Violaceous Nodules on the Lower Leg

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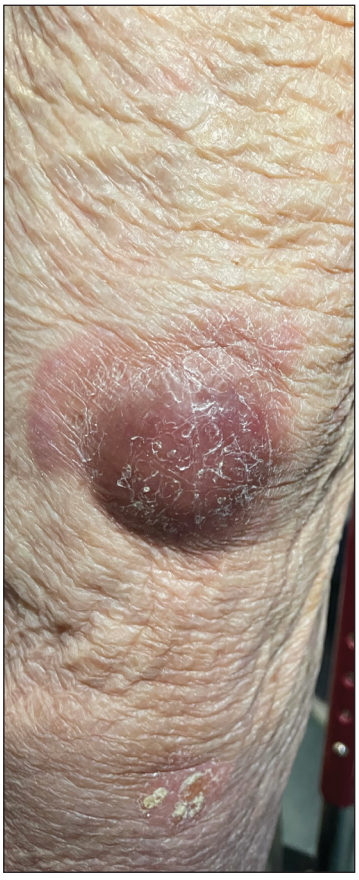

A 79-year-old man presented to the dermatology clinic with 4 enlarging, asymptomatic, violaceous, desquamating nodules on the left pretibial region and calf of 3 months' duration. He denied any constitutional symptoms such as night sweats or weight loss. His medical history included a malignant melanoma on the left ear that was excised 5 years prior. He also had a history of peripheral edema, hypertension, and rheumatoid arthritis, as well as a 50-pack-year history of smoking. Physical examination revealed 2 large nodules measuring 3.0×3.0 cm each and 2 smaller nodules measuring 1.0×1.0 cm each. There was no appreciable lymphadenopathy.

WHAT'S YOUR **DIAGNOSIS?**

a. angiosarcoma
b. cutaneous B-cell lymphoma
c. erythema elevatum diutinum
d. myeloid sarcoma
e. sarcoidosis

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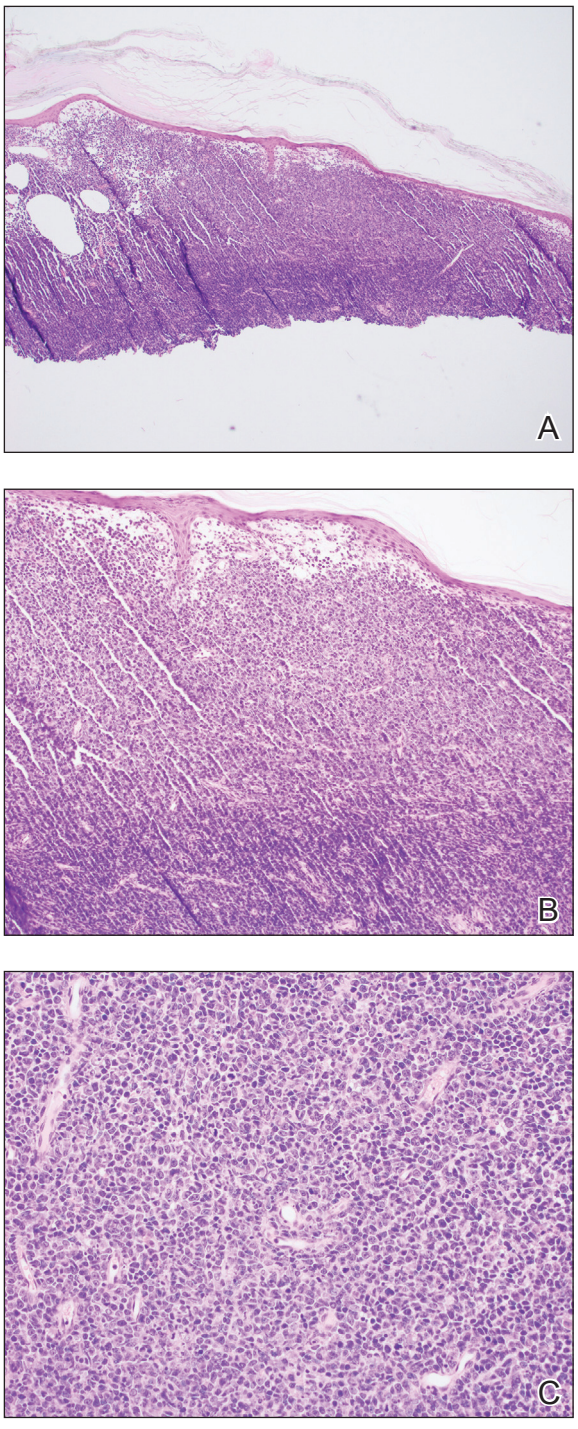
THE **DIAGNOSIS:** Cutaneous B-cell Lymphoma

Shave biopsies of 3 lesions revealed a dense, diffuse, atypical lymphoid infiltrate occupying the entirety of the dermis and obscuring the dermoepidermal junction. The infiltrate consisted predominantly of large-sized lymphoid cells with fine chromatin and conspicuous nucleoli (Figure). Immunohistochemistry was positive for CD45 and CD20, indicating B-cell lineage. Bcl-2, multiple myeloma oncogene 1, and forkhead box protein P1 also were expressed in the vast majority of lesional cells, distinguishing the lesion from other forms of cutaneous B-cell lymphomas.[1] These findings were consistent with large B-cell lymphoma with a high proliferation index, consistent with primary cutaneous diffuse large B-cell lymphoma, leg type, which often presents on the lower leg.[2] The patient had a negative systemic workup including bone marrow biopsy. He was started on the R-CEOP (rituximab, cyclophosphamide, etoposide, vincristine, prednisone) chemotherapy regimen.

Primary cutaneous diffuse large B-cell lymphoma, leg type, is an intermediately aggressive and rare form of B-cell lymphoma with a poor prognosis that primarily affects elderly female patients. Primary cutaneous diffuse large B-cell lymphoma, leg type, accounts for only 1% to 3% of cutaneous lymphomas and approximately 10% to 20% of primary cutaneous B-cell lymphomas.[2] It typically presents as multiple red-brown or bluish nodules on the lower extremities or trunk. Presentation as a solitary nodule also is possible.[1,2] Histologic analysis of primary cutaneous diffuse large B-cell lymphoma, leg type, reveals large cells with round nuclei (immunoblasts and centroblasts), and the immunohistochemical profile shows strong Bcl-2 expression often accompanied by the multiple myeloma oncogene 1 protein.[3] The 5-year survival rate is approximately 50%, which is lower than other types of primary cutaneous B-cell lymphomas, and the progression of disease is characterized by frequent relapses and involvement of extracutaneous regions such as the lymph nodes, bone marrow, and central nervous system.[1,2,4] Patients with multiple tumors on the leg have a particularly poor prognosis; in particular, having 1 or more lesions on the leg results in a 43% 3-year survival rate while having multiple lesions has a 36% 3-year survival rate compared with a 77% 3-year survival rate for patients with the non–leg subtype or a single lesion.[3] Treatment with rituximab has been shown to be effective in at least short-term control of the disease, and the R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen is the standard of treatment.[3,4]

Primary cutaneous diffuse large B-cell lymphoma, leg type, can mimic multiple other cutaneous presentations of disease. Myeloid sarcoma (leukemia cutis) is a rare condition that presents as an extramedullary tumor often



A–C, A shave biopsy of the largest lesion revealed a dense, diffuse, atypical lymphoid infiltrate consisting predominantly of large-sized lymphoid cells with fine chromatin and conspicuous nucleoli occupying the entirety of the dermis and obscuring the dermoepidermal junction (H&E, original magnifications ×4, ×10, and ×40, respectively).

simultaneously with the onset or relapse of acute myeloid leukemia.[5] Our patient had no history of leukemia, but myeloid sarcoma may predate acute myeloid leukemia in about a quarter of cases.[5] It most commonly presents histologically as a diffuse dermal infiltrate that splays between collagen bundles and often is associated with an overlying Grenz zone. A nodular, or perivascular and periadnexal, pattern also may be seen. Upon closer inspection, the infiltrate is composed of immature myeloid cells (blasts) with background inflammation occasionally containing eosinophils. The immunohistochemical profile varies depending on the type of differentiation and degree of maturity of the cells. The histologic findings in our patient were inconsistent with myeloid sarcoma.

Erythema elevatum diutinum (EED) usually presents as dark red, brown, or violaceous papules or plaques and often is found on the extensor surfaces. It often is associated with hematologic abnormalities as well as recurrent bacterial or viral infections.[6] Histologically, EED initially manifests as leukocytoclastic vasculitis with a mixed inflammatory infiltrate typically featuring an abundance of neutrophils, making this condition unlikely in this case. As the lesion progresses, fibrosis and scarring ensue as inflammation wanes. The fibrosis often is described as having an onion skin–like pattern, which is characteristic of established EED lesions. Our patient had no history of vasculitis, and the histologic findings were inconsistent with EED.

Angiosarcoma can present as a central nodule surrounded by an erythematous plaque. Although potentially clinically similar to primary cutaneous diffuse large B-cell lymphoma, leg type, angiosarcoma was unlikely in this case because of an absence of lymphedema and no history of radiation to the leg, both of which are key historical features of angiosarcoma.[7] Additionally, the histology of cutaneous angiosarcoma is marked by vascular proliferation, which was not seen in the lesion biopsied in our patient. The histology of angiosarcoma is that of an atypical vascular proliferation, and a hallmark feature is infiltration between collagen, often referred to as giving the appearance of dissection between collagen bundles. The degree of atypia can vary widely, and epithelioid variants exist, producing a potential diagnostic pitfall. Lesional cells are positive for vascular markers, which can be used for confirmation of the endothelial lineage.

Sarcoidosis is notorious for its mimicry, which can be the case both clinically and histologically. Characteristic pathology of sarcoidosis is that of well-formed epithelioid granulomas with minimal associated inflammation and lack of caseating necrosis. Our patient had no known history of systemic sarcoidosis, and the pathologic features of noncaseating granulomas were not present. As a diagnosis of exclusion, correlation with special stains and culture studies is necessary to exclude an infectious process. The differential diagnosis for sarcoidal granulomatous dermatitis also includes foreign body reaction, inflammatory bowel disease, and granulomatous cheilitis, among others.

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