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Case Report

A rare presentation of pregnancy associated primary angiosarcoma of the breasts☆

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ABSTRACT

Primary angiosarcoma of the breast is a rare malignancy that is important for radiologists to recognize in young patients because its imaging appearance may mimic benign lesions resulting in advanced stages of disease and overall decreased patient survival. We present a unique case of a bilateral primary angiosarcoma in a pregnant patient in her twenties. She presented with a self-detected, rapidly enlarging, non-tender right breast mass while in her third trimester.

Introduction

Angiosarcoma (AS) of the breast is a rare mesenchymal tumor that accounts for less than 1% of all primary breast cancers [1–3] and 8% of all sarcomas. It has an annual incidence of 4.6-17 per 10 million women [4]. Angiosarcomas arise from the endothelial cells that line vascular channels [5–7].

AS can be classified as either a primary or secondary form, with primary arising from the parenchyma of the breast and secondary associated with a history of prior radiotherapy for breast cancer with a 10-year latency period [8,9]. Primary angiosarcoma (PAS) develops in women 20-50 years of age whereas patients with secondary AS present later, 65-75 years of age [9]. AS can appear benign on clinical examination and imaging. Nevertheless, there should not be a delay of diagnosis especially in younger patients since ASs have an aggressive clinic course with an overall poor prognosis [10]. Unlike invasive mammary carcinomas of the breast, AS metastatic spread is primarily hematogenous rather than local regional. A few cases of bilateral PASs in women and sporadic cases in men have been described [11]. As to our knowledge, there have not been any reported cases as bilateral pregnancy associated breast cancer and this is the focus of this article.

☆ Competing Interests: All authors declare that there are no financial disclosures and personal relationships with other people or organizations that could inappropriately influence (bias) our work.

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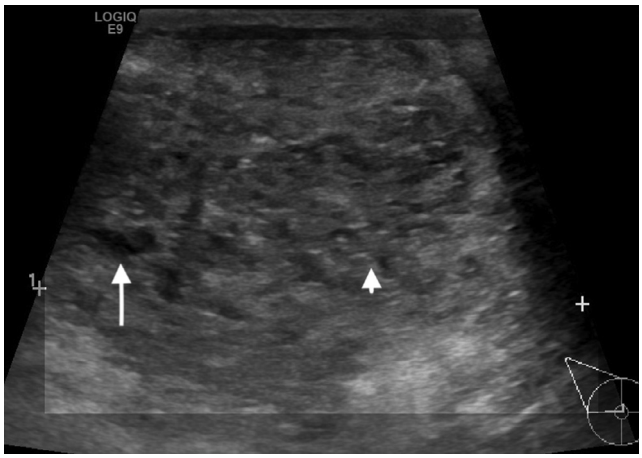

Fig. 1 – Ultrasound of the patient's right breast demonstrates a heterogeneous, not circumscribed mass with numerous small anechoic regions (arrow) and echogenic foci (arrowhead).

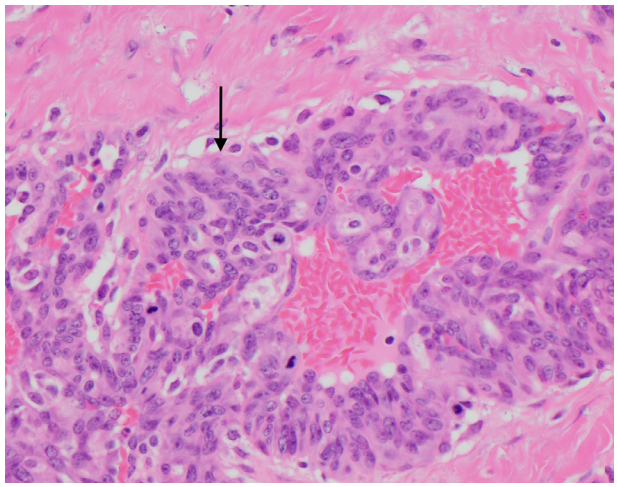

Fig. 3 – Right breast primary angiosarcoma histology (Hematoxylin and eosin stain (H&E) 40×). High-grade nuclear atypia and numerous mitotic figures are present within the intravascular.

Case description

A pregnant female patient in her twenties presented to the breast cancer center with a rapidly enlarging, 10 cm, painless right breast mass. Except for prior pregnancies, she reports no relevant medical history and no family history of breast cancer.

A diagnostic right breast ultrasound was performed as the initial imaging study. The ultrasound demonstrated a heterogeneous, not circumscribed mass with numerous small anechoic regions and echogenic foci (Fig. 1). Because the ultrasound features were suspicious, a bilateral mammogram with the patient's abdomen shielded was performed. Diagnostic bilateral Medial lateral oblique (MLO) and craniocaudal (CC) mammographic views (Figs. 2A–D) demonstrated a 10.5 cm, high-density, oval mass with indistinct margins occupying almost the entire right breast. Pathology from the ultrasound-guided core needle biopsy of the mass revealed a high-grade PAS (Fig. 3). From the time of her initial breast imaging to her postpartum staging studies (3-month interval), a left breast mass was detected on her staging chest CT (Fig. 4A). The rest of the staging CT and bone scan were negative. A new left breast diagnostic mammogram was performed and showed a 2.5 cm and a 1cm, high-density, irregular masses in the upper inner quadrant of the left breast, posterior depth (Figs. 4B and C). The masses were 2 cm apart. The patient refused left breast ultrasound-guided core biopsy.

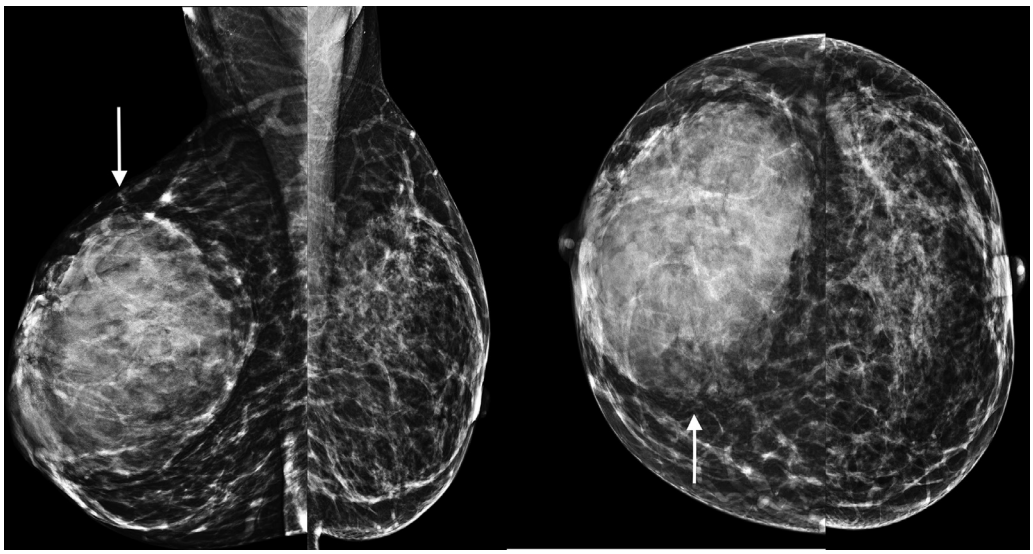

Fig. 2 – Diagnostic bilateral Medial lateral oblique and craniocaudal mammographic views (A–D) demonstrated a 10.5 cm, high-density, oval mass with indistinct margins occupying almost the entire right breast.

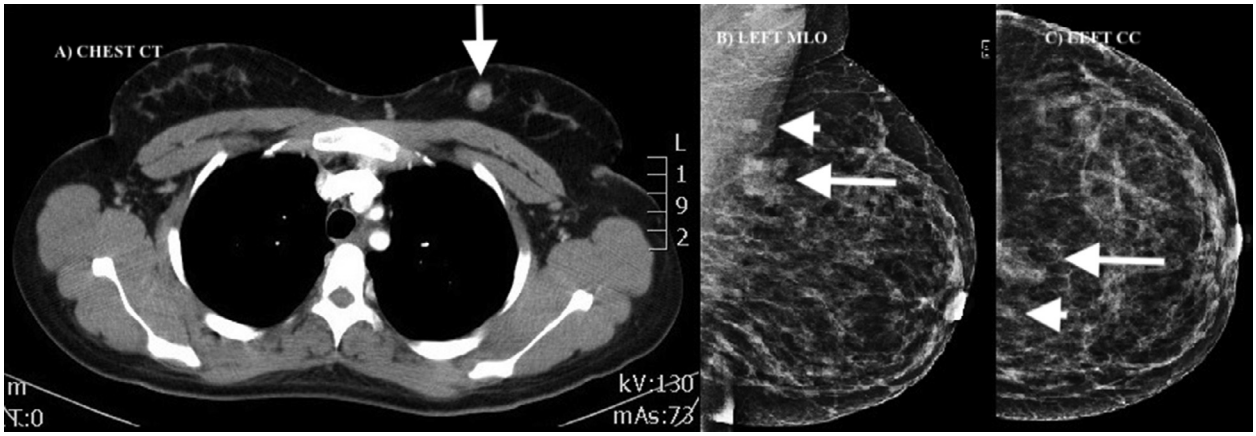

Fig. 4 – Left breast primary angiosarcoma. (A) Staging chest CT with contrast. A mass (arrow) is present in the upper inner quadrant of the left breast. (B, C) Diagnostic left breast mammogram, Medial lateral oblique and craniocaudal views. A 2.5 cm (arrow) and a 1 cm (arrowhead), high-density, irregular mass are seen in the upper inner quadrant of the left breast, posterior depth. The masses are 2 cm apart.

The patient underwent a total right mastectomy with sentinel lymph node dissection and surgical excision of the left breast mass. Final pathology revealed an 11 cm PAS with negative margins with one of two positive sentinel lymph nodes. Left breast excisional biopsy showed a 2.1 cm PAS. On further surgery, no additional positive right axillary nodes (0/13) were detected with an axillary lymph node dissection and the completion left mastectomy revealed a 0.7 cm PAS (thus, accounting for the second mass seen mammographically) with negative margins and no positive left sentinel lymph nodes (0/3).

Less than seven months into treatment with Paclitaxel and chest irradiation, the patient presented with a bleeding right chest wall mass. Biopsy of the chest wall mass revealed recurrent PAS. Hypervascular lung and liver metastases and multiple lytic bone metastases were identified on her CT study (Figs. 5A–C). Unfortunately, the patient died from her disease less than 1-year from the time of her diagnosis.

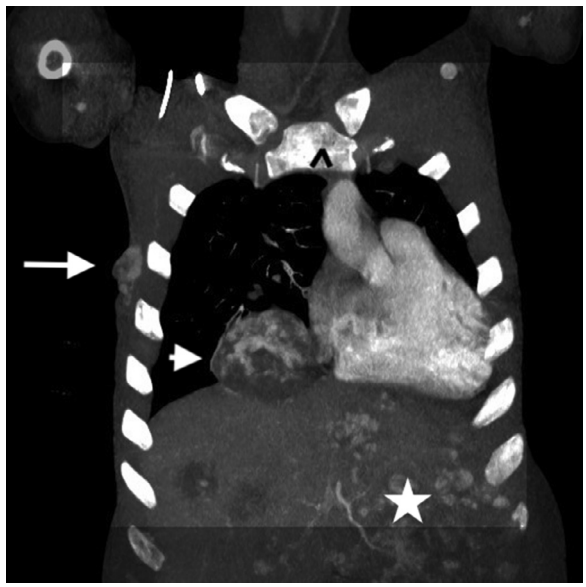

Fig. 5 – CT of the chest with contrast. The patient's recurrent PAS represents an 8 cm, heterogeneous, hypervascular mass involving the right chest wall (arrow). The patient has numerous hypervascular enhancing pulmonary nodules with the largest located in the right middle lobe (arrowhead) that abuts the right heart border. Extensive intrahepatic hypervascular metastasis are present in the liver with the largest confluent mass approximating 11 cm (*). Lytic metastasis also involve the sternum, clavicles and several ribs (^)

Discussion

AS of the breast is a rare mesenchymal tumor that originates from the endothelial cells that line vascular channels. It is an infiltrating overgrowth of vascular endothelial cells and is associated with hemorrhage and necrosis [12–14]. AS represents less than 1% of all primary breast cancers [1–3] and has an aggressive clinic course with an overall poor prognosis [10]. It can present as a primary cancer or a secondary form that is associated with a history of radiotherapy 10-year prior in older women (65-75 years) [9]. PAS is seen in women 20-50 years of age with no history of radiation therapy [8,9] as in our patient's case. PAS is extremely rare among males [13] and pregnant patients [14,15]. PAS was first described in 1907 by Borrman and arises in the parenchyma of the breast with occasional skin involvement [9,16].

Our patient presented with the most common clinical presentation of PAS with a palpable, painless rapidly growing mass. Large masses can lead to platelet sequestration and the hemorrhagic manifestations of Kasabach-Merrit syndrome [16,17], which our patient did not develop. Others have also

reported PAS to present as a fullness or swelling in the breast [18]. Clinically, there is usually absence of nipple discharge, nipple retraction or axillary lymphadenopathy [19]. In some cases, bluish colored skin in association with the vascular nature of the tumor has been described [7].

Since our patient's cancer was diagnosis during pregnancy, this is also known as pregnancy associated breast cancer (PABC). PABC is breast cancer that develops during pregnancy or in the first postpartum year and accounts for less than 5% of all breast cancers. However, it represents up to 20% of breast cancers in women up to 30 years [20]. PABCs are aggressive tumors and due to delay in diagnosis, attributed to pregnancy changes or a benign lesion such as fibroadenoma, these patients present with advanced stage of disease and have a poorer outcome than do women of the same age with breast cancer.

The mammographic and ultrasound features of PAS are nonspecific compared to those seen with adenocarcinoma. Consequently, the findings could be mistaken as benign in young or pregnant patients and delay diagnosis. The most common mammographic finding is of a non-calcified, round or oval, hyperdense mass [21,22]. Some have reported PAS to be radiographically occult in patients with dense breast tissue [25,23] with a false negative rate of 19%-33% [21,22], which is a consideration of the left breast in this case. Sonographically, PAS can appear as a circumscribed or ill-defined mass with hypoechoic to heterogeneous echogenicity that may be hypervascular on color Doppler [22]. Benign lesions with pregnancy-associated changes can also have the similar imaging characteristics; thus, a definitive diagnosis can be achieved with a core needle biopsy.

Some authors have reported magnetic resonance imaging to identify imaging characteristics of PAS. PAS exhibits hyperintensity on T2 weighted images [22] that may be the result of slow-flow blood channels [24]. On T1-weighted images, it can be iso-dense or have low signal intensity [23] or high T1 signal due to hemorrhagic areas [1], and have rapid, intense contrast enhancement and wash out kinetics [25,26].

The histological features of PAS demonstrate irregular vascular formations with hyperchromatic and irregular nuclei that can be associated with hemorrhage and necrosis with high-grade lesions. Immunohistologic staining for vascular makers (CD31, CD 34, ERG, Fli-1) [27,28] and c-myc confirm the diagnosis of AS [29]. Our patient's cancers were CD31 and c-myc positive.

Unlike invasive mammary carcinomas, metastatic disease of PAS is primarily hematogenous. However, a few cases of lymphatic involvement have been reported [30,31] Our case is unique in that it demonstrates both types of metastatic spread. Pulmonary metastasis are the most common distant site [16,32,33]. Our patient had diffuse visceral and osseous metastatic disease.

Surgical management is a key component of therapy. Breast conservation for small masses can be performed; however, negative margins are needed due to the high recurrence rate of sarcoma. Total mastectomy alone or with axillary lymph dissection is the preferred surgery (Arora). Others report that axillary lymph node dissection is not recommended since nodal involvement is <10% [34]. Nevertheless, if less there is suspicion for nodal disease, as in our patient, it should be performed [35]. With a 5-year survival rate of 40%-91% [36,37], adjuvant chemotherapy and radiation is thought to be beneficial in improving overall survival [38,39].

Conclusion

PAS of the breast is a rare soft tissue malignancy that arises in the breast parenchyma with occasional skin involvement. Unlike invasive mammary carcinomas of the breast, PAS's metastatic spread is primarily hematogenous rather than local regional. Pulmonary metastasis is the most common distant site. Radiologists should consider PAS in the differential diagnosis for a new or enlarging mass in young patients because its imaging appearance may mimic benign pathologies; thus, delaying its management. PAS has an aggressive clinic course with an overall poor prognosis. PABC is breast cancer that develops during or within 1-year following pregnancy and accounts for less than 4% of all breast cancers. Because of more aggressive tumors and delay of diagnosis, these patients present with advanced stages of disease and have a poorer outcome than do women of the same age with breast cancer.

Patient consent

The author was unable to obtain written consent from the patient or from the patient's relatives, despite attempts to do so. Because of the public interest in publication, the anonymization of the patient, and that attempts had been made to contact the patient and their relatives, exceptional agreement for publication of the case report was given by the Editor-in-Chief of the journal *Radiology Case Reports*.

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