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Case Report

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Radiation-induced breast sarcoma: case report and literature review

Abstract

Introduction: Breast sarcoma is a rare malignant neoplasm that may occur as a primary tumor or as a secondary malignancy when it arises in a previously irradiated site. In this setting, it is known as radiation-induced breast sarcoma (RIBS), an uncommon but serious late complication of radiotherapy in breast cancer survivors. It is characterized by aggressive biological behavior and a poor prognosis.

Case report: We report the case of a 57-year-old female patient with a prior history of invasive carcinoma of the right breast, treated with breast-conserving surgery followed by radiotherapy. During the sixth year of follow-up, she developed an erythematous nodule in the axillary region of the previously irradiated breast, with a diagnosis of radiation-induced sarcoma.

Conclusion: RIBS requires a high index of clinical suspicion. Early diagnosis and wide surgical excision with negative margins constitute the cornerstone of treatment.

Keywords: radiation-induced sarcoma, breast cancer, angiosarcoma, pleomorphic sarcoma, radiotherapy

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Introduction

Breast sarcoma is a malignant stromal tumor that may be classified as primary, when it arises without a known precursor, or secondary, when it develops in a previously irradiated site. In the latter setting, it is referred to as radiation-induced breast sarcoma (RIBS). This entity represents a rare and late complication of radiotherapy for breast cancer, associated with high rates of recurrence and disease progression.

We report the case of a 57-year-old female patient with a history of invasive carcinoma of the right breast, treated with breast-conserving surgery followed by adjuvant radiotherapy. During the sixth year of follow-up, she developed an erythematous nodule in the axillary region of the previously irradiated breast, which was diagnosed as radiation-induced sarcoma.

Case report

A 57-year-old female patient with a history of breast implants was diagnosed in January 2018 with right breast invasive carcinoma of no special type (NST), histologic grade 1 (HG1). She underwent surgical treatment consisting of quadrantectomy and sentinel lymph node biopsy. Final pathology revealed a 0.9 cm tumor with negative surgical margins and two negative sentinel lymph nodes (0/2). Immunohistochemistry showed estrogen receptor (ER) positivity of 95%, progesterone receptor (PR) positivity of 95%, HER2/neu (0) negative, and a Ki-67 proliferation index of 2% Pathologic staging was pT1b(sn)N0. She subsequently completed adjuvant radiotherapy, receiving 50 Gy to the breast and axilla without a boost. Adjuvant endocrine therapy with tamoxifen was recommended; however, the patient declined treatment.

In December 2024, the patient presented after self-detection of a nodule located along the anterior axillary line (8 o'clock position) of the right breast, near the previous implant drainage exit site. On physical examination, a mobile, erythematous, non-tender nodule was palpated (Figure 1).

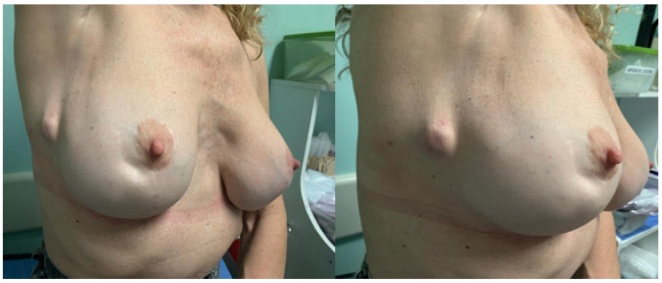


Figure 1 Patient presented after self-detection of a nodule.

In January 2025, a breast ultrasound was performed at another institution. It reported a 10 mm palpable, firm, stony-hard nodule at the right anterior axillary line. The lesion was initially considered suggestive of a granuloma; however, histologic biopsy was recommended, categorized as BI-RADS 4 (Figure 2).

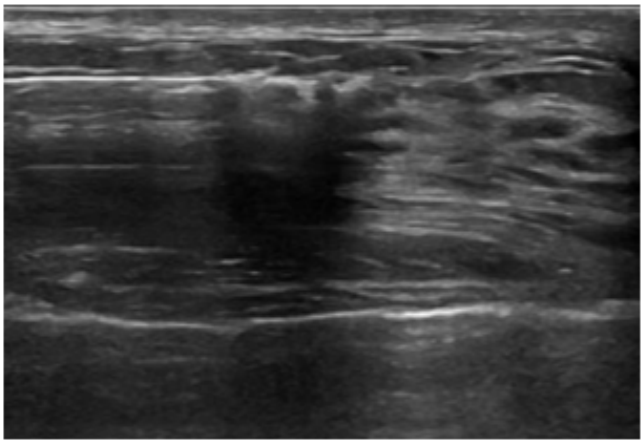


Figure 2 Breast ultrasound was performed at another institution.

In June 2025, a core biopsy of the lesion was performed at another institution. The pathology report described a poorly differentiated malignant tumor, primarily suggestive of metaplastic carcinoma. Given its atypical location, the pathology slides were reviewed at our institution, where it was reported a high-grade spindle-cell and pleomorphic neoplastic proliferation. Due to the strong clinical suspicion of radiation-induced sarcoma, an immunohistochemical panel was performed for differential diagnosis (Table 1). The results were as follows: CKAE1-AE3 negative; p63 negative; CK5/6 negative; S100 negative; SMA focally positive; desmin negative; CKAPM negative; SOX10 negative; ER negative; PR negative; HER2 negative; Ki-67 50%. These findings strongly supported the diagnosis of a high-grade spindle-cell and pleomorphic sarcomatous mesenchymal lesion.

Table 1 Strong clinical suspicion of radiation-induced sarcoma, an immunohistochemical panel was performed for differential diagnosis

Immunohistochemical panel	Results
CK AE1-AE3	Negative
p63	Negative
CK5/6	Negative
S100	Negative
SMA (Smooth Muscle Actin)	Positive
Desmin	Negative
CKAPM	Negative
SOX10	Negative
Estrogen Receptor (ER)	Negative
Progesterone Receptor (PR)	Negative
HER2	Negative
Ki-67	50%

Complementary imaging studies were requested. Breast magnetic resonance imaging (MRI) demonstrated, in the peripheral outer region of the right breast corresponding to the clinically palpable area, a nodular lesion that was hypointense on T1-weighted sequences and hyperintense on T2-weighted sequences, with heterogeneous enhancement following intravenous contrast administration. The lesion measured 2.7 × 1.6 cm and corresponded to the previously known histologic diagnosis (Figure 3). Computed tomography (CT) scan of the abdomen and pelvis, as well as whole-body bone scintigraphy, showed no significant abnormalities.

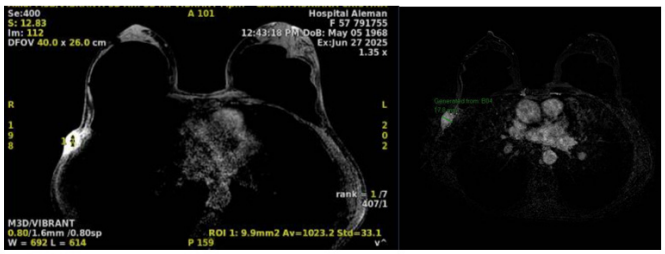
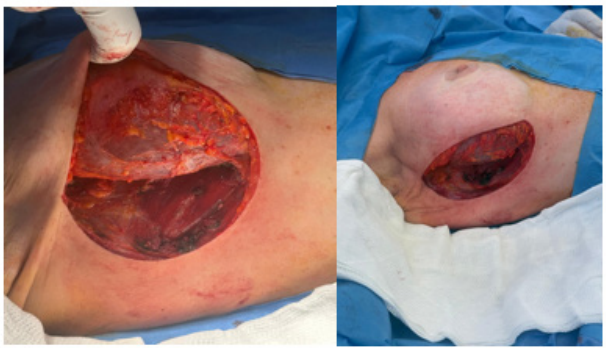


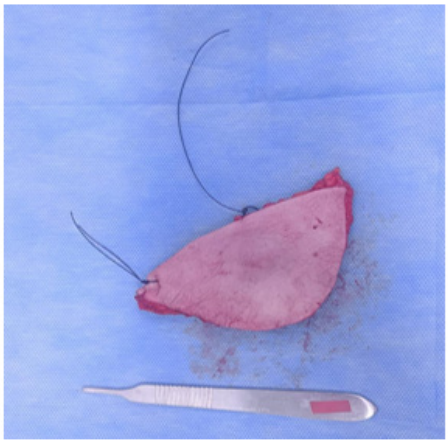
Figure 3 Nodular lesion on MRI.

In July 2025, the patient underwent wide local excision through an arciform incision with a 20 cm skin ellipse along the anterior axillary line of the right breast, encompassing a palpable 3 cm nodule. Dissection of the subcutaneous tissue was performed, and the posterior plane was developed over the implant capsule.

An en bloc resection was carried out, including a muscular cuff of the latissimus dorsi in the posterior region of the nodule, ensuring macroscopically healthy tissue margins, that was sent for istopathological evaluation. The final pathology report confirmed the presence of an undifferentiated pleomorphic sarcoma, measuring 2.5 cm in its greatest dimension. Resection margins were negative, the closest was the deep (muscular) margin, at 0.5 cm. Pathologic staging according to the AJCC 8th edition was pT1 (Figures 4–5).



A) Post-resection chest wall defect.



B) Surgical specimen with reference sutures

Figura 4 Post-resection and surgical specimen of chest.

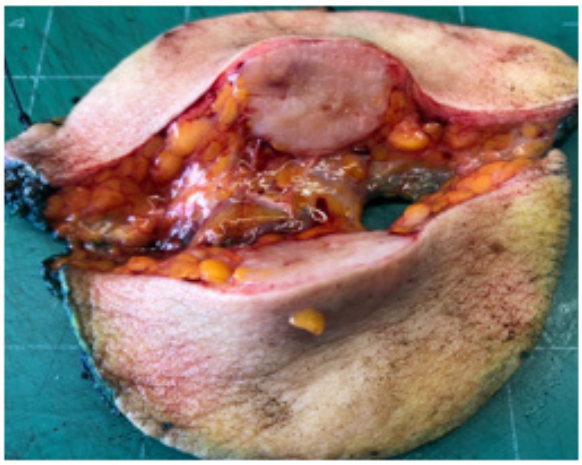


Figure 5 Gross surgical specimen showing the tumor and surrounding margins.

The case was discussed at a multidisciplinary gynecologic oncology tumor board. The decision was made to consider systemic chemotherapy and to refer the patient for evaluation by a sarcoma specialist. The sarcoma consultant recommended close surveillance with CT scans every three months initially, along with periodic laboratory monitoring (Figure 6) (Figure 7).

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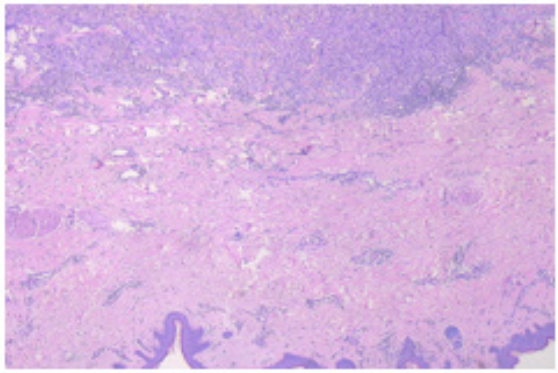
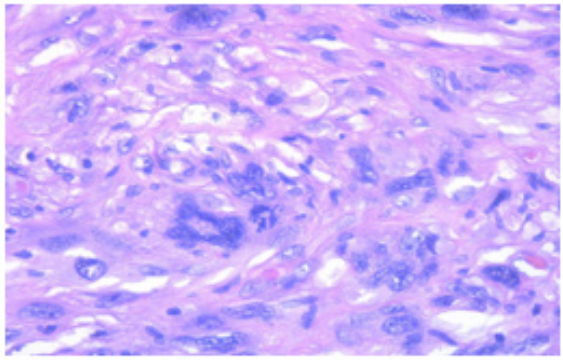
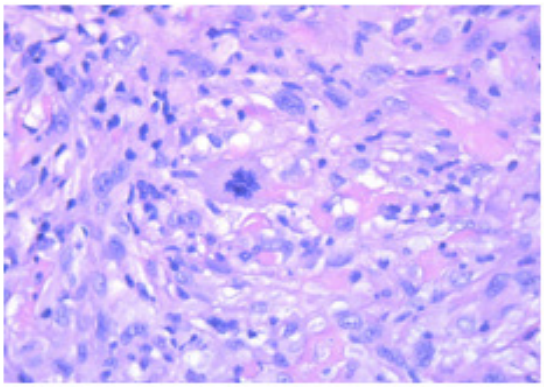


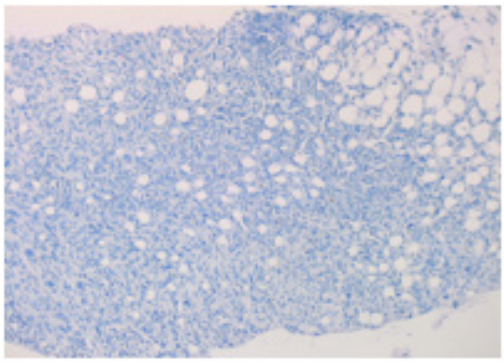
(A) Epidermis and dermis.



B) Mitoses and cytologic atypia.



C) Mitoses



D) PANK negative

Figure 6 Microscopic findings.

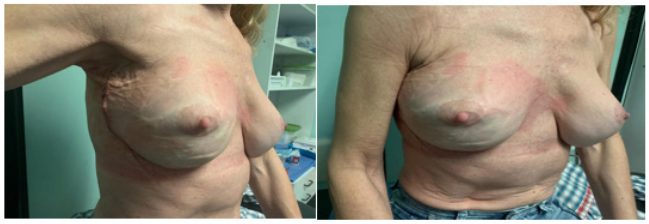


Figure 7 Fifteen-day postoperative physical examination and follow-up.

Discussion

Radiation-induced sarcoma (RIS) is a malignant mesenchymal neoplasm that develops as a late complication of radiotherapy, arising within a previously irradiated field after a variable latency period, typically spanning several years. RIS may involve both bone and soft tissues and is characterized by aggressive clinical behavior and a poorer prognosis compared with primary sarcomas.

Radiation-induced breast sarcoma (RIBS) is a rare but well-recognized complication of radiotherapy in patients treated for breast cancer, with a reported incidence ranging from 0.1% to 0.2%.[1–7] Its development is closely associated with prior radiation exposure and typically occurs after a latency period of 4 to 10 years, although longer intervals have also been documented.[1–7]

The patient presented in December 2024 with the development of a new nodule, nearly seven years after having undergone breast-conserving treatment with radiotherapy (January 2018). This time interval is consistent with the average latency period described in the literature for the development of radiation-induced sarcomas. The nodule was located in the right anterior costal region, in close proximity to the previously irradiated surgical bed, further supporting the suspicion of radiation-induced breast sarcoma (RIBS). This peripheral location, near the prior drainage site, has also been described as a common presentation, where lesions may arise in areas of chronically altered irradiated subcutaneous tissue.

The estimated overall prevalence of radiation-induced sarcoma among patients irradiated for any solid malignancy is low, typically ranging from 0.02% to 0.2% at 10 years, according to large population-based cohorts.[1–3] The cumulative incidence increases with longer follow-up, reaching values close to 0.5% at 15–20 years in historical series.[3–5]

Specifically in the breast, the most robust data derive from cohort studies and population-based registries. Among women treated with breast-conserving surgery followed by radiotherapy for breast cancer, the cumulative incidence of radiation-induced sarcoma (including angiosarcoma and other histologic subtypes) ranges from 0.1% to 0.21% at 10 years of follow-up.[4–7]

For example, in the SEER study, the incidence of secondary thoracic sarcoma after radiotherapy was 0.15% at 10 years, whereas a European cohort reported an incidence of 0.27% at 10 years and 0.48% at 15 years.[4–7] The risk of developing sarcoma is significantly higher in irradiated patients compared with non-irradiated individuals (standardized incidence ratio >10).[3,4]

Although uncommon, the incidence of radiation-induced sarcoma appears to be increasing, possibly reflecting the long latency period required for tumor development following the widespread adoption of adjuvant radiotherapy for breast cancer.

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The diagnosis is often delayed due to its frequently benign appearance. It is established through physical examination combined with imaging studies; however, both may yield highly nonspecific findings.[3] Lesions may be solitary or multiple and can vary considerably in size, ranging from small nodules to large masses involving the entire breast.[8]

Compared with previously reported cases, our patient exhibited a typical clinical course in terms of post-radiotherapy latency, anatomical location, and prior history of breast irradiation. Notably, she did not receive a radiation boost, which has been associated with a lower incidence of radiation-induced breast sarcoma, although without eliminating the risk.[3–6]

A particularly relevant feature in this case is the clinical presentation: a mobile, erythematous, non-tender nodule, which is consistent with the commonly described presentation of radiation-induced sarcoma.

This case highlights the importance of long-term clinical surveillance in patients who have undergone breast radiotherapy, even when the original tumor characteristics are favorable and treatment has been conservative. It also underscores the role of patient self-examination, as the lesion was self-detected, allowing for timely medical consultation.

Furthermore, this case fulfills the modified classical Cahan criteria traditionally used to define radiation-induced sarcomas: prior history of radiotherapy, development of the sarcoma within the irradiated field, a latency period greater than three years (seven years in this case), and histology distinct from the primary tumor. Although these criteria are currently complemented by molecular diagnostic tools, they remain a useful and widely accepted framework in the clinical evaluation of radiation-induced breast sarcoma (RIBS).[1–6]

Strategies aimed at preventing radiation-induced sarcoma focus primarily on optimizing the indication and delivery of radiotherapy, minimizing radiation dose and irradiated volume, and employing advanced planning techniques that reduce exposure to surrounding healthy tissues.

Regarding pharmacologic interventions, recent medical literature highlights ongoing research into agents targeting radiation-induced adverse effects; however, to date, no drug has been specifically approved for the prevention of radiation-induced sarcomas.

Investigational agents such as KMRC011, GC4419, and combinations including enoxaparin, pentoxifylline, and ursodeoxycholic acid have shown promising results in reducing acute radiation toxicities and focal radiation-induced injuries. Nevertheless, they have not demonstrated efficacy in preventing secondary malignancies such as radiation-induced sarcoma, and their development has been limited by adverse effects and cost-effectiveness concerns.[1]

The treatment of RIBS is based on wide surgical excision with negative margins, which remains the cornerstone of management, given the locally aggressive behavior of these tumors and their limited response to adjuvant therapies.[1–7,9,10] In most cases, mastectomy is described as the most frequently employed surgical approach, particularly in angiosarcoma, due to its tendency for diffuse infiltration of irradiated breast tissue.[1–7,9,10]

The literature also reports high rates of local recurrence in RIBS, ranging from 33% to 100% in some series, particularly when complete resection is not achieved.[2–7] In this context, the wide excision performed in our patient represents an aggressive surgical approach tailored to the tumor location and individual anatomy, aiming to balance optimal local control with functional preservation.

With regard to adjuvant therapies, the role of postoperative radiotherapy is limited and controversial, especially in tumors that arise as a direct consequence of prior radiation exposure.[1–7,9] Chemotherapy has shown some benefit in the setting of advanced disease or recurrence; however, its impact on overall survival remains uncertain and is largely based on retrospective studies.[1–7,9] In the present case, given the localized nature of the disease and the achievement of macroscopically negative margins, an initially surgery-only approach was adopted.

Finally, emerging strategies such as antiangiogenic therapies and immunotherapy are currently under investigation but have not yet become part of the standard of care[1]. Although they were not implemented in this case, they may be considered in the future in the event of disease progression or recurrence.

In conclusion, the surgical management performed in our patient aligns with current literature recommendations emphasizing the need for wide excision with negative margins. The decision to adopt a breast-conserving approach rather than total mastectomy was made possible by accurate assessment of tumor location and meticulous surgical planning, without compromising oncologic radicality.

Conclusion

Radiation-induced sarcoma is a rare but serious complication of radiotherapy, particularly relevant in the context of breast-conserving treatment for breast cancer.

Primary prevention continues to rely on careful patient selection, the use of advanced precision radiotherapy techniques (such as IMRT and image-guided radiotherapy), and long-term follow-up for the early detection of secondary malignancies. To date, no pharmacologic strategies have been approved, nor are there specific recommendations in the medical literature for the direct prevention of radiation-induced sarcoma.[9]

Current evidence underscores the need for prolonged and multidisciplinary follow-up in breast cancer survivors treated with radiotherapy, given the risk of late-onset radiation-induced breast sarcoma (RIBS). The implementation and adherence to standardized surveillance protocols are essential to facilitate early diagnosis and optimize long-term outcomes.

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None.

Conflicts of interest

Authors have no conflicts of interest to declare.

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