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Breast Angiosarcoma: A Rare Anatomical Presentation of a Neglected Case

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Abstract

Radiation-associated angiosarcoma of the breast (RAAS) is an infrequent and aggressive complication of breast-conserving therapy and adjuvant radiotherapy. Early diagnosis is challenging because of its nonspecific clinical manifestation.

A 91-year-old woman presented with a progressively evolving cutaneous lesion of the left breast 6 years after breast-conserving surgery and adjuvant radiotherapy for hormone receptor-positive breast carcinoma. Histopathological examination showed an infiltrative malignant vascular neoplasm composed of atypical epithelioid and spindle cells. Immunohistochemistry demonstrated diffuse positivity for CD31 and FLI1 and negativity for CD34, CKAE1/AE3, Cam5.2, GATA3, and HHV8, confirming the diagnosis of radiation-related angiosarcoma and excluding recurrent breast carcinoma.

This case highlights the importance of considering RAAS in patients presenting with new skin lesions within previously irradiated breast tissue. Prompt biopsy and comprehensive histopathological evaluation are essential for establishing a prompt diagnosis and guiding appropriate management, even in very elderly patients.

Categories: Obstetrics/Gynecology, General Surgery, Anatomy
Keywords: angiosarcoma, associated, breast, radiation, secondary

Introduction

Over the past few decades, breast-conserving surgery followed by radiotherapy has become a standard treatment option for early-stage breast cancer, allowing many patients to avoid mastectomy [1]. Adjuvant radiotherapy typically involves a dose of approximately 50 Gy delivered to the breast, with an additional boost of 10-20 Gy to the tumor bed in selected cases. Although radiotherapy is an established component of breast cancer treatment, it is associated with a small risk of secondary malignancies, including radiation-associated angiosarcoma (RAAS) [2]. A population-based study reported a 15-year cumulative incidence of angiosarcoma of approximately 0.9 per 1,000 breast cancer cases following radiotherapy [3].

RAAS typically develops several years after radiotherapy, with a reported median latency period of approximately four to eight years [2]. The clinical presentation may include erythematous or violaceous skin lesions and bruise-like discoloration in the previously irradiated breast. Because these lesions may resemble benign skin conditions and the disease is rare, initial recognition may be delayed. Prompt clinical assessment and histopathological evaluation of suspicious skin lesions are therefore important. Surgical excision remains the mainstay of treatment, often requiring mastectomy, depending on the extent of disease. Nevertheless, local recurrence and distant metastasis remain significant clinical concerns [4].

The prognosis of RAAS is generally poor, although the available evidence is limited by the rarity of this malignancy and is largely derived from retrospective studies, case series, and case reports. Although surgical management remains central to treatment, relatively few studies have specifically investigated surgical outcomes. The role of neoadjuvant and adjuvant chemotherapy has also been explored, but its therapeutic benefit remains uncertain [3,5].

The present case describes RAAS in a 91-year-old woman with extensive cutaneous involvement, highlighting the diagnostic challenges associated with this rare malignancy in a very elderly patient and the limitations in assessing disease extent and subsequent clinical outcomes when staging and follow-up information are unavailable.

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Case Presentation

In 2023, a 91-year-old woman living alone in an urban environment presented to the emergency department because of spontaneous bleeding from an extensive cutaneous lesion involving the left breast (Figure *1*). Clinical examination revealed multiple, scattered violaceous cutaneous nodules with diffuse skin involvement affecting both breasts, accompanied by extensive ulceration and recurrent spontaneous bleeding. The exact onset and duration of the lesions, as well as their initial appearance and progression before presentation, could not be reliably established. Precise measurements of the principal mass were unavailable. The available clinical documentation did not provide sufficient information to establish the presence or absence of regional lymphadenopathy, lymphedema, or deeper tissue involvement.



FIGURE 1: Clinical presentation of radiation-associated angiosarcoma of the breast, showing multiple, scattered violaceous cutaneous nodules, extensive ulceration, and a large hemorrhagic, exophytic mass involving the left breast

The patient's medical history was significant for multifocal hormone receptor-positive breast carcinoma diagnosed in 2017, for which she underwent breast-conserving surgery (lumpectomy) with axillary lymph node dissection. Histopathological examination of the primary tumor showed two distinct tumor foci measuring 2.5 cm and 1.4 cm in greatest dimension, respectively, with nodal metastatic involvement. Immunohistochemical analysis demonstrated diffuse estrogen receptor (ER) positivity in approximately 100% of tumor cells, absence of HER2 overexpression (score 0-1+), and a low proliferative index (Ki-67 approximately 3-4%), consistent with luminal-type breast carcinoma. Following surgery, the patient received adjuvant radiotherapy. The specific radiotherapy dose, fractionation schedule, use of a boost, and details of regional nodal irradiation were not available in the records reviewed.

Given the extensive cutaneous lesions involving the previously irradiated breast region, a biopsy of the skin and underlying subcutaneous tissue was performed for histopathological evaluation (Figures *2*-*4*).

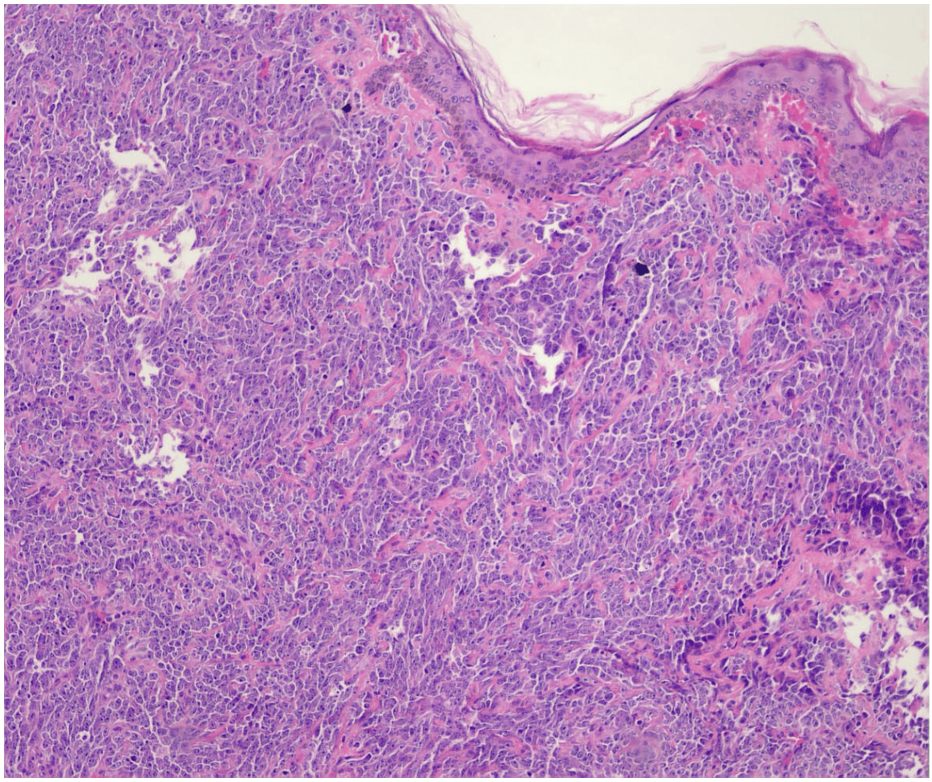


FIGURE 2: Histopathological features of angiosarcoma, showing predominantly medium- to large-sized spindle-shaped and epithelioid neoplastic cells with marked nuclear pleomorphism and cytological atypia (Hematoxylin & Eosin; original magnification ×100)

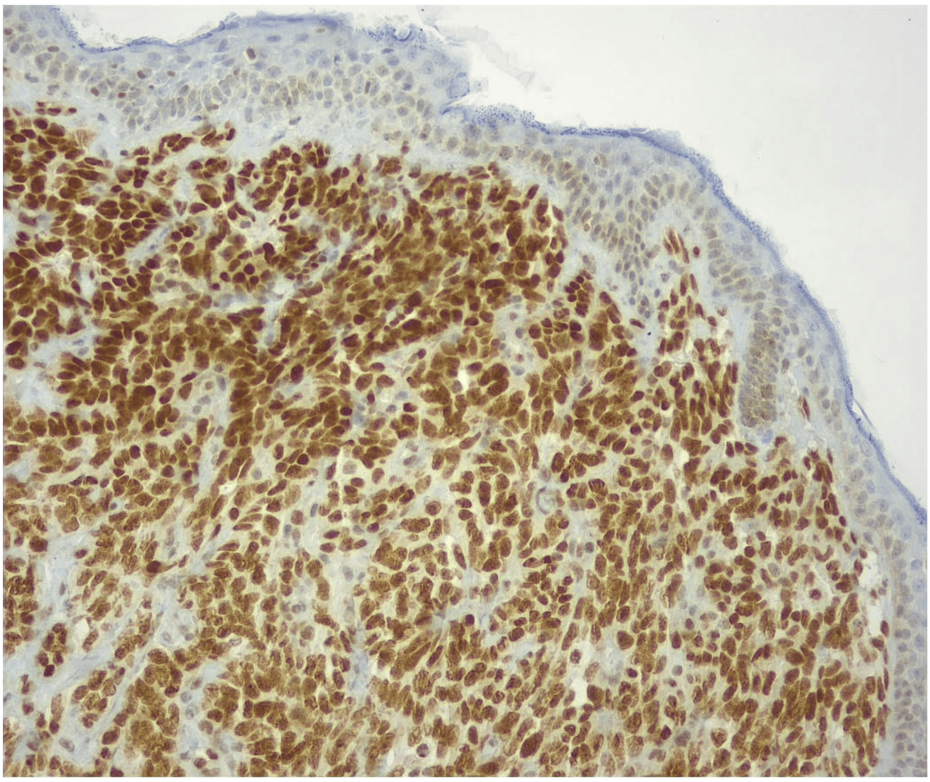


FIGURE 3: Immunohistochemical staining for FLI-1 showing strong nuclear expression in neoplastic cells (×200)

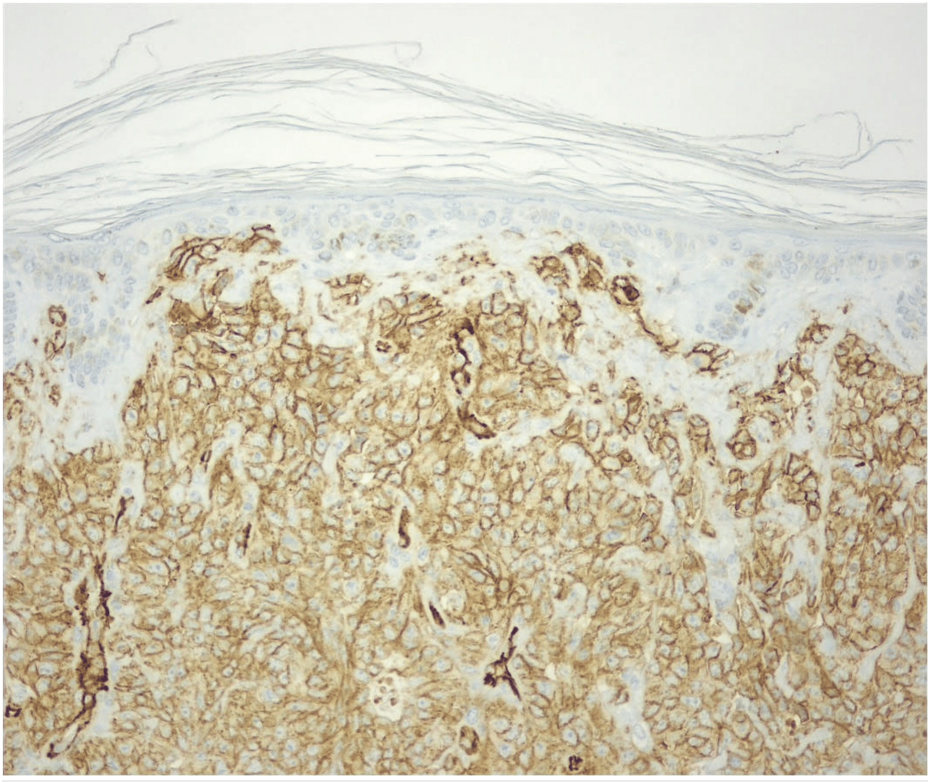


FIGURE 4: Immunohistochemical staining for CD31 showing strong and diffuse membranous expression in neoplastic cells (×200)

Following the diagnosis of radiation-associated angiosarcoma, no further diagnostic workup, including staging, imaging, or oncological treatment, was undertaken. The available clinical documentation did not establish the reasons for this decision. The patient lived alone, had no relatives, and her only known social contact was a close friend. Given her advanced age and inability to live independently, this friend arranged the patient's transfer to a long-term care facility, where she received supportive care. The patient died a few months later, in the same year. The cause of death was not documented, and no further follow-up information was available regarding her subsequent clinical course.

Discussion

RAAS represents a rare but well-recognized delayed complication of breast-conserving therapy followed by radiotherapy. Despite its infrequency, it carries considerable clinical significance because of its aggressive biological behavior, diagnostic challenges, and high risk of local recurrence [6].

The present case demonstrates several characteristic features of RAAS, including development within a previously irradiated region and a latency period of six years, consistent with published data [7]. In contrast to the subtle initial skin changes that may characterize early RAAS, this patient presented with extensive cutaneous involvement, ulceration, and recurrent spontaneous bleeding. The exact onset and progression of the lesions could not be established from the available clinical records; therefore, their initial appearance and the possibility of earlier misinterpretation remain unknown. Early RAAS lesions may resemble benign cutaneous conditions, including dermatitis, ecchymosis, or post-radiation skin changes, potentially contributing to diagnostic delay. This diagnostic challenge may be particularly relevant in older patients, in whom other dermatological conditions and age-related factors may complicate clinical assessment [8].

From a pathological perspective, RAAS exhibits a broad morphological spectrum, ranging from well-formed anastomosing vascular channels to solid sheets of highly atypical epithelioid or spindle-shaped cells [9]. In the present case, the predominantly solid growth pattern, cytological atypia, and loss of normal tissue architecture were consistent with the reported intermediate- to high-grade histological features [10].

Immunohistochemically, strong and diffuse expression of the endothelial markers CD31 and FLI1, together with the absence of epithelial markers, including cytokeratins and GATA3, supported endothelial differentiation and made recurrent or metastatic breast carcinoma less likely [11]. This distinction is clinically important because these entities differ in their management and prognosis.

The differential diagnosis includes recurrent breast carcinoma with sarcomatoid differentiation, benign post-radiation vascular proliferations, and cutaneous vascular tumors such as Kaposi sarcoma. The negative HHV8 staining did not support Kaposi sarcoma, while the infiltrative growth pattern and cytological atypia argued against a benign vascular lesion. Correlation with the clinical history, particularly previous radiotherapy and localization within the irradiated field, remains essential for an accurate diagnosis [7,12].

Complete surgical excision with negative margins remains the mainstay of treatment for RAAS when clinically appropriate. However, owing to the infiltrative nature of the tumor and its potential for multifocal microscopic spread, achieving clear margins may be challenging [3,13]. RAAS is associated with a substantial risk of local recurrence and may metastasize to distant organs, including the lungs and liver, despite treatment. However, evidence regarding systemic chemotherapy and targeted therapies remains limited, as much of the available literature is based on small retrospective series and case reports [14-16].

The present case is noteworthy because of the patient's advanced age at presentation (91 years), highlighting the importance of maintaining clinical awareness of RAAS in very elderly patients. Suspicious skin changes in previously irradiated breast tissue warrant prompt clinical assessment and consideration of biopsy, with diagnostic and therapeutic decisions tailored to the patient's overall condition and goals of care [17]. In this case, the absence of staging investigations and subsequent follow-up information limits assessment of the full extent of disease and the subsequent clinical course.

Overall, this case reinforces the importance of long-term clinical vigilance following breast-conserving therapy and highlights the diagnostic challenges posed by radiation-associated vascular malignancies. Increased awareness among clinicians and pathologists may facilitate the recognition and appropriate diagnostic evaluation of suspicious cutaneous lesions in previously irradiated breast tissue.

Conclusions

An augmented index of clinical suspicion is indispensable for radiation-associated angiosarcoma of the breast, an uncommon but extremely aggressive secondary cancer, especially when new cutaneous lesions appear within a previously irradiated territory. Prompt clinical assessment and histopathological evaluation of suspicious lesions are essential to facilitate diagnosis and minimize diagnostic delay. The present case highlights that even in very elderly patients, new skin abnormalities following breast-conserving therapy should not be underestimated and warrant prompt clinical evaluation and consideration of biopsy, taking into account the patient's overall condition and goals of care.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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