Atypical vascular lesion of the breast
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Atypical vascular lesions (AVLs) are vascular proliferations that develop after surgery and radiation for breast carcinoma and may represent precursors to angiosarcoma. AVLs are not well-known entities and currently lack official prognostic factors and guidelines for surgical treatment. We report the case of a patient who developed an AVL, vascular type, 4 years after lumpectomy and radiation therapy for ductal carcinoma in situ of the breast. The patient underwent wide local excision with 1-cm margins with subsequent pathologic examination confirming complete excision of the residual atypical vascular proliferation. This case highlights the importance of close cutaneous surveillance in patients with a history of surgery and radiation for breast carcinoma, and a low threshold for biopsy. More studies are needed to further delineate the risk of AVLs progressing to angiosarcoma and to identify histologic features or immunophenotypic markers, which may be predictive of this risk. Furthermore, formal treatment recommendations for these enigmatic entities would be helpful. (J Am Acad Dermatol 2010;63:337-40.)

Key words: angiosarcoma; atypical vascular lesion; dermatologic surgery; vascular neoplasms; pathology.

A typical vascular lesions (AVLs) develop as one or more small erythematous to violaceous macules or papules after radiation therapy for breast carcinoma. Although the specific type, technique, and dosage of prior radiation has not been specifically analyzed, all AVLs are observed within the radiation field. The latency period for development of these lesions ranges from 1 to 20 years after radiation, although presentation within 3 to 6 years is most common. The effects of radiation therapy are typically divided into acute or early changes that occur within days to weeks and delayed or late changes that occur within months to years. Early radiation-induced changes occur secondary to necrosis of the rapidly dividing keratinocytes. Dilation of capillaries and increased vascular permeability leads to erythema. Decreased activity in hair follicles and sweat glands can lead to hair loss and xerosis, respectively. By 3 to 4 weeks, warmth, tenderness, and edema can occur in addition to erythema. Thrombosis of vessels, hemorrhage, desquamation, exudation, hyperpigmentation, and ulceration can also occur. Typical late radiation-induced changes seen within the skin include hyalinization of dermal collagen fibers, swelling of endothelial cells, telangiectatic dilation of dermal vessels, and proliferation and hyalinization of deeper vessels. Because such skin changes usually stop within 3 years of radiation therapy, observed changes after this period should alert the clinician. We report the case of a patient who developed an AVL and suggest that more guidelines would be beneficial to help clinicians treat these patients.

CASE REPORT
A 63-year-old woman with a medical history of hypertension, hypercholesterolemia, and estrogen receptor-positive, ductal carcinoma in situ of the right breast presented to the dermatology clinic for evaluation of an asymptomatic, unchanging macule of the right breast that had been present for 6 months. The patient had a history of right breast lumpectomy with axillary node dissection and adjuvant chemotherapy and radiation (32 treatments of external beam radiation therapy for a total of 5000 cGy) 4 years before presentation. She was currently taking the estrogen antagonist anastrozole. Physical examination revealed a 6-mm violaceous macule...
A punch biopsy specimen revealed diffuse dermal proliferation of well-formed capillary structures with mild endothelial atypia (Fig 2). Staining was positive for the CD34 vascular marker and negative for the D2-40 lymphatic marker (Fig 3). A diagnosis of AVL, vascular type (VT), was made, consistent with the histologic appearance and the history of radiation. The patient underwent wide local excision with 1-cm margins, with pathologic examination confirming complete excision of the residual atypical vascular proliferation.

Fig 1. Low magnification (A) and high magnification (B) of a 6-mm violaceous macule of right breast.

Fig 2. Low- (A) and high- (B) power image of hematoxylin-eosin stain of atypical vascular lesion, vascular type.

REVIEW

Patients who undergo conservative surgery and radiation therapy for breast cancer have been observed to have various complications including pneumonitis, arm edema, persistent breast or chest wall pain, breast fibrosis, fat necrosis, prolonged skin breakdown, rib fracture, cardiac complications, neuropathy, vascular thrombosis, and vascular neoplasms, including angiosarcoma and AVLs.7 The term “atypical vascular lesion” was coined in 1994 by Fineberg and Rosen,8 who described 4 women with cutaneous vascular proliferations after lumpectomy and radiation for breast carcinoma.1 They believed these lesions to be benign and related to lymphatic obstruction after surgery and/or radiation-induced dilation of vascular channels.1,5 Others have used the terms “atypical hemangiomas,”9 “acquired progressive lymphangioma,”10 “benign lymphangiomatos papules,”11-13 “lymphangioma circumscription,”14 and “benign lymphangoendothelioma”8,14,15 to describe the presumptive benign nature of the same entity.

However, in their review of 42 cases, Brenn and Fletcher14 concluded that AVLs were part of a continuum and were in fact precursors to angiosarcomas that warranted more aggressive treatment.1 This opinion was based primarily on a patient with a classic AVL in whom serial biopsy specimens showed slow development of angiosarcoma during the next 5 years.1,14 Other cases of malignant transformation to angiosarcomas are also reported in the literature.14,16,17 However, despite such contradictory reports, the predominant consensus in the literature remained that AVLs represented a benign entity.1

The natural course and malignant potential of AVLs was once again called into question by a 2008 report by Patton et al15 who reviewed 32 cases of AVLs after surgery and radiation of the breast. The authors divided these into two histologic types: the less common vascular type (VT) was observed to have a higher risk of development into angiosarcoma,
whereas the more common lymphatic type (LT) had a lower risk. VT lesions were characterized by irregular dispersed, pericyte-invested, capillary-sized vessels within the papillary or reticular dermis, which were often associated with extravasated erythrocytes or hemosiderin. These lesions resembled capillary hemangiomas, with vessels displaying a vascular immunophenotype (CD31, CD34, and D2-40) although lacking a lobular organization. Although 4 of the 10 VT lesions showed endothelial atypia, they differed from angiosarcomas in that the vessels did not intercommunicate and did not display endothelial multilayering. The lymphatic subtype AVLs displayed thin-walled, variably anastomosing lymphatic vessels lined by attenuated or slightly protuberant endothelial cells. These vessels displayed a lymphatic immunophenotype (CD31, D2-40, and CD34). Most of the original descriptions of AVLs seem to describe this LT entity with a discontinuous endothelial lining, absence of pericytes, and smooth muscle actin and Ki67 negativity. Of note, 6 of the VT AVLs displayed some overlap with LT histology. In the clinicopathologic study by Patton et al, patients underwent biopsy alone, simple excision, or aggressive surgical therapy depending on physician and patient preference. Therefore, knowledge of the true biological course of these lesions is still somewhat limited. Of the 21 patients with LT AVLs who had follow-up, 5 patients developed local recurrences, and one developed several additional lymphatic AVLs and eventually a multifocal angiosarcoma. Of the 8 patients with VT AVLs who had follow-up, one had local recurrences of VT AVLs and another developed high-grade epithelioid angiosarcoma. The authors concluded that VT AVLs have the highest risk for angiosarcoma transformation based on the degree of endothelial atypia. This opinion seems to be congruent with the observation of recurrences and fatalities in patients with vascular lesions of the breast with a capillary lobular pattern but with moderately atypical endothelium reported as “post-irradiation angiosarcomas.” Although the risk may be smaller, it should be remembered that LT AVLs with unusual histologic features also have a risk of malignant transformation. It remains to be seen whether LT AVLs are precursors to VT AVLs as part of a continuum to angiosarcoma, or instead distinct entities with their own inherent risk.

In a study by the French Sarcoma Group, 20% of patients with AVLs experienced recurrence, after biopsy or excision with varying margins. The authors conceded that these new vascular lesions may not represent true recurrences but rather new lesions within the same irradiated field or “field-effect phenomenon.” Other studies have observed that up to 31% of patients develop further lesions within the radiation field. However, it should be noted that despite the more than 100 diagnosed cases of AVLs reported in the literature, no more than 5 have progressed to angiosarcoma.

Histologically, AVLs do display specific features that separate them from the typical angiosarcoma. Fineberg and Rosen used these histologic findings to differentiate AVLs from low-grade angiosarcoma. In contrast to angiosarcoma, AVLs typically lack infiltration into the subcutis, multilayering of endothelial cells, prominent nucleioli, mitoses, and hemorrhage. Others have observed that AVLs histologically display dilated vascular spaces within the papillary dermis with plump endothelial cells, differentiated from angiosarcoma by lack of destruction of adnexa, localized growth, and little penetration into reticular dermis or subcutaneous tissue. Although angiosarcomas usually lack chronic inflammation, circumscription, and stromal projections into the lumen, these features are commonly seen in AVLs. Dissection of dermal collagen can be present in both
AVLs remain challenging and enigmatic entities in terms of diagnosis, natural history, and appropriate therapy. Histologic features or immunophenotypic markers that could more specifically predict which AVLs will develop into angiosarcoma would be valuable. More research and controlled studies with careful long-term follow-up are needed to further delineate this risk. In addition, guidelines for treatment including recommendations regarding surgical margins would be beneficial, as current treatments have ranged from wide local excision with 1-cm margins to mastectomy. In patients with breast cancer and a history of surgery and radiation therapy, close monitoring of the skin for new vascular eruptions, including macular lesions resembling a bruise (as in our patient), and a low threshold for biopsy should be emphasized.

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REFERENCES


