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WJMER

World Journal of Medical Education and Research

An Official Publication of the Education and Research Division of Doctors Academy

DOCTORS ACADEMY

BETTER EDUCATION. BETTER HEALTH.

ISSN 2052-1715

Case Report
DAUIN 20230204

World Journal of Medical Education and Research:
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A Comparison between Primary and Secondary Breast Angiosarcoma: Our Local Experience

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WJMER, Vol 29: Issue 1, 2023

Abstract:
Breast angiosarcoma is a rare form of cancer and can be classified into primary or secondary types. We report two cases of breast angiosarcoma in our locality, and illustrate the differences encountered between the two types. There is no standard treatment for this disease. Surgery is the mainstay of treatment, but the role of adjuvant treatment remains uncertain.

Key Words:
Breast Angiosarcoma; Primary Breast Angiosarcoma; Secondary Breast Angiosarcoma; Spontaneous Breast Angiosarcoma; Radiation-Induced Breast Angiosarcoma

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Introduction

Angiosarcoma of the breast is a rare and highly aggressive cancer, accounting for only 0.04% of all breast malignancy.[1] It can occur as a primary lesion of the breast or as a secondary lesion after breast irradiation or in patients with chronic lymphedema after axillary dissection (Stewart - Treves syndrome). Diagnosis is difficult and the prognosis is poor, with optimal adjuvant treatment based mainly on expert opinion due to the rarity of the condition.[2] We report two cases in our locality and compare the differences encountered between primary and secondary disease.

Case 1

Miss C is a 46-year-old lady, whose mother was diagnosed with breast cancer at age of 56, presented with progressive right breast engorgement and mastalgia in 2021. Physical examination revealed breast asymmetry with an 8cm firm mass over the upper outer quadrant of the right breast which was not fixed to the underlying muscle or overlying skin. The nipple areolar complex was not affected and there were no palpable axillary lymph nodes. Ultrasound and bilateral mammogram (Figure 1) was performed which showed a large 7.9x 3.1 x 8.8cm irregular mass at the right upper outer quadrant with no suspicious microcalcification and no axillary lymphadenopathy bilaterally. Core biopsy of the lesion showed atypical vascular proliferation, most in keeping with well differentiated angiosarcoma. A whole-body positron emission tomography computed tomography (PET-CT) showed no distant metastasis. After discussion with the multi-disciplinary team, Miss C underwent a right skin sparing mastectomy with transverse rectus abdominis myocutaneous (TRAM) flap reconstruction and sentinel lymph node biopsy. Pathology confirmed angiosarcoma with clear margins (most margins >2cm), and sentinel lymph node was negative for malignancy. Adjuvant radiotherapy was offered for improving local control based on retrospective series, but Miss C was not keen.

In December 2022, she presented with haemoptysis with ~5mL fresh blood with clots during each coughing episode. On examination, a discrete 2cm right upper jugular cervical lymph node was palpable, and a plain chest radiograph revealed a 18mm opacity over the left hilar region. Ultrasound-guided fine needle aspiration of the enlarged cervical lymph node showed atypical cells. Excisional biopsy of the lymph node was performed, and the resulting pathological findings were consistent with metastatic angiosarcoma. Her PET-CT revealed

Figures for breast angiosarcoma case report

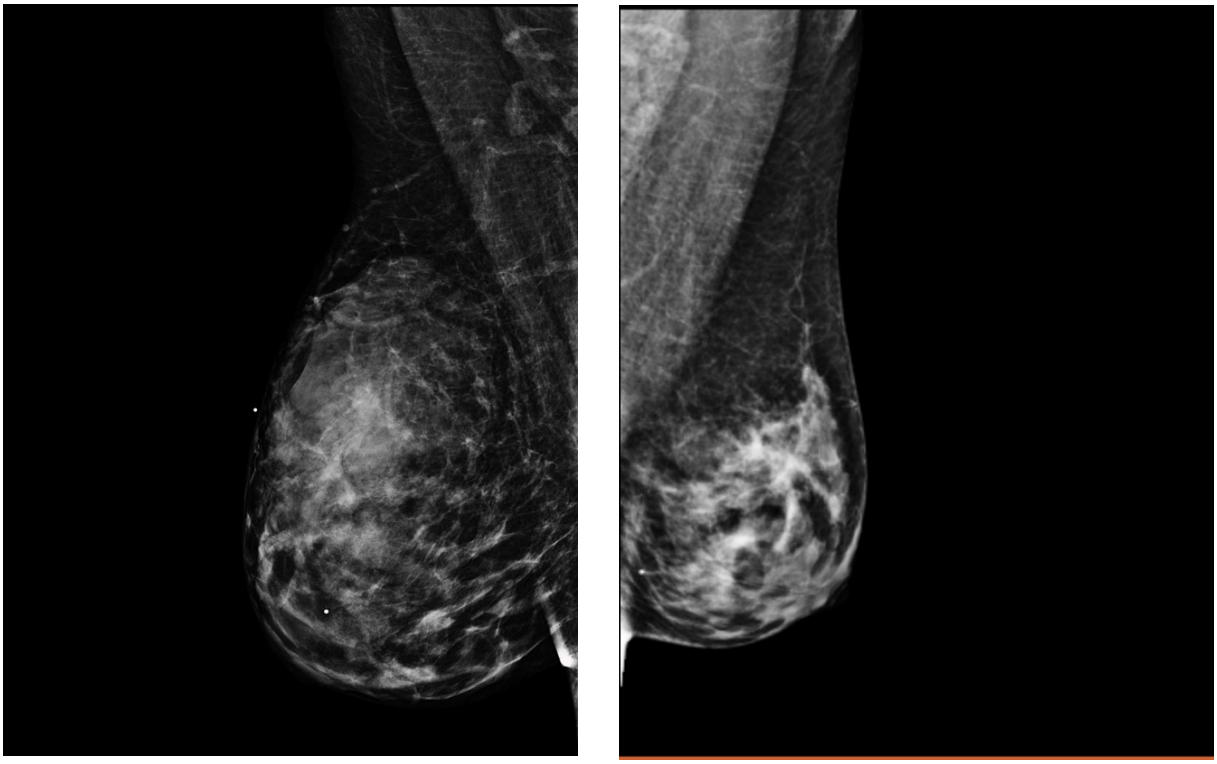

Figure 1(a): *Right MLO and Left MLO views respectively, with right MLO view showing a large iso to hyperdense mass occupying most of the upper outer portion of the right breast.*

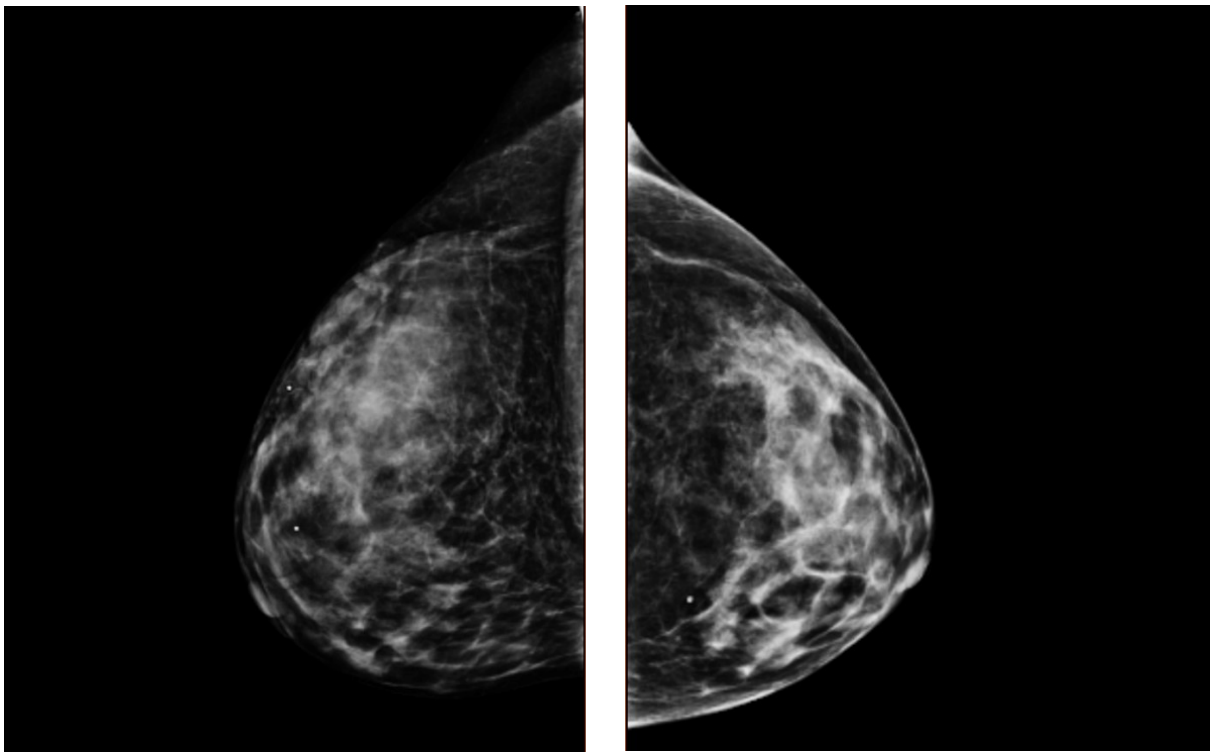

Figure 1(b): *Right MLO and Left MLO views respectively, with right MLO view showing a large iso to hyperdense mass occupying most of the upper outer portion of the right breast.*

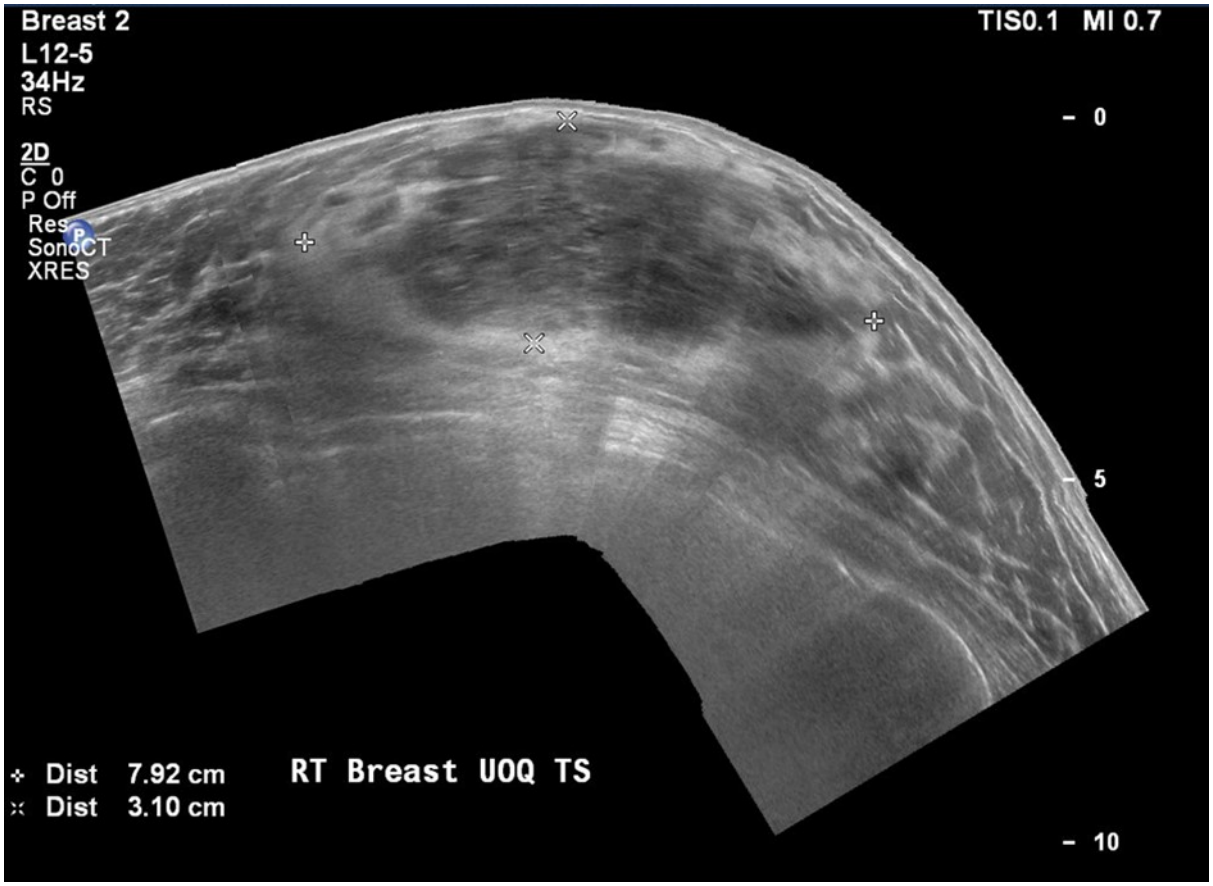

Figure 1(c): *Ultrasound imaging of the right breast showing a large irregular heterogeneous mass 7.9x3.1x8.8cm in size. Its periphery is mainly hyperechoic and blend-in with the normal breast tissue, limiting accurate delineation of the lesion extent.*

multiple new hypermetabolic bilateral lung nodules with adjacent ground glass densities which were suggestive of haemorrhagic metastasis of angiosarcoma. Within a month of her recurrence, she also developed multiple scalp, gum and skin nodules (Figure 2) with occasional bleeding. She was started on palliative chemotherapy, initially with paclitaxel which was later changed to adriamycin and zometa after she developed bone and liver metastasis. She then developed brain metastasis for which she was given radiotherapy (Figure 3).

Case 2

In comparison, Madam S is a 76-year-old lady with a right breast ductal carcinoma in situ in 2010, for which she underwent a right-sided breast-conserving therapy, sentinel lymph node biopsy with adjuvant radiotherapy. In 2014, she had a screen-detected lesion for which she underwent left sided breast-conserving therapy and sentinel lymph node biopsy (pT1cN0 ER/PR+ invasive ductal carcinoma, margins clear) with subsequent radiotherapy and hormonal treatment. Post-treatment, she has been kept on regular surveillance with no recurrence seen on her latest mammogram and ultrasound in January 2021.

Other significant medical history includes papillary thyroid cancer, for which she received a total thyroidectomy and adjuvant radioactive iodine therapy.

In November 2022, Madam S presented with a left breast nodule with associated pain and bleeding. Clinically there was a 1x1cm round nodule at the left 5 o'clock region, 2cm from the nipple with easy contact bleeding. Physical examination revealed no other suspicious breast lump or palpable axillary lymphadenopathy. There was also no lymphoedema. The working diagnosis at the time was a bleeding pyogenic granuloma. In

Clinical photographs of metastatic spread of the angiosarcoma.

Figure 2(a): *Gum nodule*

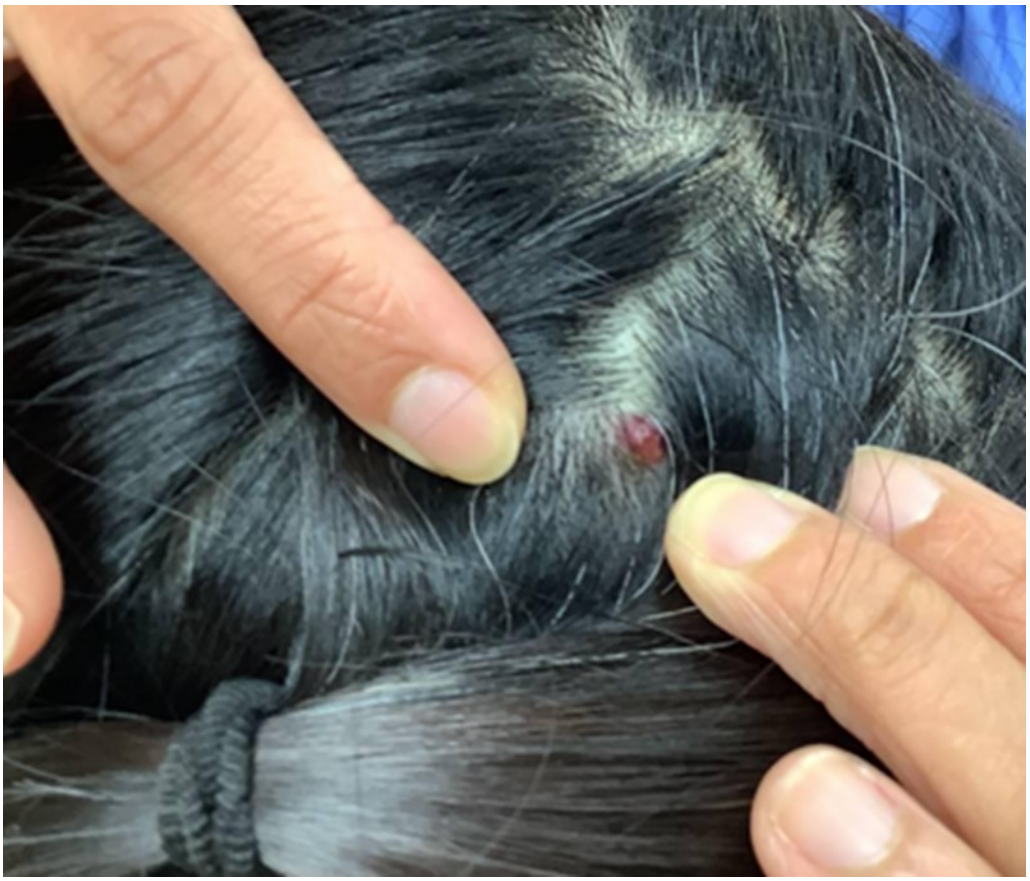

Figure 2(b) *Scalp nodule*

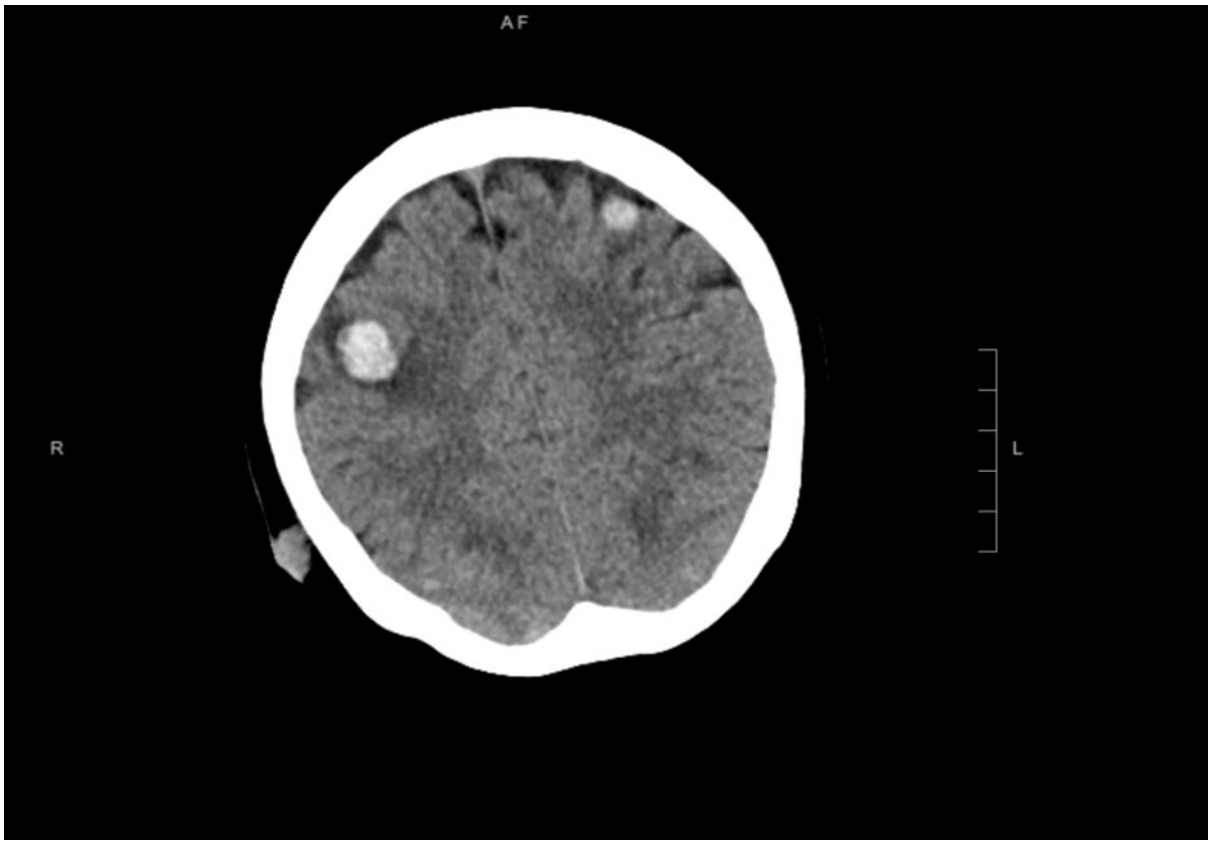

Figure 3: *Plain CT scan of brain showing multiple hyperdense lesion within the brain parenchyma*

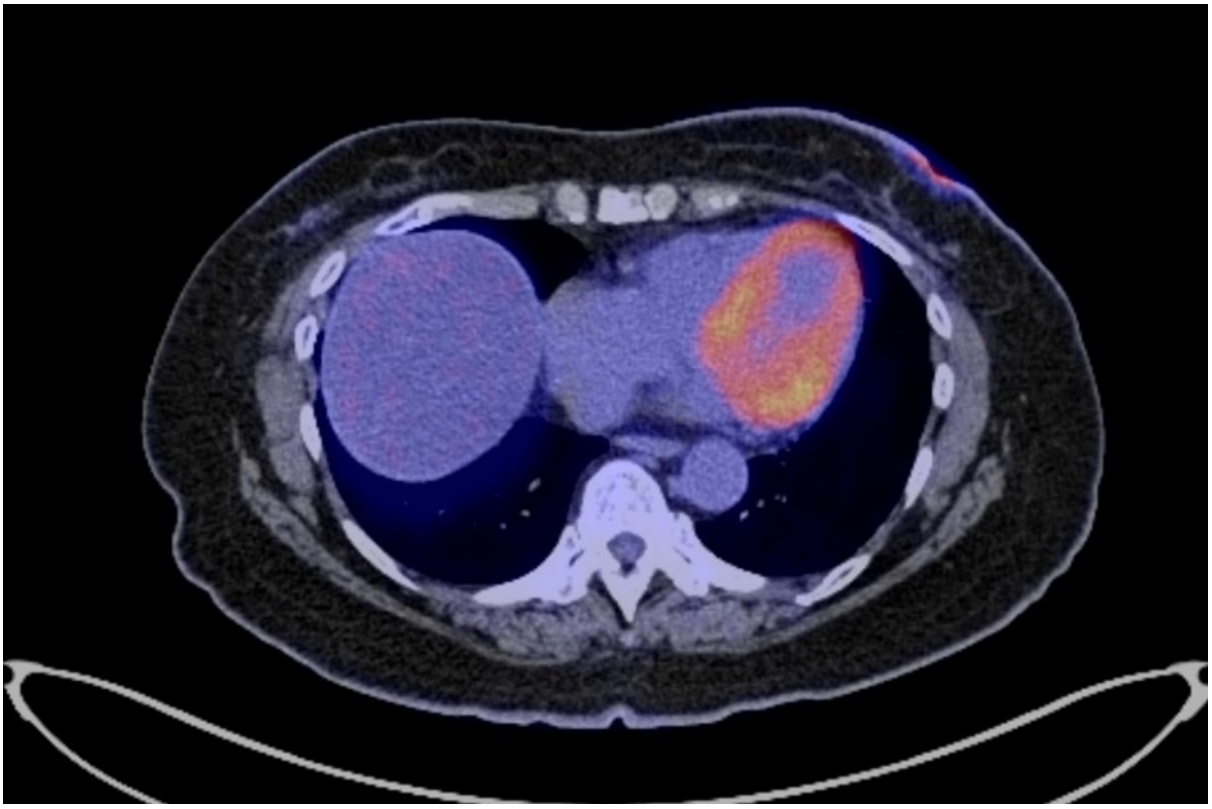

Figure 4: *PET image showing FDG uptake over site of excisional biopsy*

view of the persistent troublesome bleeding and history of bilateral breast cancer, the lesion was excised under local anaesthetic. The pathology was consistent with moderately differentiated angiosarcoma with the close margins (closest 1mm). A PET-CT was performed which showed only the hypermetabolic skin lesion over the left breast related to excisional biopsy (Figure 4), with no nodal or distant metastasis. Madam S later underwent wide local excision with no axillary treatment in private in January 2023.The pathology showed no residual tumour. No adjuvant therapy for her breast angiosarcoma was required, and there was no evidence of recurrence at her latest follow up with oncology.

Discussion

Angiosarcoma of the breast is extremely rare and can be divided into the de-novo (primary) or therapy-related (secondary) form. Primary breast angiosarcoma usually occurs between females between 20-50 years of age, [3,4,5] whilst secondary breast angiosarcoma is typically seen in older women, with the mean age of 70.[6] Secondary cases occur following a latent period after radiation or in patients with chronic lymphedema after axillary dissection (Stewart - Treves syndrome). In contrast, there are no known risk factors for the primary form. High grade breast angiosarcomas are associated with a poor prognosis, tend to metastasize early, often to the lungs or liver and have a 5-year survival rate of only 15%.[7] Low grade and intermediate grade tumours fare better in some studies.[7] However, according to Nasciemento et al, there is no correlation between histologic grade and patient outcome in their review of 49 cases.[8]

Patients with breast angiosarcoma can present with diffuse breast enlargement or a rapidly growing palpable breast mass which may have a tinge of purple discolouration, due to its highly vascular nature. Diagnosing breast angiosarcoma can be difficult as the radiological findings are non-specific. Tumours may appear hypoechoic, hyperechoic or heterogeneous on ultrasound, with high vascularity.[9] Mammographically, breast angiosarcomas can appear as large dense homogenous mass with no calcifications or spiculations,[9] and up to 33% of the tumours can have normal mammogram findings.[10] Magnetic resonance imaging (MRI) or computed tomography (CT) with contrast can help confirm the hypervascular nature of these lesions. Primary angiosarcomas are often located deep in the breast parenchyma.[11] Hence, pathological confirmation with core biopsy may have false negative rates of up to 40% of cases.[12]

Currently there is no standard treatment for breast angiosarcoma in view of the small number of reported cases. Surgical resection with negative margins is typically performed, with preference for mastectomy over wide local excision due to lower estimated recurrence rate (8% vs. 23%, respectively).[13] Axillary dissection is usually not required as lymph node involvement is uncommon (<5% of cases).[14] Ragavan *et al.* performed a retrospective review between 2006 and 2019 on axillary lymph node dissection in breast angiosarcoma patients in Singapore with no positive lymph node metastasis detected in their cohort of thirteen cases.[15] The role of chemotherapy and radiotherapy in breast angiosarcomas is not well established. For primary breast angiosarcoma, adjuvant radiotherapy after surgery allows for better local control with lower recurrence rate according to Johnstone *et al.*,[16] but the overall survival rate was comparable with those without radiotherapy.[17] The role of adjuvant chemotherapy is undefined at present, being based mainly on adult soft tissue sarcomas. Current literature suggests that patients with large high grade angiosarcoma or recurrence may benefit from chemotherapy[18] as this subset of patients has a poor prognosis. Anti-angiogenic and immunological therapies have also been described, but to date have had disappointing results.[19]

Conclusion

In conclusion, we report two cases of breast angiosarcoma in our locality. Given the aggressive nature of the disease, early detection and prompt surgical treatment are needed. Further studies are needed to guide adjuvant treatment modalities and their survival benefit. In addition, it is still unclear whether treatment for primary vs secondary angiosarcomas differ given the rarity of the disease.

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