Case Report

Primary Breast Angiosarcoma: Pathological and Radiological Diagnosis

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Abstract

Primary breast angiosarcoma is a very rare aggressive mesenchymal tumor, which may represent only 0.04% of all breast malignant tumors. We report a case of primary angiosarcoma in the breast of a 22-year-old woman who presented with a mass in her right breast. Ultrasonography revealed a large heterogeneous lobulated mass lesion consistent with a fibroadenoma or phyllodes tumor. After a period of six months, she presented with nipple retraction, so a core needle biopsy was performed. Histopathology revealed a well differentiated angiosarcoma (grade I/III), but in the mastectomy specimen, numerous neoplastic multinucleated giant cells were evident, which resembled those found in other sarcomas, such as malignant fibrous histiocytoma or extra skeletal osteogenic sarcoma, and this caused difficulty making the diagnosis. Using immunohistochemical (IHC) studies, neoplastic cells were positively stained for CD31, CD34, and factor VIII-related antigens, which confirmed that the tumor was a high grade, poorly differentiated angiosarcoma (grade III/III). In conclusion, angiosarcomas may have different grade patterns in the same tumor, and as a result it is necessary to examine the whole tumor for definite grading. Imaging findings in angiosarcomas are non-specific, therefore they may misdiagnosed, frequently by other benign lesions.

Keywords: *angiosarcoma , breast, phyllodes tumor, ultrasonography, fibroadenoma*

Introduction

Angiosarcoma is a relatively rare aggressive soft tissue tumor originating from the endothelial cells that line blood vessel walls. It tends to occur mainly in the liver, skin, breast, and deep soft tissues (1).

Primary breast angiosarcoma is a very rare malignant tumor and only a few cases have been reported in the literature (1). Secondary breast angiosarcomas occur more frequently than primary ones, and they may be seen as a complication after breast-conserving surgery for infiltrative ductal carcinoma and radiotherapy (1–3). Primary angiosarcoma of the breast has a predilection for young women aged between 20–40 years (4–10). Imaging studies do not contain characteristic features for an angiosarcoma, so it may frequently be misdiagnosed as a benign lesion (2). We report a case of primary angiosarcoma in the right breast of a 22-year-old woman who presented with a palpable mass, followed by a brief discussion of its histopathological and radiological characteristics.

Case report

A 22-year-old woman with a right breast mass was admitted to the surgical ward. The patient had felt the lump about three months before an ultrasound examination. She had no positive family history of breast carcinoma, trauma or hormone therapy. In a physical examination, the right breast was asymmetrically enlarged, without nipple retraction.

An ultrasound revealed a well-defined hypoechoic lesion in the right breast, measuring 0.9 × 0.9 cm, located in the 10 o'clock position, and 2 cm from the right nipple, consistent with a fibroadenoma. In addition, there was another

macrolobulated hypoechoic lesion, with mild heterogeneity, measuring 5.3 x 2.5 cm, and blood vessels within the lesion, located between 1 to 4 o'clock near the right nipple at a skin depth of 1.3 cm, which was consistent with a fibroadenoma or phyllodes tumor (Figure 1). Lymphadenopathy was not detected. Excisional biopsy was recommended, but based on the imaging studies the patient did not agree with the intervention. Six months later, she returned with nipple retraction.

The patient underwent core needle biopsy in order to rule out a possible malignancy. The received specimen consisted of multiple pieces of brownish-colored tissues, which measured 1 × 0.5 cm in total. Histopathological examination revealed a tumoral lesion, composed of irregular anastomosing vascular channels, lined by prominent endothelial cells, which had large atypical nuclei with moderate pleomorphism (Figure 2a$_1$). Neoplastic cells also proliferated around the blood vessel walls and within the edematous stroma (Figure 2a$_2$). Immunohistochemical studies showed a positive reaction of the neoplastic cells for; CD34, CD31, vimentin, and factor VIII-related antigen, but for; α-smooth muscle actin, desmin, estrogen receptor (ER), progesterone receptor (PR), S-100, epithelial membrane antigen (EMA), pan cytokeratin, and Her2/neu, the results appeared negative (Figures 2b, c, d). Based on the hematoxylin and eosin (H&E) staining findings and immunohistochemical studies, angiosarcoma of the breast was confirmed. Radical modified mastectomy with axillary lymph nodes biopsy was performed for the patient. The received mastectomy specimen measured 20 × 17 × 6 cm, and on section it was filled with a large grey-cream-colored tumoral lesion of fleshy consistency and a large area of hemorrhage. Microscopic examination revealed a tumoral lesion composed of oval to polygonal neoplastic cells, which had large hyperchromatic nuclei arranged in a diffuse pattern, with numerous mitotic figures, and some of these were atypical. Multinucleated neoplastic cells, with clear cytoplasm and small scattered blood vessels, were also seen (Figures 3a, b). The features of the tumor were different from the previous excisional biopsy specimen. Immunohistochemical studies were conducted to rule out any other synchronous tumor such as; malignant fibrous histiocytoma, leiomyosarcoma, extraskeletal osteogenic sarcoma, or carcinosarcoma. Neoplastic cells had a positive reaction for; factor VIII-related antigen, CD31, CD34, and vimentin, while they had negative results for estrogen receptors (ER) and progesterone receptors (PR) , alpha smooth muscle actin, desmin, CD99, epithelial membrane antigen (EMA), pan cytokeratin, HMB45 and Her2/neu, as a result, a primary angiosarcoma was confirmed (Figures 3c, d). Axillary lymph

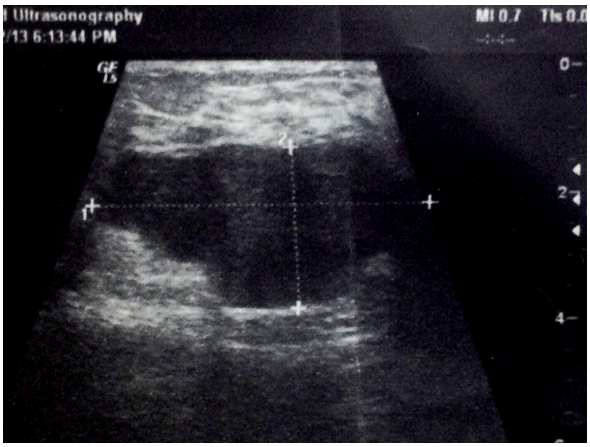
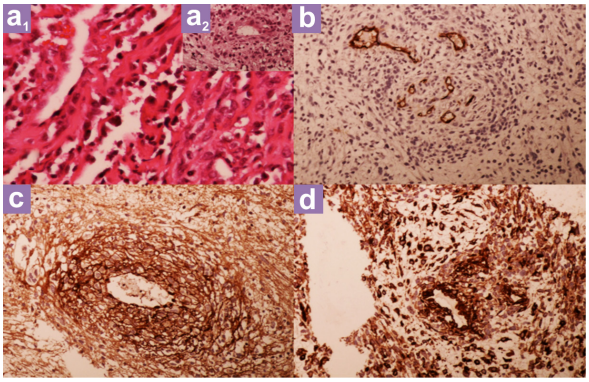


Figure 1: Ultrasonography demonstrates macro lobulated hypoechoic lesion with mild heterogeneity.

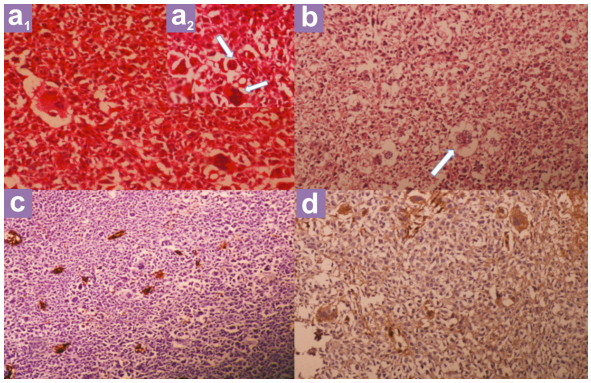


Figures 2: (a$_1$) Tumoral lesion composed of irregular anastomosing vascular channels lined by prominent endothelial cells which have an atypical, large nuclei with moderate pleomorphism. (a$_2$): Neoplastic cells also proliferated around the blood vessel walls and within the edematous stroma (hematoxylin & eosin staining, 20x magnification). (b) Neoplastic cells have a positive reaction for CD34. (c) Positive reaction for CD31. (d) Positive reaction for factorVIII-related antigen (immunohistochemical staining, 20× magnification).

nodes were intact. After surgery she received adjuvant chemotherapy, and up to the present time (after one year), no recurrence or distant metastasis have been detected.

Discussion

Breast angiosarcoma is a rare type of breast cancer originating from endothelial cells that line blood vessel walls, and it accounts for less than 0.04% of all malignant breast tumors (4,5,7). Secondary angiosarcoma may occur in the breast or arm of patients receiving breast conserving surgery for infiltrative ductal carcinoma, followed by radiation therapy (1–9). Primary angiosarcoma usually presents with an area of thickening in the breast or blue–reddish colored overlying skin tissue, which appears as a rash. Secondary angiosarcoma may present as a painless mass, with or without colored skin changes (5). Our case presented with a breast-mass, without skin color changes. The mammographic pattern does not show significant characteristics, especially in low grade types of breast angiosarcomas, but variable findings such as ill-defined masses without calcifications or speculations have been reported.



Figures 3: (a_1) Tumoral lesion composed of oval to polygonal neoplastic cells which have a large hyperchromatic nuclei that arranged in diffusely pattern with numerous mitotic figures. (a_2) show mitotic figures. (b) Multinucleated neoplastic cells with clear cytoplasm and scattered small blood vessels are admixed with polygonal cells (H&E staining, objective X20). (c) Positive staining for CD31 (immunohistochemical staining, objective X20). (d) Neoplastic cells had a positive reaction for factor VIII-related antigen.

Angiosarcomas have variable features on ultrasound examination and these may present as well-circumscribed or poorly marginated masses. These lesions could be hypoechoic or have mixed echogenicity on ultrasonography (US), based on their vascular channels or cellular components. The mixed or hyperechoic pattern, with speculated margins, is rarely seen in breast carcinoma. In general, benign lesions have a hyperechoic, isoechoic, or mildly hypoechoic pattern on US (4–6). For example, fibroadenomas usually present as hypoechoic, well circumscribed encapsulated lesions, that allow us to identify them by US. Our case demonstrated hypoechoic features on ultrasound study compatible with a malignant pattern, but because of the presentation of a well-circumscribed lesion, it was misdiagnosed as a benign lesion. Angiosarcoma margins are often not angular in shape and do not show posterior shadowing, which may be typical of other breast malignancies. On color Doppler ultrasound, they can present as hypervascular lesions. Despite non-specific findings on mammography and ultrasound studies, magnetic imaging resonance (MRI) examinations promise better characteristic findings for breast angiosarcoma. Low grade angiosarcoma may present as a large lobulated mass with indistinct borders that show hypointensity on T1-weighted images and hyperintensity on T2-weighted images, furthermore, high grade angiosarcoma may demonstrate hyperintensity on both T1WI and T2WI, with mixed intensity foci due to hemorrhage or venous lakes inside the tumor. The more aggressive types of breast angiosarcomas show rapid enhancement and washout pattern (type 3 curve) on contrast MRI studies (2–4,6).

Kinderyte et al. (1), reported a case of primary angiosarcoma in the breast of a woman after trauma, misdiagnosed as a hematoma, which appeared later as multi-organ involvement (1). Our patient did not have any positive family history of cancer or trauma, so possible predisposing factors remain unknown. Histopathologically, the low grade tumors are characterised by anastomosing vascular channels lined by neoplastic and proliferative endothelial cells, with mild cytologic atypia and rare mitotic figures (2–9). Poorly differentiated high grade angiosarcomas may contain solid areas composed of numerous large neoplastic cells, which are arranged in sheets without characteristic blood channels, and frequent mitotic figures with large areas of necrosis, and this makes it difficult to make a diagnosis. Therefore, immunohistochemical studies play an important

role to differentiating this condition from poorly differentiated carcinomas, other soft tissue sarcomas, or malignant melanomas. In well–differentiated angiosarcomas, neoplastic cells have strong positive staining patterns for CD34, CD31, vimentin, and factor VIII-related antigens. However, in high grade angiosarcoma, neoplastic cells may react weakly and focally with CD31 and CD34, but a diffuse staining pattern with factor VIII-related antigen strongly suggests endothelial origins (9). In our patient, the neoplastic cells of the resected tumor had different features in the first and second specimens that were found in the mastectomy specimen, and they resembled other soft tissue sarcomatous cells such as; malignant fibrous histiocytoma, metaplastic carcinoma, or primary osteosarcoma. A positive reaction to factor VIII-related antigens and focally positive reactions to CD31 and CD34, confirmed that it was a high grade angiosarcoma. Angiosarcoma has aggressive behavior with a poor prognosis, a high rate of local recurrence, and multi-organ involvement, especially in the lungs, liver, regional lymph nodes, and bones (1). Prognosis seems to be affected by the tumor histologic grade, while well differentiated (grade I) tumors have a better prognosis than poorly differentiated (grade III) ones, in addition, a lower local recurrence or distant metastasis rate has also been noted (2). Treatment is difficult because of the unpredictable behavior of the tumor, but a wide local excision, mastectomy or mastectomy followed by adjuvant chemotherapy have both been suggested (2,8). Angiosarcoma is disseminated by the hematologic route, so chemotherapy after surgery, especially for high grade tumors, or in cases of distant metastasis, seems to be beneficial (2). In our case, based on the poor differentiation of the tumor (grade III), no involvement of the axillary lymph nodes, and no distant metastasis obtained from a chest and abdominal computed tomography (CT) scan, she received adjuvant chemotherapy after her mastectomy. After one year, no recurrence or metastases were detected. It has been reported that the five year survival rate in well differentiated, moderately differentiated, and poorly differentiated angiosarcomas, is 76%, 70% and 15%, respectively (4). Finally, we should keep in mind that although primary angiosarcoma is a rare neoplasm, it should be considered in a differential diagnosis with fibroadenoma or phyllodes tumor, especially if US shows a homogenous or heterogenous hyperechogenic pattern. High grade angiosarcomas may have similar features to other histopathological soft tissue sarcomas; however, immunohistochemical (IHC) studies are useful for making a definitive diagnosis.

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Conflict of Interest

None.

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Authors' Contribution

Conception and design, drafting of the article and final approval of the article: STZ
Analysis and interpretation of the data: NSS
Collection and assembly of data: KR

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