Case Report

Breast Angiosarcoma with Exophytic Growth

Donya Farrokh MD•[1,2], Elaheh Modoodi MD[2], Yalda Fallah Rastegar MD[2]

Abstract

Primary angiosarcoma of the breast is a rare malignant tumor. Diagnostic breast imaging includes mammography and ultrasound, which are usually nonspecific. A 42-year-old woman with angiosarcoma of the breast is presented. Physical findings showed a hard exophytic mass in the upper part of the left breast, with skin discoloration overlaying the mass. Mammography revealed a high density well defined mass in the left breast, without any micro-calcification and speculation. On ultrasound examination, a hypoechoic mass with a well-defined margin and heterogenous echogenicity was detected. A core needle biopsy and excisional biopsy were performed, and histological examination confirmed the diagnosis of angiosarcoma. The patient underwent simple mastectomy. We present the mammographic and ultrasonographic features of a case of primary breast angiosarcoma with exophytic growth.

Keywords: Breast neoplasms, hemangiosarcoma, mammography, neoplasm metastasis

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Introduction

Angiosarcoma of the breast is a rare malignant tumor, characterized by rapidly proliferating cells derived from endothelial lining of vascular channels.[1] In the breast, angiosarcoma accounts for < 0.1% of all malignancies. Accurate diagnosis of this entity before surgery is not easy, and initial misdiagnosis is reported commonly. This rare tumor accounts for 0.04% – 1% of all primary malignant tumors of the breast,[2,3] and approximately 8% of mammary sarcomas.[4] Primary angiosarcomas of the breast occur sporadically in young women, and usually present as palpable breast lumps. Secondary angiosarcomas occur most frequently after breast conservation therapy with radiation therapy with an average latency period of usually 5 – 6 years.[5,6] Because angiosarcomas tend to recur locally and metastasis occurs widely, they are difficult to treat. Metastasis to the lungs, skin, subcutaneous tissue, liver, brain, bone, spleen and ovary have been described.[1] Prognosis is generally poor and correlates with the histological growth pattern and its aggressive nature.[1] Here, we present a case of exophytic angiosarcoma of the breast. We also describe the clinical and imaging findings of the mammary angiosarcoma.

Case Report

In September 2013, a 42-year-old multiparous woman presented to a private breast clinic, with a self-discovered left breast lump, noted since the February 2011. She did not complain of pain or tenderness of the left breast. On physical examination, a hard well-defined and exophytic mass measuring 3 × 4 cm was found in the upper part of the left breast, with purple and bluish discoloration on the overlaying skin, and mild erythema surrounding the breast lesion (Figure 1). There was no associated nipple discharge, nipple retraction or axillary lymphadenopathy. The patient's medical history was unremarkable.

She was referred for mammography. The left mammogram showed an almost fatty involution of the breast with an exophytic tumor appearing as an opaque well-defined homogenous mass at the site of this palpable breast lesion. The mass was about 2.5 × 3 × 3.5 cm in size, situated at the upper part of the left breast (Figure 2). There was no associated architectural distortion, skin thickening or skin retraction. No pathologic micro calcification was found. No further abnormal densities in the surrounding tissue or in close proximity to the mass were seen. The previous mammogram, obtained four years ago, did not reveal any signs of a breast mass that confirmed the rapid growth of the lesion. The mammogram of the right breast was unremarkable. Breast ultrasonography (US) was performed and demonstrated a 2.5 × 3 × 3.5 cm well defined heterogeneously hypoechoic mass with cystic component in the left breast (Figure 3). Otherwise, there was no abnormality at the left breast and no enlarged lymph nodes could be seen in the axilla. The right breast appeared normal at ultrasonography.

Four 16-gauge US-guided core needle biopsy specimens were taken from the breast lesion. A section of the specimen revealed variably sized anastomosing vascular spaces, suggesting a vascular tumor, but its malignant nature could not be established without an excisional biopsy, which made preoperative diagnosis and surgical planning difficult. The tumor was removed surgically, and a large vascular and hemorrhagic tumor was found at operation. Pathological examination revealed anastomosing vascular spaces that were lined by flattened cuboidal cells with nuclear prominence and pleomorphism (Figure 4). The nuclei of the endothelial cells were not very atypical. There was also mild infiltration between surrounding adipose tissue and granular parenchyma. The patient underwent left total mastectomy. Sentinel node biopsy was performed. Four axillary lymph nodes were dissected and had been reported free of metastases. There

Authors' affiliations: [1]Surgical Oncology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, [2]Department of Radiology, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

•Corresponding author and reprints: Donya Farrokh MD, Department of Radiology, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Cell Phone: +98-915-5101417, E-mail: farrokhd@mums.ac.ir, modoodie911@mums.ac.ir.

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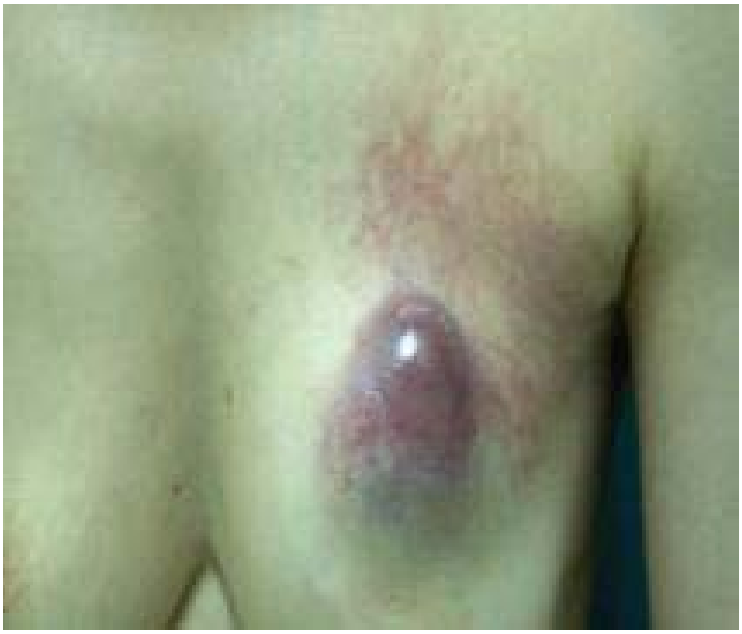

Figure 1. There is a reddish exophytic mass at the upper part of the breast accompanied by bluish red skin discoloration surrounding the tumor.

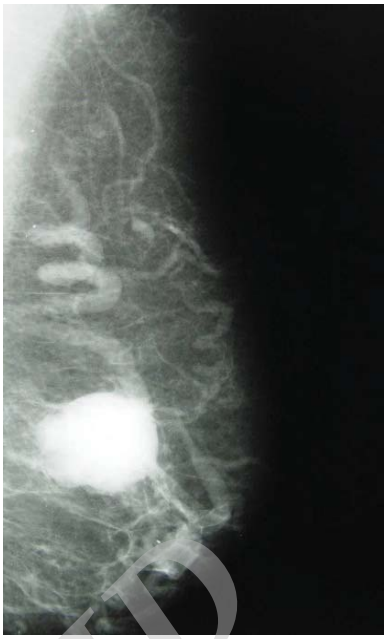

Figure 2. Mediolateral oblique mammogram image of the left breast shows a dense, well-defined mass associated with a fatty vessel in the upper part of the breast. No evidence of associated micro calcification or architectural distortion.

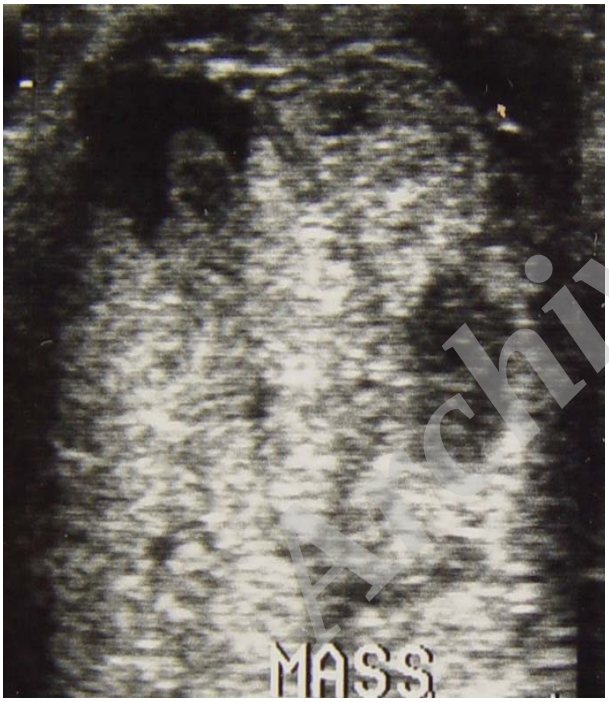

Figure 3. Ultrasound imaging of the left breast shows a well-defined hypo-echoic mass with internal cystic component.

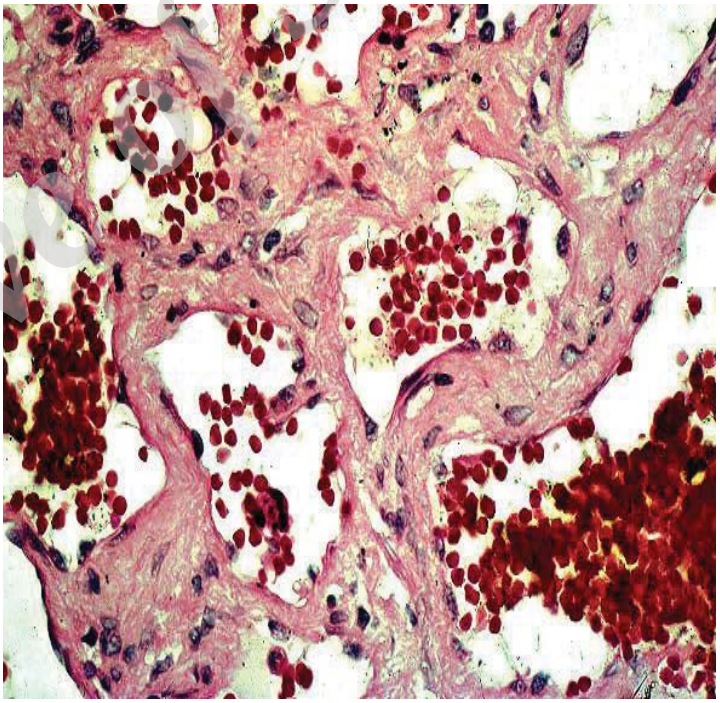

Figure 4. The mammary vascular tumor shows a proliferation of small and poorly formed anastomosing vascular spaces (H&E×100).

was no evidence of tumoral invasion at the overlaying skin. Immunohistochemical staining showed expression of CD3. Based on these findings, the pathological diagnosis was consistent with a low- grade angiosarcoma.

Discussion

Malignant breast lesions that arise from stromal tissue are extremely rare, accounting for one in 1700 – 2300 cases of all primary malignant breast tumors.[1,2] Primary angiosarcoma of the breast is a highly malignant tumor, which is generally regarded as one of the most malignant breast lesions.[2,4] Angiosarcoma is a malignancy of endovascular origin which is referred as hemangioendothelioma and hemangioblastoma.[4]

A primary and a secondary type of breast angiosarcoma are known. There are no known risk factors for developing primary angiosarcoma. Primary angiosarcomas can occur bilaterally. Bilateral lesions can also be due to metastatic spread.[1] Twelve

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percent of the cases are found during the pregnancy. An association of the tumor with pregnancy has been suggested. Therefore, hormonal stimulation may play a role in the development of angiosarcomas. It is demonstrated that secondary angiosarcoma of the breast can be differentiated from the primary angiosarcoma, because the former is associated with some specific risk factors.[5,7] Therapeutic radiation has been involved in the development of angiosarcomas as the most common subtype of all sarcomas occurring after breast radiotherapy. A correlation has been revealed between breast-conserving therapy and the pathogenesis of secondary angiosarcoma, particularly after conservative surgery of the breast followed by radiotherapy.[7] Results of the studies showed an estimated prevalence of arising angiosarcoma, ranging from 0.9 to 1.59 cases per 1000 in patients with breast-conserving surgery alone, and an estimated risk of %15.9 after breast- conserving surgery accompanied by radiotherapy.[5,7]

Multiple factors are suggested as causative factors for developing secondary angiosarcoma, including: congenital, idiopathic and traumatic factors. However, the exact etiology is still unknown. Lymphedema, radiogenic DNA mutation and a genetic predisposition status may also have a role in the development of secondary angiosarcoma.[5]

Today it is accepted that distinguishing primary from secondary type of breast angiosarcoma is not important, because the clinical behavior and prognosis of both types are very similar.

Breast angiosarcoma may be seen in patients with Stewart–Treves syndrome, a cutaneous angiosarcoma as a result of post mastectomy lymphedema.[8] Breast angiosarcoma arise in women, usually during the third and fourth decades of life; these lesions are unlike breast carcinomas, which typically arise later in life.[1,3]

Women with primary breast angiosarcoma usually present with a palpable breast mass, which at times can be rapidly growing. Bluish skin discoloration is not an uncommon finding and is thought to be attributed to the vascular nature of the tumor.[1,2,9] Some patients may complain of a painful breast lump with tenderness. Approximately 2% of primary angiosarcomas of the breast may present with diffuse breast enlargement. Nipple retraction and skin thickening have been reported, but nipple discharge is usually absent.[1,2,8] Our patient presented with an exophytic breast lump with purple and bluish skin discoloration. In the series by Yang, et al. the mean tumor size of the mass at presentation was 5.9 cm.[10] Angiosarcomas smaller than 5 cm are usually associated with a better prognosis. With small tumors, recurrence and distant metastases rarely occur.[1,2]

Breast angiosarcomas are histologically divided into three types. Well-differentiated (grade1) breast lesions are composed of well-developed anastomosing vascular channels that surround breast ducts and infiltrate the adipose tissue. Vascular channels are lined by a single laser of endothelial cells with hyper chromatic nuclei. This type of tumors may show minimal to absent papillary growth, hemorrhage, necrosis or pleomorphism, and mitosis is rare. Moderately differentiated angiosarcoma (grade 2) shows irregular vascular channels with small foci of solid proliferation of spindle-shaped cells. Mitosis is present, but necrotic changes are usually absent. Poorly differentiated (grade 3) angiosarcomas show more solid and typical cell proliferation. This type of tumors show necrotic areas and blood lakes, and mitosis and pleomorphism are common findings. Grade 3 angiosarcomas are associated with decreased five-year survival rate and increased metastasis rate.[1]

The radiologic findings are mostly non-specific, and mammary angiosarcoma may simply fail to be noticed.[3] For patients presenting with a breast mass or bluish skin discoloration, mammography remains as the baseline imaging modality.[3,10] On mammogram, the tumor may be seen as a large, lobulated mass with well-circumscribed or ill-defined borders. The mass may be round or oval; uncommonly there is calcification in the lesion but lacks the typical mammographic appearance of malignant-type calcifications.[3,11,12] Liberman, et al. study of mammography in 26 cases of primary breast angiosarcoma showed a solitary un-calcified mass in 52% of patients, and a calcified mass in 10% of patients.[3] The tumor may rarely demonstrate a soap bubble appearance on mammography. In our patient, mammogram showed a well-defined, homogeneous mass without any associated finings. Mammogram may appear normal in 55% of cases of primary angiosarcoma. There are several possible reasons why, despite the large tumour size, some angiosarcomas are not readily detected by mammography. Angiosarcoma is composed of dilated anastomosing vascular channels of low cellular densities, which may be isodense with the surrounding breast tissue, and easily overlooked by dense breast parenchyma, especially in young women with mammographically dense breast. Also, breast angiosarcoma tends to grow and extend between the fat lobules and mammary glands with ill-defined margins.[3]

Ultrasound findings of breast angiosarcoma are non-specific and may mimic benign lesions, leading to diagnostic challenges.[2,12,13]

Angiosarcoma may appear as a hypoechoic, hyperechoic, or heterogeneous breast lesion with or without posterior acoustic shadowing on ultrasound images.[12,13] In Yang, et al. series, 54% of the breast angiosarcomas were hyperechoic or mixed hypo and hyper echoic on US.[10] Hypervascularity may reflect the vascular nature of the tumor and the multiple interfaces of the vascular channels.[9] In our patient, ultrasonography revealed a well-circumscribed, hypoechoic mass containing cystic components.

Although we did not perform magnetic resonance (MR) imaging in this patient, a few characteristics of MR appearance of breast angiosarcoma will be described. MR imaging has a high contrast resolution and sensitivity to detect breast lesions but not in demonstrating the extent of the breast lesion and vascular or aggressive nature of this malignant tumor.[1] Murakamet, et al. reported that T1-weighted images after contrast agent injection showed low intensity in the central region with high signal intensity in the periphery of the tumor. This finding can be due to decreased blood circulation in the central area of the tumor.[14] MR imaging studies have demonstrated that a high intensity on T2-weighted MR images, prolongation of enhancement on the dynamic study, and the presence of multiple regions without enhancement in the tumor might be specific to breast angiosarcoma. The kinetic pattern of angiosarcoma enhancement is non-specific; low-grade lesions show plateau or persistent enhancement, whereas high-grade lesions demonstrate rapid enhancement and washout pattern.[5]

The prognosis for patients with primary angiosarcoma depends on the tumor grade. Patients with a higher-grade lesion are more prone to develop a recurrence, and have a lower survival rate than patients with a lower-grade tumor.[1,2,14] The estimated probability of five-year survival rate after initial treatment is 76% for patients with grade 1 tumors, and 15% for patients with grade 3 tumors.[13,14] There was no evidence of a metastatic lesion in our patient at the time of diagnosis. To date, 15 months after mastectomy, our patient showed no signs of recurrence or metastasis. Breast angiosarcoma

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tends to metastasis to the lungs, liver, subcutaneous tissue, skin, brain, bone and ovaries.[13]

Local recurrence is an adverse prognostic indicator and is often accompanied by distant metastasis.[3,14] Metastasis to the contralateral breast has also been reported.

Because breast angiosarcoma is a very rare tumor, no standard treatment has been established. Surgical resection with mastectomy is the choice treatment for both forms of primary and secondary angiosarcoma.[1,2] For low grade primary angiosarcoma, breast conservation therapy may be indicated. Chemotherapy may reduce the local recurrence rate. In patients with poorly differentiated angiosarcoma, adjuvant chemotherapy results in a higher proportion of patients who are relapse-free, compared to those not receiving adjuvant chemotherapy.[15]

Although in some tumors, adjuvant chemotherapy is helpful, but available treatment for disseminated disease is of minimal benefit. Radiotherapy can be useful, although irradiation may be contraindicated for possibly radiation-induced tumors. Usually, radiotherapy is used after lumpectomy and total mastectomy in large tumors (> 5 cm), positive tumor margins and skin or regional lymph node involvement.[2] Surgery may be accompanied by fractional radiation therapy in high grade angiosarcoma to decrease the recurrence rate.

In conclusion, angiosarcoma of the breast is a rare malignant tumor with difficult differential diagnosis from other breast sarcomas and angiomatous breast tumors. It typically presents as a palpable, painless breast mass in young women. The tumor tends to recur locally and metastasis widely. Imaging findings on mammography and ultrasound may be nonspecific. MRI is a useful imaging adjuvant. An adequate tissue diagnosis is needed to confirm the diagnosis.

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