomas, breast conservation therapy may be considered. Chemotherapy may be needed in patients with high grade tumour and distant metastases. Hyper-fractionated radiation therapy may be useful in secondary high-grade angiosarcomas. It results in reduction of the cell repopulation of rapidly growing tumours [13].

The prognosis for patients with primary angiosarcoma depends on the tumour grade. The estimated probability of disease-free survival 5 years after initial treatment is 76% for patients with grade 1 tumours and 15% for patients with grade 3 tumours [5].

Metastatic spread is haematogenous and occurs most frequently to bones, lungs, and liver. Metastases to the contralateral breast also have been reported [3,5,6]. Secondary angiosarcomas tend to have a poor prognosis as compared to primary. Outcome is also affected by the completeness of surgical resection. Local recurrence is an adverse prognostic indicator and is often accompanied by distant metastases [3].

CONCLUSION

Primary angiosarcoma of breast is a rare and aggressive malignant tumour. This case of a young woman with a palpable breast lump, illustrates that multi-modality breast imaging workup using the available imaging techniques such as Mammography, US and MRI; aids in making an accurate diagnosis of rare malignant masses

Reference	Age of the female patient	Clinical presentation and Clinical breast examination [CBE] findings	Imaging Features	Histo-pathology
Bhosale SJ et al., [10]	28 years	Presented with rapidly progressive breast lump for 1 month CBE- Firm, non-tender mass in upper inner quadrant of right breast. No evidence of nipple retraction, skin thickening or axillary lymphadenopathy.	Mammography- Ill-defined, non spiculated and non-calcified lobulated breast mass, 5 cm in diameter. USG, MRI not done	Grade II angio-sarcoma
Bennani A et al., [11]	33 years	Presented with a painful slowly growing mass in right breast over a period of 1 year. CBE- firm asymmetry in right lower, inner breast with blackish discolouration of overlying skin; Lesion measured about 13x12 cm in size. It was firm and appeared to be fixed to the skin. No axillary lymphadenopathy.	Mammography- Ill-defined, non spiculated and non-calcified lobulated breast mass, 5 cm in diameter. USG showed a diffuse and ill- defined hyperechoic infiltrating, lesion in right breast, lesion was hypervascular on doppler sonography. Mammography -showed a non -specific, diffuse density area of about 12 cm. No microcalcification or distortion. (BI-RADS 4-5). MRI not done	Grade III angio-sarcoma
Pandey M et al., [12]	32 years	Presented with non-tender lump in right breast. No nipple-discharge. No changes in overlying skin	Mammogram showed dense breasts with multiple nodular densities and a well-circumscribed nodular density in upper outer quadrant of the right breast USG - multiple cysts in both breasts, largest measuring 3.5×0.9 cm in size. MRI- multiple cystic structures in entire right breast, majority of these cysts contained internal loculations. PET-CT-Negative	Low grade angiosarcoma
Present Case	34 years	Presented with lump in the right breast with bluish discoloration of the overlying skin, noticed for one month. CBE-a slightly tender, immobile palpable lump with firm to hard consistency in the upper inner quadrant, right breast. It was associated with mild bluish discoloration of overlying skin. No history of nipple discharge. No nipple retraction. No axillary lymphadenopathy	Mammography-large, ill defined, high density, lobulated mass in the upper inner quadrant. No intralesional calcifications. USG-. A hypoechoic, solid mass with ill-defined margins, in (12-3o' clock position) right breast. It measured about 4.7x2.5 cm in size, subtle posterior acoustic enhancement seen; no intralesional calcifications. On colour Doppler-the mass was hyper-vascular with significant intralesional vascularity. A low velocity and low resistance flow pattern with resistive index (RI) of 0.4, on spectral trace. MRI- a large, ill-defined, T1 hypointense, T2 hyperintense breast mass showing intense post contrast enhancement and type II contrast kinetics.	Grade III Angiosarcoma

[Table/Fig-5]: Table showing comparison between the clinical and imaging findings of the present case report and various comparative case reports.

such as primary angiosarcoma of breast. It also highlights that discoloration of the overlying skin seen accompanying palpable lumps in some of the cases of breast angiosarcoma; should not be mistaken for bruising. Instead, a high index of suspicion is essential for early recognition of such a rare entity, so that timely institution of appropriate therapeutic options becomes possible.

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