



Case Study

A 54-year-old female with a history of T1b N0, ER low positive, PR negative, HER 2 negative, grade 3, right breast cancer in 2011. She had a right lumpectomy and sentinel lymph node biopsy, as well as adjuvant chemotherapy, radiation, and 5 years of tamoxifen.

More recently, the patient noted discoloration to her right breast. In March 2023, a bilateral diagnostic mammogram and ultrasound showed the right breast with new cutaneous thickening extending medially in the right peri-areolar region, which clinically corresponded with the area of purplish discoloration. A punch biopsy demonstrated perivascular proliferation. A breast MRI in April 2023 demonstrated skin thickening and edema of skin of the medial right breast with minimal associated enhancement. This represented a change from previous imaging.

A subsequent right peri-areolar skin punch biopsy performed May 2023, demonstrated an atypical vascular lesion concerning for angiosarcoma.

In September 2023, a right breast mastectomy was performed, and the final pathology revealed well-differentiated low-grade angiosarcoma measuring at least 4.5 cm. She returned to the OR for revision of the superior margin demonstrating residual focus of angiosarcoma, low-grade measuring 0.13 cm. Margins were negative however there is angiosarcoma 3 mm from the margin. This patient's case was discussed in a multidisciplinary tumor board and a consensus was reached on her requiring more surgical intervention to achieve at least a 1 cm margin.

Discussion

Angiosarcomas are a rare malignancy with a poor prognosis. They often present as a red or purple skin discoloration which can be easily mistaken for bruising, delaying diagnosis and treatment. Angiosarcomas develop from endothelial cells of blood or lymphatic vessels. They can develop either sporadically as a primary malignancy or secondary to chronic lymphedema or previous irradiation. Angiosarcomas are a rare but known risk of radiation treatment in breast cancer. There is a 0.05-0.3% risk of developing an angiosarcoma of the breast after radiation therapy. The incidence of angiosarcomas has increased as breast-conserving surgery followed by irradiation has been adopted. Women who have been diagnosed with breast cancer are at greater risk of developing a subsequent breast cancer. Hence why radiation is performed after surgery to eliminate any remaining microscopic tumor cells. Recent clinical trials have evaluated outcomes when deescalating or omitting radiation therapy. PRIMEII, a recent phase 3 randomized clinical trial involving older women with HR-positive breast cancer revealed that when treated with adjuvant endocrine therapy, the 10-year incidence of local cancer recurrence after breast-conserving surgery was lower among patients who received whole-breast irradiation than among those who did not receive irradiation. However, it showed no substantial effect on the incidence of regional/distant metastases or on breast cancer specific over-all survival. Currently, there is a lack of evidence-based data on how to properly treat angiosarcomas. The accepted course of treatment is radical resection to achieve negative margins. In this patient's case she will undergo her third operation to achieve this.

Conclusion

This case serves as an educational piece on the risks of radiation therapy as well as the abnormal presentation of angiosarcoma. Clinicians should be able to recognize an angiosarcoma despite its unusual presentation in patients with known risk factors, such as radiation therapy.



Figure 1: Erythematous plaque with telangiectasias on the right chest wall below mastectomy scar

Resources

1. Thiebaud JA, Ravi V, Litwin S, Schuetze SM, Movva S, Agulnik M, Kraft AS, Tetzlaff ED, Somaiah N, von Mehren M. OER-073: A multicenter phase 2 study evaluating the role of pazopanib in angiosarcoma. *Cancer*. 2022 Oct 1;128(19):3516-3522. doi: 10.1002/cncr.34403. Epub 2022 Aug 9. PMID: 35942596; PMCID: PMC9616178.
2. Cohen-Hallaleh RB, Smith HG, Smith RC, Stamp GF, Al-Muderis O, Thway K, Miah A, Khabra K, Judson I, Jones R, Benson C, Hayes AJ. Radiation induced angiosarcoma of the breast: outcomes from a retrospective case series. *Clin Sarcoma Res*. 2017 Aug 7;7:15. doi: 10.1186/s13569-017-0081-7. PMID: 28794852; PMCID: PMC5547463.
3. Kunkler, I.H. *et al.* (2023) 'Breast-conserving surgery with or without irradiation in early breast cancer', *New England Journal of Medicine*, 388(7), pp. 585–594. doi:10.1056/nejmoa2207586.