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Primary Breast Angiosarcoma: A Case Report

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Abstract **Original Research Article**

Breast angiosarcoma is a rare and highly aggressive malignancy with a poor prognosis. Arising from endothelial cell lining, it represents approximately 0.04–0.05% of all breast malignancies and less than 1% of all sarcomas. It can be divided into primary and secondary angiosarcoma. Primary angiosarcoma typically affects younger women with no known risk factors, radiation-induced angiosarcoma (RIAS) is classified as secondary angiosarcoma. Breast angiosarcoma is a rare malignant mesenchymal tumour that develops in breast vascular tissue. Diagnosis is often delayed because this condition is rare, and manifests most of the times as a painless lump that grows quickly. Progressive disease can develop distant metastases making the prognosis poor.

Keywords: Breast angiosarcoma, prognosis, sarcomas, tumour.

INTRODUCTION

Breast angiosarcoma (BA) is a relatively rare clinical condition, it represents 0.004 to 1% of all malignant breast tumours [1], and 8 to 10% of breast sarcomas [1]. Breast angiosarcoma is a rare malignant mesenchymal tumor that originates from the endothelium of the blood vessels surrounding breast lobules or within lobular capillaries.

It can be divided into primary and secondary angiosarcoma. Primary breast angiosarcoma (PBA) develops from endothelial cells and can infiltrate the skin, it is an aggressive and poorly prognostic tumor and manifests as an intraparenchymal enlarging mass, usually diagnosed in women aged 30–50 without a history of cancer or identifiable risk factors [2, 3]. The annual incidence of primary breast angiosarcoma is approximately 17 new cases per million women and the diagnosis is generally associated with a poor prognosis [4]. Secondary breast angiosarcoma (SBA) first appears from skin tissue and gradually invades the breast parenchyma, it tends to affect older women, with a median age of 67–71 years, and is often linked to prior radiotherapy and to chronic lymphedema which is a complication of post-demolitive breast surgery (Stewart-Treves syndrome) [5].

Moreover, surgery is the cornerstone for the treatment of breast angiosarcomas, with the status of margins being the most important prognostic factor [6]. The roles of radiotherapy (RT) and adjuvant chemotherapy (CT) are unclear, and guidelines are not available. The extreme rarity of this condition limits the possibility of clinical trials to assess the most adequate treatment strategy, therefore decisions are based on retrospective case reviews [7].

Due to the low incidence, there is no standard treatment regimen for breast angiosarcoma, and recurrence and mortality are high.

MATERIALS AND METHODS

We present a case of a 42-year-old woman affected by primary breast angiosarcoma treated with mastectomy and adjuvent radiotherapy.

RESULTS

The patient is 42 years with 2 gestities, 2 parities and 1 living child, had menarche at 13 years, have used oral contraception for 1 year, still menstruating with a regular cycle, she underwent a myomectomy in 2019 for a uterine fibroid, who was referred to our department for a tumour of the right breast evolving for one year, which had rapidly increased in size. Breast examination revealed a nodule in the right breast straddling the two lower quadrants, with a normal appearance of the skin opposite the tumour, no nipple discharge and no palpable adenopathy. The contralateral breast was normal. Mammography revealed an infero-external quadrant formation measuring 4.3x7.8mm that

is poorly limited. A surgical biopsy was performed, histological examination showed a vascular proliferation with a moderate expression of CD 34 and a negative expression of P63, KI 67 was at 25 %, nevertheless a well-differentiated infiltrating angiosarcoma could not be ruled out (Figure 1).

The patient underwent a mastectomy. Histological examination confirmed the diagnosis of a well-differentiated and infiltrating angiosarcoma. The work-up for extension was normal. The patient received radiotherapy to the chest wall and is currently under surveillance.

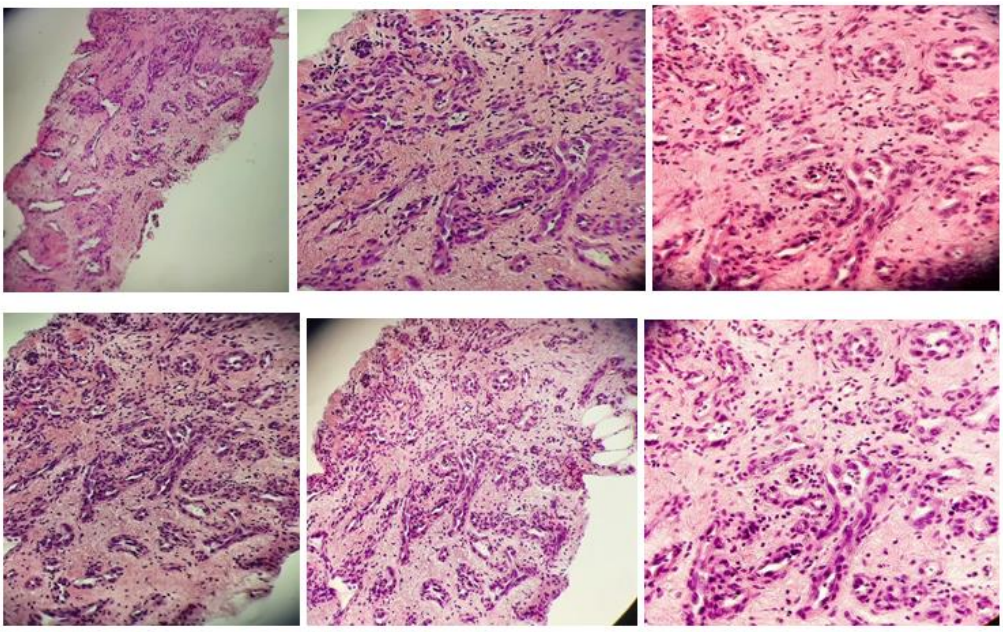

Figure 1: Histological images with haemato-eosin staining, at low/high magnification showing vascular proliferation made up of vessels of variable size, connected in places. These vessels are bordered by endothelial cells with anisokaryotic, hyperchromatic nuclei, with a prominent nucleolus in places and seat of some abnormal mitoses. The stroma is thin and inflammatory. With infiltration of adjacent adipose tissue

DISCUSSION

Primary angiosarcoma represents 0.05% of all breast tumours and 8% of breast sarcomas [8, 10]. Angiosarcoma is an extremely rare and highly malignant mesenchymal vasoformative neoplasm, characterized by rapidly proliferating and extensively infiltrating growth [11]. It occurs especially in women 30–40 years of age. The median survival time and 5-year recurrence-free survival rate are 24 months (about 2 years) and 33% respectively [12]. Tumor histology, grade, size, and invasion into surgical margins have been reported as prognostic factors [13]. Zelek *et al.*, [14] reported that tumor size correlates with 10-year recurrence-free survival, and tumor size exceeding 10 cm has a poor prognosis.

Clinically, breast angiosarcoma often presents insidiously as a painless, palpable mass with rapid growth. Bluish red discoloration of overlying skin is seen in up to a third of patients and is thought to be a result of the vascular nature of the tumor [15]. Nipple discharge or retraction and axillary lymphadenopathy are usually absent. In most reported cases, the average tumor size at presentation is greater than 4 cm in diameter. Bilateral tumors have been reported in postmenopausal women [16]. Differential diagnoses range from benign breast conditions such as hemangioma, angiolipoma, and pseudoangiomatous stromal hyperplasia to malignancies such as pseudovascular metaplastic breast carcinoma and acantholytic variant squamous cell carcinoma [17].

The ultrasound examination of PBA has no specific findings. A disordered area with mixed echoes can be shown due to the different ratios of vessel and sarcoma [18]. PBA can also present as a hypoechoic or hyperechoic mass [19]. Since pab has no apparent calcification, it usually presents as a non-calcified mass on mammography. The signal within the mass is uneven on MRI, with low T1-weighted signal intensity and high T2-weighted signal intensity, and a continuous enhancement [20]. Enhanced CT and 3D reconstruction can also be a good method to better visualize the vascular course and the surrounding tissue invasion of the patient.

The histological features of angiosarcoma of the breast are classified into grades I, II and III. In addition, immunohistochemistry can be useful to identify the clone JC/70A (CD31, the human hematopoietic progenitor cell antigen), which is an endothelial indicator of vascular proliferation. Other specific markers for this kind of lesions are Factor VIII, and Friend leukemia integration 1 transcription factor (FLI1) [21]. Angiogenesis, considered to be strongly affected by vascular endothelial growth factor (VEGF), is very important in the pathogenesis of these tumors. The

histologic grade of primary angiosarcoma of the breast plays an important role in the estimation of outcomes, it is the most important prognostic indicator in cases of PBA [22]. Concerning the correlation between high proliferation index and poor prognosis in a Grade II tumor in a study, Ozluk *et al*., [23] proposed that Ki-67 proliferation index should be used to predict nonhigh-grade tumors with unfavorable outcome. Low proliferation index of two grade I tumors in their study also supports the theory of relationship between Ki-67 antigen and aggressiveness of PBA.

The gold standard treatment for primary breast angiosarcomas is still surgery which includes total mastectomy or wide local excision, with or without axillary clearance. Total mastectomy is more favorable than wide local excision because of the resection margin status, as well as the high incidence of local recurrence in wide local excision as documented in most articles [24, 25]. Regional axillary clearance is not necessary because they tend to metastasize hematogenously, rather than lymphogenously [24, 25].

There are different views regarding postoperative adjuvant therapy for PBA. Darre *et al.*, think chemotherapy and radiotherapy should be considered for large tumors of grade III [26]. Abdou believes that although adjuvant chemotherapy improves local recurrence-free survival in high-grade PBA, it does not significantly improve survival outcomes [27]. However, Torres concluded that adjuvant chemotherapy prolongs survival and reduces the local recurrence rate in patients with angiosarcoma of the breast [28]. Sher found that anthracycline-ifosfamide and gemcitabine-taxane chemotherapy regimens were beneficial in patients with PBA [29]. Regarding postoperative radiotherapy, Torres suggested that patients with PBA with skin or muscle involvement should be treated with adjuvant radiotherapy [28].

A recent study has shown that cytotoxic chemotherapies, in particular anthracycline-based regimens and taxanes can produce significant responses to therapy in a subset of patients [30]. Sher *et al*., reported that there was no significant survival difference between patients who had and had not received anthracyclines, taxanes, gemcitabine, and ifosfamide as adjuvant chemotherapy [31].

The exploitation of VEGF-A and VEGF-C and its VEGF-R1 receptor, the main vascular growth factor, offers an interesting therapeutic target for inhibiting angiogenesis [32].

CONCLUSION

The importance of this case report is that primary breast angiosarcoma is a rare disease which can develop without prior exposure of the breast to either surgery or irradiation. A mass that shows heterogeneous hyperechogenicity on ultrasound with an associated architectural distorted appearance and typical malignant characteristics should alert the radiologist to a possible diagnosis of angiosarcoma. A good clinical history in correlation with clinical and radiological findings are important to derive an early and precise diagnosis. There is no strict contraindication for biopsy of these tumors even though false negative value is high, nevertheless, it would be helpful to do it under ultrasound guidance to avoid unnecessary complications. Total mastectomy remains the most effective mode of treatment. Skin thickening should be evaluated thoroughly and if necessary biopsied to exclude malignant infiltration. The role of adjuvant chemotherapy or radiation therapy in the management of angiosarcoma remains to be proven but may be considered in high-risk patients.

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