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Case Report

Radiation-associated angiosarcoma of the breast with initial presentation as non-mass enhancement on MRI ☆

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ABSTRACT

Radiation-associated angiosarcoma of the breast (RAASB) is a rare and aggressive malignancy occurring after radiation therapy as part of breast cancer treatment. RAASB usually presents several years after prior radiation and typically involves the skin with or without involvement of the parenchyma. Most RAASB are detected as cutaneous changes on physical exam. Herein, we present a unique case of a clinically occult RAASB diagnosed as non-mass enhancement on annual surveillance breast MRI.

Introduction

Angiosarcoma of the breast is a rare entity that can be separated into primary and secondary (radiation-associated and chronic lymphedema-associated) types. Radiation-associated angiosarcoma of the breast (RAASB) is an aggressive and increasingly described breast malignancy within the skin associated with radiation therapy given as part of breast cancer treatment. RAASB presents with skin changes on physical exam. RAASB is a clinicopathologically distinct entity when compared to primary angiosarcoma of the breast (PASB) which

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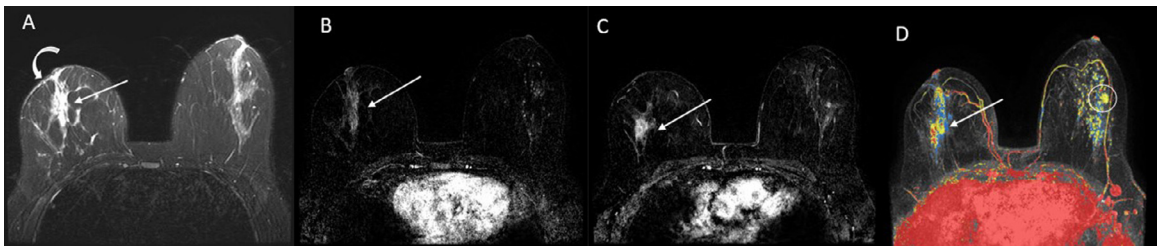

Fig. 1(A) – T2-weighted image demonstrates segmental increased signal in the right breast (straight arrow) and right breast skin thickening (curved arrow). (B and C) T1-weighted postcontrast subtraction images demonstrate segmental non-mass enhancement in the right breast (straight arrows) and mild background parenchymal enhancement in the left breast. (D) Maximum intensity projection (MIP) image of tissue contrast kinetics demonstrates segmental non-mass enhancement with washout kinetics (red color) in the right breast (straight arrow) as well as background parenchymal enhancement in the left breast. Incidentally noted fibroadenoma of the left breast (circle) was unchanged since initial MRI.

is located within the breast parenchyma. Herein, we report an interesting case of RAASB in which the initial presentation was clinically occult non-mass enhancement within the breast parenchyma on MRI without cutaneous involvement.

Case report

A 31-year-old female presented with estrogen receptor, progesterone receptor, and HER2 negative right breast invasive carcinoma with right axillary nodal metastasis. The patient received preoperative doxorubicin and cisplatin followed by breast conservation therapy and axillary lymph node dissection. In the adjuvant setting, she received additional doxorubicin and cisplatin, followed by weekly paclitaxel and then radiation to the breast and axillary regions. Due to her mammographically occult primary malignancy and heterogeneously dense breast tissue, she was followed with annual breast MRI imaging in addition to annual mammograms. Over the following 9 years, her radiologic evaluation revealed stable postsurgical and postradiation changes without evidence of tumor recurrence.

On year 9 following treatment of her breast cancer, annual breast MRI examination revealed suspicious non-mass enhancement in the right upper outer, posterior depth breast extending anteriorly into the subareolar breast in a segmental distribution. Total extent of heterogenous, non-mass enhancement measured 8.5 × 2.5 × 3.6 cm, which demonstrated T2 hyperintense signal and washout kinetics (Fig. 1). Of note, MRI did not demonstrate suspicious skin enhancement. There was stable 3-mm mild skin thickening when compared to prior exams. No suspicious lymphadenopathy was seen on MRI.

Second look diagnostic mammogram and ultrasound was performed for further evaluation of the right breast non-mass enhancement. Diagnostic mammogram demonstrated stable postsurgical and post-treatment changes of the right breast without suspicious mammographic findings or significant change from priors (Fig. 2). Second look ultrasound demonstrated 2 right breast masses correlating with the extent of non-mass enhancement seen on MRI. Ultrasound of the right breast at 10 o'clock, 6 cm from the nipple showed an irregular hypoechoic mass measuring 2.5 × 1.7 × 1.8 cm (Fig. 3a). Ultrasound of the right subareolar breast at the 11-o'clock position showed another irregular hypoechoic mass measuring 3 × 2.4 × 1.9 cm (Fig. 3b). These masses demonstrated no increased internal vascular flow but had associated increased peripheral vascularity (Fig. 3). Subsequent ultrasound-guided core needle biopsy of both masses demonstrated high grade angiosarcoma. On whole body FDG PET/CT, the 2 right breast masses were FDG-avid and there was no evidence of distant metastases (Fig. 4). The patient underwent right mastectomy and surgical pathology demonstrated an 8.3 × 5.8 × 4.5 cm angiosarcoma (Figs. 5 and 6) with negative surgical margins. The histologic extent of disease correlated with extent of non-mass enhancement on MRI. Treatment consisted of adjuvant chemotherapy with gemcitabine and docetaxel. The patient is now 6 years post angiosarcoma treatment without evidence of recurrent disease.

Discussion

Pathologically, angiosarcomas are characterized by abnormal, pleomorphic, malignant endothelial cells with decreasing cell organization with increased tumor aggressivity [1]. Breast angiosarcomas encompass approximately 20% of angiosarcoma cases throughout the body and are typically separated into primary and secondary (radiation-associated and chronic lymphedema-associated) types [1]. PASB and RAASB represent two unique entities with distinct clinical presentations. PASB often affects younger patients in their 3rd to 4th decades of life with an incidence of 1 in 1700-2300 cases of primary breast malignancies [2–4]. PASB is not associated with any particular risk factor and arises within the breast parenchyma with a variable degree of skin involvement [3]. On the other hand, RAASB tends to present in women in their 6th to 7th decades of life, has been reported to present on average close to 5 years after undergoing radiation therapy as part of breast cancer treatment, and is primarily within the skin [2,4,5]. Awareness of these differences is important as it highlights the unique parenchymal-only involvement in our case of RAASB; a dis-

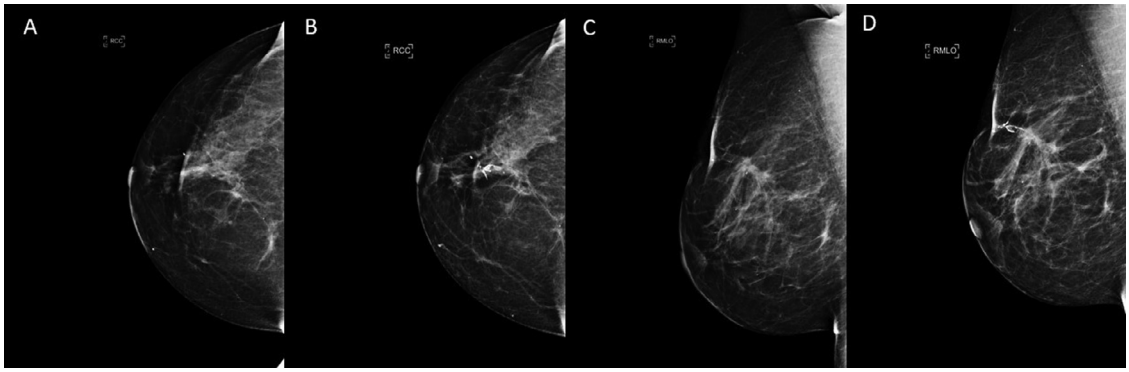

Fig. 2 – Right craniocaudal (RCC) and right mediolateral oblique (RMLO) views demonstrate benign calcifications and stable post surgical changes of the lumpectomy site 2 years prior (A and C) and at the time of diagnosis (B and D).

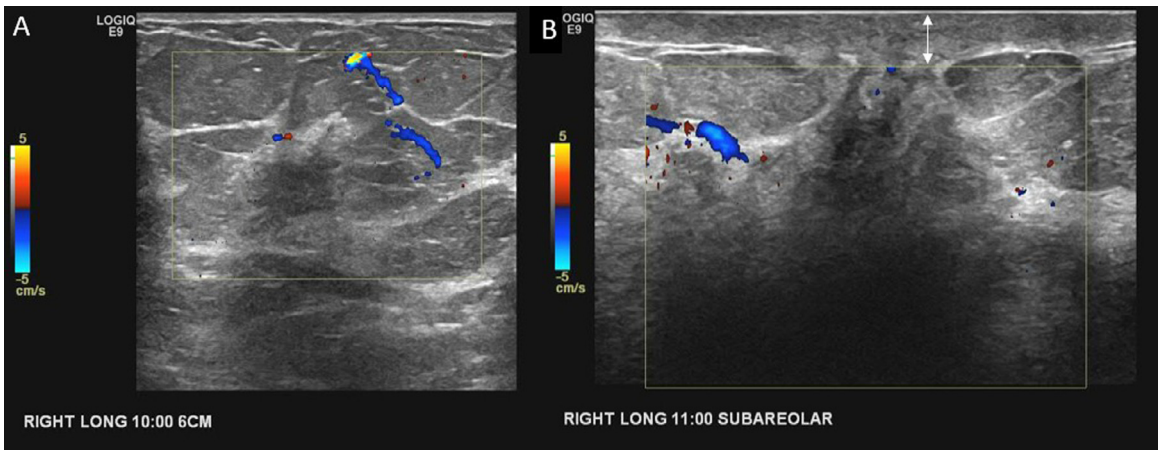

Fig. 3(A) – Gray-scale ultrasound images with Doppler demonstrate two irregular hypoechoic right breast masses with peripheral vascularity noted at the 10-o'clock (A) and 11-o'clock (B) positions. Note the mild skin thickening (double arrow).

ease distinct from PASB that typically presents with cutaneous rather than parenchymal-only manifestations as described above.

RAASB is one of the 2 most common radiation-associated sarcomas along with unclassified sarcoma [6]. Additional less common radiation-associated sarcomas include leiomyosarcomas, malignant peripheral nerve sheath tumors and osteosarcomas [6]. Although PASB and RAASB have similar gross pathologic features, the latter has been associated with almost universal amplification and protein over-expression of MYC; a proto-oncogene involved in angiogenesis among its many functions [7]. This is in contrast with PASB, in which MYC amplification and overexpression is only seen in a small subset of cases [8]. Although overall a nonspecific marker, evaluation for MYC amplification and/or over-expression can serve as a useful distinguishing factor when trying separate such lesions from atypical vascular proliferations/lesions which may also present with skin changes in the irradiated breast [7]. It is worth noting that although radiation may pose direct oncogenic effects upon the irradiated breast, lymphedema secondary to radiation therapy itself may be a further contributing factor to angiosarcoma development as patients with chronic lymphedema without radiation may also develop secondary angiosarcomas as is the case with Stewart-Treves syndrome [9,10]. More specifically, radiation may cause lymph node fibrosis leading to impaired lymphatic drainage [11]. In turn, lymphedema causes lymphatic proliferation that in the context of an impaired immune environment secondary to suboptimal lymphatic drainage, in addition to direct radiation-related DNA damage, may result in a favorable environment for angiosarcoma formation [10]. In these ways, radiation may contribute both primarily and secondarily to angiosarcoma development.

RAASB have a nonspecific mammographic and sonographic appearance [4]. Expected postsurgical and postradiation changes can be seen both mammographically and sonographically including skin thickening, benign calcifications, architectural distortion, and retraction [3,4]. If RAASB is detected sonographically, it may present as circumscribed or ill-defined masses or areas of hyper- or hypoechogenicity with variable shadowing [2]. Skin thickening alone may be the only mammographic finding in this patient population [12]. In 1992, Liberman et al [13] described normal mammographic evaluation in 33% of patients with breast angiosarcoma, although it is worth highlighting that this predates the now widespread use of tomosynthesis technology in mammography.

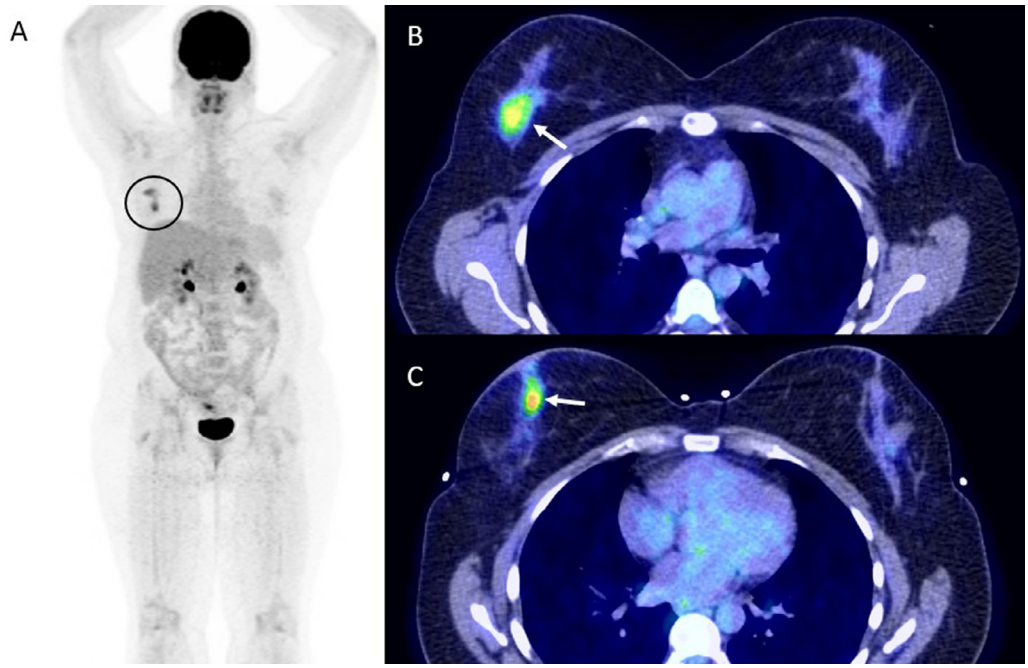

Fig. 4(A) – Maximum intensity projection (MIP) image from an FDG PET/CT exam demonstrates two FDG avid masses in the right breast (circle). (B and C) Axial fused FDG PET/CT images demonstrate a superior FDG avid mass with SUVmax of 4.4 (arrow), and a second, more inferior mass with SUVmax of 5.4 (arrow).

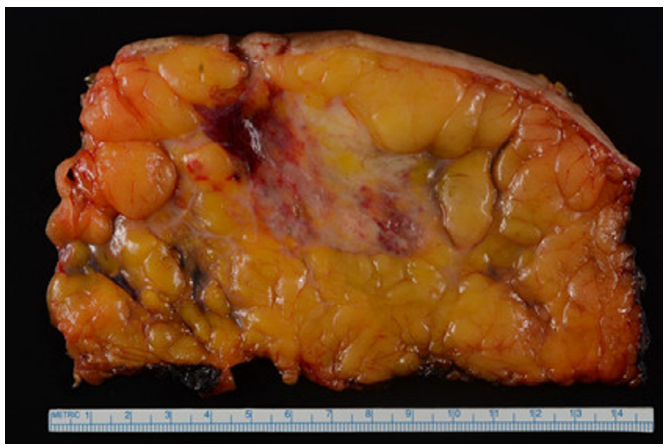

Fig. 5 – Gross pathologic image of the right breast simple mastectomy specimen. There is an angiosarcoma forming an 8.3 x 5.8 x 4.5 cm mass in the central portion of the breast. The tumor does not involve the skin (dermis or epidermis). The closest soft tissue margin is deep and negative by 2.2 cm. The closest peripheral skin margin is inferior and negative by 2.5 cm.

Breast MRI plays an important role in the assessment of extent of RAASB following detection [14]. In a series of 16 RAASB patients with pretreatment MRI, Chikarmane et al [14] described different patterns of skin enhancement in all patients with intraparenchymal involvement only found in 25% (4/16). These findings make the presence of non-mass enhancement and no skin enhancement in our patient particularly unique. Additionally, although T2 hyperintense skin thickening was noted in all 16 patients by Chikarmane et al [14], T2 signal characteristics were variable within discrete lesions. Of note, this case highlights the importance of being familiar with the temporal evolution of post treatment changes following BCT. New intraparenchymal or dermal enhancement 2 or more years following BCT should raise suspicion for a secondary malignancy, especially if within the radiation field [3]. There is scarce literature investigating the role of FDG PET/CT in the evaluation of RAASB. In the only published series of patients with breast angiosarcoma who underwent pretreatment FDG

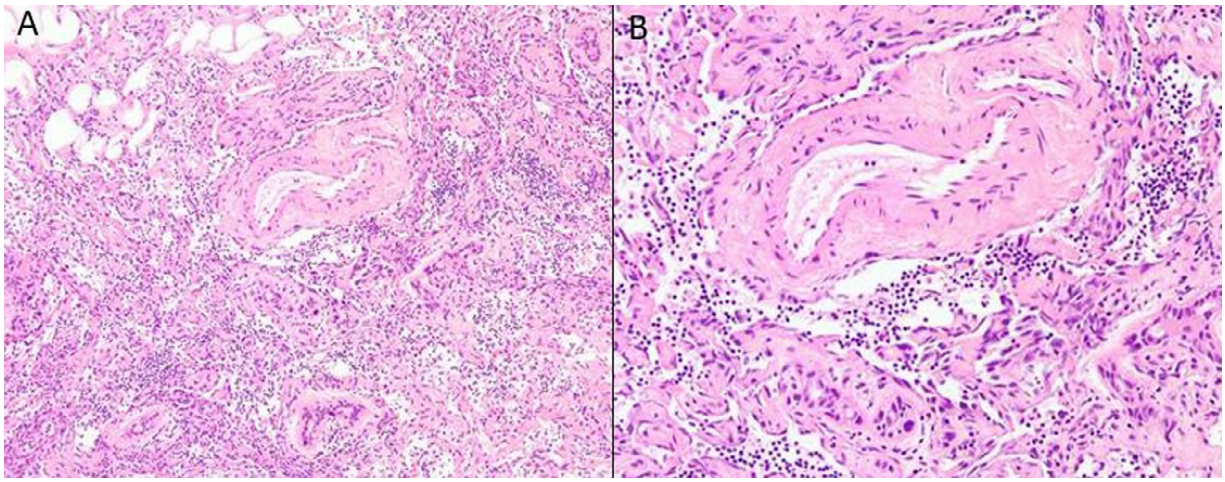

Fig. 6(A) – Postirradiation angiosarcoma of the mammary parenchyma, growing in a diffusely infiltrative fashion between non-neoplastic ducts, lobules, and thick-walled blood vessels (H+E, ×100). (B) Higher power view of high-grade mammary angiosarcoma, showing both small fascicles of hyperchromatic spindled endothelial cells and formation of irregular, slit-like vascular channels lined by protuberant, hyperchromatic endothelia (H+E, ×200).

PET/CT, Cassou-Mounat et al [15] demonstrated that there was a statistically significant difference in SUV_{max} between primary and secondary types.

Factors that have been associated with a poor prognosis in patients with RAASB include local recurrence, positive surgical margins, presenting with ecchymosis/violaceous skin and being diagnosed at 70 years or older [16–19]. There is mixed evidence regarding the prognostic utility of tumor size and histologic grade [19]. Lastly, lesions demonstrating higher SUV_{max} values on FDG PET/CT have been shown to have a poor prognosis regardless of breast angiosarcoma type [15].

At our institution, patients with newly diagnosed RAASB are often treated with neoadjuvant chemotherapy and radiation with concurrent chemotherapy followed by surgical resection. Surgical resection of RAASB often does not involve lymphadenectomy due to the primarily hematogenous spread of disease as well as the fact that axillary lymph nodes may be surgically absent at presentation as part of the treatment of the prior breast cancer [20]. Despite this, reports of occasional lymphatic metastases have prompted some authors to recommend some degree of lymph node surveillance following resection for select patients [21]. Given the rare nature of this disease, a multidisciplinary approach is needed for the appropriate management of these patients with prompt referral to a dedicated sarcoma treatment center being recommended [22].

In summary, we report a case of a clinically occult RAASB; a rare entity which typically presents with cutaneous breast changes years following radiation for breast cancer treatment. MRI evaluation after diagnosis remains the main imaging modality of choice for evaluation of extent of disease with features including variable T2 signal of skin and/or parenchymal involvement and variable enhancement kinetics. Awareness of this rare entity by the breast imager is paramount as early clinical or radiologic detection is key to expedite treatment and increase patient survival in this otherwise devastating disease.

Patient consent statement

Informed consent was obtained from the patient for use of anonymized clinical, pathologic, and radiologic information.

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