Chronic Retiform Purpura of the Abdomen and Thighs: A Fatal Case of Intravascular Large Cell Lymphoma

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PRACTICE **POINTS**

- Intravascular large cell lymphoma (ILCL) is a life-threatening malignancy that can present with retiform purpura and other symptoms of vascular occlusion.
- The diagnosis of ILCL can be challenging because of the presence of distractors, and multiple biopsies may be required to establish pathology.

To the Editor:

Intravascular large cell lymphoma (ILCL) is a rare B-cell lymphoma that is defined by the presence of large neoplastic B cells in the lumen of blood vessels.[1] At least 3 variants of ILCL have been described based on case reports and a small case series: classic, cutaneous, and hemophagocytic. The classic variant presents in elderly patients as nonspecific constitutional symptoms (fever or pain, or less frequently weight loss) or as signs of multiorgan failure (most commonly of the central nervous system). Skin involvement, which is present in nearly half of these patients, can take on multiple morphologies, including retiform purpura, ulcerated nodules, or pseudocellulitis. The cutaneous variant typically presents in middle-aged women with normal hematologic studies. Systemic involvement is less common in this variant of disease than the classic variant, which may partly explain why overall survival is superior in this variant. The hemophagocytic variant manifests as intravascular lymphoma accompanied by hemophagocytic syndrome (fever, hepatosplenomegaly, thrombocytopenia, and bone marrow involvement). Of the 3 variants, the hemophagocytic variant presents with the most rapid, aggressive decline, primarily in patients in Asian countries.[1] We describe a fatal case of classic ILCL, highlighting the importance of maintaining a high index of suspicion with false-negative biopsies.

A 69-year-old man presented to the emergency department for failure to thrive and nonhealing wounds of 1 year's duration. His medical history was notable for poorly controlled diabetes mellitus, progressive multifocal ischemic and hemorrhagic cerebral infarcts, and bilateral deep venous thromboses. Physical examination revealed large purpuric to brown plaques in a retiform configuration with central necrotic eschars on the thighs and abdomen (Figure 1). There was no palpable lymphadenopathy. Laboratory tests revealed normocytic anemia with a hemoglobin level of 10.5 g/dL (reference range, 12–18 g/dL), elevated lactate dehydrogenase level of 525 U/L (reference range, 118–242 U/L), elevated erythrocyte sedimentation rate of 73 mm/h (reference range, <20 mm/h), antinuclear antibody (ANA) titer of 1:2560 (reference range, <1:80), and polyclonal hypergammaglobulinemia. The patient's white blood cell and platelet counts, creatinine level, and liver function tests were within reference range. Cryoglobulins, coagulation studies, and cardiolipin antibodies were negative. Chest and abdominal imaging also were negative. An incisional skin biopsy and skin punch biopsy showed thrombotic coagulopathy and dilated vessels. A bone marrow biopsy revealed a hypercellular marrow but no plasma cell neoplasm. A repeat incisional skin biopsy demonstrated large $CD20^+$ and $CD45^+$ atypical lymphocytes within the small capillaries of the deep dermis and subcutaneous fat (Figure 2), which confirmed ILCL. Too deconditioned to tolerate

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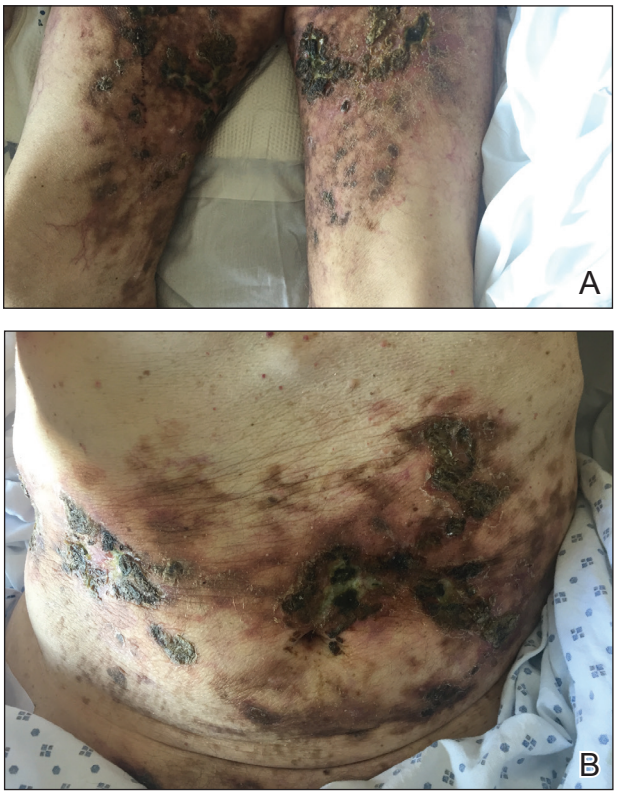

FIGURE 1. A and B, Large purpuric to brown plaques in a retiform configuration with central necrotic eschars on the thighs and abdomen, respectively.

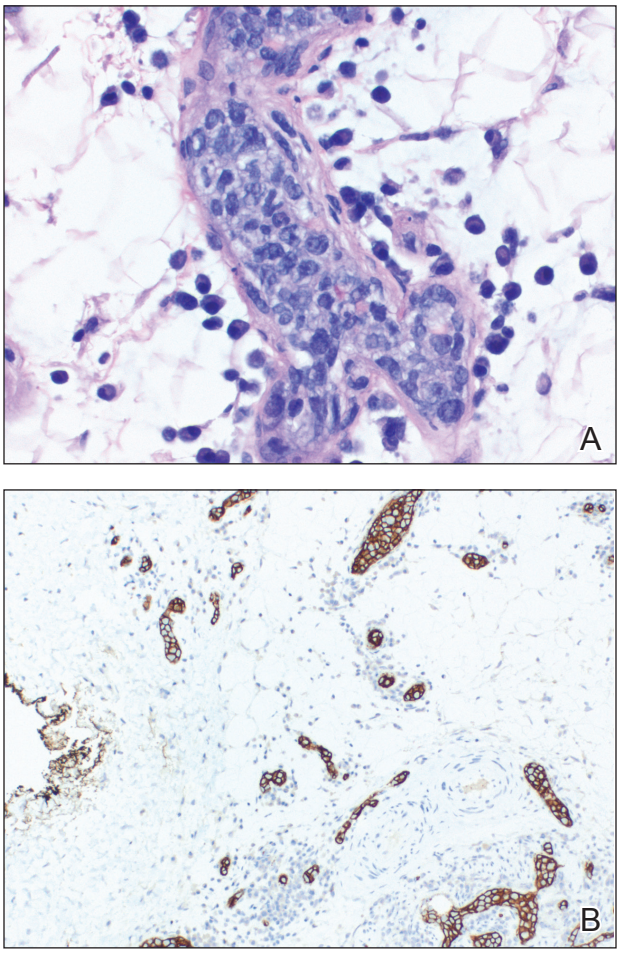

FIGURE 2. A, An incisional skin biopsy demonstrated large atypical lymphocytes within small capillaries of the deep dermis and subcutaneous fat (H&E, original magnification ×40). B, CD20 immunohistochemical staining highlighted atypical B cells (original magnification ×20).

chemotherapy, the patient opted for palliative care and died 18 months after initial presentation.

The diagnosis of ILCL often is delayed for several reasons.[2] Patients can present with a variety of signs and symptoms related to small vessel occlusion that can be misattributed to other conditions.[3,4] In our case, the patient's recurrent infarcts were thought to be due to his poorly controlled diabetes mellitus, which was diagnosed a few weeks prior, and a positive ANA, even though the workup for antiphospholipid syndrome was negative. Interestingly, a positive ANA (without signs or symptoms of lupus or other autoimmune conditions) has been reported in patients with lymphoma.[3] A positive antineutrophil cytoplasmic antibody level (without symptoms or other signs of vasculitis) has been reported in patients with ILCL.[4,5] Therefore, distractors are common.

Multiple incisional skin biopsies in the absence of clinical findings (ie, random skin biopsy) are moderately sensitive (77.8%) for the diagnosis of ILCL.[2] In a study by Matsue et al,[2] 111 suspected cases of ILCL underwent 3 incisional biopsies of fat-containing areas of the skin, such as the thigh, abdomen, and upper arm. Intravascular large cell lymphoma was confirmed in 26 cases. Seven additional cases were diagnosed as ILCL, 2 by additional skin biopsies (1 by a second round and 1 by a third round) and 5 by internal organ biopsy (4 bone marrow and 1 adrenal gland). The remaining cases ultimately were found to be a diagnostic mimicker of ILCL, including non-ILCL.[2] Although random skin biopsies are reasonably sensitive for ILCL, multiple biopsies are needed, and in some cases, sampling of an internal organ may be required to establish the diagnosis of ILCL.

The prognosis of ILCL is poor; the 3-year overall survival rate for classic and cutaneous variants is 22% and 56%, respectively.[6] Anthracycline-based chemotherapy, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), is considered first-line treatment, and the addition of rituximab to the CHOP regimen may improve remission rates and survival.[7]

REFERENCES

1. Ponzoni M, Campo E, Nakamura S. Intravascular large B-cell lymphoma: a chameleon with multiple faces and many masks [published online August 15, 2018]. *Blood*. 2018;132:1561-1567. doi:10.1182/blood-2017-04-737445
2. Matsue K, Abe Y, Kitadate A, et al. Sensitivity and specificity of incisional random skin biopsy for diagnosis of intravascular large B-cell lymphoma. *Blood*. 2019;133:1257-1259.

3. Altintas A, Cil T, Pasa S, et al. Clinical significance of elevated antinuclear antibody test in patients with Hodgkin's and non-Hodgkin's lymphoma. *Minerva Med*. 2008;99:7-14.
4. Shinkawa Y, Hatachi S, Yagita M. Intravascular large B-cell lymphoma with a high titer of proteinase-3-anti-neutrophil cytoplasmic antibody mimicking granulomatosis with polyangiitis. *Mod Rheumatol*. 2019;29:195-197.
5. Sugiyama A, Kobayashi M, Daizo A, et al. Diffuse cerebral vasoconstriction in a intravascular lymphoma patient with a high serum MPO-ANCA level. *Intern Med*. 2017;56:1715-1718.
6. Ferreri AJ, Campo E, Seymour JF, et al. Intravascular lymphoma: clinical presentation, natural history, management and prognostic factors in a series of 38 cases, with special emphasis on the 'cutaneous variant.' *Br J Haematol*. 2004;127:173-183.
7. Ferreri AJM, Dognini GP, Bairey O, et al; International Extranodal Lyphoma Study Group. The addition of rituximab to anthracycline-based chemotherapy significantly improves outcome in 'Western' patients with intravascular large B-cell lymphoma [published online August 10, 2008]. *Br J Haematol*. 2008;143:253-257. doi:10.1111/j.1365-2141.2008.07338.x