CHRISTOS TZIOTZIOS, BA, MA, MB, BChir (Cantab)
Addenbrooke's Hospital, Cambridge University Hospitals NHS (National Health Service) Foundation Trust, Hills Road, Cambridge CB2 0QQ, UK

ARETI MAKRYGEORGOU, MD
The Alan Lyell Centre for Dermatology, Western Infirmary, Glasgow G11 6NT, UK

The Clinical Picture
Leukemia cutis

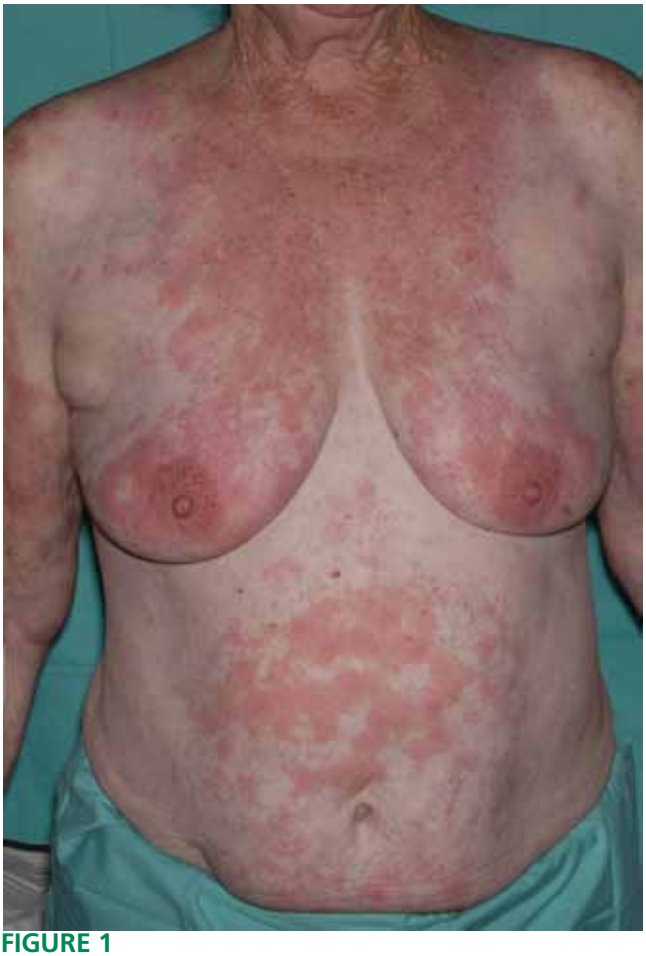

FIGURE 1

A 72-year-old woman presents with a 3-week history of diarrhea, pyrexia, and a florid but asymptomatic skin eruption consisting of infiltrated erythematous papules and nodules that coalesce into large plaques (**FIGURES 1 AND 2**). These initially afflicted her thorax before spreading to her back, arms, and legs. Pancytopenia is noted on her admission hemogram.

doi:10.3949/ccjm.78a.10127

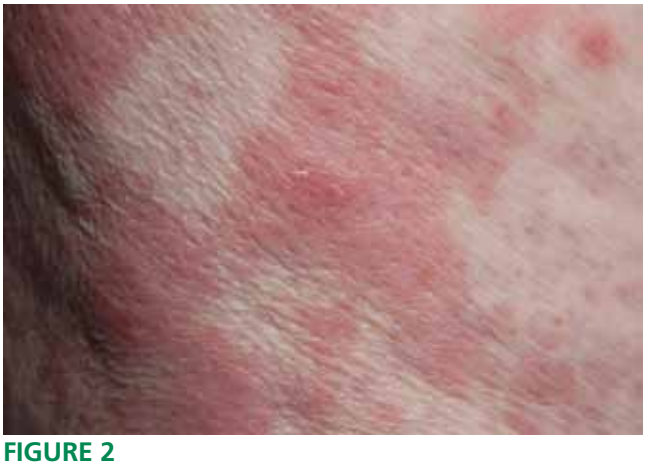

FIGURE 2

She is a smoker but has been in good health and is on no regular medications.

Q: What is the most likely diagnosis?

- ☐ Leukemia cutis
- ☐ Drug reaction
- ☐ Sweet syndrome
- ☐ Erythema multiforme
- ☐ Urticaria

A: The correct answer is leukemia cutis, defined as a cutaneous infiltration by neoplastic leukocytes.[1] When the leukocytes are primarily granulocytic precursors, the terms myeloid sarcoma, granulocytic sarcoma, chloroma, and primary extramedullary leukemia have been used.[2] The term monoblastic sarcoma has been used when the cutaneous infiltrate is composed of neoplastic monocytic precursors.[2]

Leukemia cutis most commonly manifests as erythematous papules and nodules, single or multiple, of varying sizes, and afflicting one or more body sites; it typically is asymptomatic.[3] It occurs in 10% to 15% of patients with acute myeloid leukemia[4] and is itself a poor prognostic sign.[5] The cutaneous changes may pre-

date the hematologic manifestations and may even herald a relapse.[6]

In patients presenting with extramedullary leukemia and no bone marrow or blood involvement, the importance of preemptive chemotherapy for acute myelogenous leukemia has recently been emphasized.[7]

CASE CONTINUED

The patient undergoes further testing with bone marrow aspiration and trephination, which are diagnostic of acute myeloid leukemia with myelodysplastic changes: the studies reveal a clear excess of myeloblasts (accounting for 40% to 50% of nucleated cells) and clearly dysplastic erythropoiesis and myelopoiesis. Bone marrow cytogenetic analysis reveals a complex abnormal female karyotype with multiple numerical and structural abnormalities, in particular deletion of the long arm of chromosome 5, suggestive of a poor prognosis.

Skin biopsy reveals a normal epidermis but dermal perivascular involvement with a reactive T-lymphocyte infiltrate associated with immature myeloid elements, characterized by positive staining to myeloperoxidase, in keeping with leukemia cutis. It should be noted that histopathologic confirmation of leukemia cutis can be challenging, as the condition can adopt a variety of patterns, and clinicopathologic correlation is often warranted.

The patient is treated with a cycle of cytarabine-based chemotherapy, and her skin eruption transiently improves. However, her clinical condition subsequently deteriorates; she has a relapse of leukemia, with the rash returning more florid and angry-looking than previously. She is subsequently managed palliatively and passes away 3 weeks later.

THE OTHER DIAGNOSTIC CHOICES

Sweet syndrome or acute febrile neutrophilic dermatosis is often seen in association with hematologic malignancies, but the lesions are typically tender, and histopathology reveals an intense dermal neutrophilic infiltrate.[6]

Erythema multiforme is associated with malignancy, but its characteristic concentric "target" lesions are typically acral and symmetrical in their distribution; their histopathology is inflammatory.[8]

The patient had not been on any regular medications and her rash could not have been medication-induced.

Urticaria presents with pruritic evanescent wheals, which rarely last more than 12 hours.[9] Our patient had a fixed and entirely asymptomatic rash, which in addition did not have the histopathologic features of urticaria—namely, dermal edema involved with an infiltrate made of lymphocytes and eosinophils.[9]

Bone marrow studies confirm acute myeloid leukemia with myelodysplasia

REFERENCES

1. **Strutton G**. Cutaneous infiltrates: lymphomatous and leukemic. In: Weedon D, editor. Skin Pathology, 2nd ed. New York, NY: Churchill Livingstone, 2002:1118-1120.
2. **Brunning RD, Matutes E, Flandria F, et al**. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press, 2001:104-105.
3. **Watson KM, Mufti G, Salisbury JR, du Vivier AW, Creamer D**. Spectrum of clinical presentation, treatment and prognosis in a series of eight patients with leukaemia cutis. Clin Exp Dermatol 2006; 31:218–221.
4. **Agis H, Weltermann A, Fonatsch C, et al**. A comparative study on demographic, hematological, and cytogenetic findings and prognosis in acute myeloid leukemia with and without leukemia cutis. Ann Hematol 2002; 81:90–95.
5. **Kaddu S, Zenahlik P, Beham-Schmid C, Kerl H, Cerroni L**. Specific cutaneous infiltrates in patients with myelogenous leukemia: a clinicopathologic study of 26 patients with assessment of diagnostic criteria. J Am Acad Dermatol 1999; 40:966–978.
6. **Cutaneous aspects of leukemia**. In: Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC, editors. Dermatology, 2nd ed. Berlin: Springer, 2000:1640–1648.
7. **Tsimberidou AM, Kantarjian HM, Wen S, et al**. Myeloid sarcoma is associated with superior event-free survival and overall survival compared with acute myeloid leukemia. Cancer 2008; 113:1370–1378.
8. **Erythemato-papulo-squamous diseases**. In: Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC. Dermatology, 2nd ed. Berlin: Springer, 2000.
9. **Urticaria, angioedema and anaphylaxis**. In: Braun-Falco O, Plewig G, Wolff HH, Burgdorf WHC. Dermatology, 2nd ed. Berlin: Springer, 2000.

ADDRESS: *Christos Tziotzios, BA, MA, MB, BChir (Cantab), Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge CB2 0QQ, UK; e-mail ct287@cantab.net.*