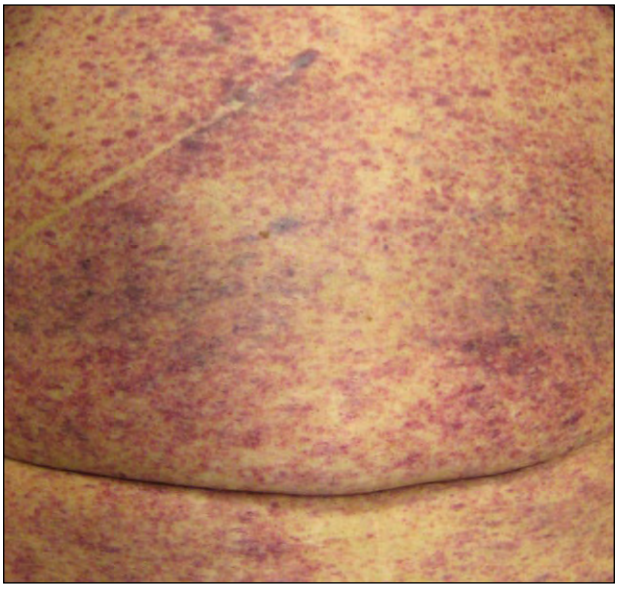
What Is Your Diagnosis?



A 71-year-old woman with acute lymphoblastic leukemia resistant to imatinib mesylate was seen for an inpatient consultation for diffuse petechiae and purpura of 6 weeks' duration. She also experienced B symptoms (eg, fever, night sweats, headaches, nausea) that started around the same time as the skin lesions. Physical examination revealed confluent petechiae and purpura concentrated over the abdomen with a few similar lesions scattered on the arms and legs. Her platelet count was $36\times10^3/\mu L$ (reference range, $150–350\times10^3/\mu L$) and her white blood cell count was 98,000/μL (reference range, 4500–11,000/μL).

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The authors report no conflict of interest.
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The Diagnosis: Leukemia Cutis

Skin lesions in leukemia patients have 2 main etiologies: nonspecific lesions caused by leukemids (eg, vasculitis, purpura, exfoliative erythroderma, erythema nodosum, Sweet syndrome) and actual infiltration of the skin with leukemic cells (leukemia cutis).[1] In our patient with confluent petechiae and purpura on the abdomen (Figure 1), a punch biopsy revealed a scant perivascular infiltrate of large polymorphous cells (Figure 2). Additional markers including immature B-cell antigens, CD34, LN-3, common acute lymphoblastic leukemia (ALL) antigen, and terminal deoxynucleotidyl transferase were strongly positive (Figure 3); CD20 and CD79a were weakly positive, which is consistent with leukemia cutis. This pattern was identical to a prior bone marrow aspirate.

Leukemia cutis usually is associated with acute myelocytic leukemia (AML) and rarely is seen in ALL. When present in ALL, it usually indicates resistant disease.[2] Leukemia cutis typically manifests as papules, nodules, or indurated violaceous plaques. Petechiae, as seen in our patient, are an unusual finding and could have easily been attributed to thrombocytopenia. A high index of suspicion for this entity is imperative in patients with leukemia. Histologic findings in leukemia cutis classically include a perivascular and/or periadnexal pattern of involvement with a dense interstitial or nodular infiltrate involving the dermis and subcutis that spares the upper papillary dermis, known as the grenz zone.[3] Biopsy shows different cell morphologies depending on the type of leukemia. For example, an AML infiltrate will consist of monocytes, while an ALL infiltrate will demonstrate lymphoblasts. Because there may be exceptions in certain skin specimens, immunohistochemical staining is the most reliable method for diagnosis. Although standard hematoxylin and eosin staining alone may be useful for diagnosis, it usually is insufficient for leukemia typing.[4]

Acute lymphoblastic leukemia is a rare cause of leukemia cutis, representing only 1% of cases.[4] Cutaneous infiltration by leukemic blasts is most commonly seen in AML patients, especially in myelomonocytic (M4) and monocytic (M5) subtypes with an incidence of 11%.[5] Leukemia cutis is associated with a poor prognosis, as up to 90% of cases exhibit other extramedullary involvement.[6] The central nervous system provides secure sanctuaries for leukemic cells, and some studies have shown meningeal involvement as high as 40% in patients with leukemia cutis.[6,7] In fact, our patient underwent a lumbar puncture 3 weeks after the diagnosis because of headaches and fever, which demonstrated leukemic cerebrospinal fluid involvement. The patient received intrathecal and intravenous chemotherapy and achieved remission. Six months later her leukemia recurred and she

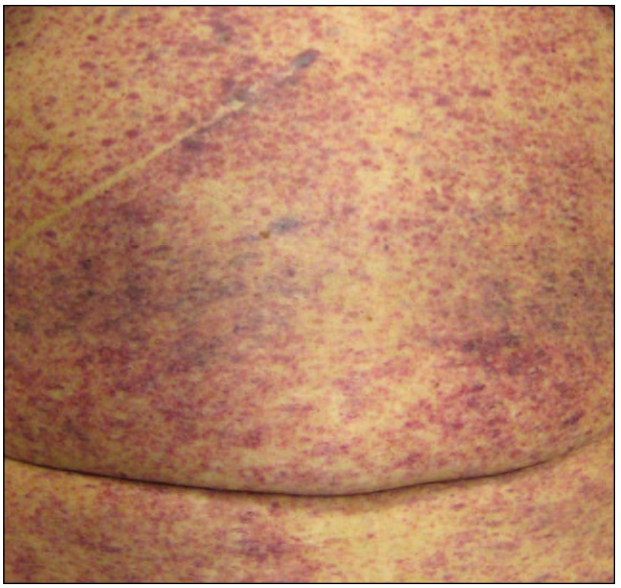

Figure 1. Petechiae and purpura on the abdomen.

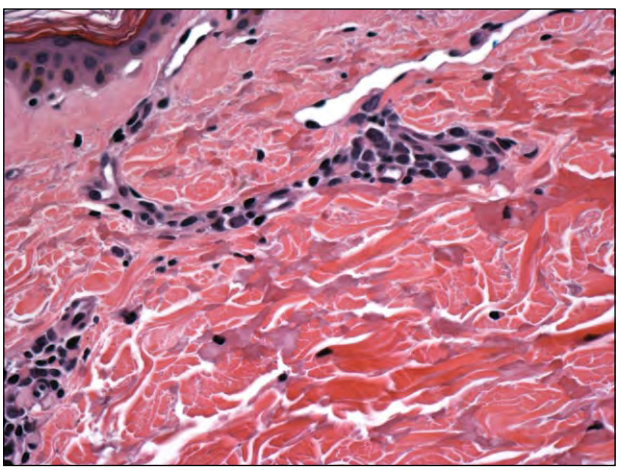

Figure 2. Biopsy of an abdominal purpuric lesion showing a scant perivascular infiltrate comprised of large polymorphous cells (H&E, original magnification ×100).

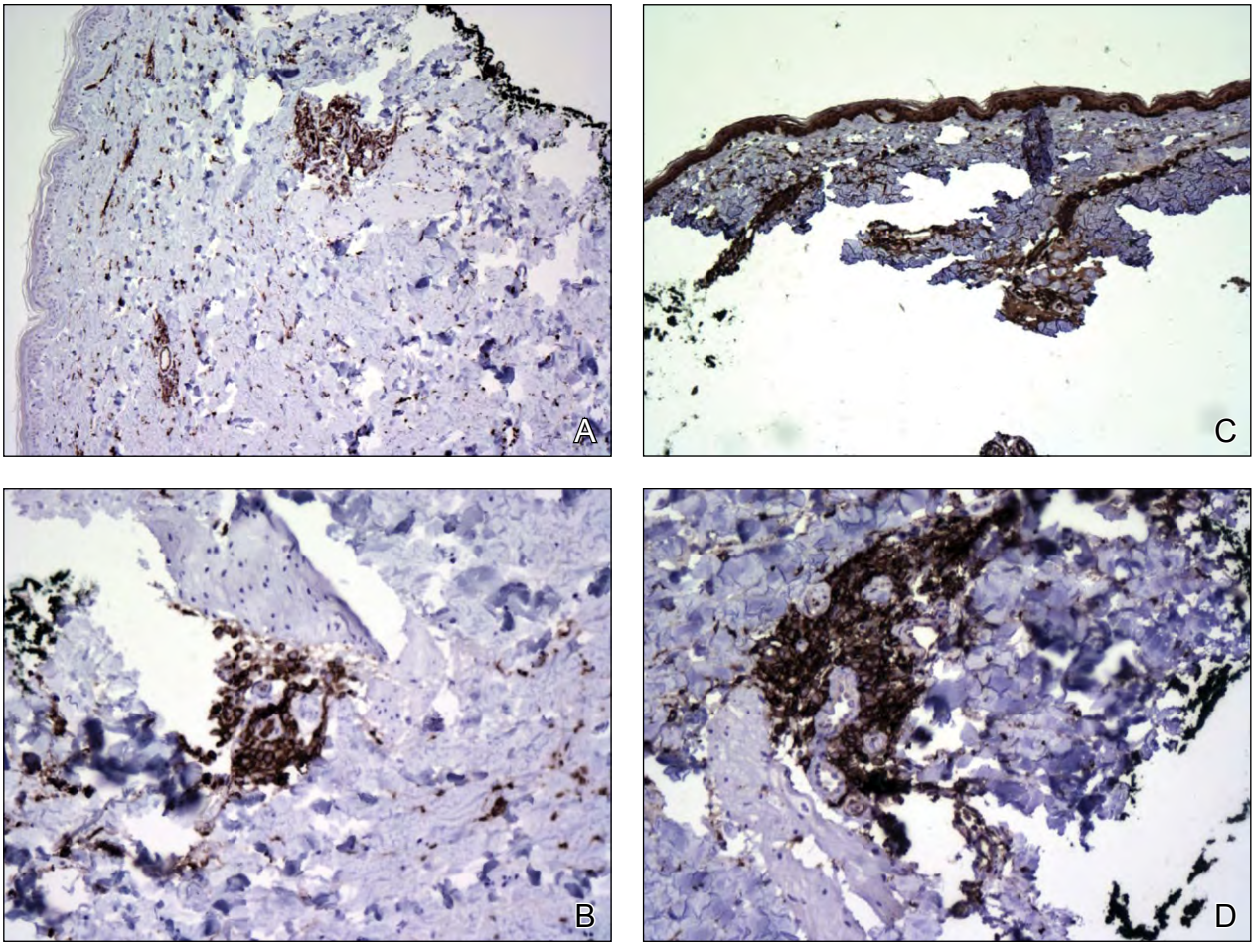

Figure 3. Positive immunostaining of tumor cells for CD34 (A), LN-3 (B), common acute lymphoblastic leukemia antigen (C), and terminal deoxynucleotidyl transferase (D)(original magnifications ×40, ×100, ×4, and ×100, respectively).

died soon after. Our case emphasizes the importance of diagnosing leukemia cutis and searching for extramedullary involvement.

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