Tender Nodules on the Extremities: Answer

A Zarbo
Kedar Inamdar
Ben J. Friedman

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Allison Zarbo, MD, Kedar Inamdar, MD, PhD, and Ben J. Friedman, MD

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ANSWER

Chronic myelogenous leukemia cutis.

DISCUSSION

Histopathologic review of the punch biopsy specimen revealed a deep polymorphous infiltrate filling the subcutaneous septae and intercalating between adipocytes. The infiltrate consisted of extravasated erythrocytes, neutrophils, eosinophils, mononuclear, and occasional multinucleated cells. Many of the granulocytes had an immature appearance with hyposegmented nuclei and a high nuclear-to-cytoplasmic ratio. A concurrent bone marrow biopsy and peripheral blood evaluation revealed findings diagnostic of chronic myeloid leukemia (CML) with 5%–8% blasts. Differential diagnosis for the skin histopathology included extramedullary hematopoiesis versus cutaneous involvement of CML (leukemia cutis). To differentiate among these possibilities, fluorescence in situ hybridization (FISH) was performed on the skin biopsy specimen for t(9;22) BCR-ABL1. This gene fusion was identified in 75% of the nuclei, confirming the diagnosis of chronic myelogenous leukemia cutis (Fig. 1).

CML presenting with cutaneous infiltrates is an exceptionally rare phenomenon occurring in only up to 2% of patients1,2 and is more typically reported in the setting of blast crisis. In this case, the infiltrate was rather polymorphous, and blasts were not increased, thus not meeting diagnostic criteria for acute myeloid leukemia (ie, myeloid sarcoma). In view of the concurrent diagnosis of CML in the bone marrow and peripheral blood and the FISH study on the skin being positive for t(9;22), the cutaneous infiltrate was best classified as an extramedullary manifestation of CML. Establishing the diagnosis relied on detection of the BCR-ABL1 fusion on the skin biopsy through FISH, which to the best of our knowledge, has not been reported previously in this context. The patient was promptly started on hydroxyurea 40 mg/kg/d and transitioned to imatinib, an inhibitor of the BCR-ABL tyrosine kinase. Owing to a subpar response to therapy with imatinib, a switch was then made to the newer tyrosine kinase inhibitor dasatinib.

Leukemia cutis in general may precede frank development of leukemia by months to years.1 It is most often seen with acute myeloid leukemia, specifically in acute myelomonocytic leukemia and acute monocytic leukemia.1–3 Morphology is variable and can range from gingival hypertrophy to cutaneous papules, plaques or nodules involving the head, neck, trunk, and extremities to a generalized morbilliform eruption.1 In this case, the skin lesions presented as subcutaneous nodules closely resembled erythema nodosum. The mechanism of leukemia cutis is largely unknown, although chemokine receptors such as CCR4 and adhesion molecules such as cutaneous lymphocyte associated antigen may play a role in skin tropism of leukemic cells.4 Traditionally, leukemia cutis is associated with a poor prognosis and is believed to reflect more advanced systemic involvement of the disease.5 Treatment of the leukemia cutis involves treating the underlying leukemia, and it should be noted that the time to onset of resolution of the leukemia cutis is not predictive of the overall prognosis.3

REFERENCES