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Early Onset Angiosarcoma of the Breast Following Breast Conserving Therapy

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Abstract

Introduction: Radiation-associated angiosarcoma (RAAS) following breast conservation therapy (BCT) is a rare event and a median latency period of approximately 8 years. Upon review of the breast cancer registry from 2000-2020 at our tertiary-care cancer center, 4 cases of RAAS followed BCT were identified. Two of these cases were classified as early onset.

Case Presentations: Patient A was a 44 year old female who presented with a T1bN0M0 estrogen receptor positive right breast invasive ductal carcinoma. She underwent a lumpectomy, sentinel lymph node biopsy, radiation, and adjuvant hormone therapy. She presented with skin discoloration and was diagnosed with right breast angiosarcoma three and a half years after BCT completion. Right breast mastectomy was performed and revealed 9.7 and 1 cm lesions of grade 2 angiosarcoma. She completed adjuvant chemotherapy. Patient B was a 72 year old female who presented with a T1cN1aM0 estrogen receptor positive right breast invasive ductal carcinoma. She underwent a lumpectomy, sentinel lymph node biopsy, re-excision lumpectomy, radiation, and adjuvant hormone therapy. She presented with skin discoloration and was diagnosed with right breast angiosarcoma four years after BCT completion. Right breast mastectomy was performed and revealed 8 cm of grade 1 angiosarcoma.

Conclusion: Radiation-associated angiosarcoma is a known but rare entity. Although the median latency period of 8 years, early-onset RAAS does occur. RAAS should remain high on the differential for patients with suspicious breast lesions and a history of breast conservation therapy as to avoid a delay in diagnosis.

Introduction

- Angiosarcoma of the breast is a rare but aggressive malignancy and represents <1% of all malignancy mammary neoplasms.¹
- Breast angiosarcoma can be classified into primary and secondary types.² Primary angiosarcoma of the breast originates in the breast parenchyma and arises de novo.² Secondary angiosarcoma develops in the setting of lymphedema or prior radiation.²
- Radiation-associated angiosarcoma (RAAS) arises on previously irradiated skin and most commonly presents as painless multifocal erythematous patches or plaques.³ RAAS occurs in 0.1% to 0.5% of patients treated with breast conservation therapy.³ The median latency period from breast cancer treatment to development of RAAS is 8 years.⁴
- At our tertiary-care cancer center, the tumor registry from 2000-2020 was reviewed for radiation-associated angiosarcoma. Four cases following breast conservation therapy were identified with a latency period range of 3 to 11 years. Two of these cases were early onset diagnosed at 3 and 4 years respectively.

Photo



Figure 1. Patient A at initial appointment with a breast surgeon three and a half years after breast conservation therapy. Physical exam significant for a large area of reddish purple discoloration in the lower quadrant of the right breast and no underlying palpable mass.

Case Presentations

- Patient A was a 44 year old female that presented in 2014 with a T1bN0M0 estrogen receptor positive progesterone receptor positive Her2neu negative right breast invasive ductal carcinoma.
- She underwent right breast lumpectomy with negative margins and sentinel lymph node biopsy. She received right breast radiation (48.6 Gy in 27 fractions with boost of 12 Gy in 6 fractions) and initiated adjuvant hormone therapy with tamoxifen.
- Three and a half years later, she developed progressive right breast skin discoloration. After a delay of four months, as multiple providers attributed her discoloration to bruising secondary to trauma sustained during a fall, she was referred to the breast surgery clinic. She presented with a large area of reddish purple discoloration in the lower quadrant (Figure 1). There was no palpable mass in the breast. Diagnostic mammogram and targeted ultrasound were obtained. Punch biopsy was performed and diagnostic for angiosarcoma.
- She underwent right breast mastectomy and immediate reconstruction with a free transverse rectus abdominus myocutaneous (TRAM) flap reconstruction. Pathology revealed 9.7 cm of grade 2 angiosarcoma and a separate 1 cm lesion. Margins were negative, and the closest margin was 0.9 cm from the inferior skin flap. She completed 12 weeks of adjuvant chemotherapy with weekly taxol. She has been closely followed with physical exam and imaging and has shown no evidence of recurrence.
- Patient B was a 72 year old female that presented in 2015 with a T1cN1aM0 estrogen receptor positive progesterone receptor positive and Her2neu negative right breast invasive ductal carcinoma.
- She underwent right breast lumpectomy with a focally positive anterior and sentinel lymph node biopsy with metastasis measuring 1.1 cm. She underwent re-excision for negative margins. She received right breast radiation (60 Gy in 30 fractions) and initiated adjuvant hormone therapy with femara.
- Four years later, she presented to the breast surgery clinic with a four week history of right breast rash. She was noted to have a 6 cm area of erythema, swelling, and dimpling medial to the nipple. Diagnostic mammogram was obtained. Punch biopsy was performed and diagnostic for angiosarcoma.
- She underwent right breast mastectomy and immediate reconstruction with an external oblique myocutaneous flap. Pathology revealed 8 cm of grade 1 angiosarcoma. Margins were negative, and the closest margin was 1.5 cm from the superior skin flap. She did not received adjuvant chemotherapy or radiation therapy. She has been closely followed with physical exam and imaging and has shown no evidence of recurrence.

Discussion

- The incidence of RAAS of the breast is 0.16%.¹ At our tertiary-care cancer center, the tumor registry from 2000-2020 was reviewed for radiation-associated angiosarcoma. Four cases following breast conservation therapy were identified with a latency period range of 3 to 11 years.
- RAAS develops in the irradiated skin, and patients tend to present with cutaneous abnormalities including skin discoloration ranging from red to purple, elevated skin, and skin thickening.^{1,2}
- The 5-year survival rate of RAAS patient ranges from 27%-48%, and the 5-year disease-free survival rate is approximately 35%.¹
- Most cases of RAAS occur in association with a total radiation dose of 40-50 Gy.⁵
- The median latency period from breast cancer treatment to development of RAAS is 8 years.⁴ The shortest documented latency to developed of RAAS reported was 6 months.²
- Two of the RAAS cases from the Henry Ford tumor registry were early onset diagnosed at 3 and 4 years respectively.
- Optimal management of RAAS includes complete surgical excision, specifically wide local excision with negative surgical margins either by segmentectomy or mastectomy.^{1,3}
- The role of chemotherapy and radiotherapy remains ambiguous.^{1,3}

Conclusions

- Radiation-associated angiosarcoma following breast conservation therapy is a known but rare entity.
- Although the median latency period is 8 years, early-onset RAAS does occur.
- RAAS should remain high on the differential for patients with suspicious breast lesions and a history of breast conservation therapy as to avoid a delay in diagnosis.

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