Leukemia Cutis Manifesting as Nonpalpable Purpura

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PRACTICE **POINTS**

- Leukemia cutis complicates 5% to 15% of all cases of acute myeloid leukemia (AML) in adults.
- The appearance of leukemia cutis may be highly variable. Therefore, it should be included in the differential diagnosis for any cutaneous presentation in patients with an existing diagnosis or high likelihood of AML.
- Leukemic infiltrates are associated with sites of inflammation.

To the Editor:

A 72-year-old man presented with symptomatic anemia and nonpalpable purpura of the legs, abdomen, and arms of 2 weeks' duration (Figure 1). There were no associated perifollicular papules. Physical examination of the hair and gingiva were normal.

The patient's medical history was notable for a poorly differentiated pancreatic adenocarcinoma (pT3N1M0) resected 7 months prior using a Whipple operation (pancreaticoduodenectomy). Adjuvant therapy consisted of 5 cycles of intravenous gemcitabine and paclitaxel. Treatment was discontinued 1 month prior due to progressive weight loss and the presence of new liver metastases on computed tomography. There was no recent history of corticosteroid, antiplatelet, or anticoagulant use. The patient had no known history of trauma at the affected sites.

The patient's laboratory workup revealed the following results: hemoglobin, 5.5 g/dL (reference range, 13–18 g/dL); platelets, 128×10^9/L (reference range, $150–400\times10^9$/L); total white blood cell count (24.0×10^9/L [reference range, $4.0–11.0\times10^9$/L]), consisting of neutrophils (2.4×10^9/L [reference range, $2.0–7.5\times10^9$/L]), lymphocytes (3.1×10^9/L [reference range, $1.5–4.0\times10^9$/L]), and monocytes (18.5×10^9/L [reference range, $0.2–0.8\times10^9$/L]). Fibrinogen, activated partial thromboplastin time, and prothrombin time were within reference range. Results of a bone marrow biopsy showed 64% blasts. The lactate dehydrogenase level was 286 U/L (reference range, 135–220 U/L) and CA-19-9 antigen was 238 U/mL (reference range, 0–39 U/mL).

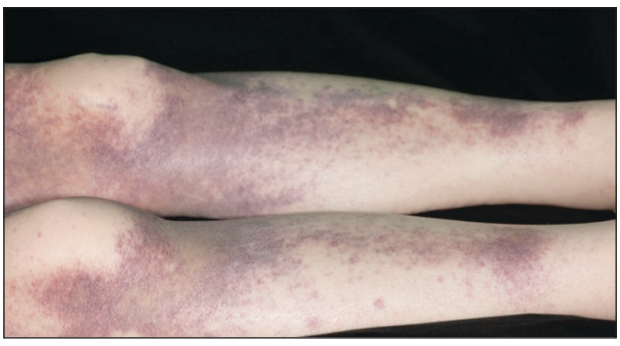

FIGURE 1. Nonpalpable purpura on the lower limbs.

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The authors report no conflict of interest.

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Results from a skin punch biopsy from the right leg showed a normal epidermis and papillary dermis. The reticular dermis was expanded by a diffuse cellular infiltrate with dermal edema and separation of collagen bundles (Figure 2), which consisted of small cells with irregular, cleaved, and notched nuclei, containing a variable amount of eosinophilic cytoplasm. Mitotic figures were present (Figure 3). There was no evidence of vasculitis, and Congo red stain for amyloid was negative. These atypical cells were positive for the leukocyte common antigen, favoring a hematopoietic infiltrate (Figure 4). Other positive markers included CD4 (associated with helper T cells, and mature and immature monocytes), CD68 (a monocyte/macrophage marker), and CD56 (associated with natural killer cells, myeloma, acute myeloid leukemia [AML], and neuroendocrine tumors). The cells were negative for CD3 (T-cell lineage–specific antigen), CD5 (marker of T cells and a subset of IgM-secreting B cells), CD34 (early hematopoietic marker), and CD20 (B-cell marker). Other negative myeloid markers included myeloperoxidase, CD117, and CD138. These findings suggested leukemic cell recruitment at the site of a reactive infiltrate. The patient completed 2 cycles of intravenous azacitidine with little response and subsequently opted for palliative measures.

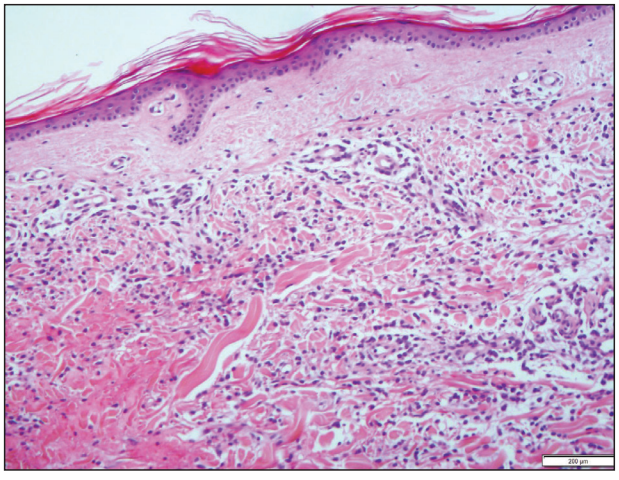

FIGURE 2. Histopathology of a skin biopsy showed a dense cellular infiltrate extending from the reticular dermis leading to separation of collagen bundles in the subcutis (H&E, original magnification ×100).

Nonpalpable purpura has a broad differential diagnosis including primary and secondary thrombocytopenia; coagulopathies, including vitamin K deficiency, specific clotting factor deficiencies, and amyloid-related purpura; genetic or acquired collagen disorders, including vitamin C deficiency; and eruptions induced by drugs and herbal remedies.

Leukemia cutis is a relatively rare cause of purpura and is defined as cutaneous infiltration by neoplastic leucocytes.[1] It most commonly is associated with AML and complicates approximately 5% to 15% of all adult cases.[2] Cutaneous involvement occurs predominantly in monocytic variants; acute myelomonocytic leukemia and acute monocytic leukemia may arise in up to 50% of these cases.[3] The clinical presentation may vary from papules, nodules, and plaques to rarer manifestations including purpura. A leukemic infiltrate often is associated with sites of inflammation, such as infection or ulceration,[4] though there was no reported history of any known triggering events in our patient. Lesions usually involve the legs, followed by the arms, back, chest, scalp, and face.[4] One-third of cases coincide with systemic symptoms, and approximately 10% precede bone marrow or peripheral blood involvement, referred to as aleukemic leukemia. The remainder of cases arise following an established diagnosis of systemic leukemia.[5] Leukemia cutis is considered a marker of poor prognosis in AML,[4,6] requiring treatment for the underlying systemic disease. Our case

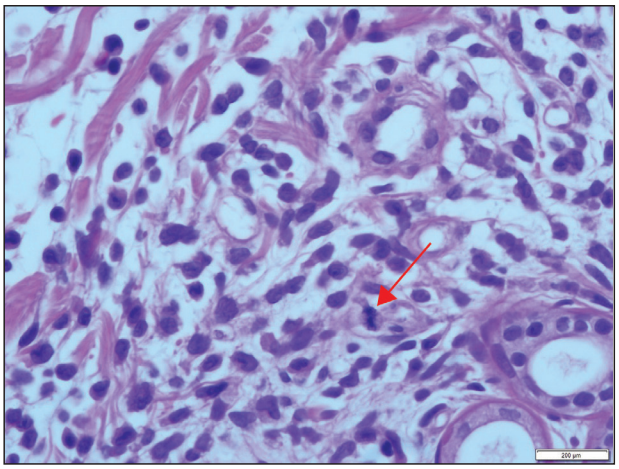

FIGURE 3. A mitotic figure in the right lower quadrant (arrow) and numerous notched nuclei (H&E, original magnification ×400).

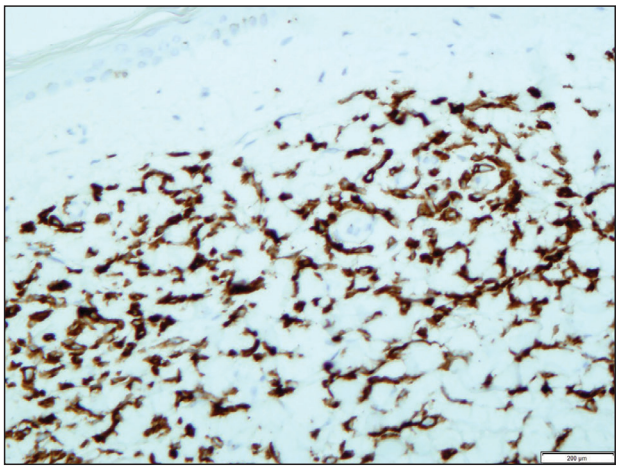

FIGURE 4. Leukemic cells stained positively for leukocyte common antigen on immunohistochemical staining (original magnification ×200).

also was complicated by a concurrent pancreatic malignancy and relatively advanced age, which limited the feasibility of further treatment.

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