Clinical Note

Leukemia cutis in a middle aged Saudi patient with acute Myeloid Leukemia

Leukemia may be associated with a wide variety of cutaneous manifestations, and such lesions are classified as either specific or nonspecific. Specific lesions (leukemia cutis) are defined as localized or disseminated skin infiltration by leukemic cells.[1] Nonspecific skin infiltrates, also known as leukemids, are much more common than leukemia cutis and represent a spectrum of cutaneous diseases that may be seen in leukemia and can be related to bone marrow dysfunction, cytotoxic effects of chemotherapy, opportunistic infections, immunologic responses to tumor antigens, reactive, and due to paraneoplastic lesions.[2,3] The incidence of leukemia cutis varies from 1%-50%, depending on the type of leukemia.[2] Specific skin lesions are more common in acute myeloid leukemia (AML), with the highest incidence seen in the monocytic leukemias,[3] the incidence has been reported to be 10%-50%.[3] Leukemia cutis has also been reported in 8%-100% of patients with chronic lymphocytic leukemia (CLL)[3] especially adult T-cell leukemia/lymphoma (ATLL)[3] and in only 3% of those with acute lymphoblastic leukemia (ALL).[3] It may be regarded as dissemination of aggressive systemic leukemia to the skin and its presence is usually associated with a poor prognosis.[3] This report is an example of an uncommon presentation of leukemia that may be difficult to differentiate from other skin lesions. An apparently healthy 52-year-old Saudi male presented with a 10-day history of a diffuse asymptomatic cutaneous eruption that began on his axillae and groin and progressed to involve his trunk. Review of systems was normal, and he is a known case of non-insulin dependent diabetes mellitus (NIDDM) for the last 2 years. Physical examination revealed diffusely scattered erythematous and violaceous smooth surfaced papules and nodules. There was no lymphadenopathy or organomegaly. However, there was a small right testicular swelling not noticed by the patient. A biopsy specimen was obtained from a lesion on the trunk (Figure 1). Histological examination revealed sheets of diffuse atypical mononuclear cellular infiltrate involving the whole reticular dermis and extending deep to the subcutis. A thin zone of sparing separates the infiltrate from the epidermis. The cells are large in size with abundant cytoplasm and exhibiting pleomorphism, and mitotic figures (Figure 2). Leucocyte common antigen stain (CD45) was positive, features consistent with leukemia cutis. A complete blood count (CBC), was carried out, and showed a white blood cell count (WBC) of 32 x 10^9/L, platelet count 17 x 10^9/L and a hemoglobin level of 10.3 gm dl. White blood count differential revealed: neutrophils 14%, lymphocytes 20%, eosinophils 4%, metamyelocytes 1%, promyelocytes 1% and leukemia blasts 60%. The morphology of the blasts was suggestive of AML, French, American and British (FAB) subtype M4. A bone marrow aspiration and biopsy was performed, the former showed hypercellular bone marrow spicules, with markedly decreased granulopoiesis, erythropoiesis and thrombopoiesis and a remarkable infiltration by leukemia blasts that constituted 90% of the bone marrow cells. The blasts were pleomorphic, with abundant cytoplasm and some showing cytoplasmic vacuoles and granules. Cytochemistry showed Sudan black positive, and double esterase showed myeloid reaction positive such as chloroacetate (specific) esterase and weak monocytic reaction while Periodic Acid Schiff (PAS) was negative. Combining the morphological appearances in the blood, bone marrow and cytochemistry, the

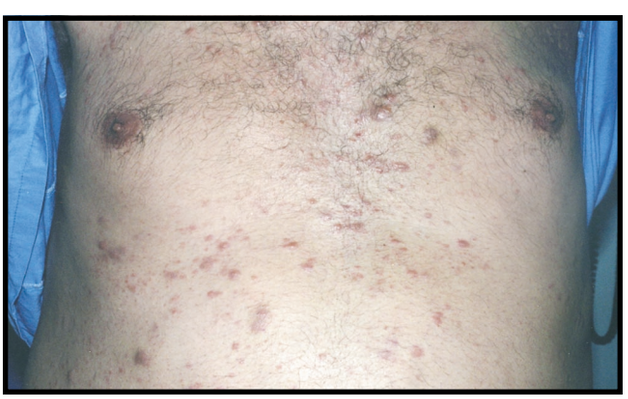

Figure 1 - Gross picture showing the scattered erythematous and violaceous lesions on the trunk.

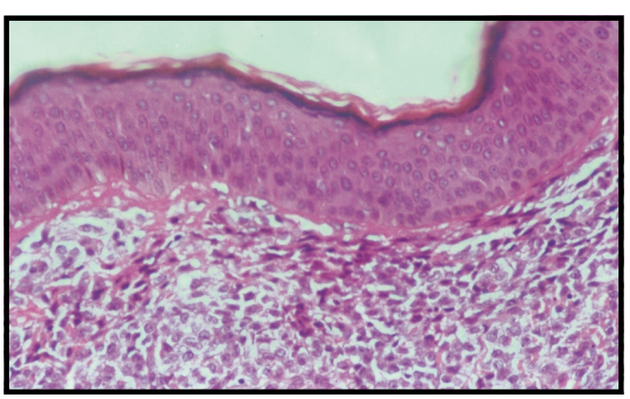

Figure 2 - Histological picture of lesions showing sheets of diffuse atypical mononuclear cells.

diagnosis was that of AML, M4, to be confirmed by immunophenotyping. Immunophenotyping results supported the morphological and cytochemical features for the diagnosis of AML, FAB subtype M4. The results showed positivity of: CD45, CD14, CD13, CD33 and, CD34. Other investigations included; Erythrocyte sedimentation rate (ESR)=0 mm/hr (normal range 0-20 mm/hr). Coagulation studies included partial thromboplastin time 35.8 seconds, (normal control 24.8 seconds). Prothrombin time 16 seconds, (control 11.4 seconds). Fibrinogen degradation products (FDP) >160-<320 mg/ml normal value less than 10) and fibrinogen level 140mg/dl, (normal range 200-400). Liver function tests were normal except lactate dehydrogenase (LDH) 708 mg/dl (normal range 100–190). Uric acid 11.6 mg/dl (normal range 3.8–7.5). Electrolytes within normal, but fasting glucose 133 mg/dl (Normal range 70–110). Renal function tests slightly deranged, with a serum creatinine level of 1.3 mg/dl (normal range 0.6–1.2). Tumor markers alpha-fetoprotein and carcino-embryonic antigen within normal limits. Computerized tomography (CT) scan of the chest, abdomen, and pelvis were normal. Leukemia cutis occurs in the setting of AML, ALL, CLL, and chronic myelogenous leukaemia (CML).[3] Leukemia cutis and what is known as granulocytic sarcomas are often difficult to differentiate from cutaneous lymphomas.[3] Leukemia cutis presents with multiple skin lesions with a varied clinical appearance including papules, nodules, plaques, palpable purpura, macules, ecchymoses, bullous lesions, gingival hypertrophy, urticaria like, and ulcerated lesions.[3,4] The skin lesions that may precede the diagnosis of AML, are occasionally the first symptoms, and in a recent series it developed in one of 40 patients without any known prior or subsequent hematologic disorder.[4] It has also been reported that leukaemia cutis may be an early manifestation of leukaemic transformation in some patients with CML or myelodysplastic syndrome (MDS).[4] Leukemic changes in the bone marrow or peripheral blood usually precede skin involvement, but in rare instances leukemia cutis is the first sign of leukemia preceding the diagnosis of systemic leukemia by several months or even years.[3,5] This condition is known as aleukemic leukemia cutis, and has a poor prognosis.[3,5] Skin biopsies, from leukemia cutis of AML regardless of the lineage, are characterized histologically by either interstitial infiltrate (reticular) as in our patient, or a nodular infiltrate of leukemic cells that spare the epidermis, but often involve the subcutis.[3] It has also been reported that the distribution of the lesions may help with the diagnosis,[6] such as lesions that appear on the face and extremities are more often associated with acute leukemia and CLL, while those that occur over the trunk are more often associated with CML, and entire body involvement suggests monocytic leukemia.[6] This patient presented with multiple erythematous skin (flesh) colored papules and nodules which are the familiar cutaneous manifestations.[3] The absence of significant constitutional symptoms in this patient, may be attributed to the relatively short period (10 days) between the eruption and seeking medical advice. In this case also, despite the good state of health, and the absence of appreciable symptoms, the bone marrow, and peripheral blood were abnormal when examined, which raised the possibility of this being an acute transformation of chronic granulocytic leukemia, however, the patient denied any previous illness, and there was no organomegaly. The patient was managed conservatively until his transfer to an Oncology Center upon his request.

The case presented here should remind physicians that unusual cutaneous manifestations or skin eruptions may be a sign of leukemias, lymphomas or tumors. In rare cases like aleukemic leukemia cutis, blood and bone marrow may fail to reveal leukemia, and treatment may be based on results of skin biopsy and immunohistochemistry.[5] The patient returned after 2 months, in complete remission but presented to the emergency room due to chemotherapy induced complications. There was no further follow-up.

In conclusion, leukemia cutis is an uncommon manifestation of leukemia, patients usually present concomitantly with systemic leukemia or after diagnosis and rarely, before the onset of systemic leukemia. The skin lesions have different presentations and can be difficult to distinguish from cutaneous lymphomas and other nonspecific cutaneous lesions. Histopathological means and immunohistochemistry maybe needed for diagnosis. Awareness of this uncommon clinical condition may help in early diagnosis and management.

Omar M. Al-Akloby
Ali M. Al-Ameer
Department of Dermatology
Layla A. Bashawri
Department of Pathology
College of Medicine
King Faisal University
Damman
Kingdom of Saudi Arabia

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