Regression of Cutaneous Intravascular Lymphoma With Rituximab

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Intravascular lymphoma, also known as malignant angioendotheliomatosis or angiotropic lymphoma, is a rare non-Hodgkin lymphoma that is usually fatal. It often presents with cutaneous and/or nervous system involvement, but the disease can involve any organ system. Clinical symptoms result from the occlusion of small vessels by tumor cells and fibrin. We present a case of cutaneous intravascular lymphoma successfully treated with rituximab, a recombinant antibody to CD20 antigen found on B lymphocytes.

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Case Report

An 81-year-old man presented with asymptomatic eruptions on his thighs, waist, and back, which he reported being of more than 3 months' duration. His medical history was significant for Crohn disease for 10 years that had been treated with prednisone and 6-mercaptopurine. He also had a 5-year history of pancytopenia, with a previous bone marrow examination demonstrating mild erythroid dysplasia and abnormal cytogenetic analysis that revealed a large population of cells lacking the Y chromosome. He was thus diagnosed with myelodysplasia, possibly stemming from the long-term use of 6-mercaptopurine, which was then discontinued. His pancytopenia remained stable but unimproved. A review of systems was negative for any neurological or constitutional symptoms.

On physical examination, the patient had multiple 2- to 5-cm erythematous and violaceous patches and plaques with telangiectasias on his bilateral thighs, waist (Figure 1A), and lower back. Palpable lymphadenopathy and organomegaly were absent.

Results of histopathologic examination of a skin biopsy from a left flank lesion showed large basophilic cells with nuclear atypia, occluding the superficial and mid dermal blood vessels (Figure 2, A and B). The atypical cells stained negative for S100 protein, factor VIII and pan-cytokeratin, ruling out melanoma, endothelioma, and metastatic squamous cell carcinoma and adenocarcinoma, respectively. However, they stained positive for leukocyte common antigen (CD45RB) and CD20 (Figure 2C), indicating a B-cell origin. There also were reactive T cells that stained positive for CD3. A diagnosis of intravascular B-cell lymphoma was made.

Results of a complete blood count revealed a low white blood cell count of $2.1\times10^3/\mu L$ (reference range, $3.28–9.29\times10^3/\mu L$) with an absolute neutrophil count of 900 μL, a low platelet count of $101\times10^3/\mu L$ (reference range, $143–398\times10^3/\mu L$), and a hemoglobin level of 13.5 g/dL (reference range, 12.3–16.3 g/dL). His blood chemistries showed an elevated lactate dehydrogenase level of 303 U/L (reference range, 110–220 U/L), and a normal uric acid level of 6.5 mg/dL. Head, chest, and abdominal computed tomography results showed no evidence of metastatic disease. Results of magnetic resonance imaging of the brain revealed chronic ischemic white matter disease without any evidence of acute infarction or neoplasm. A full-body positron emission tomography scan also showed no evidence of disseminated lymphoma. Results of a bone-marrow biopsy demonstrated marrow with 20% to 30% cellularity, appropriate for the patient's age. All hematopoietic elements were present with progressive maturation. There was no evidence of lymphoproliferative disorder. Hemophagocytosis, which is often found in association with intravascular lymphoma, was absent on the bone marrow biopsy. Interestingly, karyotyping of the bone marrow specimen demonstrated a continued clonal loss of Y chromosome, commonly seen in myelodysplastic syndromes.

With a persistently low absolute neutrophil count, the patient was a poor candidate for the traditional multiagent chemotherapeutic regimen for B-cell lymphoma.[1] Instead, he was treated with 4 weekly doses of rituximab (375 mg/m^2) infusion,

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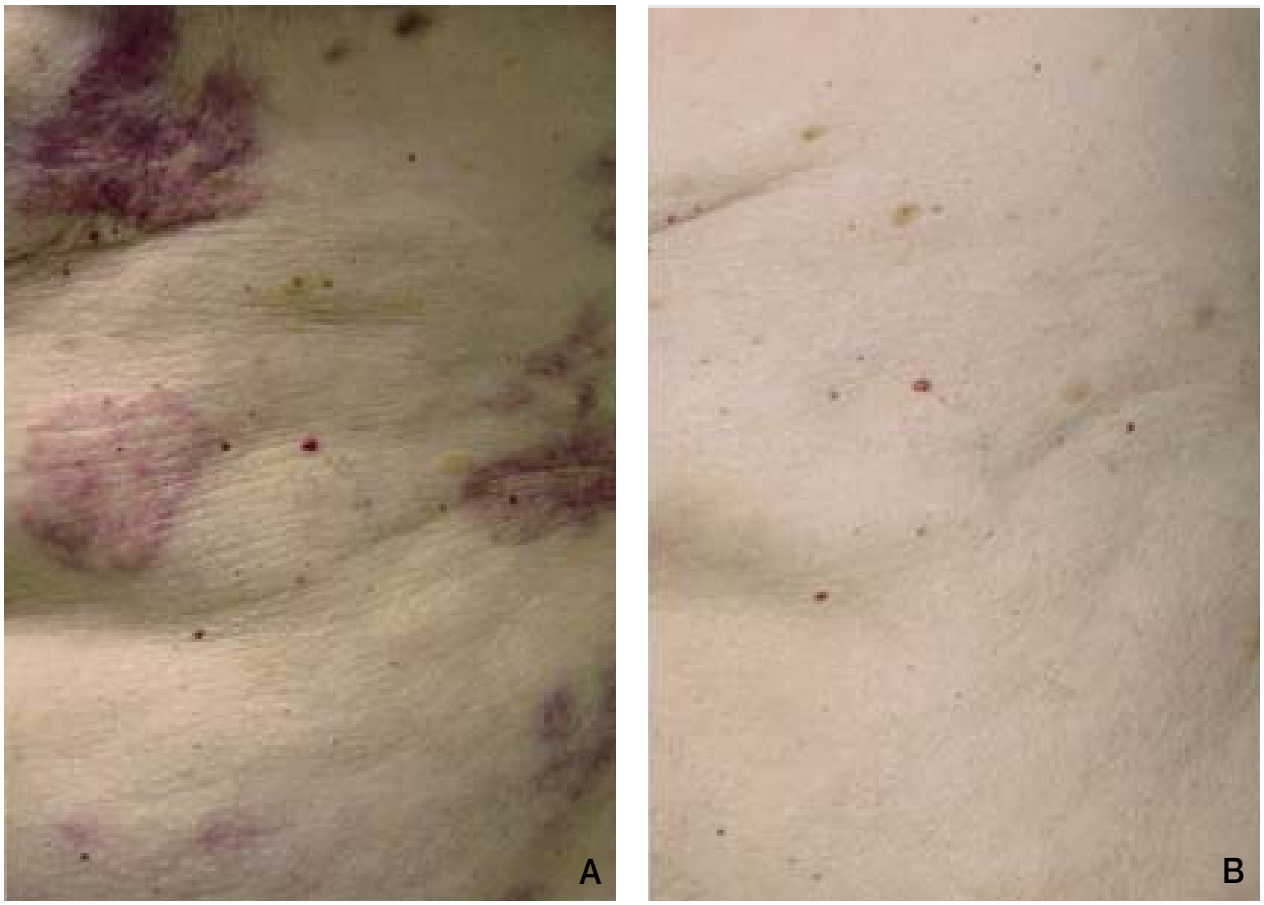

Figure 1. Cutaneous intravascular lymphoma on the waist before (A) and after (B) rituximab treatment.

a recombinant antibody against the CD20 antigen found on normal and malignant B cells. Within 2 weeks of the first infusion, the patient's cutaneous lesions regressed (Figure 1B). Results of a repeat skin biopsy from the same previously involved area demonstrated focal dilated telangiectasias without evidence of intravascular lymphoma. The patient's cutaneous lesions remain in remission 6 months after treatment. To our knowledge, this is the first report of the successful use of rituximab for cutaneous intravascular lymphoma.

Comment

Intravascular lymphoma is an aggressive non-Hodgkin lymphoma that is often fatal. It usually involves the vasculature of neurological and cutaneous tissues. Very rarely does this lymphoma involve the bone marrow or lymph nodes. Patients often present with fever, dementia, cutaneous lesions, nephrotic syndrome, and hypertension.[2]

Eighty-five percent of patients with intravascular lymphoma have neurological manifestations, including progressive cognitive impairment and stroke. Peripheral neuropathy, myalgia, and lower extremity paresthesia also have been reported. Nonspecific constitutional symptoms include fever, weight loss, and weakness. Multisystem involvement is found in 90% of reported cases.[2]

Cutaneous lesions are present in more than 30% of patients with intravascular lymphoma. Cutaneous manifestations include erythematous plaques or nodules,[3] often indurated with telangiectasias.[4] There also have been reports of erythema nodosum–like lesions,[5] ecchymotic plaques, palpable purpura, and purpuric patches.[6] Lower extremity location is common, though few cases have been reported on the face.[2]

The diagnosis of intravascular lymphoma is based on histologic examination. Biopsy results of involved tissues show atypical mononuclear cells filling the lumen of small dilated vessels. There is prominent fibrin deposition, as well. Most reported cases are of B-cell origin, though a few are T-cell disease.[7]

Prognosis is usually poor, with diagnosis often occurring postmortem. There is a mean survival

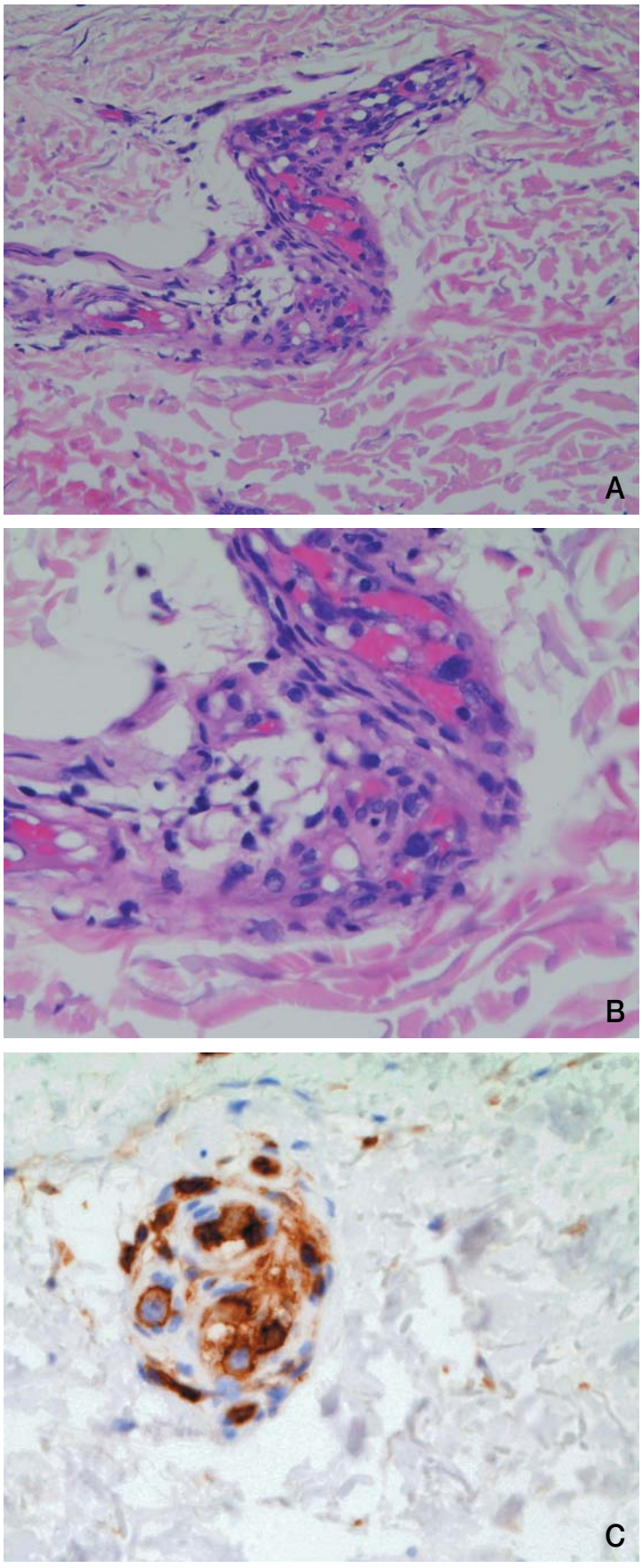

Figure 2. Mid dermal vessel occlusion by atypical basophilic cells (A and B)(H&E, original magnifications ×20 and ×40). Immunohistochemistry demonstrates positive anti-CD20, indicating B-cell origin (C) (anti-CD20, original magnification ×40).

rate of 13 months after diagnosis. Death is usually secondary to neurologic involvement. Treatment options are limited, usually involving chemotherapeutic regimens directed at lymphomas, such as cyclophosphamide, doxorubicin, vincristine, and prednisone. Long-term disease-free survival has only been reported in patients without neurologic involvement.[6]

Our extensive workup of this patient demonstrated cutaneous manifestations of the disease without signs of neurologic involvement. His neutropenia limited the use of traditional chemotherapeutic regimens. The B-cell origin of his disease made rituximab a reasonable alternative because rituximab is an anti-CD20 antibody previously reported to treat other lymphoproliferative disorders and malignancies.[8] A good prognosis for this patient is likely due to the lack of neurologic involvement and the successful regression of his cutaneous lesions with rituximab treatment. However, given the risk of systemic involvement, close follow-up is required to monitor possible metastasis and early intervention.

We present this case of intravascular lymphoma and demonstrated the novel use of rituximab for the treatment of this disease.

Addendum—Since the submission of this paper, the patient has remained in remission without evidence of disease. He is now 18 months in remission.

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