Case Report
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Mucocutaneous Relapse as an Unusual Presentation of T-Lineage Acute Lymphoblastic Leukemia

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Abstract

Acute leukemias represent approximately 30% of malignant diseases in patients under the age of 15 years. Leukemic infiltration of the central nervous system and testis are common events, particularly as sites of relapse in the third year after diagnosis. Management of acute lymphoblastic leukemia is based on long-term chemotherapy, leading to a cure rate of approximately 80% of children and adolescents. Despite this elevated cure rate, approximately 20% have disease relapse. Bone marrow is the most frequent site of relapse followed by the central nervous system. Nevertheless, relapse can occur in any tissue or organ. Recurrence in the mucocutaneous area is extremely uncommon and rare in childhood acute lymphoblastic leukemia. To our knowledge, a few case reports (mostly in adolescents or adults) have been published regarding relapse in the mucosal area (oral cavity) and skin. Most patients had concomitant bone marrow relapse. In this paper we report a case of recurrence of T-cell acute lymphoblastic leukemia in the hard palate, lip and skin of a child without bone marrow relapse.

Keywords: Leukemid, Leukemia cutis, Mucocutaneous involvement, T cell leukemia, Childhood malignancy

Introduction

Acute leukemias are the most common malignancy in childhood. They represent approximately 30% of malignant disease in patients under the age of 15 years. Acute lymphoblastic leukemia (ALL) is the most frequent type of leukemia in children.[1-4] The etiology remains unknown and seems to involve both genetic mechanisms and environmental factors that lead to disorganized proliferation of a single progenitor cell.[2-4] Clinical manifestations are due to the inhibition of normal hematopoiesis by leukemia cells and leukemic infiltration in several organs. Anemia secondary to decreased red blood cell production, bleeding due to thrombocytopenia, and infections due to neutropenia are the cardinal

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manifestations of leukemia. Infiltration of organs results in hepatomegaly, splenomegaly and lymphadenopathy. Leukemic infiltration of the central nervous system (CNS) and testis are also common events, particularly as sites of relapse in the third year after diagnosis.[4] Diagnosis is confirmed when more than 25% of leukemic blast cells are detected in the bone marrow. Immunophenotyping, molecular and cytogenetic studies are useful to characterize both leukemic cells and prognosis.[1] Management of ALL is based on long-term chemotherapy. Treatment in the last decades has undergone striking advances, leading to a cure rate of approximately 80% of children and adolescents. Despite the cure rate, approximately 20% still have disease relapse.[3] The bone marrow is the most frequent site of relapse followed by the CNS.[3-6] Nevertheless, relapse can occur in any tissue or organ. Recurrence in the mucocutaneous area is extremely uncommon and rare in childhood ALL. To our knowledge, a few publications (mostly in adolescents or adults) have reported separate relapses in the mucosal area (oral cavity) and skin (leukemid); most patients had concomitant bone marrow relapse.[7-9] This case report discusses recurrence in the hard palate, lip and skin of a child with T-cell ALL, without bone marrow relapse.

Case report

An 8-year-old boy initially diagnosed with T-lineage ALL was treated according to the standard protocol for T-cell ALL.[10] However, two years after the end of treatment he presented with a burning sensation in the hard palate area with no other clinical or hematological signs or symptoms. Oral examination showed erosion on the right palatal mucosa without hypertrophy. The patient was referred to a dentist. A biopsy was taken which revealed chronic inflammation. Two months later he presented with fever, facial edema, perioral and periorbital swelling. A non-pruritic erythematous maculopapular rash was present on his face and trunk (Figure 1). The skin rash progressed 10 days prior to admission. Oral examination showed severe gum and hard palate mucosal hypertrophy covered with a whitish membrane (Figure 2). The hard palate lesion was firm and painful upon palpation. He had no systemic symptoms such as fatigue, weight loss, night sweats, or bleeding. Laboratory data that included CBC, ESR, and LDH were normal. He underwent an incisional biopsy of the oral and skin lesion with the impression of mucormycosis, but surprisingly received a histological diagnosis of hard palate and dermal infiltration by lymphoid precursor neoplastic T-cells. Histochemical analyses revealed that the cells were positive for cytoplasmic CD3 (polyclonal) CD5, CD7, LCA, CD43, and Ki67 high (40%-50%), but negative for CD10, CD15, BCL2, CD30, TDT, and CD20. Bone marrow aspiration and biopsy with

Figure 1. A) Non-pruritic erythematous maculopapular rash on the face of this case of aleukemic leukemia cutis (LC) at the time of relapse. B) Gross improvement of skin lesions after two courses of chemotherapy.

microscopic and flow cytometry studies, and a cerebrospinal fluid examination did not show evidence of leukemic infiltration. Chest X-ray, PNS X-ray and abdominopelvic sonography were all negative for other organ involvement. After confirmation of relapse in the skin and oral mucosa, he repeated the standard T-cell ALL protocol for treatment.[10] The maculopapular rash and oral lesions improved two weeks after chemotherapy (Figures 1-B, 2-B) and the patient became a candidate for allogenic bone marrow transplantation.

Discussion

Leukemia cutis (LC) or leukemic skin involvement (leukemid) and oral cavity lesions are rare manifestations of extra-medullary leukemia. Leukemia cutis is defined as cutaneous infiltration by neoplastic leukemia cells that result in clinically identifiable skin lesions. Leukemia cutis is distinct from other cutaneous syndromes associated with leukemia such as Sweet's syndrome (infiltration of normal neutrophils in subcutaneous tissue), erythema multiforme, erythema nodosom and pyoderma gangreonosum which are thought to represent reactive or paraneoplastic processes.[11-13] The clinical and morphological features of LC are variable and can present as violaceous, erythematous or hemorrhagic nodules, papules and plaques of varying size.[14,15] The lower extremities are most commonly involved followed by the upper extremities, back, chest, scalp and face.[16] Leukemia cutis is seen in 10% to 15% of patients with acute myeloid leukemia (AML) and 4% to 20% patients with chronic lymphocytic leukemia (CLL). Leukemia cutis is rare in patients with B- or T-cell ALL, affecting 1% to 3% of these patients.[14,16,17] Most cases of LC occur in the setting of established systemic leukemia; rarely LC may precede observable peripheral blood or bone marrow involvement. This condition is known as aleukemic LC (ALC).[14,15] The absence of systemic leukemia has been defined in several ways.[13] According to the broadest definition, ALC is LC in the absence of leukemia cells in the peripheral blood. A second schema defines ALC as the absence of leukemic cells in the peripheral blood but evidence of disease in the bone marrow. The most stringent interpretation defines ALC as the absence of leukemic cells in both the peripheral blood and bone marrow as seen in our patient.

Aleukemic LC rarely has been reported with ALL when using the most stringent definition of ALC (negative peripheral blood and negative bone marrow at time of diagnosis). Very rare cases have been reported with T-cell ALL.[18-20] Leukemia cutis often predicts rapid disease progression and poor prognosis.[14] Relapses of ALL in the oral cavity have been reported where most of these cases are adolescents and adults. Lesions in the oral cavity that result from infiltration of oral tissues by leukemic cells may

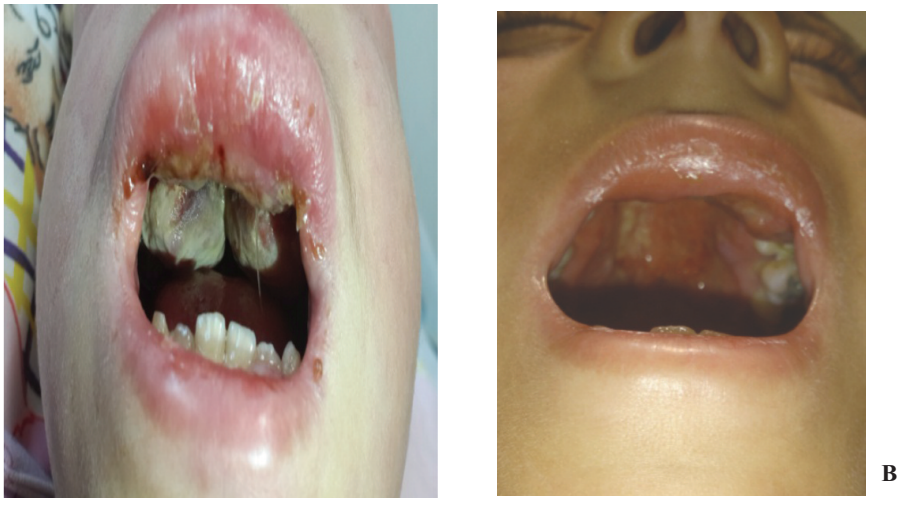

Figure 2. A) Severe hard palate and gum hypertrophy covered with a whitish membrane due to lymphoblastic infiltration. B) Gross improvement of gum and hard palate lesions after two courses of chemotherapy.

occur in any part of the oral cavity. These are common in the gingiva and less frequently in the alveolar bone tissues.[15] However we have been unable to find any case report of hard palate infiltration as a site of extramedulary relapse in the literature. Children with extra medullary relapse usually had a better prognosis than those with medullary involvement;[21,22] however, patients with T-cell ALL had unfavorable outcomes in several studies.[5] Many investigators reported that the duration of the first remission was the most significant variable that influenced an event-free survival. Children with late relapses had better prognosis than those with early recurrence. Our case could be classified as a late recurrence and extra-medullary relapse.[4,5,19]

Conclusion

To the best of our knowledge this is the first described case of ALC associated with hard palate infiltration in a child with T-cell ALL. Serial oral and skin examinations, monitoring and investigation of lesions in these regions during and after treatment is suggested for early detection and appropriate treatment of disease-related lesions and the adverse effects of chemotherapy.

Conflict of Interest

No conflict of interest is declared.

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