

A case of leukemia cutis presenting as blue toes in a patient with chronic lymphocytic leukemia



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INTRODUCTION

Blue toe syndrome (BTS) is a condition characterized by the blue or violaceous discoloration of one or more toes as a result of tissue ischemia. First described in 1976 in a report of 31 patients who presented with cyanotic toes secondary to embolic phenomena, it has since been linked with several different diseases including embolic, thrombotic, infectious and vasoconstrictive disorders.^{1,2} Three fundamental mechanisms are thought to underlie the alteration in skin color: diminished arterial perfusion, impaired venous outflow, and abnormal circulating blood.¹ Here we report an unusual case of leukemia cutis secondary to chronic lymphocytic leukemia manifesting as blue toe syndrome in the absence of background cryoglobulinemia or cold agglutinin disease.

CASE REPORT

A 74-year-old white man with a medical history significant for coronary artery disease, basal cell carcinoma, squamous cell carcinoma, melanoma, and chronic lymphocytic leukemia (CLL) diagnosed 10 years prior presented for evaluation of bilateral discoloration of the toes. Over the course of 6 months, the lesions had become increasingly painful and intermittently edematous and had darkened to a bluish color. On initial examination, his toes were cool to the touch, and palpable purpura with necrotic centers were observed on the left and right dorsal great toes, second toes, third toes, and fourth toes. The toes also had bulbous swelling without signs of infection. The right second

Abbreviations used:

BTS: blue-toe syndrome
CLL: chronic lymphocytic leukemia

toe was the most discolored and had an additional ulcerative exophytic plaque (Fig 1). The patient otherwise denied fever, chills, night sweats, or unintentional weight loss. No splenomegaly or hepatomegaly was appreciated, and no palpable lymphadenopathy in the anterior neck, supraclavicular, axillary, or inguinal areas was present.

Results of computed tomography angiogram and photoplethysmogram showed no significant atherosclerotic occlusive disease or thromboembolic source. On further evaluation, a complete blood count found a normal differential with the exception of an elevated absolute lymphocyte count of 4543 cells per microliter (reference range, 850–3900 cells per microliter). Serum rheumatoid factor, antinuclear antibody, cryofibrinogen, and cryoglobulin were negative, and there was no evidence of cold agglutinin disease.

Results of a serum protein electrophoresis, urinalysis, and comprehensive metabolic panel were unremarkable. Kappa/lambda light chain assay showed a total serum kappa concentration of 194 mg/dL (reference range, 74–295 mg/dL), total serum lambda concentration of 114 mg/dL (reference range, 32–156 mg/dL), and a kappa/lambda ratio of 1.7 (reference range, 1.3–2.7).

On immunohistochemical and microscopic analysis, sections from a punch biopsy measuring 0.3 × 0.3 × 0.1 cm of the palpable purpura located

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Fig 1. Leukemia cutis. Bluish discoloration and bulbous swelling of the right toes. An ulcerative exophytic plaque on the lateral aspect of the second toe.

on the right distal plantar great toe showed a dense and diffuse infiltrate of the dermis and endothelium of some vessel walls by small- to medium-sized lymphoid cells along with an intact epidermis (Fig 2). The cells were CD20⁺, CD79A⁺, CD43⁺, CD5⁺, CD10⁻, CD138⁻, CD45⁺, CD34⁻, and CD23⁺ B cells. The CD20 staining was mild to moderate, labeling more than 80% of the cells. CD34 staining found prominent vascularity and notable thick-walled vessels with fibrinoid change around them.

In view of the history of chronic lymphocytic leukemia, this infiltrate is consistent with leukemic infiltration. However, the clinical picture (6 months of blue toes) and lack of vasculopathy is unusual. Because the biopsy results indicated CLL involvement of the skin, focal radiation therapy was recommended.

Eighteen days after radiation therapy, the patient was seen for follow-up and reported that his feet were feeling fine with only minimal tenderness in the distal toes of the left foot.

Physical examination did not find any further complications, infection, or discoloration, and his toes appeared to be healing well with no sign of relapsed CLL.

DISCUSSION

This case of blue toe syndrome in our patient with a 10-year history of CLL proves unusual, as leukemia cutis has yet to be reported as an etiology of blue toes. Because the pathophysiology of blue toe syndrome typically centers on dysfunction of arterial perfusion, venous outflow, and blood circulation, it is not entirely surprising that a hematologic malignancy such as CLL could be an inciting factor in the development of blue toes. Although other hematologic malignancies are typically more associated with coagulopathy, CLL has been found to confer as much as a 10-fold increase in the risk of

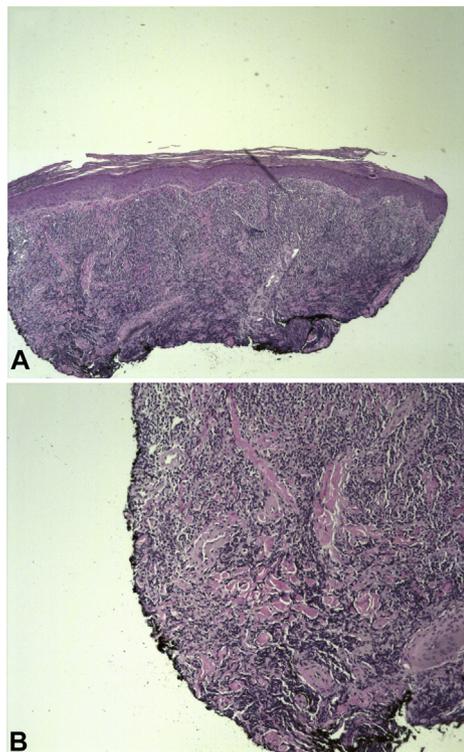


Fig 2. Leukemia cutis. Punch biopsy of the palpable purpura located on the right distal plantar great toe measuring 0.3 × 0.3 × 0.1 cm found a dense and diffuse infiltrate of the dermis and endothelium of some vessel walls by small- to medium-sized lymphoid cells, a picture consistent with CLL-induced leukemia cutis. The epidermis is notably intact. (A and B, hematoxylin-eosin stain; A, low-power magnification; B, high-power magnification.). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: [VM02580](#) and eSlide: [VM02582](#).

venous thromboembolism, with reports of deep venous thromboembolism, pulmonary embolism, and even thrombosis of the common femoral vein.^{3,4} Pathophysiology of the thrombotic phenomenon in CLL is likely an extension of leukemic infiltration into involved vasculature, as monoclonal infiltration of B lymphocytes was noted in all 42 patients with cutaneous infiltrates by Cerroni et al,⁵ and hyperleukocytosis is reported in a case of CLL-induced femoral thrombosis by Cukierman et al.⁴

Because such a hypercoagulable state is known to exist in hematologic malignancies such as CLL, and because of the proposed pathogenic mechanisms of blue toe syndrome, it would be reasonable to attribute our patient's toe discoloration to vaso-occlusive disease.⁶ Interestingly, however, our patient exhibited no such signs of thromboembolic disease, and laboratory testing found no indication of an underlying hypercoagulable state.

Although our patient's multiple comorbidities initially suggested a vaso-occlusive process of other etiologies, the negative vascular and autoimmune workup, as well as the definitive biopsy showing leukemic infiltrate into the dermis and vasculature, confirmed that our patient's presentation of blue toes was secondary to CLL-induced leukemia cutis. The resolution of symptoms with radiation therapy further suggested that the blue toe discoloration was directly attributable to the presence of leukemic cells within the vascular endothelium and dermis. Additionally, although the exophytic plaque located on the patient's right second toe was not biopsied, we presume that this was part of the same process, as it initially began as a purpuric papule before ulcerating. It also promptly resolved with the radiation treatment.

This case shows the importance of considering a leukemic process in a patient presenting with blue/purple toes in the background of a CLL

diagnosis, as timely recognition and administration of proper therapy can allow resolution of symptoms without further vascular sequelae.

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