JAMA Dermatology Clinicopathological Challenge

Reddish-Brown Hematomalike Annular Plaque in a Healthy Patient's Axilla

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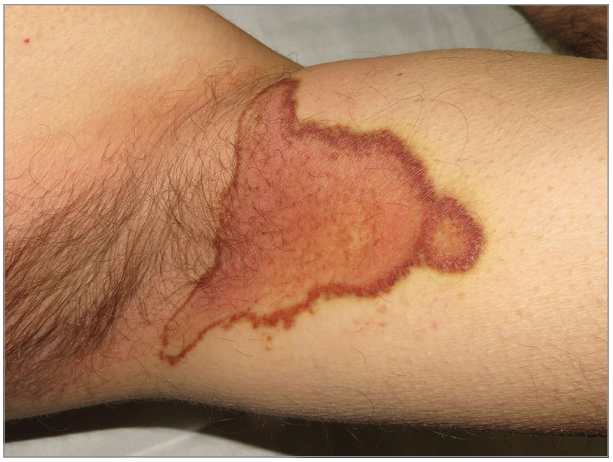

Figure 1. Clinical image of the left axilla showing an asymptomatic, reddish hematomalike plaque with a brownish peripheral border.

An otherwise healthy man in his 50s was referred to the Department of Dermatology with a 5-year history of an asymptomatic, gradually enlarging, reddish hematomalike plaque with a brownish peripheral border in his left axilla (**Figure 1**). The patient described the spontaneous onset of the lesion and reported no previous history of trauma or any other systemic symptoms; he had previously applied a topical antifungal cream but observed no lesion improvement. Physical examination revealed a nonindurated and well-defined 10 × 8-cm reddish-brown annular plaque with peripheral ecchymosis. No local lymphadenopathy was observed. Two biopsy specimens were obtained from different areas of the lesion for immunohistochemical studies; vascular channel endothelial cells were positive for CD31, CD34, and D2-40 and negative for human herpesvirus 8 (HHV-8) (latent nuclear antigen) and Wilms tumor 1 (WT1). Serologic tests for HIV and hepatitis B and C were negative.

WHAT IS YOUR DIAGNOSIS?

- **A.** Benign lymphangioendothelioma
- **B.** Kaposi sarcoma
- **C.** Hobnail hemangioma
- **D.** Low-grade angiosarcoma

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Diagnosis

A. Benign lymphangioendothelioma

Discussion

Results of histologic analysis showed poorly defined, superficial, and deep dermal vascular proliferation, consisting of small dilated, cleft-like, irregular, thin-walled vascular channels dissecting collagen bundles (**Figure 2**A). No cellular pleomorphism, mitotic figures, or intravascular red blood cells were observed. Vascular spaces were lined with a single layer of bland endothelial cells, and promontory signs were observed (Figure 2B). Perls Prussian blue staining revealed a background with prominent hemosiderin deposits. Vascular channel endothelial cells were positive for D2-40 (Figure 2C). The Ki-67 index showed low proliferation in endothelial cells.

Benign lymphangioendothelioma (BLAE) (also known as acquired progressive lymphangioma) is a rare, little understood lymphatic vascular proliferation first described by Wilson Jones in 1990.[1] Rather than a true neoplasm, it is probably an acquired malformation induced by an inflammatory stimulus. The 2018 International Society for the Study of Vascular Anomalies classification refers to BLAE as a lymphatic malformation.[2] While lymphatic malformations are usually congenital, delayed onset has also been described. Histopathologic analysis results often suggest complex vascular hamartoma, but the characteristically progressive growth of BLAE would rule out this conclusion.

Clinically, BLAE presents as an asymptomatic erythematous, gradually enlarging, reddish hematomalike plaque. Histopathologic findings include a proliferation of irregular, thin-walled

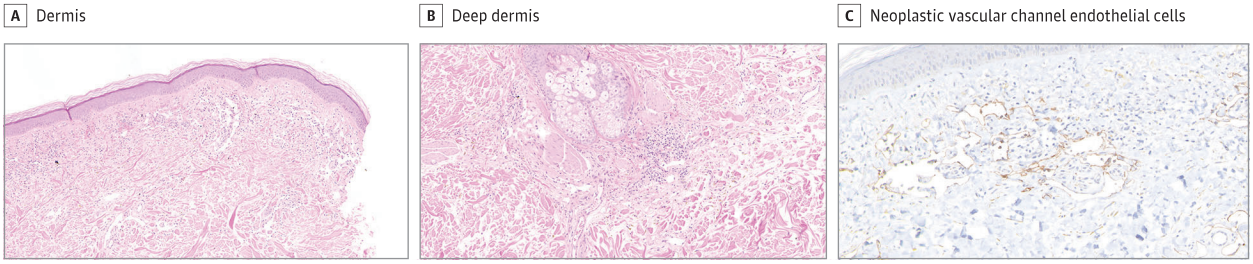

Figure 2. A, Poorly defined anastomosing vascular proliferation with collagen dissection, consisting of small, dilated, irregular, thin-walled vascular channels lined by a single layer of bland endothelial cells (hematoxylin-eosin; original magnification ×100). B, Vascular proliferation with a lymphocytic inflammatory infiltrate. Cellular pleomorphism and mitotic figures are absent (hematoxylin-eosin; original magnification ×200). C, Cells are strongly labeled by D2-40 immunostaining (original magnification ×200).

vascular spaces lined by a single discontinuous layer of bland endothelial cells dissecting collagen bundles and exclude nuclear atypia and mitosis. As happens with other lymphatic proliferations, hemosiderin deposits may be evident (in this patient, they were notable). Vascular channel endothelial cells were positive for CD31, CD34, and D2-40, supporting lymphatic differentiation,[3,4] and negative for WT1, similar to other lymphatic vascular malformations.[5] Histopathologic and immunohistochemical studies are crucial given differential diagnoses of Kaposi sarcoma (KS), hobnail hemangioma, and low-grade angiosarcoma.

Kaposi sarcoma, especially in the macular/patch stage, is clinically and histopathologically similar to BLAE given that diffuse dermal infiltration by an increased number of irregular vascular structures dissecting the collagen is characteristic of KS. Cell atypia with spindle cells is usually evident in the nodular stage. Promontory signs are often observed but are not specific to KS; this sign was very evident in this patient. Evidence of hemosiderin deposits often favors a KS diagnosis. Proliferating cells are positive for HHV-8 in KS but in BLAE are always negative,[6] and WT1 is usually positive in KS but negative in BLAE.

Hobnail hemangioma clinically differs from BLAE in typically presenting as a small, solitary, violaceous papule but, as happens with BLAE, with peripheral ecchymosis secondary to hemosiderin deposits. Vascular proliferation is generally symmetric and wedge shaped, affects the superficial and deep dermis, and shows a biphasic growth pattern. The endothelial cells, plump and exophytic, and with a "hobnail" morphology, show positivity for CD31 and variable reactivity for CD34 and D2-40.[7]

Low-grade angiosarcoma is usually observed as vascular proliferation with a fusocellular component dissecting collagen fibers. Endothelial cells are atypical, with plump hyperchromatic nuclei protruding into the lumen. Unlike what happens with BLAE, the Ki-67 proliferating index is often high, and c-*myc* amplification, as demonstrated by fluorescence in situ hybridization or immunohistochemistry, is positive in certain settings, such as radiation-induced tumors.[8]

BLAE, as its name indicates, is considered a benign entity. While surgical excision is thought to be curative,[9] spontaneous remission has been reported.[10] In view of BLAE size and location, this patient rejected surgery in favor of a watch-and-wait approach.

The BLAE in this patient presented with an unusual annular pattern and prominent hemosiderin deposition. We suggest considering BLAE in differential diagnoses for other vascular and lymphatic aggressive neoplasms to establish early diagnosis and treatment.

ARTICLE INFORMATION

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