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A Rare Presentation of Radiation-Associated Angiosarcoma of the Breast Following Intraoperative Radiation Therapy

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Abstract

Radiation-associated angiosarcoma of the breast (RAASB) is a rare but highly aggressive complication of breast-conserving therapy. It accounts for less than 1% of all breast malignancies and typically presents 5–10 years after radiation exposure [1,2]. Clinically, RAASB most often manifests as cutaneous lesions rather than a discrete breast mass, contributing to frequent diagnostic delays [3]. Although most reported cases follow whole-breast external beam radiation therapy, there is limited literature on RAASB after intraoperative radiation therapy (IORT) [4]. We report a rare case of angiosarcoma developing five years after lumpectomy with sentinel lymph node biopsy and IORT.

Keywords: Intraoperative radiation; IORT; Angiosarcoma of breast; Breast cancer; Case report

Introduction

Radiation-associated angiosarcoma of the breast (RAASB) is a rare but aggressive complication of breast-conserving therapy, accounting for less than 1% of breast malignancies [1,2]. It typically presents 5–10 years after radiation exposure and most often manifests as cutaneous lesions rather than a discrete breast mass, frequently leading to delayed diagnosis [3]. The majority of reported cases occur following whole-breast external beam radiation therapy [4]. Reports of RAASB developing after isolated intraoperative radiation therapy (IORT) without adjuvant radiation are exceedingly rare. We present a case of angiosarcoma arising five years after lumpectomy with sentinel lymph node biopsy (SLNB) and IORT alone.

Case Presentation

A 75-year-old woman with a history of left invasive ductal carcinoma diagnosed in February 2020, presented with new erythematous skin lesions of the left breast. Due to delays related to the COVID-19 pandemic, she was initially bridged with neoadjuvant endocrine therapy using anastrozole for three months. In June 2020, she underwent a left breast lumpectomy with SLNB and IORT. A 4-cm applicator was used. The closest distance from the applicator to the skin was approximately 16 mm inferiorly. A single fraction of 20 Gy was delivered over 24 minutes. She had an uneventful recovery.

Final pathology demonstrated stage IA (pT1cN0M0), well-differentiated, estrogen receptor–positive, progesterone receptor–positive, HER2-negative invasive ductal carcinoma, with Nottingham score 5/9 and tumor size of 11 mm. Clear margins were achieved with negative nodal metastasis. No additional radiation therapy was recommended. The patient completed five years of adjuvant endocrine therapy, which was later discontinued in July 2025 due to arthralgias and osteoporosis. In September 2025, the patient noticed multiple small erythematous skin lesions on the left breast after showering. She denied breast pain, palpable masses, nipple discharge, or systemic symptoms. Physical examination revealed subtle erythematous macules involving the nipple–areolar complex (NAC) and surrounding skin (Figure 1A-B). Mammography and ultrasound performed earlier that year showed no suspicious masses or calcifications, although a retrospective review revealed progressive skin thickening compared with prior imaging (Figure 2A-C).

A dermatologic evaluation was performed, and a skin punch biopsy revealed angiosarcoma of the breast (Figure 3A-E). Staging computed tomography of the chest, abdomen, and pelvis showed no evidence of metastatic disease. Given the aggressive nature of the disease, the patient was advised to undergo a non-skin-sparing mastectomy to achieve adequate margins. The patient underwent an uncomplicated surgery ten days after re-presentation. Her postoperative course was unremarkable, and she was discharged on postoperative day one. Final pathology confirmed a radiation-associated angiosarcoma of the breast measuring 7.7 cm in greatest dimension, with negative surgical margins (Figure 3A-E). She was treated with 6 cycles of adjuvant doxorubicin. Additional radiation was not recommended.

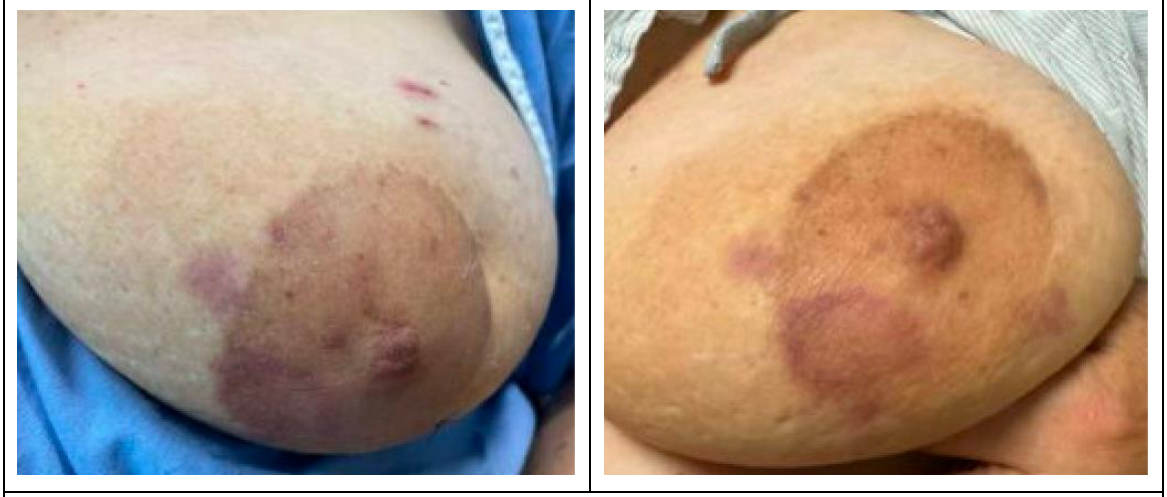

Figure 1 (A and B): Left breast with patches of erythematous lesions and hyperpigmentation, focally and circumferentially involving the nipple–areolar complex (NAC).

2A

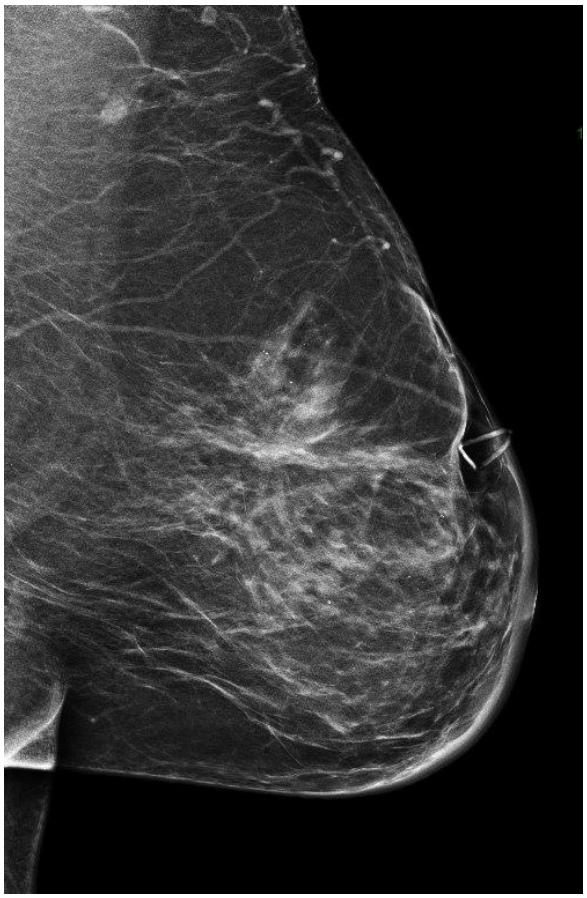

Figure 2 (A): Mediolateral oblique (MLO) view of the left breast on screening mammogram completed 5/2024, demonstrating post-surgical changes in the inner upper quadrant without suspicious masses or calcifications.

2B

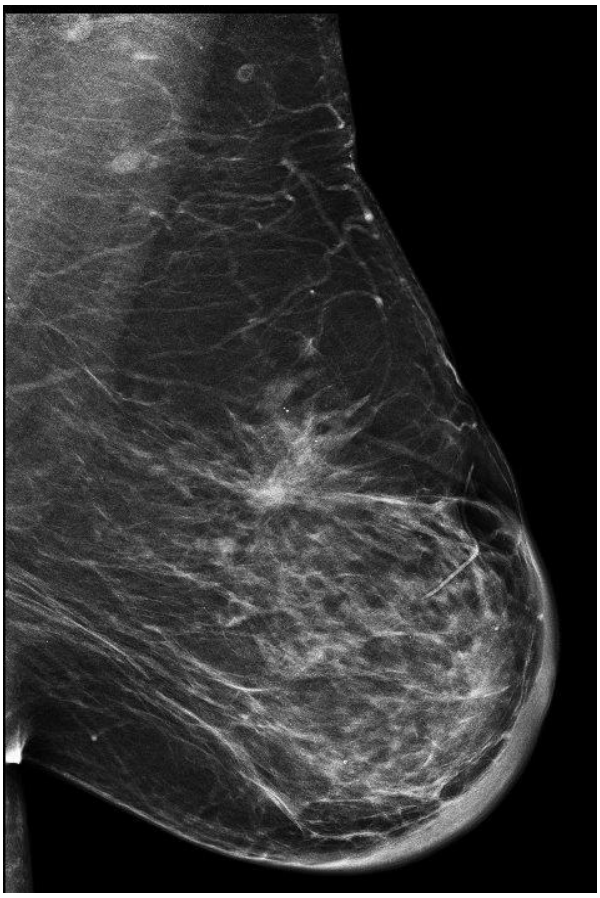

Figure 2 (B): MLO view of the left breast on screening mammogram completed 4/2025, showing stable post-surgical changes in the inner upper quadrant without suspicious masses or calcifications. Skin thickening is noted anteriorly along the NAC.

2C

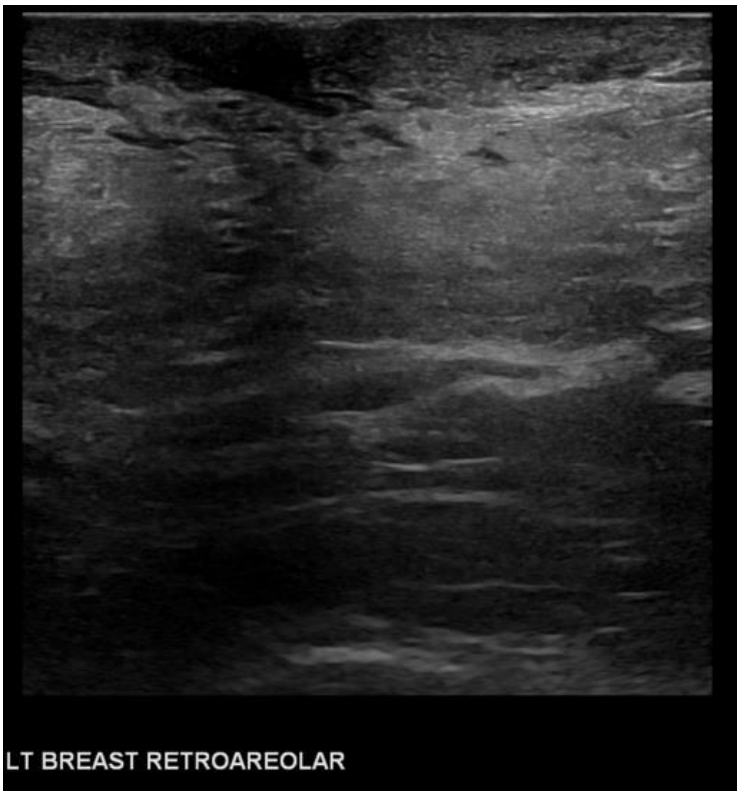

Figure 2 (C): Ultrasound of the left breast completed 4/2025 showing the retroareolar region with skin thickening and edema.

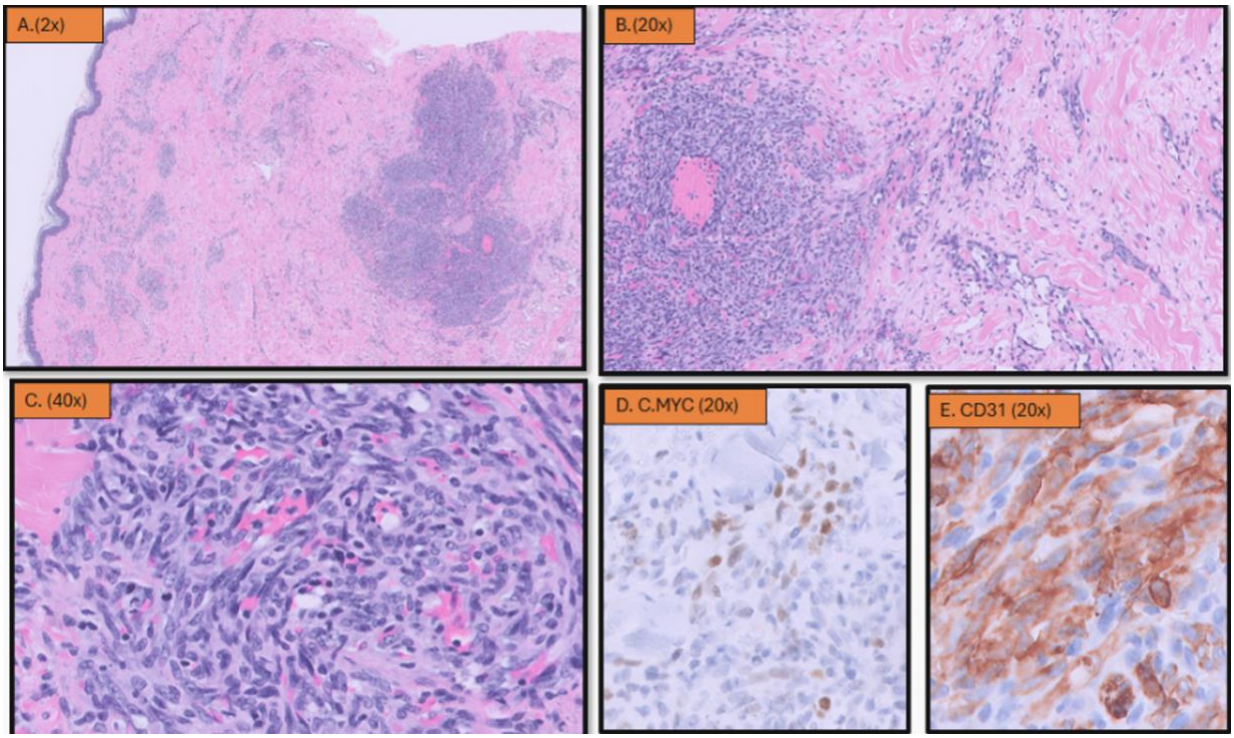

Figure 3: Pathology Slides from Left Breast Skin Punch Biopsy and Left Mastectomy.

Figure 3A (2× H&E): Vascular tumor within the dermis from left breast skin punch biopsy.

Figure 3B (20× H&E): Anastomosing vascular channels with atypical endothelial cells dissecting through stroma and merging into the solid component.

Figure 3C (40× H&E): Oval-to-spindled atypical endothelial cells lining vessels.

Figure 3D (20× immunohistochemistry): Tumor cells positive for c-MYC.

Figure 3E (20× immunohistochemistry): Tumor cells positive for vascular marker CD31.

Discussion

Radiation-associated angiosarcoma of the breast (RAASB) is an aggressive subtype of breast sarcoma and an unfortunate complication of breast cancer treatment. Since its first report in 1936, RAASB has remained uncommon, with an incidence of 0.05%- 0.3% [1-3]. RAASB is a form of secondary angiosarcoma, often developing after exposure to conventional external beam radiation therapy (EBRT), or in the setting of chronic lymphedema [5]. Cumulative doses ranging from 40-50 Gy are reported to be high risk for the development of RAASB [6]. In contrast, primary angiosarcoma develops de novo and involves the breast parenchyma without cutaneous presentation [5].

The pathogenesis of RAASB remains incompletely understood. Proposed mechanisms include radiation-induced DNA double-strand breaks, oxidative damage to proteins and lipids, and chronic endothelial injury, leading to genomic instability and oncogenic transformation [4,7]. Amplification of the MYC oncogene has been frequently identified in radiation-associated, but not primary, angiosarcomas, supporting a causal association with radiation exposure [4].

Although a dose–response relationship has not been definitively established, prior studies suggest that even relatively low radiation doses may be sufficient to induce sarcomagenesis in susceptible individuals [8,9]. This raises important questions about individual host susceptibility and genetic predisposition. Our case supports this hypothesis, as angiosarcoma developed after a single localized radiation exposure via IORT, without adjuvant EBRT.

RAASB typically presents as subtle erythematous or violaceous cutaneous changes, frequently mimicking benign dermatologic conditions [3,10]. As demonstrated in this case, conventional breast imaging may be non-specific and non-diagnostic, contributing to delayed diagnosis [10,11]. Therefore, a new or evolving skin lesion in a previously irradiated breast should prompt urgent biopsy.

Surgical excision with wide margins remains the cornerstone of treatment and offers the best chance for local control [6]. Non-skin-sparing mastectomy is often required due to the multifocal and cutaneous nature of the disease. Prognosis remains poor, with reported 5-year overall survival rates ranging from 30%-40%, particularly in patients with large tumors, multifocal disease, or incomplete resection [6,7,12]. Tumor size greater than 5 cm and multifocality have been consistently associated with worse outcomes [11,12].

The role of adjuvant chemotherapy remains unclear due to the rarity of the disease and lack of prospective trials. Taxane-based regimens, particularly weekly paclitaxel, are commonly utilized because of reported activity in angiosarcoma, while anthracycline-based therapy remains an accepted alternative [13]. Adjuvant systemic therapy is often considered in patients with high-risk features such as large tumor size, multifocal disease, or high-grade histology.

Large clinical series evaluating targeted intraoperative radiotherapy (TARGIT-IORT) demonstrate excellent oncologic outcomes and low rates of radiation-related toxicity compared to traditional EBRT [14]. However, these studies are not designed to detect rare secondary malignancies, such as angiosarcoma, of which only three cases were reported without details on the management and long-term outcome of these patients. This case emphasizes the importance of continued vigilance and extended surveillance in patients treated with IORT, with a low threshold for skin biopsy in any previously irradiated breast exhibiting new or progressive cutaneous changes.

Conclusion

Radiation-associated angiosarcoma should be considered in any patient with prior breast radiation presenting with new cutaneous changes, even years after a single treatment with IORT. Early recognition and prompt surgical management are critical to optimizing outcomes.

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