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Radiation-Induced Angiosarcoma of the Breast: A Detailed Case Report

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Abstract

Radiation-associated angiosarcoma (RAAS) of the breast is a rare but aggressive malignancy that arises within previously irradiated tissue, typically years after treatment for breast cancer. We report the case of a 54-year-old woman who developed RAAS five years after completing adjuvant radiotherapy for invasive breast carcinoma. She presented with gradually progressive erythematous cutaneous lesions over the irradiated breast. Histopathology confirmed well-differentiated angiosarcoma with characteristic endothelial markers. The patient underwent wide local excision with clear margins and remains disease-free at two-year follow-up. This case underscores the diagnostic challenges of RAAS, which can mimic benign post-radiation changes, and highlights the importance of early biopsy and prompt surgical management to optimize outcomes.

Keywords: Histopathology, Biopsy, Morphologic, Malignancy.

Introduction

Angiosarcomas are rare, highly aggressive malignant tumors originating from vascular or lymphatic endothelial cells, and constitute fewer than 2% of soft tissue sarcomas.[1] They may occur de novo or develop as secondary angiosarcomas, the latter typically associated with chronic lymphedema, prior radiation exposure, environmental carcinogens (e.g., vinyl chloride, thorium dioxide, arsenic), and several hereditary cancer syndromes. Historically used terms such as hemangiosarcoma and lymphangiosarcoma have fallen out of favour due to overlapping morphologic and

immunophenotypic features. Radiation-associated angiosarcoma (RAAS) represents the most frequent sarcoma subtype arising after radiotherapy for breast cancer, typically emerging within previously irradiated tissue.[2] RAAS is an increasingly recognized consequence of the widespread adoption of breast-conserving therapy (BCT) combined with adjuvant radiotherapy, coupled with prolonged survival in breast cancer patients. The condition primarily affects older women and is characterized by a latency period usually ranging from 4 to 10 years.[3]

The diagnostic criteria for RAAS, first established by Arlen et al. in 1971, require:

1. A history of radiotherapy for a primary malignancy;
2. A minimum latency of three years;
3. Histopathologic distinction from the original tumor;
4. Occurrence within the irradiated field.[1]

Despite aggressive treatment, RAAS carries a poor prognosis, with reported 5-year survival rates of 20–45%.[4] Local recurrence is common due to the infiltrative nature of the tumor, and distant metastases occur frequently. Factors associated with improved outcomes include smaller tumor size at diagnosis, lower histologic grade, early clinical recognition, and achievement of negative surgical margins.[5] Because clinical manifestations often resemble benign post-radiation changes, delayed diagnosis remains a major contributor to poor outcomes.

We present a rare case of RAAS in a patient who developed disease five years after completing radiotherapy for breast cancer, successfully managed with wide local excision, and who remains disease-free at two-year follow-up.

Case Report

A 54-year-old woman initially presented in April 2018 with a palpable lump in the left breast. She underwent excision biopsy in July 2018, which revealed invasive breast carcinoma. Modified radical mastectomy with axillary lymph nodes dissection (MRM with ALND) was subsequently performed with clear margins. Final pathology staged the tumor as pT2N0M0, and immunohistochemistry demonstrated estrogen receptor (ER) and progesterone receptor (PR) positivity with HER2 negativity.

Adjuvant systemic therapy consisted of six cycles of Epirubicin and Cyclophosphamide, followed by maintenance therapy with Anastrozole and Zoledronate, with routine surveillance thereafter.

The patient also received adjuvant image-guided radiotherapy (IGRT) to the left breast, consisting of 45 Gy in 15 fractions, followed by a 10-Gy boost to the tumor bed.

Presentation of New Lesions

In October 2023 — approximately five years after completing radiotherapy — the patient noted the gradual appearance of new erythematous cutaneous lesions on the previously irradiated breast. (Figure 1)

The lesions were initially subtle and were presumed to represent common post-radiation changes. However, progressive discoloration and mild induration prompted further evaluation.

Benign causes, including post-radiation erythema, telangiectasia, and dermatitis, were considered and clinically excluded. Owing to persistent suspicion, a core biopsy was performed.

Histopathologic Findings

Histologic examination revealed:

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- Atypical vascular proliferation consistent with well-differentiated angiosarcoma
- Immunohistochemistry positive for CD31, CD34, and ERG
- Ki-67 proliferation index of 35%
- Cytokeratin (CK) negative, helping to exclude recurrent carcinoma

These findings confirmed a diagnosis of radiation-associated angiosarcoma (RAAS)

Management and Follow-Up

The patient underwent wide local excision of the lesion with the goal of achieving negative margins. Surgical pathology confirmed clear margins and no residual disease.

She has since been maintained on a structured surveillance protocol, including dermatologic and breast examinations and periodic imaging. At her two-year follow-up, she remains alive and disease-free, with no evidence of recurrence.

Discussion

Post-radiation vascular proliferations span a continuum ranging from benign atypical vascular lesions to fully malignant angiosarcoma. When malignant vascular tumors arise after radiotherapy in breast cancer patients, they are termed radiation-associated (RAAS) or radiation-induced angiosarcoma (RIAS).[2,3]

RAAS is rare, affecting fewer than 1% of irradiated breast cancer survivors. Reported cumulative incidence ranges from 0.03% to 0.3%, but may increase with longer follow-up intervals, as latency often exceeds traditional surveillance windows and may extend beyond 20 years.[3,4]

Clinical Presentation

RAAS may present as:

- Bluish or violaceous patches
- Erythematous plaques
- Angulated nodules
- Ecchymosis-like discoloration

Because these features often resemble benign or expected post-radiation changes, misdiagnosis or delayed diagnosis is common. Advanced imaging such as MRI may assist in identifying infiltrative subcutaneous disease, but definitive diagnosis requires biopsy.[5]

Pathogenesis and Risk Factors

RAAS is thought to result from radiation-induced DNA damage, chronic inflammation, and microvascular injury. Patients who receive radiotherapy have an increased risk of developing RAAS. The risk appears higher with greater radiation exposure and may increase over time.[1,5]

Histologically, RAAS is characterized by:

- Infiltrative, atypical vascular channels
- Hyperchromatic, pleomorphic endothelial cells
- Frequent expression of vascular endothelial markers such as CD31, CD34, Factor VIII, VEGF, and ERG; cytokeratin negativity helps distinguish from carcinoma.[2,5]

Management and Prognosis

Surgical excision — often requiring mastectomy or wide local excision with generous margins — remains the cornerstone of treatment. Achieving negative margins is critical but challenging due to the tumor's infiltrative nature.[2,4]

Despite aggressive surgical management:

- Local recurrence rates remain high.[4]
- Median survival ranges from 27 to 48 months, and five-year overall survival is reported at approximately 40%.[3,4]

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- Adjuvant chemotherapy or further radiotherapy have been evaluated, but evidence for a survival benefit remains limited.[5]

Early detection offers the best opportunity for improved outcomes, underscoring the importance of clinician vigilance, especially in patients with prior breast irradiation and new cutaneous lesions.

Conclusion

Radiation-associated angiosarcoma of the breast is an uncommon but highly aggressive malignancy that requires heightened clinical awareness. Breast cancer survivors presenting with new or atypical skin changes in previously irradiated areas should undergo prompt evaluation, and biopsy should not be delayed for lesions that do not clearly represent benign post-radiation effects. Surgery with negative margins remains the primary therapeutic modality. Given the increasing use of breast-conserving therapy, clinicians must remain vigilant for this rare complication. This case highlights the importance of early recognition, multidisciplinary management, and long-term surveillance, as timely intervention can significantly improve outcomes.

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Legends Figure

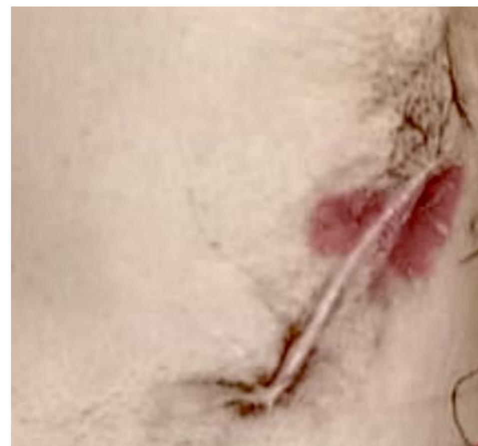

Figure 1: Appearance of erythematous patch on previously irradiated scar in a case of carcinoma breast.

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