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Abstract

A 53-year-old man presented with a recurrent pruritic eruption accompanied by oral sores. His past medical history was significant for subclinical B-cell chronic lymphocytic leukemia (CLL), which had never been treated. On exam, there were erythematous papules and plaques studded with vesicles on the neck, trunk, and upper extremities. Two skin biopsies showed common features of a perivascular and periadnexal lymphocytic infiltrate in the superficial to mid-dermis. Immunohistochemical staining of the lymphocytes showed co-expression of CD20, CD23, CD5, and CD43, consistent with a diagnosis of cutaneous involvement by the patient's CLL. This case highlights the importance of considering leukemia cutis in patients with underlying CLL presenting with unusual clinical features.

Introduction

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia with an incidence of 3-5 per 100,000 [**1**]. It is an indolent disease characterized by the accumulation of mature monoclonal B cells in the blood and bone marrow, often also involving the spleen, liver, and lymph nodes. Skin lesions are common in CLL and can be seen in the background of exaggerated insect bite reactions, cutaneous malignancies, Sweet syndrome, urticaria, infection, purpura, and erythroderma. However, specific cutaneous involvement by CLL, or leukemia cutis, is a rare phenomenon that presents with solitary, grouped or generalized papules, plaques, nodules, or tumors. We report a case of leukemia cutis presenting as a papulovesicular eruption in a man with a several-year history of asymptomatic, untreated CLL.

Case presentation

A 53-year-old man with a history of CLL presented with a three-week history of a mildly pruritic eruption on the upper body. He reported two previous similar episodes, each lasting 3 weeks over the past 18 months. Each episode was accompanied by oral sores. He denied recent insect bites as well as fevers, joint pain, or other associated symptoms. Treatment with topical steroids and oral antibiotics was unhelpful. At the onset of the current episode, he was prescribed oral valacyclovir and trimethoprim-sulfamethoxazole, but reported no change with these medications. He was diagnosed with CLL in 2004, but remained asymptomatic and had never been treated for the disease.

On exam, there were erythematous papules and small plaques studded with vesicles on the neck, trunk, and upper extremities (Figure 1). There were also small erosions on the palate and gingival mucosa.

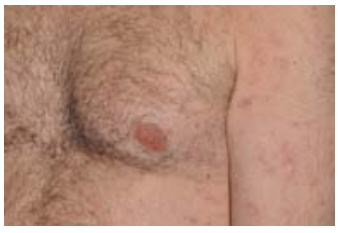

Figure 1

Figure 1. Erythematous papules and small plaques studded with vesicles on the neck, trunk, and upper extremity.

Two skin biopsies from the right arm and the right neck showed common features of a predominantly perivascular and slightly periadnexal lymphocytic infiltrate in the superficial to mid-dermis (Figure 2). The infiltrate was composed of small lymphocytes with slightly pale cytoplasm, fine chromatin, and irregular nuclear contours. A second population of small lymphocytes had scant cytoplasm and hyperchromatic nuclei (Figure 3). Other features included mild interface changes with basal vacuolar alteration and scattered dyskeratosis. The biopsy from the right neck also showed a prominent granulomatous component with aggregates of histiocytoid cells forming perivascular epithelioid granulomas (Figure 4).

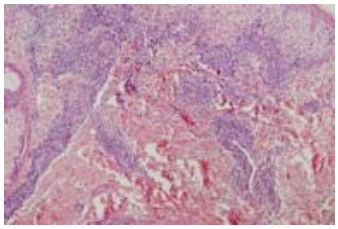

Figure 2

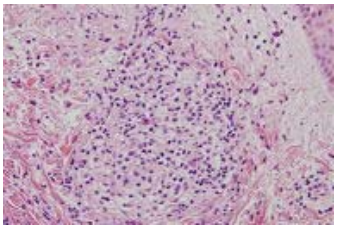

Figure 3

Figure 2. Perivascular and periadnexal lymphocytic infiltrate in the superficial to mid-dermis. (H&E, x40)

Figure 3. Infiltrate composed of lymphocytes and histiocytes. (H&E, x400)

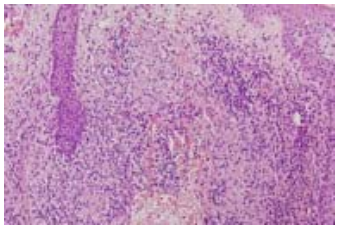

Figure 4

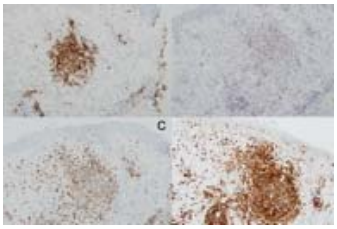

Figure 5

Figure 4. Perivascular epithelioid granulomas. (H&E, x200)

Figure 5. Immunohistochemical staining showing positivity of neoplastic cells for CD20 (A), CD23 (B), CD5 (C), and CD43 (D).

The initial impression was that of a reactive process. However, given the patient's history of CLL, a panel of immunohistochemical stains was performed on both biopsies revealing aggregates and individual CD20+ B cells in both perivascular and periadnexal locations. These lymphocytes showed co-expression of CD23, CD5, and CD43 (Figure 5). The staining pattern supported the neoplastic nature of the B lymphocytes and confirmed the diagnosis of cutaneous involvement by CLL. The second population of lymphocytes was highlighted by CD3, CD5, and CD43 and showed mixed CD4 and CD8 positivity, consistent with reactive T lymphocytes.

Discussion

Cutaneous eruptions are seen in up to 25 percent of patients with underlying CLL [**1**]. Most commonly, these findings represent non-specific or reactive manifestations of disease and include cutaneous malignancies, purpura, pruritus, urticaria, cutaneous vasculitis, Sweet syndrome, and exaggerated arthropod reactions [**1**, **2**, **3**]. Leukemia cutis in CLL is far less common, and often presents in later stages of disease. In a series of 42 patients with CLL presenting with specific cutaneous infiltrates, the mean duration of disease before skin manifestations was 39 months; in only seven patients, skin lesions were the first sign of disease [**4**].

Leukemia cutis in CLL typically presents with erythematous papules, plaques, nodules, or large tumors. Lesions may be generalized and commonly occur on the head and neck. Histologically, three architectural patterns of leukemic infiltrates have been described: patchy perivascular and periadnexal, nodular-diffuse, and band-like. The latter was described in less than 5 percent of cases [**4**]. Other features include subepidermal blisters, epithelioid and giant cell granulomas, rare proliferation centers, scattered solitary epidermotropic lymphocytes, and occasional eosinophils [**4**]. The leukemic infiltrate is composed of small monomorphous lymphocytes with hyperchromatic nuclei and scant cytoplasm. By immunohistochemistry, the neoplastic B cells co-express CD20, CD43, CD23, and CD5 [**4**, **5**, **6**]. Reactive T lymphocytes are a consistent finding [**4**].

Whereas previous reports suggested that leukemia cutis in CLL confers a negative prognosis, recent data counters this notion. In the absence of large cell transformation (Richter syndrome) or progression of systemic disease, skin involvement is not likely to affect prognosis [**4**, **5**]. Cutaneous involvement by CLL may represent a reactive process triggered by antigenic stimuli such as infection or malignancy, a theory supported by findings of CLL infiltrates in herpes or varicella scars and adjacent to malignant epithelial tumors [**4**, **6**].

In our case, despite an unusual clinical presentation, CLL in the skin was confirmed by the classic histopathologic finding of a perivascular and periadnexal infiltrate of CLL lymphocytes. A granulomatous component was also seen in one of the biopsy specimens, consistent with previous reports of leukemia cutis in CLL. Although exaggerated arthropod bite reactions can present as papulovesicles in patients with CLL, lesions predominantly affect exposed skin and are typically pruritic and painful. On histopathologic examination, a lymphocytic infiltrate is often present, but immunohistochemical studies do not consistently confirm the presence of neoplastic B lymphocytes. Further, dermal eosinophils and flame figures are common [**7**]. Thus, the clinicopathologic features seen in our patient are most consistent with specific cutaneous involvement by CLL.

Although our patient was undergoing oral anti-viral treatment, a diagnosis of herpes simplex or herpes zoster was not confirmed and there was no history of skin lesions suggestive of infection at the sites of the leukemic eruption. Whereas mucosal involvement by CLL has been reported [**1**, **3**], the oral lesions in our patient were not biopsied. Our patient's palate and gingival lesions were likely reactive or incidental, but may have represented involvement by the patient's CLL. Specific cutaneous lesions in CLL are usually persistent, but as with our patient, the spontaneous resolution of lesions without scarring has been described [**1**].

This case highlights the importance of considering leukemia cutis in patients with underlying CLL presenting with unusual clinical features.

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