Enlarging Breast Lesion

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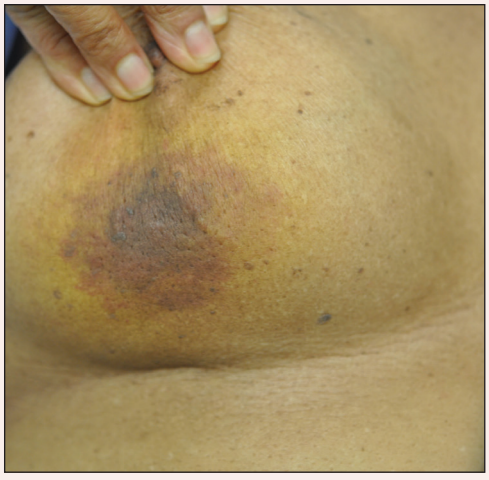

A 75-year-old woman with a history of stage II invasive ductal carcinoma of the right breast presented to the dermatology clinic with an enlarging, indurated, ecchymotic plaque on the inferior aspect of the right breast of 2 months' duration. The patient underwent a lumpectomy, radiation, and adjuvant chemotherapy 13 years prior to presentation. Review of systems was otherwise noncontributory.

What's the diagnosis?

a. hyalinized fibroadenoma
b. inflammatory breast carcinoma
c. mastitis
d. radiation-associated angiosarcoma
e. recurrent invasive ductal carcinoma

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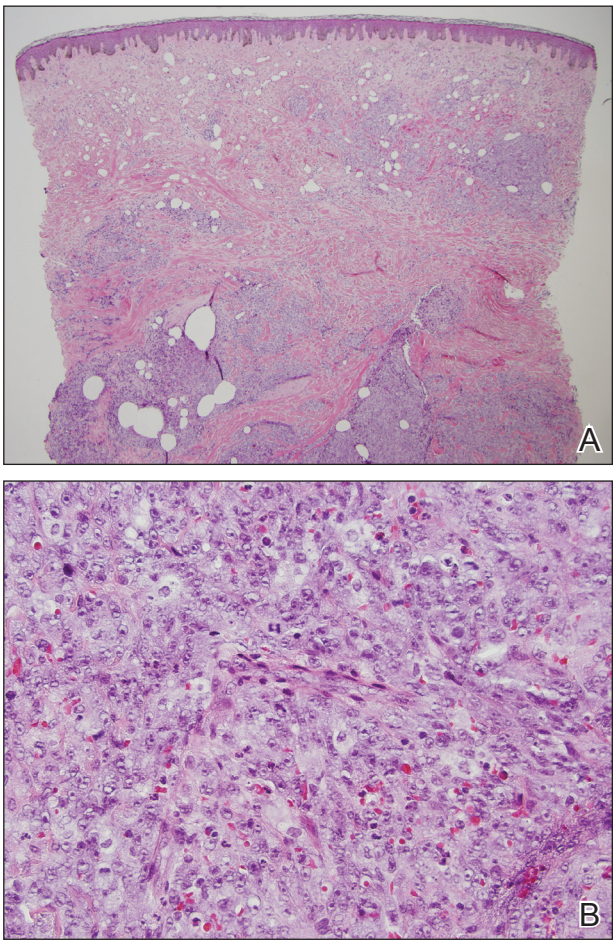
The Diagnosis: Radiation-Associated Angiosarcoma

At the time of presentation, a 4-mm lesional punch biopsy was obtained (Figure), which revealed an epithelioid neoplasm within the dermis expressing CD31 and CD34, and staining negatively for S-100, CD45, and estrogen and progesterone receptors. The histologic and immunophenotypic findings were compatible with the diagnosis of angiosarcoma. Given the patient's history of radiation for breast carcinoma several years ago, this tumor was consistent with radiation-associated angiosarcoma (RAAS).

Development of secondary angiosarcoma has been linked to both prior radiation (RAAS) and chronic lymphedema (Stewart-Treves syndrome).[1] Radiation-associated angiosarcoma is defined as a "pathologically confirmed breast or chest wall angiosarcoma arising within a previously irradiated field."[2] The incidence of RAAS is estimated to be 0.9 per 1000 individuals following radiation treatment of breast cancer over the subsequent 15 years and a mean time from radiation to development of 7 years.[1] Incidence is expected to increase in the future due to improved likelihood of surviving early-stage breast carcinoma and the increased use of external beam radiation therapy for management of breast cancer.

Differentiating between primary and secondary angiosarcoma of the breast is important. Although primary breast angiosarcoma usually arises in women aged 30 to 40 years, RAAS tends to arise in older women (mean age, 68 years) and is seen only in those women with prior radiation.[2] Additionally, high-level amplification of MYC, a known photo-oncogene, on chromosome 8 is a key genetic alteration of RAAS that helps to distinguish it from primary angiosarcoma, though this variance may be present in only half of RAAS cases.[3] Immunohistochemical analysis of tumor cells for MYC expression correlates well with this amplification and also is helpful in distinguishing atypical vascular lesions from RAAS.[4] Atypical vascular lesions, similar to RAAS, occur years after radiation exposure and may have a similar clinical presentation. Atypical vascular lesions do not progress to angiosarcoma in reported cases, but clinical and histologic overlap with RAAS make the diagnosis difficult.[5] In these cases, analysis with fluorescence in situ hybridization or immunohistochemistry for the MYC amplification is important to differentiate these tumors.[6]



Findings from a lesional punch biopsy were consistent with angiosarcoma (A and B)(H&E, original magnification ×40 and ×400, respectively).

At the time of presentation, the majority of patients with RAAS of the breast have localized disease, often with a variable presentation. In all known cases, there have been skin changes present, emphasizing the importance of both patient and clinician vigilance on a regular basis in at-risk individuals. In one study, the most common presentation was breast ecchymosis, which was observed in 55% of patients.[7] These lesions involve the dermis and are commonly mistaken for benign conditions such as infection or hemorrhage.[2] In 2 other studies, RAAS most often manifested as a skin nodule or apparent tumor, closely followed by either a rash or bruiselike presentation.[1,2]

The overall recommendation for management of patients with ecchymotic skin lesions in previously

irradiated regions is to obtain a biopsy specimen for tissue diagnosis. Although there is no standard of care for the management of RAAS, a multidisciplinary approach involving specialists from oncology, surgical oncology, and radiation oncology is recommended. Most often, radical surgery encompassing both the breast parenchyma and the at-risk radiated skin is performed. Extensive surgery has demonstrated the best survival benefits compared to mastectomy alone.[7] Chemotherapeutics also may be used as adjuncts to surgery, which have been determined to decrease local recurrence rates but have no proven survival benefits.[2] Adverse prognostic factors for survival are tumor size greater than 10 cm and development of local and/or distant metastases.[2] Following the diagnosis of RAAS, our patient underwent radical mastectomy with adjuvant chemotherapy and remained disease free 6 months after surgery.

In summary, RAAS is a well-known, albeit relatively uncommon, consequence of radiation therapy. Dermatologists, oncologists, and primary care providers play an important role in recognizing this entity when evaluating patients with ecchymotic lesions as well as nodules or tumors within an irradiated field. Biopsy should be obtained promptly to prevent delay in diagnosis and to expedite referral to appropriate specialists for further evaluation and treatment.

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