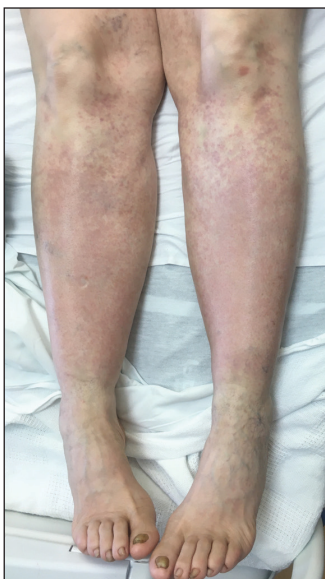


# Nonblanching Rash on the Legs and Chest

Karin Roszell, MD; Elisabeth A. Pedersen, MD, PhD; Rajiv M. Patel, MD; Trilokraj Tejasvi, MD



A 67-year-old woman with history of atrial fibrillation and leukemia presented with a nonpruritic nonpainful rash of 10 days' duration that began on the distal lower extremities (top) and then spread superiorly. She reported having a sore throat and mouth, cough, night sweats, unintentional weight loss, and lymphadenopathy. Physical examination revealed pink-purple nonblanching macules and patches on the lower extremities extending from the ankles to the knees. She also had firm pink papules on the chest (bottom) and back. Punch biopsies of the skin on the chest and leg were obtained for histologic examination and immunohistochemical staining.



## WHAT'S YOUR DIAGNOSIS?

- capillaritis (pigmented purpuric dermatosis)
- leukemia cutis
- leukocytoclastic vasculitis
- pretibial myxedema
- venous stasis dermatitis

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From the Department of Dermatology, University of Michigan, Ann Arbor. Dr. Roszell also is from the Medical School, and Dr. Patel also is from the Department of Pathology, Sections of Dermatopathology and Bone and Soft Tissue Pathology.

The authors report no conflict of interest.

Correspondence: Trilokraj Tejasvi, MD, 1910 Taubman Center, 1500 E Medical Center Dr, Ann Arbor, MI 48109 (ttejasvi@med.umich.edu).

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## THE DIAGNOSIS: Leukemia Cutis

Hematoxylin and eosin staining revealed an infiltration of monomorphic atypical myeloid cells with cleaved nuclei within the dermis, with a relatively uninvolved epidermis (Figure, A). The cells formed aggregates in single-file lines along dermal collagen bundles. Occasional Auer rods, which are crystal aggregates of the enzyme myeloperoxidase, a marker unique to cells of the myeloid lineage (Figure, B) were appreciated.

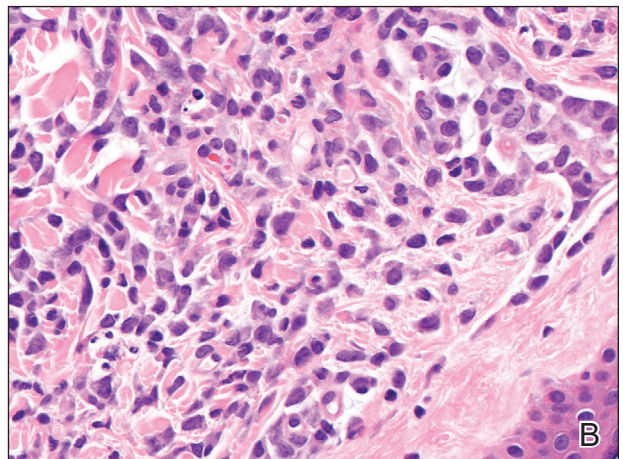
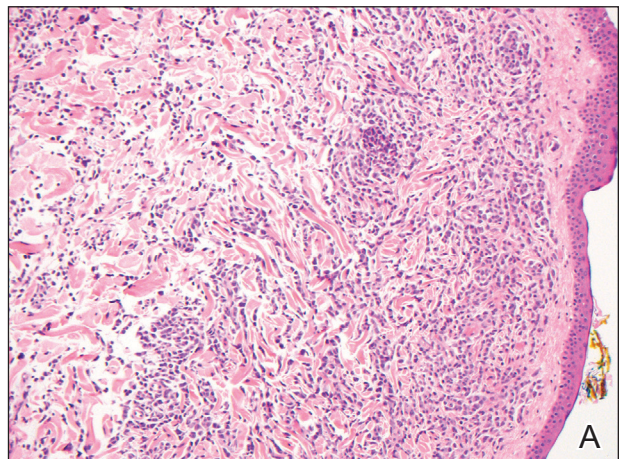
Immunohistochemical staining for myeloperoxidase was weakly positive; however, flow cytometric evaluation of the bone marrow aspirate revealed that approximately 20% of all CD45<sup>+</sup> cells were myeloid blasts. These findings confirmed the diagnosis of recurrent acute myeloid leukemia (AML). The diagnosis of AML can be confirmed with a bone marrow biopsy demonstrating more than 20% of the total cells in blast form as well as evidence that the cells are of myeloid origin, which can be inferred by the presence of Auer rods, positive myeloperoxidase staining, or immunophenotyping. In our patient, the Auer rods, myeloperoxidase staining, and atypical myeloid cells on skin biopsy, in conjunction with the bone marrow biopsy results, confirmed leukemia cutis.

Leukemia cutis is the infiltration of neoplastic proliferating leukocytes in the epidermis, dermis, or subcutis from a primary or more commonly metastatic malignancy. Leukemic cutaneous involvement is seen in up to 13% of leukemia patients and most commonly is seen in monocytic or myelomonocytic forms of AML.<sup>1</sup> It may present anywhere on the body but mostly is found on the back, trunk, and head. It also may have a predilection for areas with a history of trauma or inflammation. The lesions most often are firm, erythematous to violaceous papules and nodules, though leukemia cutis can present with hemorrhagic ulcers, purpura, or other cutaneous manifestations of concomitant thrombocytopenia such as petechiae and ecchymoses.<sup>2</sup> Involvement of the lower extremities mimicking venous stasis dermatitis has been described.<sup>3,4</sup>

Treatment of leukemia cutis requires targeting the underlying leukemia<sup>2</sup> under the guidance of hematology and oncology as well as the use of chemotherapeutic agents.<sup>5</sup> The presence of leukemia cutis is a poor prognostic sign, and a discussion regarding goals of care often is appropriate. Our patient initially responded to FLAG (fludarabine, cytarabine, filgrastim) chemotherapy induction and consolidation, which was followed by midostaurin maintenance. However, she ultimately regressed, requiring decitabine and gilteritinib treatment, and died 9 months later from the course of the disease.

Although typically asymptomatic and presenting on the lower limbs, capillaritis (also known as the pigmented

purpuric dermatoses) consists of a set of cutaneous conditions that often are chronic and relapsing in nature, as opposed to our patient's subacute presentation. These benign conditions have several distinct morphologies; some are characterized by pigmented macules or pinpoint red-brown petechiae that most often are found on the legs but also are seen on the trunk and upper extremities.<sup>6</sup> Of the various clinical presentations of capillaritis, our patient's skin findings may be most consistent with pigmented purpuric lichenoid dermatitis of Gougerot and Blum, in which purpuric red-brown papules coalesce into plaques, though her lesions were not raised. The other pigmented purpuric dermatoses can present with cayenne pepper-colored petechiae, golden-brown macules, pruritic purpuric patches, or red-brown annular patches,<sup>6</sup> which were not seen in our patient.



A and B, Histopathology demonstrated an infiltration of immature myeloid blasts in the dermis (H&E, original magnifications  $\times 10$  and  $\times 400$ ).

Venous stasis dermatitis also favors the lower extremities<sup>7</sup>; however, it classically includes the medial malleolus and often presents with scaling and hyperpigmentation from hemosiderin deposition.<sup>8</sup> It often is associated with pruritus, as opposed to the nonpruritic nonpainful lesions in leukemia cutis. Other signs of venous insufficiency also may be appreciated, including edema or varicose veins,<sup>7</sup> which were not evident in our patient.

Leukocytoclastic vasculitis, a small vessel vasculitis, also appears as palpable or macular purpura, which classically is asymptomatic and erupts on the shins approximately 1 week after an inciting exposure,<sup>9</sup> such as medications, pathogens, or autoimmune diseases. One of the least distinctive vasculitides is polyarteritis nodosa, a form of medium vessel vasculitis, which presents most often with palpable purpura or painful nodules on the lower extremities and may be accompanied by livedo reticularis or digital necrosis.<sup>9</sup> Acute leukemia may be accompanied by inflammatory paraneoplastic conditions including vasculitis, which is thought to be due to leukemic cells infiltrating and damaging blood vessels.<sup>10</sup>

Pretibial myxedema is closely associated with Graves disease and shares some features seen in the presentation of our patient's leukemia cutis. It is asymptomatic, classically affects the pretibial regions, and most commonly affects older adults and women.<sup>11,12</sup> Pretibial myxedema presents with thick indurated plaques rather than patches. Our patient did not demonstrate ophthalmopathy, which nearly always precedes pretibial myxedema.<sup>12</sup> The most common form of pretibial myxedema is nonpitting, though nodular, plaquelike, polypoid, and elephantiasic forms also exist.<sup>11</sup> Pretibial myxedema classically favors the shins; however, it also can affect the

ankles, dorsal aspects of the feet, and toes. The characteristic induration of the skin is believed to be the result of excess fibroblast production of glycosaminoglycans in the dermis and subcutis likely triggered by stimulation of fibroblast thyroid stimulating hormone receptors.<sup>11</sup>

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