A case of primary breast angiosarcoma

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Angiosarcoma of the breast is a rare malignancy that may be easily misdiagnosed. Of the two forms, the more common form presents in patients (typically postmenopausal) with a history of breast cancer, secondary to irradiation or chronic lymphedema. In contrast, the rarer form, primary angiosarcoma, arises sporadically in premenopausal women who present with palpable masses. Primary angiosarcoma accounts for 1 in 2,500 cases (0.04%) of breast cancer (1). The described patient presented with primary breast angiosarcoma. Ultrasound, mammography, and magnetic resonance imaging findings are presented.

Case report

A 45-year-old woman with a history of systemic lupus erythematosus presented for workup of a palpable abnormality of the left breast. The patient identified this abnormality on self-examination three months earlier. In the lower inner quadrant of the left breast, there was reportedly a lobulated smooth mobile mass. No lymphadenopathy was evident on clinical examination. Since the patient recently had a screening mammogram with benign findings (Fig. 1), she underwent a breast sonogram. No sonographic correlate was found in the area of the palpable abnormality. Thus, the patient was followed clinically, and the diagnosis of lupus mastopathy was considered.

Due to persistence of the palpable abnormality, the patient underwent a contrast-enhanced breast MRI (Fig. 2). In the left lower inner breast, a lobulated irregular mass measuring 2.7 x 2.2 cm, hypointense on T1-weighted images and hyperintense on T2-weighted images, was seen. The mass had kinetics demonstrating a rapid rise to peak with washout. The mass also had increased circumferential signal on STIR images, suggesting possible edema. A second mass demonstrating similar kinetics was seen in the supra-areolar region. Scattered enhancing nodules were incidentally noted in the right breast.

Excisional biopsy of the area of the MRI abnormality was performed. On pathology, multifocal angiosarcoma of intermediate to high grade was identified. The largest focus measured 1.6 cm. Histologic sections showed neoplastic blood vessels lined by endothelial cells with marked cytologic atypia as well as frequent associated mitoses. Intermediate- to high-grade areas consisted of solid growth or prominent endothelial tufting with papillary formations as

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well as blood lakes (Fig. 3). Other areas were low-grade and seen as anastomosing, thin-walled, vascular channels invading into and around benign mammary lobules and stroma. Fine-needle aspiration of the right breast nodules revealed no malignant foci. The patient was free of metastatic disease, as determined by CT of the abdomen and the pelvis and bone scintigraphy. The patient elected to undergo bilateral mastectomy. The mastectomy specimen of the left breast revealed tumor in the lower inner quadrant, measuring 3.5 cm. The resection margins were negative. The right mastectomy specimen contained only benign findings.

Discussion

Angiosarcomas are highly malignant vascular neoplasms. They may present as primary tumors, or arise secondary to irradiation (postirradiation angiosarcoma) or lymphedema (lymphedema-associated cutaneous angiosarcoma), typically in patients who have undergone treatment for breast cancer (2). Secondary angiosarcomas present in older women at a mean age of 60 years, compared to two to three decades earlier for primary angiosarcomas. Secondary angiosarcomas present with a mean age of onset of 6 years after irradiation, with an average tumor size of 7.5 cm. Multicentricity is seen in up to one-third of patients with secondary disease, and these tumors are typically high grade (3).

Following mastectomy, the patient completed adjuvant chemotherapy with doxorubicin. She is three years post mastectomy with recurrence-free survival. Due to the high risk of recurrence, she continues to be closely followed with serial CT scans of the chest, abdomen, and pelvis every 6 months.
While patients with primary angiosarcoma may present as early as their teens and into their 70s, the average age of diagnosis is late 30s to early 40s (2, 4, 5, 6). Patients frequently identify an abnormality before the onset of screening mammograms; thus, masses are large enough to be palpable, with an average diameter of 4.6 to 5.9 cm at diagnosis (4, 5). Primary and secondary angiosarcomas usually present as palpable masses (4, 7) or with fullness, swelling, and irregularity of the breast (2, 8). Sometimes, there is bluish discoloration of the skin, due to the presence of blood vessels. This finding is most evident in primary angiosarcoma, as patients with secondary angiosarcoma may have postoperative changes and skin thickening from chronic lymphedema and radiation.

The patient described here was premenopausal, had no history of prior radiation therapy or lymphedema, and had a single palpable abnormality at initial presentation, consistent with primary (rather than secondary) angiosarcoma.

The diagnosis of primary angiosarcoma is particularly difficult due to the young patient population it afflicts and the nonspecific findings on ultrasound and mammography. On ultrasound, angiosarcomas can include a wide spectrum of findings. They may be well-circumscribed or poorly marginated. They may be diffuse. They may be hypoechoic or of mixed echogenicity. Angiosarcomas typically do not contain angular margins or posterior shadowing, which is typical of breast carcinomas, but do show hypervascularity on color Doppler imaging.

Mammographically, angiosarcomas, when identified, appear most commonly as ill-defined masses, without spiculations or calcifications. The patient described had a screening mammogram months before identification of the palpable mass, yet the mammogram revealed benign findings. This is not an uncommon occurrence. In a study of 21 cases by Liberman et al., one-third of patients had no remarkable findings on mammography. Angiosarcomas were more commonly missed if of low histological grade (5).

Yang et al. found that in a study of 16 breast angiosarcomas, 31% of mammograms were scored as BI-RADS® 2. Angiosarcomas may be especially hard to distinguish due to dense parenchyma, which is typically seen in these younger patients.

Angiosarcomas are best discriminated from normal breast parenchyma via MRI. They are seen as large, lobular masses with indistinct borders. Low-grade tumors are hypointense on T1-weighted images and hyperintense on T2-weighted images, whereas high-grade angiosarcomas may have irregular areas that are hyperintense on T1-weighted images, corresponding to hemorrhage or venous lakes. Their more aggressive nature is suggested by rapid enhancement and washout (type 3 curve) (2).

On pathology, angiosarcomas can resemble benign vascular lesions such as hemangiomas. In a study by Rosen et al., three of 63 patients with angiosarcoma were initially misdiagnosed as having hemangioma on biopsy. Angiosarcomas and hemangiomas are composed of thin-walled capillaries lined by cytologically bland/low-nuclear-grade endothelial cells. Mitotic figures are rare in well-differentiated angiosarcomas and may not be present with limited sampling. However, hemangiomas differ from angiosarcomas in that they are usually less than 2 cm, they are well circumscribed, and their vascular channels go around ducts and lobules rather than invading them.

Prognosis depends on tumor grade. Previous reports have found a five-year disease-free survival of 76% and 70% for low- and intermediate-grade disease, respectively, compared to only 15% for high-grade angiosarcoma (9). The median length of disease-free survival ranges from greater than 15 years to 15 months for low- and high-grade tumors, respectively. Tumor size and resection margin status are also significant prognostic factors (1, 10).

Breast angiosarcomas rarely metastasize to the regional lymph nodes (1, 9, 11) and more commonly undergo hematogenous spread to the lung, the liver, and the bones (4, 9). PET with 18F-FDG can be used for staging, with uptake seen for tumors in the pleura, heart, and liver. CT is frequently used to monitor for recurrence. Angiosarcomas are usually treated with total mastectomy due to their large size, although breast-conserving treatment with axillary lymph-node dissection can be considered for small, low-grade tumors. There is a high rate of systemic recurrence. In one study of 69 breast angiosarcoma patients, 55% of patients experienced recurrence after 40-months’ followup (12). The effect of adjuvant chemotherapy has yet to be examined for breast angiosarcomas, due to their low prevalence, though retrospective studies have failed to show a significant difference in overall and recurrence-free survival (12). Studies from primary soft-tissue sarcomas have shown increased time to recurrence and overall recurrence-free survival with doxorubicin-based chemotherapy or epirubicin plus ifosfamide (13, 14). In this reported case, despite this patient having high-grade angiosarcoma, she is recurrence-free three years following mastectomy.

Though rare, primary angiosarcoma should be considered when a 20- to 50-year-old woman presents with a palpable mass that appears to be growing rapidly. On mammography, calcifications or spiculations that typify breast carcinoma may not be present. Ultrasound is frequently inconclusive, but hypervascularity is seen with color Doppler imaging. If the area of the palpable abnormality is visualized on ultrasound, a core biopsy should be performed. If the biopsy is inconclusive or if the mass continues to enlarge, a repeat biopsy and MRI should be considered.

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