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Case Report

Breast Angiosarcoma Case Report

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Abstract

We present a case of a 77-year-old female who was diagnosed with right breast invasive carcinoma treated with breast-conserving surgery and adjuvant radiation therapy in 2015. In 2023, she was diagnosed with radiation-induced angiosarcoma (RIAS), and a right breast mastectomy was recommended. RIAS is difficult to diagnose due to its rarity and non-specific symptoms. This paper examines various factors causing RIAS and strategies to manage this disease. Even though achieving clear margins is challenging due to its multifocal nature, surgical resection remains the primary treatment for RIAS. The role of chemotherapy remains unclear, although targeted therapies may offer alternative options. The prognosis for RIAS is influenced by factors including the size of the tumor and stage at diagnosis. Adjuvant chemotherapy's role is still evolving, and developments within radiotherapy approaches have allowed for enhanced local control. Further research is required to develop optimal treatment protocols and preventive strategies.

Keywords: Angiosarcoma; Breast Cancer; Radiation therapy

Introduction

Breast angiosarcoma is a type of rare cancer that can manifest as either a primary tumor (PBA) or a secondary malignancy (SBA). Due to their varying clinical features, PBA and SBA present with their own clinical challenges. SBA develops primarily as a result of previous breast radiation therapy. The SBA cases are rising due to the increased use of breast-conserving surgery and radiation therapy. Angiosarcoma of the breast accounts for 0.04% of all breast cancers and 8% of breast sarcomas [1]. Secondary angiosarcomas, predominantly observed in women with a history of breast cancer treatment, include lymphedema-associated cutaneous angiosarcoma and post-irradiation angiosarcoma. This malignancy exhibits high local recurrence rates, distant metastases, and poor survival. This study underscores the imperative to comprehend the clinico pathological features, survival, and prognostic factors of breast angiosarcoma.

Clinical Case Presentation

Patient is a 77-year-old female diagnosed with a right breast invasive ductal carcinoma of 1.8 cm in April 2015. There was no family history of breast, ovarian, colon, prostate, or pancreatic cancer. The patient's medical history indicated osteoporosis, diabetes, and hypertension. Biopsy of the breast mass showed an invasive ductal carcinoma ER/PR positive and HER2 negative, and DCIS grade 3 with cribriform and comedo types. In May of 2015, she underwent a right lumpectomy with x-ray needle localization and sentinel node biopsy that staged her at T1N0M0 with positive inferior and medial margins for DCIS. She underwent a re-excision of the right breast tumor cavity in July 2015. The patient underwent radiation therapy for 21 days but refused adjuvant chemotherapy at that time. She completed radiation therapy in August 2015 and was started on hormonal treatment with Anastrazole, which she continued for 5 years. The patient noted slight discoloration but no pain around the areola in November 2015 to radiation oncology but was reassured that it was secondary to treatment. She also followed oncological and radiation therapy follow up which consisted of clinical examinations every 4-6 months, bilateral mammography, physician breast exams, and monthly self-breast exams. In March 2016, she was concerned about an area of mobile mass near the posterior end by the healed scar tissue. She underwent an ultrasound and mammogram which revealed it to be a cystic lesion. In May 2016, a significant mass effect was noted along the lateral aspect of the right breast in the area of the lumpectomy, and a repeat mammography indicated post-surgical changes. In November 2016, the patient transitioned to yearly mammograms compared to 6-month visits.

In December 2021, she noticed some bruising around her right breast. The bruising had been present for 2-3 weeks and didn't cause any pain or drainage. She couldn't recall any trauma that might have caused the bruising. During the physical examination, it was observed that there was a widespread area of ecchymosis, including the lower half of the breast. The skin had a mix of dark bluish to light pink discoloration, but there was no palpable mass, induration, nipple discharge, or pain. The radiology findings from December 2021 reported scattered areas of fibroglandular density but no suspicious masses, architectural distortion, or micro calcifications. The patient was advised to use empirically over-the-counter antifungal medication, which she did for a few days.

Abnormal skin thickening and discoloration involving a large portion of the right breast with incidentally noted ill-defined hypoechoic skin lesion seen on ultrasound in February 2023. Bilateral diagnostic mammography at the time showed BI-RADS: 4. In February 2023, an MRI bilateral breast revealed diffuse skin thickening and an abnormally enhancing 3.3 cm lesion within the right breast dermis, inferior and lateral to the nipple and extending into the subcutaneous tissue. Differential considerations included skin cancer, dermatitis/abscess, and less likely breast cancer recurrence. Needle core biopsy reviewed grade 2 post-radiation angiosarcoma and metastatic workup was recommended. Further metastatic workup including, CT chest, abdomen, and pelvis with contrast in April 2023 showed no evidence of metastatic disease. Due to the extent of the local disease, plastic surgery service was consulted to help with wound closure, if needed. Patient was scheduled for a right breast mastectomy with a possible skin graft. Mastectomy incision was made, and superior and inferior skin margins were sent intraoperatively for frozen analysis. Pathology exam showed negative results for malignancy. Mastectomy was completed and the wound was successfully closed primarily. Patient recovered well. Final pathology of the right breast mastectomy showed angiosarcoma (secondary/treatment-related), measuring at least ~ 11.5 cm, with features favoring multiple foci of tumor (predominantly involving central and lower quadrants), predominantly involving skin (papillary and reticular dermis), with involvement of likely nipple/areolar related tissue and underlying subcutaneous tissue, with foci of focal mammary parenchymal involvement, prior biopsy/procedural site change and mild to moderate chronic inflammation with germinal center formation. Margins/tissue edges of resection appear uninvolved by tumor, closest clearance ~ 6 mm from anterior-inferior peripheral skin and soft tissue edges. Features compatible with separate appearing prior procedural site change associated with a nodular cyst-like area with dense peripheral fibrosis, hyalinization, dystrophic calcifications, pseudocystic change, mild chronic inflammation, pigment-laden macrophages, cholesterol clefts, fat necrosis and features of remote organizing hematoma. Stromal fibrosis with hyalinization, atrophic change, focal foci of cystic glandular dilatation, focal apocrine metaplasia, and focal intraglandular microcalcification. Skin with scar and features compatible with focal seborrheic keratosis. Skin and subcutaneous tissue for the right breast, superior skin flap, inferior skin flap, posterior margin, and medial margin were all negative for definitive morphologic evidence of tumor. Patient was scheduled for a follow-up visit in the following week but missed the scheduled follow-up visit at the hospital.

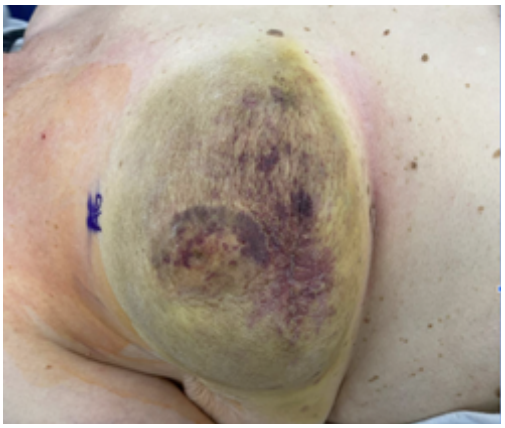
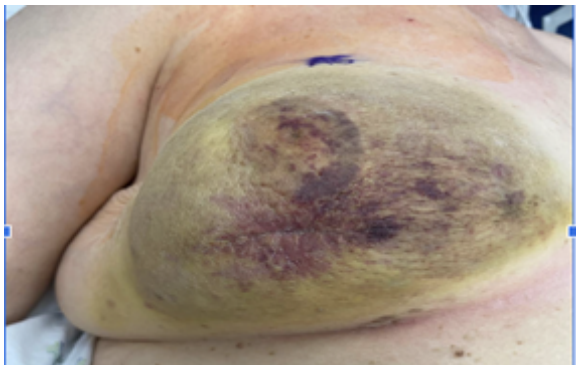


Figure 1



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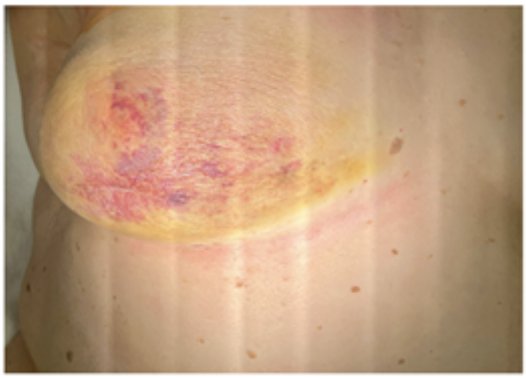

Figure 3

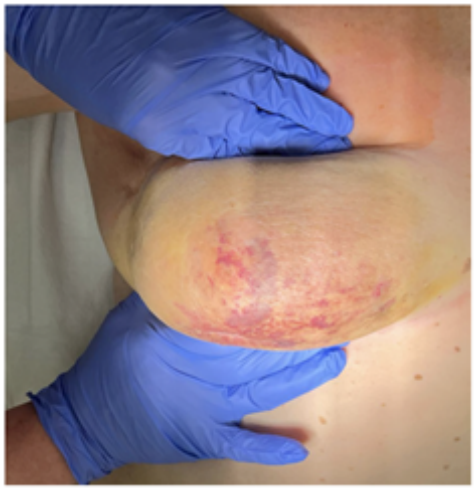

Figure 4

Discussion

RIAS of the breast is an aggressive tumor that is difficult to diagnose accurately due to its rarity and complexity. The risk of angiosarcoma increases 26-fold in patients with a prior history of radiotherapy [2]. Diagnostic delay can occur due to its rarity and non-specific clinical presentation, which includes skin discoloration and nodules. Medical professionals must have high clinical suspicion for angiosarcoma for prompt diagnosis when they observe breast skin lesions or tumors in patients with a history of breast radiation therapy [3].

In the study by Cohen-Hallaleh et al., it was found that the typical age at which patients were diagnosed with RIAS was 72 years (with a range of 51 to 92 years), and the average period between the completion of radiation therapy (RT) and the diagnosis of RIAS was 7.5 years (with a range spanning from 1 to 26 years) [2]. In our specific case, the age at diagnosis was above the median age, and the time interval between the conclusion of radiation treatment and the RIAS diagnosis slightly above the median duration. The latency period for the development of RIAS after radiation therapy varies but can be substantial, with a median latency of around 7.5 years. Patients who have received adjuvant radiotherapy for breast cancer are at an increased risk of developing RIAS, although the benefits of radiation therapy in treating breast cancer still outweigh the risk of RIAS [4].

Surgical resection is the primary treatment for angiosarcoma of the breast, which often involves mastectomy with the removal of all irradiated tissue [5]. However, angiosarcoma can present as a multifocal lesion, so it can be challenging to achieve complete resection with clear margins. The role of adjuvant chemotherapy in RIAS management remains unclear [3], and its use is not routinely recommended [6]. However, some case reports suggest potential benefits. Recent studies reveal that angiosarcoma patients treated with (neo)adjuvant have shown favorable results [7]. Another large retrospective study suggests that patients with localized angiosarcoma of any site, who are affected by > 50 mm and/or high-risk primary, localized angiosarcoma could benefit from (neo) adjuvant chemotherapy [8]. A study conducted on 52049 women observed that patients with smaller tumors (< 14mm) were likely to have less advantage of long-term survival through postoperative RT. The benefit of radiotherapy was significant in patients with large tumors (>=14 mm). This study concluded radiotherapy could be omitted for older patients with small (<=14mm) low-risk breast tumors after breast-conserving therapy [9]. Radiotherapy plus tamoxifen significantly reduces the risk of breast and axillary recurrence after lumpectomy in women with small, node-negative, hormone–receptor–positive breast cancers compared to tamoxifen alone [10].

Tumor size is one of the important factors of RIAS in determining P outcomes and survival rates. As per a study, conducted retrospectively on 15 patients with primary angiosarcoma of the breast at Samsung Medical Center, the 5-year survival rate was 28.3% in the group with tumor size ≥5 cm and 66.7% in the group with tumor size <5 cm [6]. Old age is a risk factor for Overall Survival (OS) but was protective in disease-specific survival (DSS) for angiosarcoma patients [11]. Chronic lymphedema is another risk factor for angiosarcoma. The connection between long-standing chronic lymphoedema and angiosarcoma has been identified as Stewart-Treves syndrome [11].

Early detection and prompt referral are crucial to improving both local and distant disease control. The risk of developing RIAS must be weighed against the benefits of radiation therapy in breast cancer treatment. Changes in the dose, extent, and duration of radiotherapy may impact the risk of RIAS, necessitating close monitoring. Given the rarity and complexity of RIAS, patients are best managed at tertiary sarcoma centers with expertise in treating this malignancy. Multidisciplinary collaboration between

oncologists, surgeons, and pathologists is essential to providing comprehensive care. Despite the challenges associated with RIAS, achieving curative treatment through extensive surgery remains the primary goal. While recurrence rates are high, surgery with curative intent can extend survival for patients with local recurrence. However, overall survival for RIAS remains limited, emphasizing the need for further research into effective treatments and prevention strategies.

In summary, RIAS of the breast is a rare and aggressive malignancy that poses diagnostic and treatment challenges. Surgical resection remains the primary treatment option, but the role of adjuvant therapy and the impact of radiation therapy on RIAS risk require further investigation. Early detection and specialized care are crucial in improving patient outcomes and controlling this challenging disease.

Conclusion

This case report highlights the significance of monitoring and examining skin alterations in breasts following radiation treatment. The occurrence of radiation-induced angiosarcoma (RIAS), a rare yet aggressive cancer, is a known consequence of radiation therapy, and surgical intervention is the primary mode of treatment. However, the likelihood of recurrence is significant, underscoring the need to identify effective preventive measures and treatments. Further research is imperative to evaluate the impact of radiation therapy on the risk of developing RIAS. Early detection and specialized care are integral to enhancing survival rates.

Conflict of Interest: No conflicts of interest to disclose.

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