

# Radiation-induced angiosarcoma of the breast

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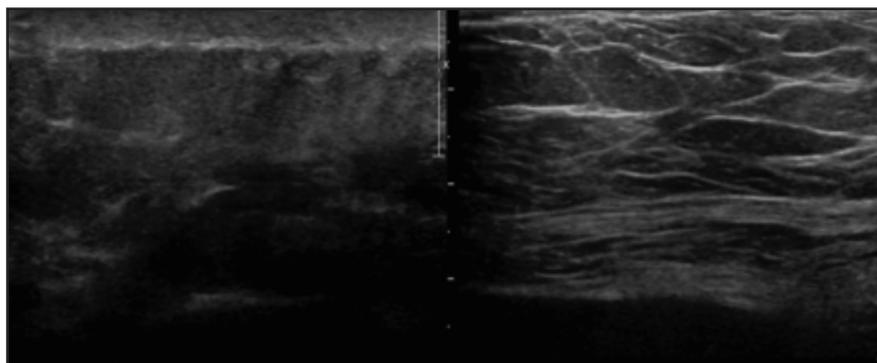
## CASE SUMMARY

Our patient is a 45-year-old female with a past medical history of T2N1M0 (stage IIb, grade 3), ER positive, PR negative, HER2/NEU positive infiltrating ductal carcinoma of the left breast at the age of 38 treated with left modified radical mastectomy transverse rectus abdominis muscle (TRAM) flap reconstruction, and later with a latissimus flap following the development of a thrombus in the original TRAM flap. Following surgical therapy, she received doxorubicin and cyclophosphamide, followed by paclitaxel and trastuzumab. In addition, she received chest wall radiation.

Approximately six years later, during a routine surveillance visit, she was found to have small nodules on her chest wall inferior to her latissimus flap. These nodules progressed rapidly, eventually encompassing over 50% of the inferior aspect of the native breast, chest wall fold, latissimus dorsi flap, and skin over the xiphoid. The rest of the physical exam and laboratory findings were unremarkable.

## IMAGING FINDINGS

Diagnostic workup included a mammogram, breast sonogram, breast



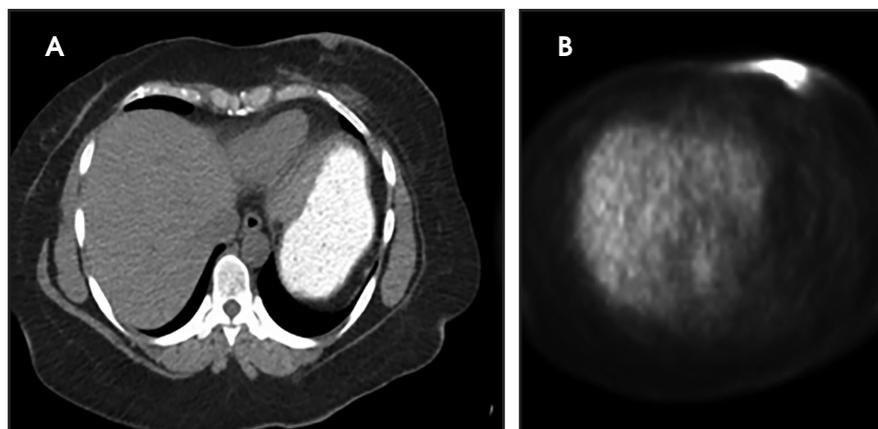
**FIGURE 1.** Ultrasound of the reconstructed left breast demonstrating thickened skin in the medial aspect (8 o'clock) as compared to normal skin thickness laterally (3 o'clock).

MRI and PET-CT scan. The mammogram did not reveal any suspicious findings. Sonography of the left breast showed thickening of the skin in the region of the cutaneous nodularity (Figure 1). No other site of abnormal increased uptake was visualized in the body (Figures 2 and 3). PET scan revealed a large area of curvilinear configuration of diffuse, intense uptake in the superficial and medial inferior aspect of the reconstructed left breast, fusing to thickened skin and subcutaneous tissue, with a maximum standardized uptake value of 15. MRI of the thorax demonstrated diffuse nodular thickening and enhancement of the skin, primarily along the medial inferior aspect of the

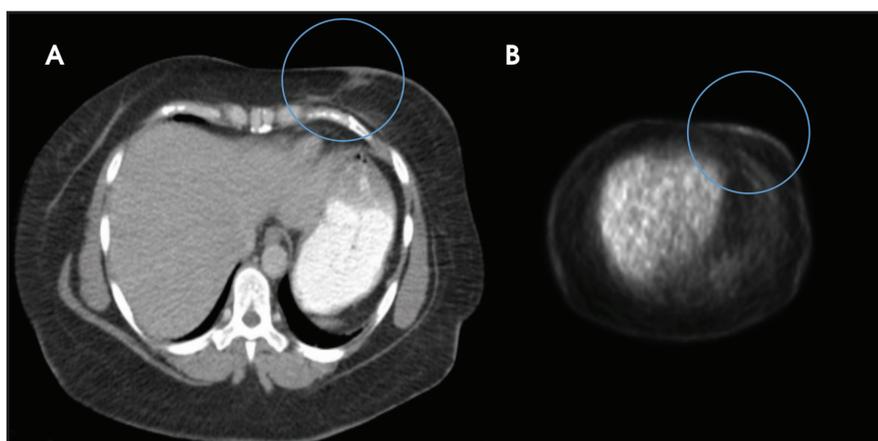
left reconstructed breast and chest wall. The nodular enhancement extended into the soft tissues deep to the skin at the level of the inferior edge of the implant, measuring 4 × 1.2 × 2 centimeters. Superior to this enhancement, another area of nodular enhancement was seen abutting the skin, measuring 1.6 × 3 × 1.6 centimeters. No involvement of the muscle was visualized. Small areas of nodular skin enhancement were also noted on the lateral aspect of the breast (Figure 4).

## DIAGNOSIS

Punch biopsy of two sites in the region of nodular skin thickening revealed a grade 2 angiosarcoma.



**FIGURE 2.** Preoperative PET/CT showing nodular skin thickening in the medial aspect of the reconstructed left breast. Increased metabolic activity is seen in this region on the PET image. Technique: This is a combined PET/CT scan. PET was performed from the base of the skull to mid-thigh after a 66-minute uptake phase. CT was performed with oral contrast. No IV contrast was given. Blood sugar level is 90mg/dL prior to FDG injection. 9.9 mCi F18 FDG was given IV.



**FIGURE 3.** Postoperative and post-chemotherapy PET/CT results showing a reduction of the nodularity in the medial aspect of the left breast. Metabolic activity is diminished in the same region of the PET image. Technique: This is a combined PET/CT scan. PET was performed from the base of the skull to mid-thigh after a 66-minute uptake phase. CT was performed with oral contrast. No IV contrast was given. Blood sugar level is 90mg/dL prior to FDG injection. 9.9 mCi F18 FDG was given IV.

## DISCUSSION

Angiosarcoma is a type of rare, rapidly proliferating, soft tissue sarcoma (STS) derived from anaplastic endothelial cells lining the blood vessel walls. They make up 4.1% of STS, which comprise 1% of all malignant tumors.<sup>1</sup> Angiosarcomas are becoming recognized as a complication following radiation therapy in women receiving conservative therapy for

breast cancer treatment, as well as lymphedema following axillary node dissection.<sup>1,2</sup> As the incidence of breast cancer in the western world rises, so is the incidence of radiation induced angiosarcoma of the breast (RIASB), with a cumulative 15-year incidence of 0.9/1,000 breast cancer patients receiving radiation as a means of conservative therapy, with an average age of onset of 68 years.<sup>2,3</sup> Overall survival

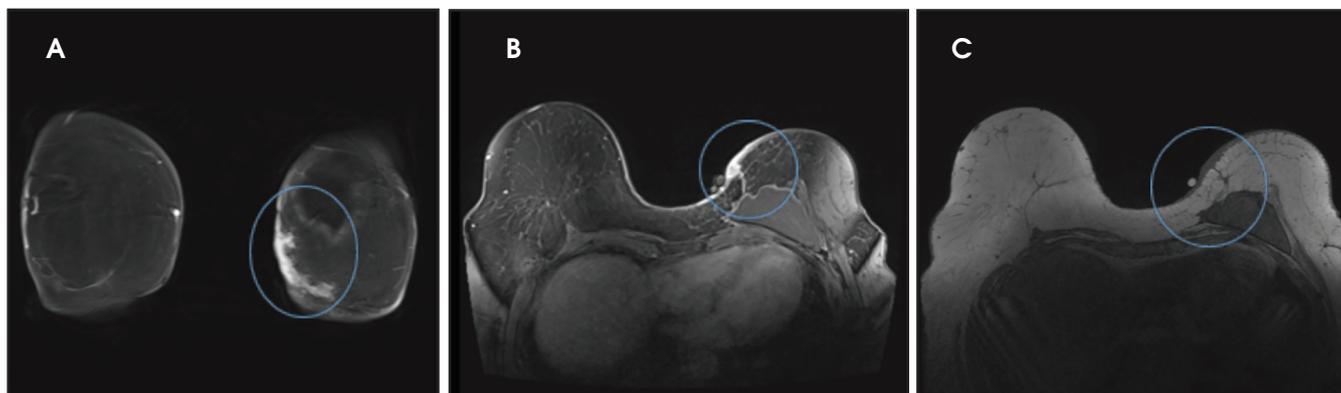
for post-irradiation breast sarcomas are poor, with a mean 5-year survival of 27-35%.<sup>3</sup>

RIASB typically presents with non-specific clinical findings, such as skin thickening and discoloration, fibrosis, telangiectasia, and nodularity.<sup>4</sup> The guidelines for making the diagnosis of radiation induced sarcoma (RIS) are often applied to RIASB.<sup>5,6</sup> Pathologic findings include a poorly defined hemorrhagic mass, and histologic findings may include anastomosing vascular channels within the breast parenchyma that are lined by malignant endothelial cells containing small and pale nuclei.<sup>7</sup> Treatment generally consists of surgical resection with mastectomy, and chemotherapy to reduce the risk of recurrence.<sup>7</sup>

Imaging generally has poor specificity for detecting RIASB. Mammography is used routinely for breast cancer surveillance. However, it is nonspecific for RIASB and may show an ill-defined, noncalcified mass or focal asymmetry, or appear normal.<sup>7-8</sup> It does not appear that mammography is beneficial in the initial detection of, or monitoring for the recurrence of RIASB.

If sonographic findings are present, these may appear as a hypoechoic, hyperechoic, or heterogeneous mass, with or without acoustic shadowing.<sup>7</sup> Sonograms may be useful as an initial screening modality at sites of previous radiation or tumor location, as well as for comparison, should patients develop clinically significant abnormalities such as skin nodularity at a site of previous radiation.

Magnetic resonance imaging (MRI) has shown promise in the diagnosis of RIASB. Kikawa et al demonstrated findings that may be specific for angiosarcomas, including marked hyperintensity on T2-weighted images, prolongation of enhancement on the dynamic phase, and the presence



**FIGURE 4.** (A) Nodular enhancement in the lower inner quadrant of the reconstructed left breast. Technique: Coronal post-contrast fat saturated T1-weighted image; 3T magnet, TR=5.0 ms, TE=2.1 ms, slice thickness=3 mm. (B) An intact saline implant is present. Technique: Axial postcontrast, fat-saturated, T1-weighted image; 3T magnet, TR=4.6 ms, TE=1.7 ms, slice thickness=1 mm. (C) Findings: nodular skin thickening in the lower inner quadrant of the reconstructed left breast. An intact saline implant is present. Fat containing markers mark the area of clinical concern. Technique: Axial non fat-saturated T1-weighted image; 3T magnet, TR=6.4 ms, TE=2.7 ms, slice thickness=1 mm.

of multiple regions without enhancement in the tumor.<sup>9</sup> MRI may be a useful imaging technique to detect lower grade angiosarcomas before metastases and tumor growth, as well as delineate ambiguities in breast masses.

FDG-PET/CT is useful for determining whether or not the lesion in question is malignant, as well as localizing its location. Combining the two imaging modalities has been shown to improve both sensitivity and specificity for detecting loco-regional occurrence and recurrence, anatomical correction for the poor spatial resolution on the FDG-PET modality, and differentiation between benign and malignant lesions.<sup>10</sup> This data lends support that FDG-PET/CT is a useful imaging modality for further evaluation of patients that develop clinically significant changes at the site of previous radiation therapy.

## CONCLUSION

Although rare, due to the poor prognosis, RIASB remains a concern as radiation therapy is an acceptable and highly utilized therapy for breast

cancer. The tumors may grow and metastasize rapidly by the time physical signs are noticed by the patient or physician, and they have high recurrence rates. While data and standardized guidelines are still lacking for RIASB surveillance, a greater frequency of clinician visits, high index of suspicion, early and routine imaging studies utilizing MRI and PET/CT, and breast biopsies may be beneficial in earlier detection and treatment of this tumor.

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*Prepared by Dr. Burns while at the Trinity School of Medicine in Baltimore, MD.; and by Dr. Gupta while Medical Director of Breast Imaging in the Department of Radiology, and Dr. Leonard while Medical Director of the Herman & Walter Samuelson Breast Care Center at Lifebridge Health in Randallstown, MD.*