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Global Journal of
Medical and Clinical Case Reports
OPEN ACCESS JOURNAL

ISSN: 2455-5282 Journal DOI: https://dx.doi.org/10.17352/gjmccr

Case Report

Radiation-Associated Secondary Angiosarcoma of the Breast: Case Report and Literature Review

Dragos Cristian Voicu[1,2]*, Dorina Stan[1,2], Marius Adrian Dragan[1,2], Claudia Plesea[1], Daniela Mihalache[1,2], Pusica Zainea[1,2] and Stefan Alexandru Luchian[1,2]

[1]Braila County Emergency Clinical Hospital, Romania

[2]"Dunarea de Jos" University of Galati, Romania

Submitted : 20 March, 2026
Accepted : 28 March, 2026
Published : 30 March, 2026

***Corresponding author:** Dragos Cristian Voicu, Braila County Emergency Clinical Hospital, "Dunarea de Jos" University of Galati, Romania,
E-mail: dragosfvoicu@yahoo.com

Keywords: Breast angiosarcoma; Radiotherapy; Surgery

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Abstract

Radiation-Associated Angiosarcoma (RAAS) of the breast is a rare but highly aggressive malignancy that arises as a late complication of radiotherapy. Its incidence is increasing alongside the widespread use of breast-conserving treatment. The paper presents a case of a 57-year-old female with a history of bilateral breast cancer, treated with surgery and radiotherapy, who developed progressive cutaneous lesions of the right breast. Histopathological evaluation confirmed secondary angiosarcoma. Despite surgical management, early recurrence occurred, requiring systemic chemotherapy. This report highlights the aggressive clinical course of RAAS and underscores the importance of early diagnosis and multidisciplinary management.

Introduction

Radiation-associated angiosarcoma is an uncommon vascular malignancy, developing in previously irradiated tissues. It typically occurs after a latency period of 5–10 years following radiotherapy for breast cancer [1].

The increasing use of breast-conserving surgery, combined with adjuvant radiotherapy, has led to a gradual rise in incidence, although the condition remains rare [2]. Clinically, it often presents as cutaneous discoloration, bruising, or nodular lesions, frequently mimicking benign dermatologic conditions and delaying diagnosis [3].

Prognosis is generally poor due to high rates of local recurrence (up to 40% - 90%) and limited effective systemic therapies [4].

Case report

A 5A 7-year-old woman, with a prior history of bilateral breast carcinoma, treated with breast-conserving surgery and adjuvant radiotherapy eight years earlier, presented for routine follow-up. She reported progressive skin changes of the right breast. Clinical examination revealed extensive erythematous-violaceous plaques, with multiple raised nodules, involving approximately 2/3 of the breast surface, extending toward the sternal region. No palpable intraparenchymal mass or axillary lymphadenopathy was detected.

A pA biopsy demonstrated atypical vascular proliferation with endothelial atypia, consistent with angiosarcoma. Immunohistochemistry confirmed vascular differentiation (CD31/CD34 positive).

Sta. Positron emission tomography showed no distant metastases.

Following a multidisciplinary discussion, mastectomy was recommended. The patient opted for unilateral surgery, and a right-sided mastectomy was performed. Initially, postoperative recovery was uneventful.

However, three months later, multiple nodular lesions

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appeared in the surgical field. Histological reassessment confirmed local recurrence. Given the aggressive course, systemic chemotherapy with weekly taxane therapy was initiated.

Discussion

RAAS is a distinct clinic-pathological entity, arising from radiation-induced endothelial damage. Molecular alterations such as MYC amplification have been implicated in its pathogenesis [5,6].

MYC amplification is a common genetic aberration where the MYC gene (often *c*-MYC at 8*q*24) is duplicated multiple times, leading to overproduction of the MYC protein. This acts as a powerful oncogenic driver, fueling cancer progression by promoting rapid cell proliferation, inhibiting cell death, and increasing genomic instability, often indicating a poor prognosis [12,13].

Detailed information regarding prior radiotherapy is essential for understanding the pathogenesis of radiation-associated angiosarcoma. In the present case, the patient underwent adjuvant radiotherapy following initial breast-conserving surgery for left-sided breast carcinoma. The total delivered dose was 50 Gy in 25 fractions, followed by a boost dose of 10–16 Gy to the tumor bed, consistent with standard protocols.

The radiation energy employed was within the megavoltage range (typically 6–10 MV photons), ensuring adequate tissue penetration while minimizing superficial toxicity. The field arrangement consisted of tangential opposed fields encompassing the whole breast, with careful sparing of adjacent organs such as the heart and lungs.

Importantly, no intentional overlap existed between irradiation fields of the two breasts, as the contralateral (right) breast had not been irradiated at the time of the initial treatment. However, it must be acknowledged that scatter radiation and low-dose peripheral exposure may occur, albeit at clinically negligible levels. From a pathogenic standpoint, radiation-associated angiosarcomas are typically confined to the previously irradiated field, supporting the causal relationship between high-dose exposure and sarcomagenesis.

In cases where bilateral irradiation or field overlap occurs, there is a theoretical increase in cumulative radiation dose to shared tissues, potentially amplifying the risk of secondary malignancies, including angiosarcoma. However, in this patient, the absence of field overlap reinforces the classical model of radiation-induced sarcoma, localized strictly within the high-dose region.

Typical clinical presentation includes: violaceous or erythematous patches, rapidly evolving nodules, and absence of a deep palpable mass in early stages. These features were consistent with our case.

Diagnosis relies on histopathology and immunohistochemistry. Imaging is primarily used for staging, with PET/CT useful for detecting metastatic disease [18] (Figures 1,2).

Following the right mastectomy, postoperative radiotherapy (PMRT) was carefully evaluated but ultimately not indicated. The decision was based on: absence of high-risk pathological features (e.g., large tumor size, positive margins, extensive nodal involvement); lack of chest wall invasion; favorable surgical margins (R_0 resection). Given these findings, the anticipated benefit of PMRT in reducing locoregional recurrence was outweighed by the potential risks, particularly in a patient with a prior history of radiation exposure and a documented radiation-induced malignancy. Thus, omission of PMRT was considered clinically justified and aligned with current oncological guidelines (Figure 3 and Table 1).

Treatment: wide surgical excision remains the mainstay of treatment. However, margin-negative resection is often difficult, and recurrence rates are high. Chemotherapy (e.g., taxanes) may provide disease control. Emerging strategies, such as reirradiation and targeted therapies, are under investigation but lack consensus [7,8].

The selection of therapeutic strategies in breast cancer is inherently multifactorial and individualized. The following parameters are central to clinical decision-making: tumor-related factors - size, histological subtype, grade, lymphovascular invasion; biological profile - hormone receptor status (ER/PR), HER2 expression, Ki-67 index; disease extent - nodal involvement, metastatic spread; patient-related factors - age, comorbidities, performance status; previous treatments - prior irradiation or systemic therapy; patient preference (particularly regarding breast conservation). In this context, multidisciplinary evaluation remains the cornerstone of optimal care.

Mastectomy continues to play a crucial role in breast cancer treatment; however, it is not universally superior to breast-conserving therapy (BCT). Multiple landmark trials have demonstrated equivalent overall survival between mastectomy and BCT (lumpectomy followed by radiotherapy) in early-stage breast cancer. Therefore, mastectomy is generally reserved for: large tumors relative to breast size; multifocal or multicentric disease; contraindications to radiotherapy; persistent positive margins after re-excision; and patient preference. In contrast, breast-conserving approaches are preferred when oncologically safe, due to better cosmetic outcomes and comparable survival rates.

In the specific context of radiation-associated angiosarcoma, however, mastectomy becomes the treatment of choice, as wide surgical excision with negative margins is critical for local control, and further irradiation is generally contraindicated.

While breast-conserving therapy remains standard for many patients, prior radiation exposure and secondary malignancy risk fundamentally alter management strategies, necessitating a more radical surgical approach [14-17].

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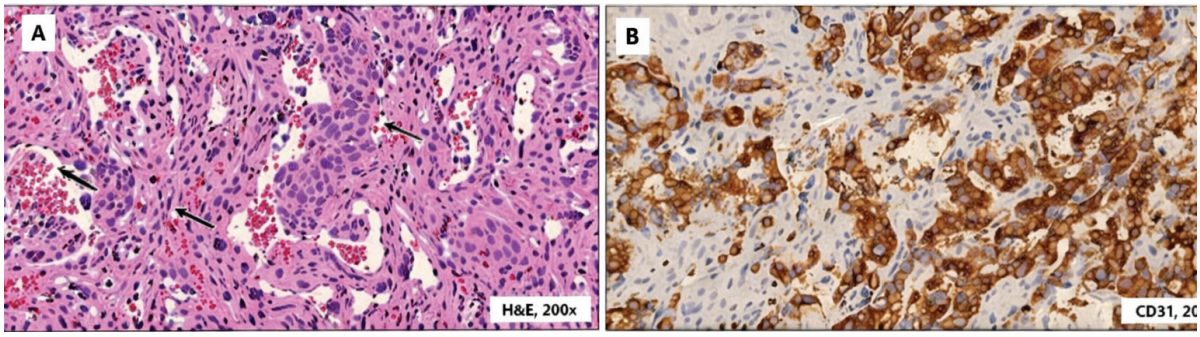

Figure 1: Histopathology of secondary angiosarcoma of the breast.
A) H&E: Irregular, anastomosing vascular channels lined by atypical endothelial cells with hyperchromatic nuclei and mitotic figures (arrows).
B) Immunohistochemistry: Strong diffuse positivity for CD31 highlighting vascular endothelial proliferation.

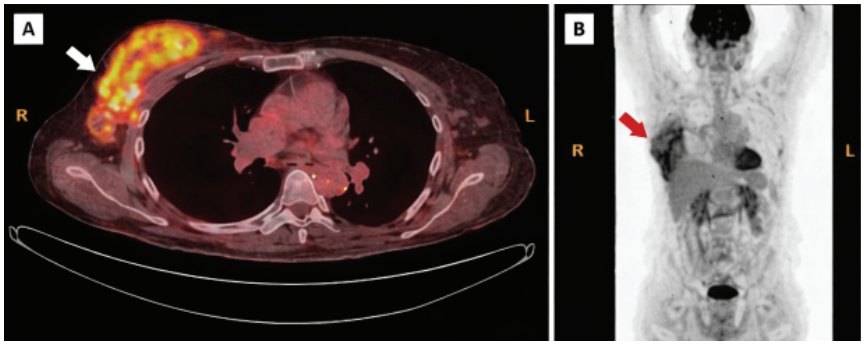

Figure 2: PET/CT (FDG) – Staging.
A) Axial fused PET/CT: Intense hypermetabolic activity in the skin and subcutaneous tissue of the right breast (arrow), corresponding to angiosarcoma.
B) Whole-body PET (MIP): Increased uptake limited to the right breast region (arrow); no distant metastases detected.

Table 1: Reported Cases of Radiation-Associated Breast Angiosarcoma (NED = no evidence of disease; RT = radiotherapy).

No	Author (Year)	Age	Latency (years)	Clinical Presentation	Treatment	Outcome
1	Bonito, et al. [2]	68	7	Violaceous plaques	Mastectomy	Recurrence
2	Bonito, et al. [2]	72	9	Nodular lesions	Surgery + chemo	Alive (12 months)
3	Stewart-Parker, et al. [3]	61	8	Skin discoloration	Mastectomy	Recurrence
4	Stewart-Parker, et al. [3]	75	10	Bruise-like lesion	Surgery	Deceased (18 months)
5	Rhou,l et al. [4]	63	7	Nodules	Surgery + taxane	Recurrence
6	Wong, et al. [5]	59	6	Erythematous plaque	Surgery	NED (10 months)
7	Wong, et al. [5]	70	8	Diffuse lesions	Surgery + chemo	Recurrence
8	Cozzi, et al. [1]	66	9	Macules/papules	Surgery	Recurrence
9	Cozzi, et al. [1]	74	5	Plaques	Surgery + RT	Deceased
10	Takehara, et al. [7]	58	6	Nodules	Surgery	NED
11	Caterino, et al. [8]	71	10	Skin thickening	Surgery + chemo	Recurrence
12	Sheu, et al. [9]	65	8	Violaceous patch	Surgery	Recurrence
13	Li, et al. (2019)	69	9	Bruising	Surgery	Recurrence
14	Nomoto, et al. [10]	62	7	Nodules	Surgery	Deceased
15	Torres, et al. (2021)	73	11	Plaques	Surgery + chemo	Deceased
16	Kim, et al. (2022)	55	6	Nodules	Surgery	NED
17	Patel, et al. (2020)	67	8	Diffuse erythema	Surgery + taxane	Recurrence
18	Singh, et al. (2022)	64	7	Skin lesions	Surgery	Recurrence
19	Müller, et al. (2021)	76	12	Nodules	Surgery + chemo	Deceased
20	Rossi, et al. (2023)	60	6	Plaques	Surgery	NED
21	García, et al. (2024)	72	10	Nodules	Surgery + chemo	Recurrence
22	Ahmed, et al. (2022)	68	9	Bruising	Surgery	Recurrence
23	Chen, et al. (2023)	57	5	Macules	Surgery	NED
24	Novak, et al. (2021)	74	11	Plaques	Surgery + chemo	Deceased
25	Silva, et al. (2020)	66	8	Nodules	Surgery	Recurrence
26	Brown, et al. (2022)	70	9	Diffuse lesions	Surgery + taxane	Recurrence
27	Ibrahim, et al. (2023)	63	7	Plaques	Surgery	NED
28	Kaur, et al. (2024)	59	6	Nodules	Surgery + chemo	Recurrence
29	Zhang, et al. (2021)	71	10	Skin discoloration	Surgery	Deceased
30	Present case	57	8	Diffuse plaques + nodules	Surgery + taxane	Early recurrence

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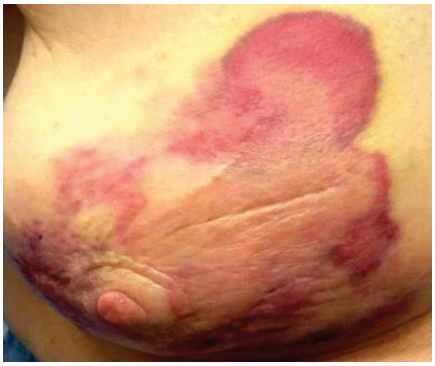

Figure 3: Clinical presentation of radiation-associated angiosarcoma of the breast: extensive cutaneous involvement of the right breast showing erythematous to violaceous discoloration with multiple raised nodules and indurated plaques. The lesions occupy approximately 2/3 of the breast surface and extend toward the sternal region. No obvious underlying mass is visible.

Prognosis remains poor, with frequent early recurrence, as observed in this case. Survival outcomes depend on tumor size, margin status, and early detection.

Conclusions

Radiation-associated angiosarcoma of the breast is an aggressive malignancy with increasing incidence due to modern breast cancer treatment strategies [18].

This case highlights:

- The importance of early biopsy of suspicious skin lesions;
- The critical importance of detailed radiotherapy documentation, individualized therapeutic decision-making, and the nuanced role of mastectomy;
- The high recurrence rate despite surgery
- The need for individualized, multidisciplinary treatment

Future research should focus on molecular profiling and targeted therapies to improve outcomes in this rare but devastating disease [19].

Ethical approval statement

This study was conducted in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of County Emergency Clinical Hospital Brăila, under approval number [protocol number. 826 from 2024, August 26].

Informed consent statement

Written informed consent was obtained from the patient for participation in this study and for the publication of clinical data and images. A copy of the consent is available upon request.

Conflict of interest declaration

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Funding Statement: This research received no external funding.

Author contributions

Conceptualization: D.C.V, M.A.D; Methodology: C.P, D.M.; Data Collection: D.S, P.Z. S.A.L.; Analysis: D.C.V, M.A.D.; Writing – Original draft: M.A.D.; Writing – Review & Editing: D.C.V.; Supervision: D.C.V. All authors have read and approved the final manuscript.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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