Primary breast angiosarcoma: A case report

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SUMMARY

Breast angiosarcoma is a rare and aggressive malignancy arising from vascular endothelial cells. It is categorized into primary and secondary types, with primary breast angiosarcoma (PBA) occurring de novo and accounting for less than 0.04% of all breast malignancies. The condition often mimics other breast cancers clinically and radiologically, leading to diagnostic difficulty. Imaging lacks specificity, and diagnosis depends mainly on histopathological and immunohistochemical findings. Mastectomy remains the mainstay treatment to achieve negative margins, while the role of adjuvant radiotherapy or chemotherapy remains uncertain. Due to its rarity and aggressive course, further studies are required to improve management strategies and survival outcomes.

INTRODUCTION

Breast angiosarcoma (BA) is a rare form of malignancy, accounting for less than 1% of all breast cancers. It originates from vascular endothelial cells and may occur spontaneously as primary breast angiosarcoma (PBA) or as a secondary malignancy following radiotherapy.[2-5] Primary BA arises de novo in non-irradiated breast tissue and has a reported incidence of less than 0.04% of all breast malignancies.[3,5,6] Secondary BA, in contrast, occurs predominantly in elderly women after breast-conserving surgery with adjuvant radiotherapy, typically within the irradiated field.[4,5,7] Both subtypes are aggressive, with poor prognosis and high recurrence potential.[1,3]

CASE PRESENTATION

A 49 years old, postmenopausal Malay woman, previously not known to have medical illness, presented with left breast swelling for the past 7 years. Initially, the mass was smaller in size, however, rapidly increasing in size for the past 6 months. Besides, the patient was also complaining about retraction of left nipple and intermittent serous left nipple discharge. Patient had a history of taking oral contraceptive pills/ Otherwise, no complaints over the right breast, no constitutional symptoms, no history of exposure to radiation/radiotherapy, no history of cancer among first degree relatives and the patient was not on any hormone replacement therapy.

Physical examination revealed palpable fungating mass measuring 15cm x15cm occupying the entire left breast with necrotic patches (Figure 1). The left nipple was found to be inverted. On palpation the mass was hard, non-tender and fixed to the overlying skin. The anterior group of left axillary lymph nodes were palpable. Otherwise, the assessment over the right breast and axilla were insignificant.

Subsequently, mammography(MMG) and Ultrasonography (USG) of bilateral breasts and axilla were done as part of the triple assessment. Mammography (Figure 2) of the left breast is reported as a large irregular lobulated high density lesion seen occupying all quadrants of the left breast. There is associated mild architectural distortion, nipple retraction and overlying skin thickening. Otherwise, no suspicious cluster of microcalcification and left axillary lymph nodes seen.

USG of the left breast (Figure 3) showed a large lobulated heterogeneously hypoechoic mass with posterior shadowing occupying the central part of the breast measuring 4.1x9.0x7.6cm at the subcutaneous region of skin and nipples.

Primary radiological assessment concluded as suspicious left breast lesion with subcutaneous skin involvement, and it highly suggestive of malignancy.-(Breast Imaging Reporting and Data System) BI-RADS Category 5.

Consequently, the patient had undergone Tru-cut biopsy, which revealed malignant tumour consisting of solid growth of spindle and epithelioid cells. Apart from necrosis and blood lakes are seen, tumour cells display marked nuclear atypia. Immunohistochemical markers of the tumor cells are positive for CD 31, and negative for CK7, LCA, CK AE1 AE3 and S100. Hence, the biopsy results further concluded as primary breast angiosarcoma.

Subsequently, a contrast enhanced computed tomography (CECT) of Thorax (Figure 4) done prior to surgery. Revealed large fungating, irregular, lobulated, heterogeneously enhanced mass is seen occupying the entire left breast, measuring approximately 9.5x9.0x9.7cm. Anteriorly,it infiltrates the left nipple and the overlying skin, causing skin thickening. Posteriorly, there is infiltration to the underlying left pectoralis major muscle. Surrounding subcutaneous fat streakiness around the mass.

Our patient had undergone radical mastectomy of the left breast. In view of larger chest wall defects (Figure 5), primary closure was unfeasible. Hence, reverse abdominoplasty technique was done for the closure of extensive post-mastectomy chest wall defect (Figure 6). Post-operative

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Fig. 1: (Preoperative appearance):Fungating mass measuring about 15cm x15 cm occupying the entire left breast with necrotic patches

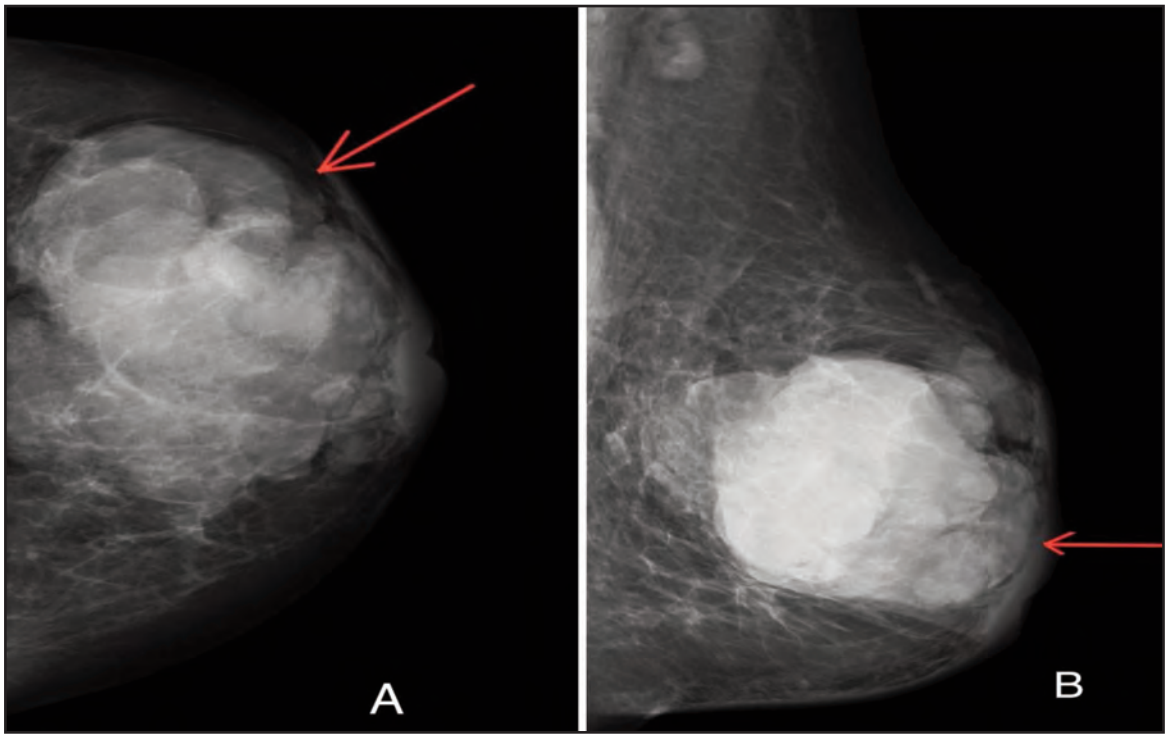

Fig. 2: (A-Left CranioCaudal view, B-Left MedioLateralOblique view) Irregular lobulated high density lesion seen occupying all quadrants of the left breast with architectural distortion

specimens were sent for further histopathological evaluation, and subsequent report was consistent with angiosarcoma.

DISCUSSION

Breast cancer remains the most common cancer among Malaysian women, with angiosarcoma being one of its rarest histological subtypes. Primary BA typically occurs in younger women aged 30–50 years, whereas secondary BA usually affects older women aged above 60 years and arises in previously irradiated tissue.[8] Angiosarcoma is an extremely rare entity with breast being one of the commonest sites.[2-4] The incidence rate of BA accounted to be less than % among all the other breast malignancies.[2,3] It is further classified into Primary BA and secondary BA.[1-3] Primary BA has an incidence rate of less than 0.04%, sporadic in origin and with a mean age of occurrence 30-50 years old.[3,5,6]

BA demonstrates highly aggressive behaviour with early hematogenous spread to lungs, bones, and liver. Lymphatic spread is less common. Genetic alterations such as BRCA1 and BRCA2 mutations have been implicated in some cases of secondary BA.[4,5,7,9]

Generally, BA exhibits aggressive growth as compared to other breast malignant tumors with poor prognosis.[1,3,10] Studies show point mutations in BRCA1 and BRCA2 genes are often associated with secondary BA, wherein there is loss in endeavoring protection against radiation induced DNA damage.[11,12] Another study by Emanuela et al. shows a close relation between p53 gene down regulation, vascular endothelial growth factor (VEGF) over expression in BA origin.[11] Though there is molecular relevance, the pathogenic rarity of BA remains unclear.[13] There are reports with suggestive correlation of BA with chronic lymphoedema, chronic infection, and trauma.[11] Besides there are reported

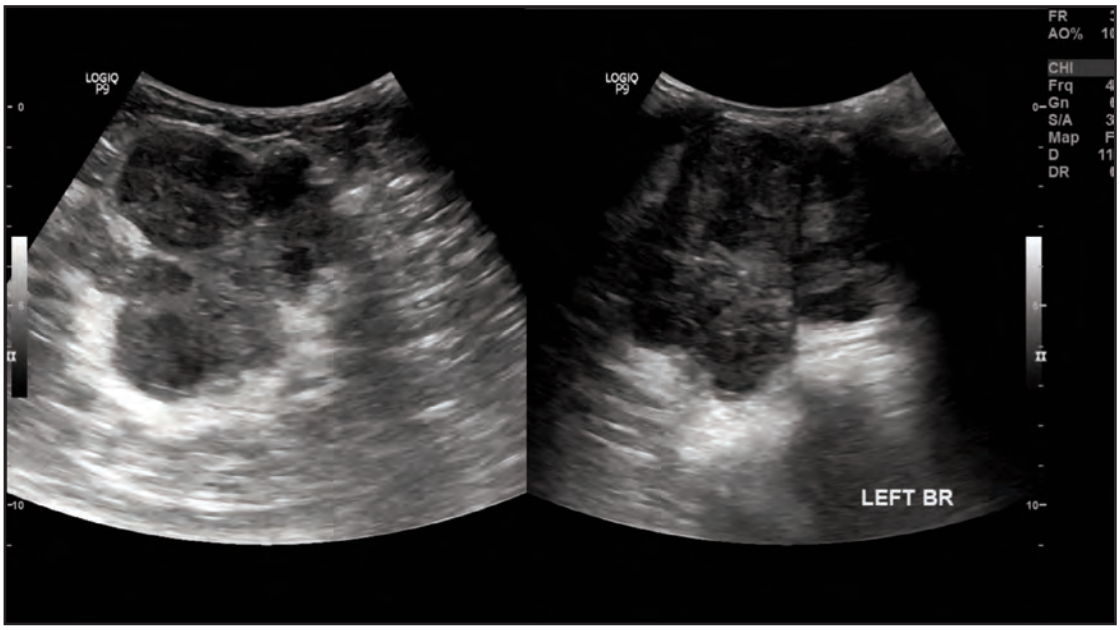

Fig. 3: (US Breast)

Fig. 4: (CECT Thorax)

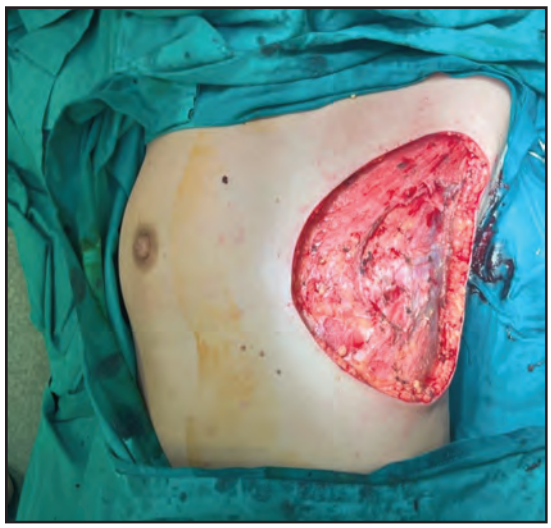

Fig. 5: Post radical mastectomy with large chest wall defect

Fig. 6: Reverse abdominoplasty technique used for wound closure

cases of BA among pregnant women and hypothesized to be having possible hormonal triggers.[4,13] However still lack sufficient data confirming all these relevance.[11,13] BA in patients with chronic lymphoedema often termed as Stewart-Treves Syndrome.[1,2,5]

Patients with Primary BA typically present with rapidly growing palpable lump(≥4cm)over the breast.[5,13] Often the mass is painless in nature.[5,9] A study by Katrina et al shows a mean tumor size of 5.9cm[4]. Occasionally, the mass is associated with purplish-bluish discoloration of overlying skin, which is being cognate to the vascular nature of the tumor.[9,11,13] Whereas in secondary BA predominantly affecting elderly women often patients present with complaints of bruising, ecchymosis or nodular like lesion over previous surgical site.[4,5,13] In contrast to primary BA, the lesions here are confined to the dermal layer and occasionally extend to breast parenchyma.[13]

Habitually BA exhibits metastasis via hematogenous route, though lymphatic spread is possible but unusual.[5,14,15] Common sites involving bone, liver, soft tissue structures and lymph nodes[4,14] have been reported. A retrospective study conducted by Aron Hui et al . shows, out of 14 cases studied, lungs were the commonest sites of involvement in both primary and secondary BA.[5]

Imaging is an important modality part of breast cancer work-up.[8] Mammography and USG Breast may not show specific characteristics attributing to BA, wherein the findings may be persistent with other malignant breast tumors.[7,10] USG of breast may show well circumscribed, ill-defined mass with hyper-or hypo-genicity.[9,10] Mammographically non-specific, ill-defined with focal asymmetry commonly associated, occasionally calcification features.[10] Even in our case, the lesion was reported as lobulated, heterogenous mass with irregular architecture. Various studies show that magnetic resonance imaging (MRI) has been the best imaging modality for BA as it can identify the lesions that were occult to mammography.[7,10] BA characteristically have low intensity on T1W and high intensity on T2W images.[9] However, MRI was not performed for our patient pertaining to limited resources in the secondary level hospital.

Fine needle aspiration cytology (FNAC) has a high rate of false negatives and is often misleading due to close similarities to other breast abnormalities, hence core needle biopsies are recommended in the case of BA.[10] In our patient, tru-cut biopsy was performed as a part of histopathological assessment.

These BA generally arise from endothelium, lining of vascular channels.[4] This is attributed to their nature of rapidly proliferating and infiltrating into surrounding connective tissues.[3] BA is typically positive for markers such as CD31, CD34 and VIII-related markers.[11,15] These are indicative markers for endothelial differentiation related to their vascular origin.[11] CD31 reported to be more specific, whereas CD34 marker more sensitive in BA.[9] In relation to that, our patient's biopsy sample shows to be positive for CD31 marker.

According to the degree of differentiation, BA is classified into three levels namely low-, intermediate- and high grade.[13] Furthermore, certain studies show a close correlation between histological grading in patients with primary BA and prognosis.[10,13] In most cases primary BA are associated with high tumor grade with positive margins.[10,13]

There is a lack of clear guidelines for surgical management of BA pertaining to their rarity.[7,13] However, a more rational surgical approach with mastectomy remains the mainstay treatment for primary and secondary BA with an aim to achieve surgical R^0 resection.[3,4,13,15] Though mastectomy is

preferable, study shows those who underwent BCS did not show worse prognosis.[3,9,15] Hence BCS are being suggested for small grade 1 lesions.[4] Axillary clearance remains controversial as BA usually don't have nodal involvement, thereby indicated in those selective cases with clinical or radiographic nodal involvement.[9,10,11,13,15] Another study by Ran An et al. shows no significant difference in survival rates among those who underwent simple mastectomy and modified radical mastectomy.[13]

In our patient, radical mastectomy was done, and tumor resection leading to creating a large chest wall defect. Hence instead of primary wound closure, reverse abdominoplasty technique was used.

Post operative adjuvant chemo radiation has been a controversial discussion due to limited data available.[15] However, few studies show patients receiving adjuvant radiotherapy in large doses (>50Gy) postoperatively have better locoregional control as well as being beneficial in combating microscopic positive margin.[7,14,15] Risk of radiation induced angio sarcoma has been a concern, thereby those receiving radiotherapy require closer long-term follow-up.[15] A series shows doxorubicin-based chemotherapy agents are being suggested as first line adjuvant chemotherapy post mastectomy.[11] Another series has reported the usage of gemcitabine and docetaxel as neoadjuvant therapy, showing a significant regression over skin lesion.[16]

Generally, patients with BA have poor prognosis and truly depend on the tumor grading.[4,7,16] For grade 1 tumors, a disease-free survival of 5 years is around 76% in contrast to grade 3 tumors which is only 15%4] Few studies revealed that secondary BA has poorer prognosis compared to primary BA with survival rate of 32%.

CONCLUSION

Breast angiosarcoma is a rare and aggressive malignancy with diagnostic challenges due to nonspecific clinical and imaging features. Mastectomy remains the primary treatment option, aiming for negative surgical margins. Axillary clearance is not routinely indicated unless nodal involvement is suspected. The role of adjuvant radiotherapy and chemotherapy remains controversial. Greater clinical awareness and multicentre data are needed to standardize management and improve survival outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL STATEMENT

Patient's consent and permission has been obtained to publish this case report and accompanying images.

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