CASE REPORT

Leukemia cutis in a patient of relapsed leprosy- Coincidence or predisposition?

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Introduction

Leprosy, a disease of skin and peripheral nerves has varied manifestations which principally affect the immune status of the host. Leukemic skin infiltrations in patients with leukemia are referred to as leukemia cutis. It can be seen in all types of leukemia, especially in patients with acute myelomonocytic leukemia (AML). In majority of cases, the cutaneous lesions are nonspecific manifestations associated with an impaired immune system.\(^1\) Though various malignancies have been documented with leprosy, no case of borderline-tuberculoid (BT) Hansen’s disease with coexisting leukemia cutis has ever been reported in literature to the best of our knowledge.

Case report

A 79 year old male presented with multiple asymptomatic skin coloured to brownish well-defined plaques over the face, neck, back, forearm and thighs of 15 days duration (Figures 1 and 2).

The patient was a known case of BT Hansen’s disease, released from treatment 3 years ago. The patient reported an increase in the size of his previous leprosy patches as well as the appearance of new lesions (Figure 3).

Both the ulnar nerves were asymmetrically thickened and tender. Sensory deficit was noted over both palms without motor deficit. Cervical lymphadenopathy was present. After 2 weeks of admission, the lesions over the back disappeared. On the day of presentation, we considered either relapse or Type 1 lepra reaction in our differentials, and the patient underwent a skin biopsy and slit skin smear which came back positive with a BI of 2+. Histopathology showed diffuse lymphocytic infiltration with epitheloid granulomas in the upper dermis with a clear Grenz zone (Figure 4).
Fite-Faraco staining revealed the presence of solid staining bacilli. We therefore diagnosed the patient as a ‘relapse’ BT Hansen’s disease and MDT-MB was started.

During routine blood investigations, the haemoglobin was 11.2 gm% and the total leucocyte count was 76,000 cells/cumm. A peripheral blood smear and bone marrow biopsy showed features of chronic lymphocytic leukemia (CLL). The patient also showed hepatosplenomegaly with diffuse hyperechoic shadows on ultrasound examination with elevated liver enzymes and a normal renal panel. Following this, immunohistochemistry was done which showed T cells positive for CD3/CD45RO with the histiocytes immunoreactive for CD68 in upper dermis suggestive of leprosy (Figures 5 and 6) and lower dermis with B-cells immunoreactive for CD20/CD5/CD23 suggestive of leukemic infiltrate (Figures 7 and 8).

Based on this, we revised our diagnosis to BT Hansen’s with Leukemia cutis secondary to B cell CLL. The patient was advised to continue with MDT-MB and referred to oncologist, who started the patient on cyclophosphamide and fludarabine for the management of B-Cell CLL.

**Figure 1.** Multiple non-tender erythematous papules and plaques on nape of the neck. The lesions disappeared after two weeks.
According to WHO (1995), a case of relapse is defined as “A patient who successfully completes an adequate course of MDT, but subsequently develops new signs and symptoms of the disease either during the surveillance period or thereafter”. The criterion for leprosy was given by Becx-Bleumink (Table 1) which has been adapted by WHO.

Lesions found in BT and tuberculoid (TT) leprosy are the direct result of a hypersensitive granulomatous response to the antigens of M. leprae. Introduction of multidrug therapy (MDT) leads to resolution of the granuloma over time. However, a few bacilli may get buried alive in the fibrosed nerves and arrector pili muscles, thereby serving as a nidus for relapse.

The association of leprosy with various cancers though recognised is not well established in the literature. In a series of 252 autopsies done in leprosy patients, 85 cases (33.7%) were reported to have malignancies, among which carcinoma of the alimentary system was the most common. Of the non-epithelial malignancies, malignant lymphoma was the most common. In our case, the patient initially developed leprosy and though he was adequately treated, immunodeficiency associated with leukemia may have allowed multiplication of dormant persisters resulting in his current presentation. This is similar to the case of lepromatous leprosy with B-cell lymphoma reported by Sutjita and that of large-cell anaplastic lymphoma in a lepromatous leprosy.
Leukemia cutis refers to the infiltration of the skin by neoplastic leukocytes (myeloid or lymphoid), resulting in clinically identifiable cutaneous lesions. It is most often reported in congenital leukemia and AML. It occurs in 10%–15% of patients with AML, and has been reported in 4% to 20% of patients with chronic lymphocytic leukemia (CLL). Leukemia cutis has a wide range of cutaneous manifestations, including single or multiple violaceous to hemorrhagic papules, nodules, bulla, and plaques of varying sizes. The presence of leukemia cutis suggests extramedullary involvement, thereby indicating a poorer prognosis. In the setting of AML, leukemia cutis presents as a firm nodule with a greenish hue, known as a chloroma or granulocytic sarcoma. In the neonate, it often presents as sites of extramedullary hematopoiesis in the skin, imparting a ‘blueberry muffin’ appearance.
More than 90% of cases of leukemia cutis occur after a diagnosis of leukemia has been established. Concomitant involvement of skin and systemic leukemia have been observed in up to one third of the cases, and, in <10% of cases, skin infiltration can occur before bone marrow or peripheral blood involvement and in the absence of systemic symptoms\(^9\) as in this case.

Cutaneous involvement by CLL may represent a reactive process triggered by antigenic stimuli such as infections. Cutaneous leukemic infiltration has been associated with sites of previous or concomitant inflammatory or infectious conditions, including borrelia burgdorferi, leishmaniasis, herpes zoster, and herpes simplex.\(^10\) This is the first case report to our knowledge where there is cutaneous localisation to previous leprosy lesions. The underlying molecular basis responsible for the migration of leukemic cells to the skin is not defined. The expression of cutaneous lymphocyte associated antigen (CLA) on circulating immunoglobulin-secreting B cells may relate, at least in part, to skin homing of some of these cells after antigen stimulation.\(^11\)

In leukemia cutis, histopathology reveals three main architectural patterns, viz, perivascular and periannexal, nodular & diffuse, and band-like with sparing of upper papillary dermis with a relatively monotonous population of small lymphoid cells with round nuclear contours.\(^8\) This is in contrast to a relapsed case of leprosy which shows well defined

**Figure 4.** H&E staining under scanner view showing diffuse lymphocytic infiltration of the papillary dermis, focal nodular infiltration of the deeper dermis with a clear grenz zone. (inset) H&E staining under 40x showing diffuse lymphocytic infiltration with epitheloid granulomas and occasional Langhan’s giant cells.
granulomas made of lymphoid and epitheloid cells initially focused around the fibrosed nerve bundles and progress later to invade larger portions of dermis. The well-defined granulomas are often indistinguishable from the original lesions. A Grenz zone is often appreciated in BT Hansen’s disease.

**Figure 5 and 6.** Immunohistochemistry showing diffuse lymphocytic infiltrate reactive for CD3/CD45RO with the histiocytes immunoreactive for CD68 in upper dermis suggestive of borderline tuberculoid leprosy.

Leukemia cutis in a patient of relapsed leprosy
To summarise, leukemia cutis, like leprosy has a varied clinical presentation. Leprosy occurring together with leukemia is rare. Leukemia cutis can also be confused for reactions in leprosy. In our case, immunohistochemistry confirmed the presence of both T cell and B cell markers and thus established the diagnosis of concurrent leukemia cutis and leprosy. The occurrence of leprosy in our patient may be coincidental, but the possibility of reduced immunity leading to reactivation of persister leprosy bacilli should be considered.

Figure 7 and 8. The reticular dermis shows focal nodular aggregates of lymphocytes immunoreactive for CD20/CD5/CD23 suggestive of leukemia cutis.
Table 1. Becx-Bleumink criteria

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<td>a. New skin lesions</td>
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<td>b. New activity in previously existing skin lesions</td>
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<td>c. Bacteriological index (BI) 2+ or more in two sets of skin smears</td>
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<td>d. New nerve function loss</td>
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<td>e. Histological evidence of relapse in skin or nerve biopsy</td>
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<td>f. Lepromatous activity in the eye(s)</td>
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Conclusion

CLL rarely presents with skin lesions as the initial manifestation. In leprosy endemic areas, it is important for dermatologists to recognise the subtle clinical differences between these two entities. When in doubt, investigations like immunohistochemistry prove to be a valuable tool to accurately diagnose and differentiate these two conditions with similar clinical and histological presentation. Further, reduced immunity in leukemia predisposing to relapse of leprosy should be further investigated.

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References