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Atypical Vascular Lesion Arising in an Area of Previous Radiation Treatment on the Breast

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Case Presentation:

Patient: A.B. is an 82 y.o. Causasian female.

History of Present Illness: Patient presented in October 2010 with a pink to purple asymptomatic plaque on the right medial breast. This had developed in an area of previous radiation treatment for breast cancer. Since the lesion arose in an area of previous radiation treatment, a biopsy was obtained. The lesion remained asymptomatic and stable in size for approximately one year. No treatment was pursued and watchful waiting was implemented, with the intent to biopsy any new or changing areas. At approximately twelve months, within the span of two weeks, the lesion grew four times in size and became tender. This prompted re-biopsy due to the aggressive clinical nature of the lesion.

Medical History: Dementia, malignant melanoma, breast cancer, osteoporosis, anemia

Surgical History: Bilateral lumpectomy (right breast stage T2 N0 with radiation treatment, total radiation dose 62.40 Gy, last radiation dose 2005, left breast T0), hip replacement

Medications: Aspirin, donepezil, calcium plus vitamin D, iron

Physical Examination: October 2010: 2.0 x 3.0 cm pink to purple plaque on the right breast. December 2011: 10.0 x 14.0 cm pink to purple, indurated plaque on the right breast

Biopsy:

Advanced Dermatology Associates, LTD. (AD10-10799, 10/04/2010) Right medial breast: "In the superficial half of an edematous dermis is a subtle population of ectatic vessels with plump, but small, endothelial cells. This is somewhat obscured by a patchy mixed cell inflammatory infiltrate that includes lymphocytes, histiocytes, and a rare eosinophil. There are also extravasated erythrocytes. A PAS stain is negative for fungus."

Advanced Dermatology Associates, LTD. (AD11-13464, 12/15/2011) Right medial and lateral breast: "Both specimens contain a proliferation of irregular, erythrocyte-containing, vascular channels that are lined by a single layer of flattened endothelial cells. These vary in size and shape with small jagged channels subtly intercalated between collagen bundles admixed with large ectatic ones. This process is most prominent in the superficial half of the dermis though it is full thickness, overall, with involvement of the subcutis (right breast medial). Endothelial morphology is monomorphic with no cytologic atypia and no mitoses. Superimposed on this, and also most prominent is a conspicuous population of lymphocytes that are clustered within, and around, the vessels."

Additional Studies: D2-40 negative, FISH for MYC amplification pending **Treatment:** Interest and treatment recommendations



Figure 1A: October 2010: 2.0 x 3.0 cm pink to purple plaque on the right breast.

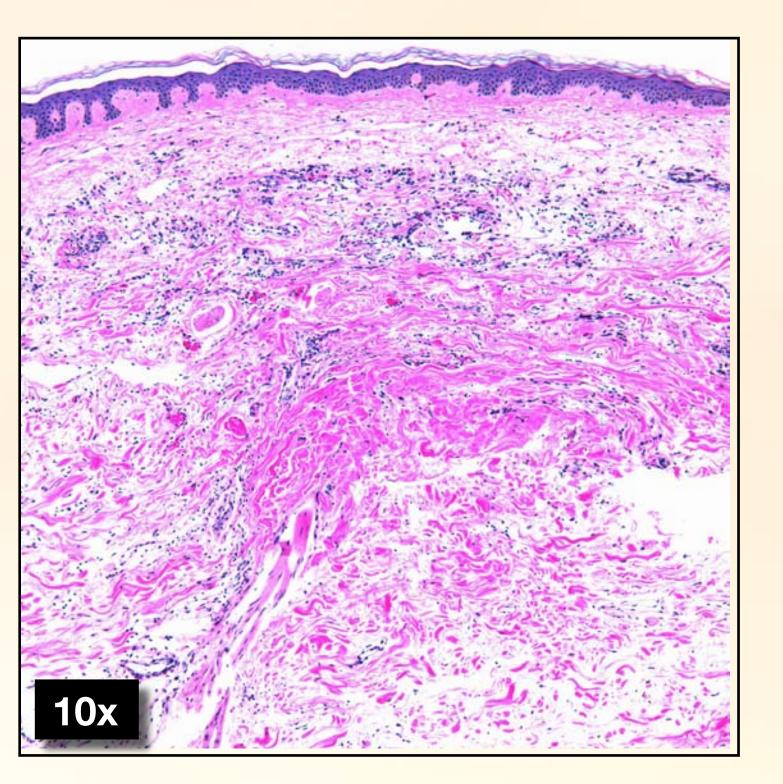


Figure 2A: H&E October 2010: There are a number of ectatic vessels with plump small endothelial cells surrounded by a patchy mixed cell infiltrate. The infiltrate is composed of lymphocytes, histioctyes, and a rare eosinophil Extravasated erythrocytes are present.

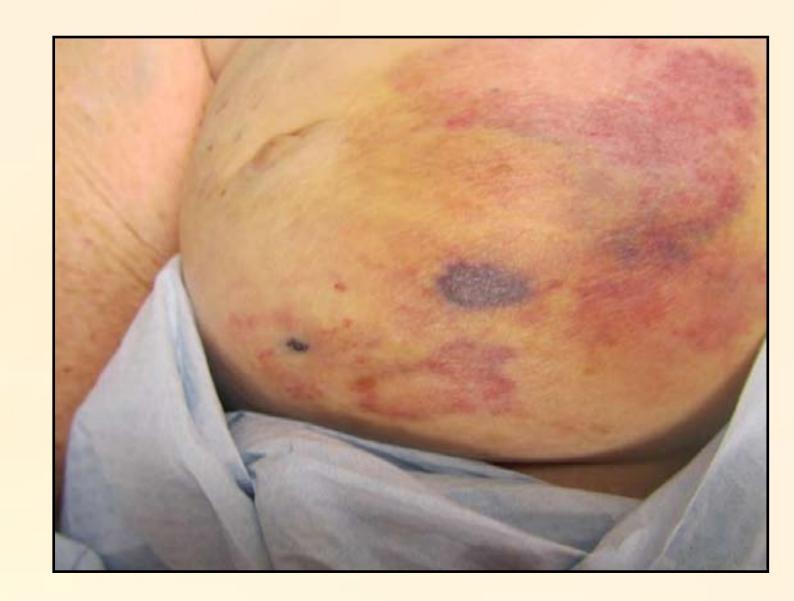


Figure 1B: December 2011: 10.0 x 14.0 cm pink to purple, indurated plaque on the right breast.

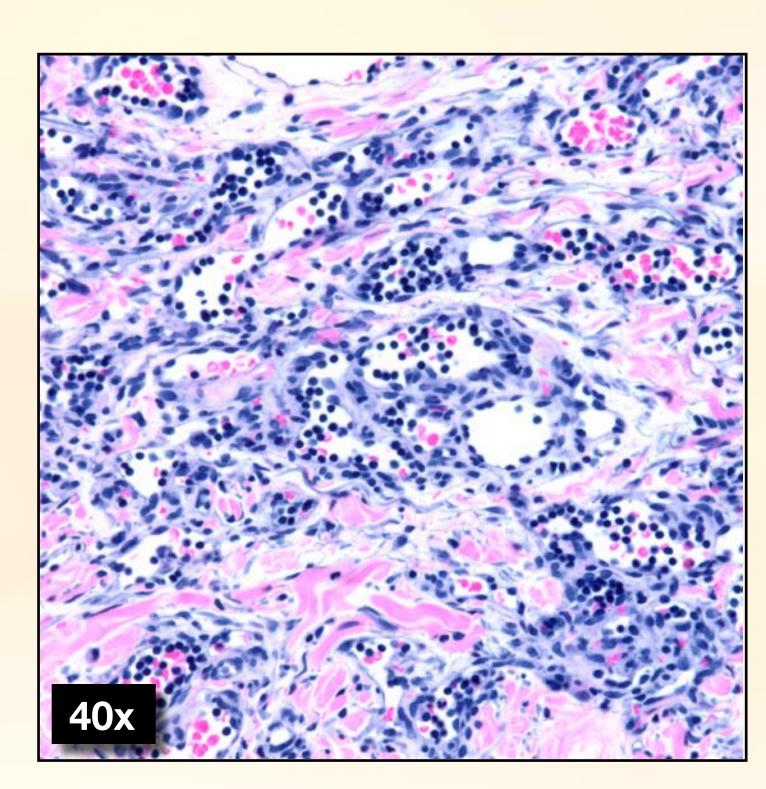


Figure 2B: H&E December 2011: Monomorphic endothelial cells with no cytologic atypia and no mitoses. There is a conspicuous population of lymphocytes clustered within and around the vessels.

Discussion:

Over the past decade, a direct link has been established between the development of angiosarcoma and radiation treatment, specifically on the breast. Although the relative risk is about 10-fold, the overall incidence of angiosarcoma arising in a breast radiation field falls within an estimated range of 0.09 to 0.16%. The specific inciting requirements are speculated to be a result of breast-conserving surgery, chemotherapy, and post lumpectomy radiation treatment. Interestingly, atypical, but not outwardly malignant vascular lesions have been reported to develop in radiation fields following breast-conserving surgery as well. Clinical and histologic overlap, combined with an unpredictable long term clinical course, may cause difficulty in

distinguishing atypical vascular lesions (AVLs) from early angiosarcoma. An established treatment protocol is needed for patients that fall into this category.

AVLs typically present in women in their 50s that have received breast-conserving surgery, in conjunction with an average treatment of 40-60 Gy cumulative radiation dose. Clinically, these lesions tend to be smaller, well circumscribed, and symmetrical. The post radiation interval for the development of AVLs is notably shorter compared to frank angiosarcoma. The time to presentation for AVLs is approximately 3 years compared to angiosarcoma, which is approximately 6 years. This has led to the hypothesis that AVLs and angiosarcoma are part of a continuous spectrum of vascular lesions, and that AVLs represent a precursor lesion.

Histopathologic analysis of AVLs versus angiosarcoma can be difficult due to many different overlapping features. To date, angiosarcoma has been histopathologically identified by anastomosing vascular channels lined by prominent endothelial cells with nuclear hyperchromasia and hobnailing. Dissection of dermal collagen and involvement of the subcutaneous tissue can occur in conjunction with necrosis or "blood lakes". AVLs, in contrast, appear well circumscribed, wedge-shaped, and tend to involve only the superficial to mid dermis. Recently, fluorescence in situ hybridization (FISH) has been able to distinguish AVLs from angiosarcoma by the presence of MYC amplification, although repeat testing on multiple biopsy sites may be needed for consistent results.

No definitive criteria are available to adequately predict whether AVLs will develop into angiosarcoma or may continue to follow a benign course. Recent attempts at sub-classifying lesions with similar histopathologic findings into two categories (i.e. lymphatic appearing versus capillary appearing lesions) has not been found to be a definitive means of distinguishing AVLs of a more aggressive nature, or those that may develop into angiosarcoma. Analysis of new cases with long term follow-up is needed to further analyze the spectrum of these lesions, leading to an appropriate and accepted treatment algorithm in the future.

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