Exaggerated Insect Bite Reaction in Patients with Hematologic Malignancies

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Abstract

Exaggerated insect bite reactions are characteristic in patients with hematologic malignancies, mainly chronic lymphocytic leukemia. The pathogenesis is unclear and the skin lesions may either precede or appear after the diagnosis of a hematologic malignancy. We report 4 cases of exaggerated insect bite reactions in the setting of chronic lymphocytic leukemia, Hodgkin’s lymphoma, and large B cell lymphoma and discuss the phenomenon in these cases. The diagnoses were made using histopathology and immunohistochemistry.

Introduction

Cutaneous eruptions can be commonly observed in patients with hematologic malignancies. One rare and rather infrequently reported cutaneous eruption is the exaggerated insect bite reaction (EIBR). This cutaneous eruption has been most commonly associated with chronic lymphocytic leukemia (CLL). However, they can be seen in other hematoproliferative disorders as well as disorders associated with altered immunity, such as human immunodeficiency virus infection, [1-3] congenital agammaglobulinemia, [4] and natural killer lymphocytosis. [5]

We report 4 cases of EIBR in the setting of various hematologic malignancies (CLL, Hodgkin’s Lymphoma, and Large B cell lymphoma). These cases are uncommon and can be a diagnostic and therapeutic challenge. It is important to consider a possible underlying hematologic malignancy when these reactions are seen.

Case Reports

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Table 1. Patients with Exaggerated Insect Bite Reaction Associated with Various Hematologic Malignancies.
Four patients were identified from our clinical files. These patients are summarized in Table 1. Our index patient 1 was followed for 2 years before developing a blast crises and expiring. During this time his eruption waxed and waned, with no apparent response to treatment of his underlying CLL with Rituximab. Topical clobetasol cream provided modest improvement. No exposure to insects could be correlated with his eruption. Patient 2 presented with a combination of CLL, which was not under current therapy, and a new onset of pruritic papules (Figure 1). Again there was no history of insect exposure. Treatment with antihistamines and topical triamcinolone gave modest improvement in pruritus. Patients 3 and 4 were both new onset of pruritic papules in patients with a history of Hodgkin’s lymphoma and large B cell lymphoma respectively.

Figure 1. Clinical examination of a 68 year old reveals multiple pruritic papules on upper arm.

Figure 2. Low power view showing superficial and deep nodular lymphoid infiltrate. (H&E 40x).
Figure 3. Higher power view showing a mixed nodular infiltrate with eosinophils. (H&E 100x).

Figure 4. Immunostain for CD3 reveals the majority of the infiltrate to be T cells. (Hematoxylin counterstain, 100x).

Figure 5. Immunostain for CD 20 reveals only a small number of B cells (Hematoxylin counterstain, 100x).
We present 4 cases of EIBR in patients with various hematologic malignancies. EIBR are an infrequently reported condition. A literature review reveals multiple reports of EIBR in patients with CLL, [6-21] a reported case of this reaction in a patient with large cell lymphoma, [12] and no reported cases of this reaction in patients with Hodgkin’s Lymphoma. This makes our report of cases interesting and an exceedingly rare finding.

All 4 of our patients presented with superficial and deep infiltrates composed of small lymphocytes and eosinophils, which histopathologically classifies it as an EIBR based upon the definition created by Byrd et al in 2001. [6] These 4 patients were also all diagnosed with an underlying malignancy of CLL, Hodgkin’s Lymphoma, or Large B-cell Lymphoma.

EIBR was first described by Weed in 1965. [7] In 1999, Barzilai et al. described 8 patients with various hematologic malignancies who had eruptions consistent with insect bites but the history, distribution, and treatments did not support a true insect bite. They then coined the term “insect bite-like reaction” or “eosinophilic eruption of haemoproliferative disease.” [12] Since then, many reports have come out of patients with various hematologic malignancies having the same insect bite-like reaction with no clinical history suggestive of a true insect bite.

The pathogenesis of these eruptions is unclear. These lesions have been more frequently seen in B-cell hematologic malignancies. One theory suggests that IL-4 and IL-5 play a role in malignant B-cell proliferation and the eosinophilic predominant response. [12] Another theory is that neoplastic B cells are causing the hypersensitivity reaction. [12] Although exaggerated insect bite-like reactions have always been classified as nonspecific lesions, Mitteldorf et al recently used FISH analysis to reveal neoplastic leukemic cells within the eosinophilic infiltrate. [22] This put into question the previous classification of these exaggerated insect bite reactions as a nonspecific phenomenon. However, immunohistochemical staining done by Butzmann et al in 2014 on a patient with CLL, displayed a predominant T-cell infiltrate with only a few B cells. [21] In addition, the immunohistochemical staining performed in our cases of predominately B-cell malignancies revealed similar results with a predominant T-cell infiltrate and only a few B cells in the infiltrate.

Treatment of these lesions have been challenging with many cases of refractory lesions having been published. [12,16] Treating the underlying hematologic malignancy in these patients has shown various results in resolution of the lesions, in addition to a lack of symptomatic management being fully achieved. [11] This truly differs from leukemia cutis, in which treatment of the CLL usually leads to full improvement of the leukemia cutis. In patients with EIBR, systemic prednisolone 40 mg/day or greater has been shown to decrease the symptoms, although relapses often always occur with reduction of the dose. [12,16] Other treatment options that have been used include dapsone, interferon alfa, IVIG, and phototherapy in refractory cases. [15,23] Our cases showed only modest response to strong topical steroids.

In summary, we have presented multiple cases of an infrequent disease process, including 2 exceedingly rare cases. As a whole, exaggerated insect bite reactions in hematologic malignancies must be differentiated from leukemia or lymphoma involving the skin. Although a rare phenomenon, when encountering an exaggerated response to an insect bite, further workup may be warranted since it can precede underlying hematologic malignancies [12].

References


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