Purpuric Eruption in a Patient With Hairy Cell Leukemia

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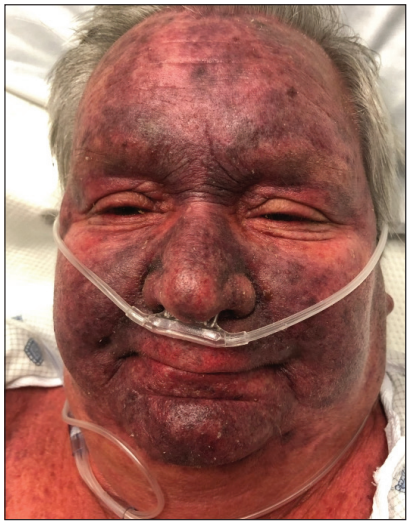

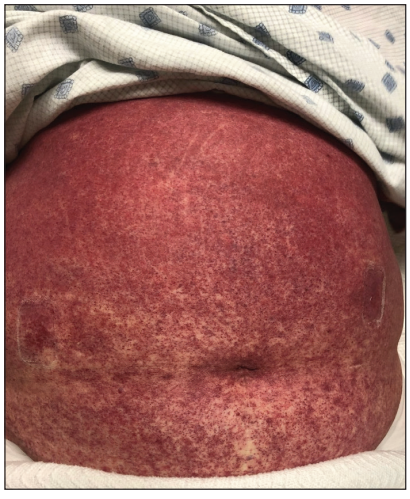

A 68-year-old woman presented to the emergency department with neutropenic fever and a rash over the body after receiving 2 doses of cladribine therapy for hairy cell leukemia. Physical examination demonstrated marked facial (top), lip, and tongue swelling, as well as a diffuse dusky nonpalpable purpuric rash on the abdomen (bottom) and back involving 90% of the body surface area. Bilateral ear edema was appreciated with accentuation of the earlobe crease. The patient exhibited subconjunctival hemorrhage, ectropion, and scleral injection. A punch biopsy of the thigh was performed.

WHAT'S THE **DIAGNOSIS?**

a. disseminated intravascular coagulation
b. purpuric drug eruption
c. thrombotic thrombocytopenic purpura
d. toxic epidermal necrolysis
e. toxic erythema of chemotherapy

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Dr. Gray has received research grants from the National Psoriasis Foundation. Drs. Flood and Korman report no conflict of interest.
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Cutis. 2024 May;113(5):E22-E24. doi:10.12788/cutis.1020

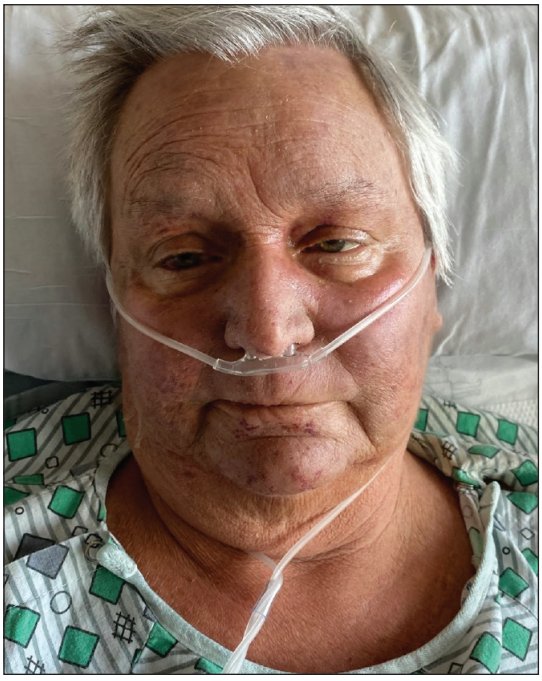
THE **DIAGNOSIS:** Purpuric Drug Eruption

Histopathology revealed interface dermatitis, spongiosis, and a perivascular lymphocytic infiltrate with extravasated red blood cells consistent with a purpuric drug eruption. Our patient achieved remission of hairy cell leukemia after receiving only 2 of 5 expected doses of cladribine. The rash resolved completely in 3 weeks following a prednisone taper (Figure).

Hairy cell leukemia is a rare indolent lymphoproliferative disorder of B cells that accounts for approximately 2% of adult leukemias in the United States. Cladribine, a purine nucleoside analog that impairs DNA synthesis and repair, has become the mainstay of therapy, demonstrating a 95% complete response rate.[1] Although few reports have addressed the cutaneous reactions seen with cladribine therapy, they can occur in more than 50% of patients.[1,2] The most common skin manifestation associated with cladribine therapy is a morbilliform rash, but Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) have been reported.[1]

Few cases of purpuric eruption secondary to cladribine treatment have been described, and nearly all reports involve concomitant medications such as allopurinol, which our patient was taking, and antibiotics including trimethoprim-sulfamethoxazole and penicillins.[1,3,4] In a cohort of 35 patients receiving cladribine,[1] only concomitant treatment with cladribine and allopurinol caused cutaneous reactions, further supporting the hypothesis of cladribine-induced drug sensitivity. Allopurinol often is prescribed during induction therapy for prophylaxis against tumor lysis syndrome; similarly, antibiotics frequently are given prophylactically and therapeutically for neutropenic fever. It is believed that T-cell imbalance and profound lymphopenia induced by cladribine increase susceptibility to drug hypersensitivity reactions.[1,3]

The typical purpuric eruption develops within 2 days of starting cladribine therapy. Diascopy will reveal petechiae, and biopsy should be performed to rule out other serious drug-induced reactions, such as erythema multiforme, Stevens-Johnson syndrome, and TEN. A cladribine-induced purpuric eruption typically is self-resolving and carries a favorable prognosis, though high-dose corticosteroids often are prescribed to hasten recovery. The rare reports of serious cutaneous reactions secondary to cladribine therapy have been with maculopapular, not purpuric eruptions.[2] Based on limited available data, cladribine-induced purpura should not be a limitation to continued treatment in patients who need it.[1] Careful consideration of concomitant drug use is necessary, as the current literature demonstrates resolution of rash with withdrawal of other therapies, namely allopurinol.[2-4] Future studies are needed to examine the safety of withholding offending medications and to further elucidate the mechanisms contributing to drug hypersensitivity due to cladribine.



The purpuric drug eruption resolved completely in 3 weeks following a prednisone taper.

Widespread purpura and petechiae can pose a wide differential; the patient's recent history of cladribine administration pointed to a classic purpuric eruption. Other diagnoses such as toxic erythema of chemotherapy (TEC) and TEN are not purpuric, though plaques can be violaceous. Lack of bullae, blisters, and facial or mucosal surface involvement suggest TEN.[5] Thrombotic thrombocytopenic purpura and disseminated intravascular coagulation do manifest with petechiae and purpura, though such a robust eruption in the context of recent cladribine therapy is less likely. The classic retiform purpura and necrosis were not present to suggest purpura fulminans from disseminated intravascular coagulation.

Several of the proposed diagnoses as well as a purpuric drug eruption would demonstrate extravasated red blood cells on histopathology, but the presence of interface dermatitis narrows the differential to a purpuric drug eruption. Necrotic keratinocytes and full-thickness necrosis were not present on biopsy to support a diagnosis of TEN in our patient. Characteristic features of TEC—including eccrine squamous syringometaplasia, dermal edema, and keratinocyte atypia—were not present on biopsy.[6] Finally, although TEN should resolve with steroid treatment, TEC is self-limited and thrombotic thrombocytopenic purpura

and disseminated intravascular coagulation would not resolve with use of steroids alone.

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