CLINICAL VIGNETTE

Leukemia Cutis as the Presenting Symptom of B-cell Acute Lymphoblastic Leukemia

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Introduction

Leukemia cutis (LC) is cutaneous infiltration of neoplastic leukemic cells and an extramedullary manifestation of leukemia. LC has a range of morphologic manifestations, from nodular to vesicular or plaque-like lesions. Cutaneous lesions are more commonly associated with acute myeloid leukemia (AML) and are rarely seen in acute lymphoblastic leukemia (ALL). We present a 25-year-old-male who presented with diffuse nodular lesions, with skin biopsy revealing B-cell acute lymphoblastic leukemia (B-ALL). LC was the presenting symptom of B-ALL.

Case Report

A 25-year-old-male with Autism Spectrum Disorder presented to the Emergency Department with diffuse nodular skins lesions and progressive weakness and fatigue. The patient reported onset of symptoms about six months prior, with a single hyperpigmented spot on his right cheek. This progressed to painful raised dark nodules. The nodules then spread to involve his upper chest, back, and right groin. He had initially presented to his primary care physician (PCP) and was diagnosed with cellulitis and abscess of the trunk. He completed a course of trimethoprim-sulfamethoxazole as well as an antifungal cream without improvement. He subsequently developed worsening weakness, fatigue, anorexia, as well as fevers, drenching night sweats, and headaches and severe right knee pain. He was seen in follow up and complete blood count (CBC) revealed a WBC 1.48K (with absolute neutrophil count of 40), Hgb 5.0, Plt 112K, prompting referral to the Emergency Department. Presenting vital signs in the ED included: Temp 38.7C, HR 139, RR 20, BP 115/66, SpO2 100% on room air. He was started on broad spectrum antibiotics for neutropenic fevers. CT scan of the chest, abdomen, and pelvis revealed mild splenomegaly, but otherwise no mass, lymphadenopathy, or focal inflammatory process was identified. Lactate was 8.9. Biopsy of the anterior chest lesion showed B-lymphoblastic leukemia. Physical exam revealed multiple hyperpigmented plaques and nodular/raised lesions throughout the upper anterior chest, back, right groin, and left thigh. Due to headaches, MRI of the brain, showed no acute intracranial enhancement, however, did reveal abnormal T1 signal throughout the osseous structure. CT-guided bone marrow biopsy of the left iliac bone revealed markedly hypercellular bone marrow with diffuse infiltration by B lymphoblasts, consistent with acute B-lymphoblastic leukemia. B-lymphoblasts were positive for CD19, cCD79a, nTdT, cCD22, CD34, HLA-DR and CD38. Lumbar puncture revealed negative CSF studies. The patient was started on systemic chemotherapy, with Daunorubicin, Vincristine, Prednisone, Asparaginase Erwinia, and Rituximab. His cutaneous lesions improved with chemotherapy, and subsequent bone marrow biopsy revealed complete remission of disease.

Discussion

Leukemia is a neoplasm that affects the hematopoietic system. The illness begins with the generalization phase in the bone marrow, followed by the appearance of leukemic cells of myeloid or lymphoid origin in the peripheral blood, followed by extramedullary manifestations.[1] In B-ALL, the central nervous system is the most common extramedullary site.[2-4] Other extramedullary sites include renal, orbital, hepatic, and testicular infiltration.[2,5] Skin involvement is rare in ALL.[2] Leukemia Cutis is extramedullary manifestation of leukemia defined as cutaneous infiltration of leukemic cells. This results in identifiable skin lesions. LC has a wide range of clinical manifestations, which makes it difficult to distinguish from other skin conditions. Lesions may appear as papules, macules, nodules, ulcers, blisters, plaques, or palpable purpura.[2] On initial exam, the skin lesions may be confused with infectious, allergic or vasculitic pathology.[2] In patients with known leukemia, dermatologic symptoms may be divided into “unspecific” and “specific” lesions.[1] Unspecific lesions are conditions that result from the consequences of abnormal hematopoiesis. Examples are fungal or viral skin lesions due to inadequate granulocyte production or thrombocytopenic purpura due to thrombocytopenia.[1] Unspecific lesions also include cutaneous paraneoplastic disease such as Sweet syndrome, erythema nodosum, and pyoderma gangrenosum.[1,3] LC is a specific skin lesion, which contains actual leukemic infiltrates. LC in B-ALL is typically characterized by firm, erythematous nodules.[3] In B-ALL, diagnosis is made via skin biopsy, which reveals histopathologic findings showing atypical hematopoietic infiltrates of moderate to large lymphoid cells with prominent nucleoli and a thin basophilic cytoplasm.[1,2,6] Immunohistochemistry in B-ALL is positive for CD79a and TdT.[1]

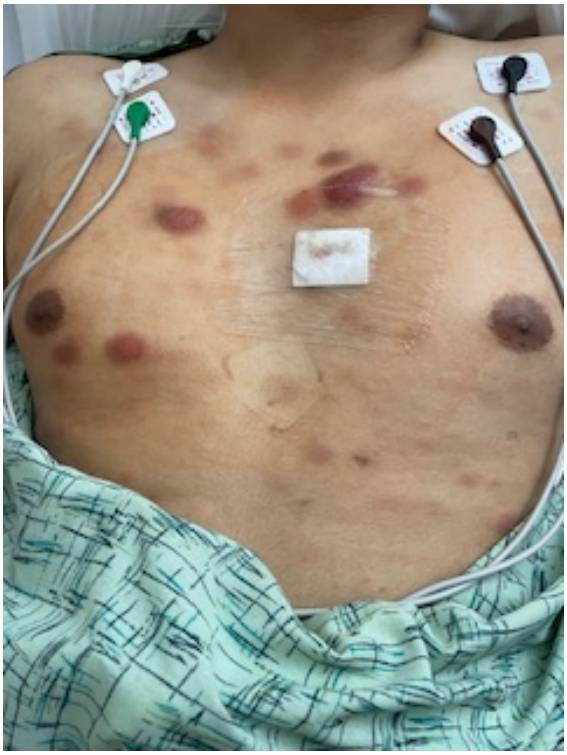
LC is a rare skin disease that is seen in varying frequencies in different forms of leukemia. Though still rare, LC is more commonly seen in AML and CLL. It was reported in 4-27% in patients with CLL[1] and 10-15% in patients with AML.[1,3,7] However, LC is very rarely seen in patients with B- or T- cell lymphoblastic leukemias (less than 1%).[7,8] One study reported

only 10 cases of LC associated with pre-B-ALL.[3] LC is usually diagnosed concurrent to or shortly after the diagnosis of systemic leukemia. Very rarely, it is seen prior to bone marrow or peripheral blood involvement and is termed "aleukemic leukemia cutis".[1,2,6]

LC is the cutaneous manifestation of a systemic disease, so treatment is aimed at treating the underlying leukemia. Skin lesions usually resolve or at least improve with systemic treatment. LC is also sensitive to radiation and local radiation therapy is also used to treat LC lesions.[1,2,7] In B-ALL, the presence of LC is associated with poor prognosis. Afzal et al. stated a 15% six-month survival rate from initial diagnosis of leukemia.[4] A case report by Jiang et al. reported a mean interval between diagnosis of LC to death of 8.3 months.[8] Huang et al. quoted a study where 88% of patients with LC died within 1 year of diagnosis.[3]

Conclusion

LC is a rare extramedullary manifestation of leukemia. However, it is more often seen in AML or CLL and is very rarely associated with B-ALL. Lesions vary in appearance, making diagnosis difficult. In B-ALL, LC is more often associated with firm, erythematous nodules. Diagnosis is based on skin biopsy with both histology and immunophenotype. Treatment generally systemic as well as local radiation of skin lesions. Given its poor prognosis, early clinical suspicion and recognition of LC is important to aid in rapid diagnosis and treatment of this disease.



A. Leukemia cutis in patient with B-ALL.

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