OMNIPOTENT Publishers

Journal of Case Report and Clinical Images

Case Report

Radiation-associated angiosarcoma of the breast masquerading as post-biopsy ecchymosis: a delayed diagnosis with surgical and oncologic challenges

Abstract

Background: Radiation-associated angiosarcoma of the breast (RAAS) is a rare but aggressive cancer in patients who have received Breast Conserving Therapy (BCT). It is clinically difficult to diagnose due to skin changes present from previous radiation. This can lead to delayed diagnosis and treatment.

Case Report: A 79-year-old female with a history of right-sided breast Ductal Carcinoma in Situ (DCIS) previously treated with BCT (partial mastectomy and adjuvant whole-breast radiation therapy) and Anastrozole, presented with persistent right breast ecchymosis several months status post stereotactic biopsy. Full-thickness skin biopsies were consistent with high grade angiosarcoma. Right total mastectomy with en bloc resection of all involved skin was performed. Re-excision of positive margins was performed one week later. A split thickness skin graft was later placed in the setting of known positive margins due to the extent of skin involvement.

Conclusion: RAAS often has delayed diagnosis and treatment due to similar initial presentation as post-treatment breast changes. Surgical resection with clear margins is the primary treatment for RAAS but can be challenging if the tumor has spread diffusely.

Keywords: Radiation, breast angiosarcoma, breast conserving therapy, total mastectomy, ductal carcinoma in situ, skin graft

Volume 1 Issue 1 - 2025

Fahim Bachu,[1] Molly Good,[1] Brandon Arnsberger[2]

[1]*Department of Medicine, Lake Erie College of Osteopathic Medicine (LECOM) at Seton Hill, USA*

[2]*Department of Surgery, University of Pittsburgh Medical Center (UPMC) Harrisburg, USA*

Correspondence: Fahim Bachu, Lake Erie College of Osteopathic Medicine (LECOM) at Seton Hill, 20 Seton Hill Drive, Greensburg, PA, USA, Tel 240-469-0452, Email FBachu14477@med.lecom.edu

Received: July 17, 2025**; Published:** July 28, 2025

Introduction

Radiation-associated angiosarcoma (RAAS) of the breast is a rare but aggressive malignancy that can arise several years after breast conserving therapy (BCT). While the overall incidence is low, estimated at 0.05-0.3% of patients who undergo BCT, the clinical implications remain significant due to the tumor's rapid progression and high risk of local recurrence.[1,2] RAAS typically presents 5-10 years after radiation therapy, though cases have been documented both earlier and much later, making long term surveillance essential.[3]

The diagnosis of RAAS is frequently delayed due to its subtle and often misleading presentation. Early signs such as ecchymosis, erythema, or nonspecific skin thickening may be mistaken for benign post-treatment changes or fat necrosis, especially in older adults or those on anticoagulation. Furthermore, initial imaging and biopsy findings may be inconclusive or falsely reassuring, leading to more diagnostic uncertainty.[2,4] With disease progression, more concerning features such as violaceous plaques, nodules, or fungating lesions may emerge, prompting reconsideration and additional workup.[4] By this time, the tumor often involves a large surface area and may be multifocal, complicating the treatment approach. This case illustrates the diagnostic complexity and therapeutic challenges of RAAS in a patient with prior history of ductal carcinoma in situ treated with BCT. It also emphasizes the importance of clinical vigilance when new skin changes develop in an irradiated breast, even when initial investigations appear benign.

Main Body

A 79 year old female with history of right-sided breast Ductal carcinoma in Situ (DCIS) previously treated with BCT (partial mastectomy and adjuvant whole-breast radiation therapy) and Anastrozole, presented for routine surveillance imaging. Initial screening mammography showed grouped calcifications in the upper outer quadrant of the right breast (BI-RADS 0), prompting a follow up diagnostic mammogram and stereotactic biopsy. Diagnostic mammography demonstrated heterogeneous calcifications spanning 2.5 cm (BI-RADS 4), and pathology from the biopsy revealed fat necrosis and microcalcifications, concordant with the imaging findings.

In the months following the biopsy, the patient developed persistent ecchymosis over her right breast. The ecchymosis was attributed to anticoagulation (Eliquis) by her primary care physician which she was taking for atrial fibrillation. Six months later, upon relocating and establishing care at a new institution, the patient presented to a breast surgeon with complaints of worsening right breast skin discoloration and palpable nodularities. Physical examination at this visit revealed diffuse violaceous plaques and nodules involving 70-80% of the right breast with two fungating lesions. Two full-thickness punch biopsies were performed in the clinic, revealing intermediate to high grade angiosarcoma. Subsequent staging with Chest CT and PET/CT revealed nonspecific increased metabolic activity in the right axillary node and chest wall but no definitive evidence for metastatic disease. The case

was discussed at a multidisciplinary tumor board. Although neoadjuvant chemotherapy and proton therapy were recommended, the patient opted for surgical resection alone.

The patient underwent a right total mastectomy with wide en bloc resection of affected skin. Dissection was carried superiorly to the clavicle, medially to the sternum, laterally to the anterior border of the latissimus dorsi, and inferiorly to the inframammary fold. Gross disease was noted at the inferior skin flap, prompting intraoperative frozen sections, which revealed positive margins for sarcoma. Additional inferior margin tissue was excised until frozen pathology was negative. The wound was irrigated, and a wound vacuum-assisted closure (VAC) device was applied due to the large surface area and anticipated need for further margin assessment.

Final pathology revealed a 30 cm intermediate to high grade angiosarcoma with positive superior, medial, lateral, and inferior margins. The patient returned to the OR one week later for re-excision of the positive margins. During this operation, gross examination of the wound revealed induration and purulent drainage at the lateral wound edge. Cultures were obtained, and wide excision of all four wound margins (superior, medial, lateral, and inferior) was performed with 2-3 cm margins, guided by frozen section. Additional tissue was excised until all margins were confirmed negative. The wound, now measuring 40 x 21 cm, was irrigated and managed again with a wound VAC due to size and ongoing infection risk.

Postoperative recovery was complicated by poor pain control, prolonged wound care needs, and a delayed final pathology due to consultation with a sarcoma specialist at a tertiary center. Pathology once again revealed positive margins at the superior, inferior, and lateral margins. After discussion with plastic surgery and medical oncology, the patient underwent definitive wound closure with placement of a split-thickness skin graft. The graft demonstrated excellent growth at her follow up visit. The patient is currently under multidisciplinary surveillance and evaluating adjuvant therapy options, including systemic chemotherapy and proton therapy.

Discussion

RAAS of the breast is a rare, complex diagnosis with limited treatment options. Radiation associated skin changes can often mask developing RAAS during physical exam, and the appearance of RAAS on mammography appears similarly to the breast after radiation including retraction, skin thickening, and tissue distortions. Breast tissue changes from radiation will appear on mammography for up to two years after treatment completion, and any changes on mammography after the two-year mark should raise suspicion for malignancy.[5] Due to the overlap in appearance of angiosarcoma and irradiated skin on physical exam and mammography, patients and providers should be diligent and maintain a high index of suspicion when following up years after treatment.

Surgical resection with negative margins remains the primary treatment modality for RAAS, although this can be challenging due to the tumor's infiltrative growth and diffuse spread within the dermis and subcutaneous tissue.[1] Neoadjuvant chemotherapy and adjuvant radiation may be considered in select cases, especially when clear margins are difficult to achieve or in cases of local recurrence.[3,4] While the use of additional radiation in a previously irradiated field is controversial, proton therapy is sometimes considered due to its highly conformal dose distribution and lower exit dose, which may reduce toxicity to surrounding healthy tissues.[5]

Published outcomes for chemotherapy and radiation therapy remain discordant, and treatment plans are often individualized based on patient preference, comorbidities, and disease progression.[3,4] The overall survival rate in patients diagnosed with RAAS remains low ranging from 27 to 48%.[6] This patient had delayed diagnosis due to several factors including history of anticoagulation leading to post-biopsy bruising and transition of care to a new institution. The plan of care also highlights how shared decision-making impacts treatment as this patient was recommended neoadjuvant chemotherapy and proton therapy, however decided to only pursue surgical resection.

Conclusion

Radiation-Associated Angiosarcoma of the breast is a rare malignancy with clinical and radiographic similarities to post-treatment skin changes leading to challenges in both diagnosis and treatment. A high index of suspicion should be maintained in patients who are multiple years post treatment and sustain skin changes of the breast to ensure that angiosarcomas are diagnosed and treated as early as possible. Further investigation of appropriate treatment is recommended given the limited published literature on secondary angiosarcomas.

Acknowledgments

All authors have reported that they have no funding relevant to the contents of this paper to disclose. All authors have reported that they have no disclosures relevant to the contents of this paper to disclose.

Conflicts of interest

The authors declare no conflicts of interest.

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