Atypical vascular lesions (AVLs) of the breast are rare cutaneous vascular proliferations that appear as flesh-colored or erythematous papules or macules in women who have undergone radiation treatment for breast carcinoma. These lesions can develop in the irradiated area up to 20 years after the radiation treatment but most commonly occur within 3 to 6 years. The general consensus agrees on the benign nature of AVLs; however, their identity as benign lesions has been a source of controversy, with some investigators proposing that AVLs may be a precursor lesion to postirradiation angiosarcoma. Currently, there are no specific guidelines to direct clinicians on the effective treatment of AVLs, but most AVLs are treated with total excision. This rare case describes the development of 4 AVLs within the same breast and stresses the relevance of the field effect in AVL development as well as the importance of field monitoring.

Case Report

A 55-year-old woman with a history of obesity, hypertension, and infiltrating ductal carcinoma in situ of the right breast (grade 2, estrogen receptor and progesterone receptor positive) underwent a right breast lumpectomy and sentinel lymph node dissection. Three months later, she underwent re-excision for positive margins and started adjuvant hormonal therapy with tamoxifen. One month later, she began external beam radiation therapy and received a total dose of 6040 cGy over the course of 9 weeks (34 total treatments).

The patient presented to an outside dermatology clinic 2 years after completing external beam radiation therapy for evaluation of a new pink nodule on the right mid breast. The nodule was biopsied and discovered to be an AVL. Pathology showed an anastomosing proliferation of thin-walled vascular channels mainly located in the superficial dermis with notable endothelial nuclear atypia and hyperchromasia. There were several tiny foci with the beginnings of multilayering with prominent endothelial atypia (Figure 1). She underwent complete excision for this AVL with negative margins.

Six months after the initial AVL diagnosis, she presented to our dermatology clinic with another asymptomatic red bump on the right breast. On physical examination, she was found to have developed three additional AVLs in the same breast. Pathology confirmed the diagnosis of AVL in all four lesions. She underwent complete excision for all four AVLs with negative margins.

PRACTICE POINTS

- Atypical vascular lesions (AVLs) of the breast can appear an average of 5 years following radiation therapy.
- Although the malignant potential of AVLs remains debatable, excision generally is recommended, as lesions tend to recur.
a 4-mm firm, erythematous, well-circumscribed papule was noted on the medial aspect of the right breast along with a similar-appearing 4-mm papule on the right lateral aspect of the right breast (Figure 2). The patient was unsure of the duration of the second lesion but felt that it had been present at least as long as the other lesion. Both lesions clinically resembled typical capillary hemangiomas. A 6-mm punch biopsy of the right medial breast was performed and revealed enlarged vessels and capillaries in the upper dermis lined by endothelial cells with focal prominent nuclei without necrosis, overt atypia, mitosis, or tufting (Figure 3). Immunostaining was positive for CD34, factor VIII antigen, podoplanin (D2-40), and CD31, and negative for cytokeratin 7 and pankeratin. This staining was compatible with a lymphatic-type AVL. A diagnosis of AVL was made and complete excision with clear margins was performed. At the time of this excision, a biopsy of the right lateral breast was performed revealing thin-walled, dilated vascular channels in the superficial dermis with architecturally atypical angulated outlines, mild endothelial nuclear atypia, and hyperchromasia without endothelial multilayering. Clear margins were noted on the biopsy, but the patient subsequently declined re-excision of this third AVL.

During a subsequent follow-up visit 9 months later, the patient was noted to have a 2-mm red, vascular-appearing papule on the right upper medial breast (Figure 2). A 6-mm biopsy was performed and revealed thin-walled vascular channels in the superficial dermis with endothelial nuclear atypia consistent with an AVL.

Comment
Fineberg and Rosen were the first to describe AVLs in their 1994 study of 4 women with cutaneous vascular proliferations that developed after radiation and chemotherapy for breast cancer. They concluded that these AVLs were benign lesions distinct from angiosarcomas. However, further research has challenged the benign nature of AVLs. In 2005, Brenn and Fletcher studied 42 women diagnosed with either angiosarcoma or atypical radiation-associated cutaneous vascular lesions. They suggested that AVLs resided on the same spectrum as angiosarcomas and that AVLs may be precursor lesions to angiosarcomas. Furthermore, Hildebrandt et al published a case report of a patient who developed an angiosarcoma from a preexisting AVL.

The controversy continued when Patton et al published a study in 2008 in which 32 cases of AVLs were reviewed. In this study, 2 histologic types of AVLs were
described: vascular type and lymphatic type. Vascular-type AVLs are characterized by irregularly dispersed, pericyte-invested, capillary-sized vessels within the papillary or reticular dermis that often are associated with extravasated erythrocytes or hemosiderin. On the other hand, lymphatic-type AVLs display thin-walled, variably anastomosing, lymphatic vessels lined by attenuated or slightly protuberant endothelial cells. These subtypes have been suggested based on the antigens known to be present in certain tissues, specifically vascular and lymphatic tissue. Despite these seemingly distinct histologies, 6 lesions classified as vascular type displayed some histologic overlap with the lymphatic-type AVLs. The authors concluded that the vascular type showed greater potential to develop into an angiosarcoma based on the degree of endothelial atypia.1

In 2011, Santi et al13 found that both AVLs and angiosarcomas share inactivation mutations in the tumor suppressor gene TP53, providing further evidence to suggest that AVLs may be precursors to angiosarcomas. Although the malignant potential of AVLs remains questionable, research has shown that they do have a propensity to recur.5 In 2007, Gengler et al1 determined that 20% of patients with AVLs experienced recurrence after a biopsy or excision with varying margins; however, the group stated that these new vascular lesions might not be recurrences but rather entirely new lesions in the same irradiated field (field-effect phenomenon). Several other studies demonstrated that more than 30% of patients with 1 AVL developed more lesions within the same irradiated area.3,14-16 Despite the high rate of recurrence documented in the literature, only 5 of more than 100 diagnosed AVLs have progressed to angiosarcoma.1,3

Many differences can be noted when comparing the histology of AVLs versus angiosarcomas, though some are subtle (Table). Angiosarcomas display poorly circumscribed vascular infiltration into the subcutaneous tissue, multilayering of endothelial cells, prominent nucleoli, hemorrhage, mitoses, and notable atypia. Atypical vascular lesions lack these features and tend to be wedge shaped and display chronic inflammation.6,15,17-19 Atypical vascular lesions show superficial localized growth without destruction of adjacent adnexa, display dilated vascular spaces, and exhibit large endothelial cells.5,6,8,14,15,19,20 However, there is overlap between AVLs and angiosarcomas that can make diagnosis difficult.2,14,16,17,19 Areas within or just outside of an angiosarcoma, especially in well-differentiated angiosarcomas, can appear histologically identical to AVLs, and multiple biopsies may be required for diagnosis.17,19,21

Conclusion
More research is needed in the arenas of classification, diagnosis, treatment, and follow-up recommendations for AVLs. In particular, more specific histologic markers may be needed to identify those AVLs that may progress to angiosarcomas. Although most AVLs are treated with excision, a consensus needs to be reached on adequate surgical margins. Lastly, due to the tendency of AVLs to recur coupled with their unknown malignant potential, recommendations are needed for consistent follow-up examinations.

REFERENCES