

CLINICAL IMAGE

Exaggerated arthropod assault: Eosinophilic dermatosis in a patient with small lymphocytic lymphoma

Curtis Lachowicz¹  | Kevin White² | Stephen Spurgeon³

¹Department of Internal Medicine, Oregon Health and Science University, Portland, Oregon

²Department of Dermatology, Oregon Health and Science University, Portland, Oregon

³Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon

Correspondence: Curtis Lachowicz, Department of Internal Medicine, Oregon Health and Science University, 3181 SW Sam Jackson Park Rd, Portland, OR 97239 (lachowie@ohsu.edu).

Key Clinical Message

Dermatologic reactions are commonly encountered in clinical practice. Providers must be aware of both the common and uncommon etiologies leading to these eruptions, particularly in patients with underlying malignancies. Establishing the appropriate etiology directs treatment of these conditions, which may be therapy directed at the malignancy itself.

KEYWORDS

arthropod bite, chronic lymphocytic leukemia, eosinophilic dermatosis, leukemia, skin eruption

1 | INTRODUCTION

Cutaneous manifestations of systemic disease are common and provide valuable clinical information to aid clinicians in the diagnosis of the underlying etiology. A subset of these eruptions known as eosinophilic dermatoses are often seen in patients with underlying hematological malignancies. Here, we present a case of a patient with an eosinophilic dermatosis and discuss the differential diagnosis, clinical course, histological findings, and approach to treatment.

2 | CASE PRESENTATION

A 66-year-old man from rural Oregon with a history of intermediate-risk untreated small lymphocytic lymphoma (SLL) presented with an erythematous plaque on the dorsum of his right hand and progressive, pruritic, flesh-colored papules over his neck and arms (Figure 1). Other than mild progression of cervical and axillary adenopathy (up to 2.5 cm), there was no evidence of disease progression necessitating SLL-directed therapy. The patient denied any new exposures to topical agents, detergents, or medications. He reported no

recent travel but spent much of his time outdoors in wooded areas. He denied any history of insect bites or exposures. His complete blood count revealed normal lymphocyte numbers although reactive lymphocytes were noted (1.15 K/cu mm). There was no eosinophilia. Erythrocyte sedimentation rate (ESR) was mildly prolonged at 40 mm/h. A comprehensive metabolic panel was normal.

His history of spending prolonged periods of time spent outside raised the suspicion of a type IV hypersensitivity dermatitis to an arthropod exposure, and he was empirically prescribed doxycycline, antihistamines, a short course of oral prednisone (1 mg/kg × 5 days), and intermediate strength topical steroids. An initial skin biopsy demonstrated superficial and deep perivascular lymphohistiocytic and eosinophilic inflammation. The prescribed treatment provided little symptomatic relief without improvement of his lesions. Given the lack of initial response, he underwent repeat skin biopsy showing nodular mixed dermatitis and lobular panniculitis with numerous eosinophils and “flame figures” (eosinophilic degranulation) (Figure 1).¹ No leukemic or neutrophilic infiltrate was appreciated. In this clinical context, the changes were most suggestive of an exuberant or persistent response to an arthropod bite.

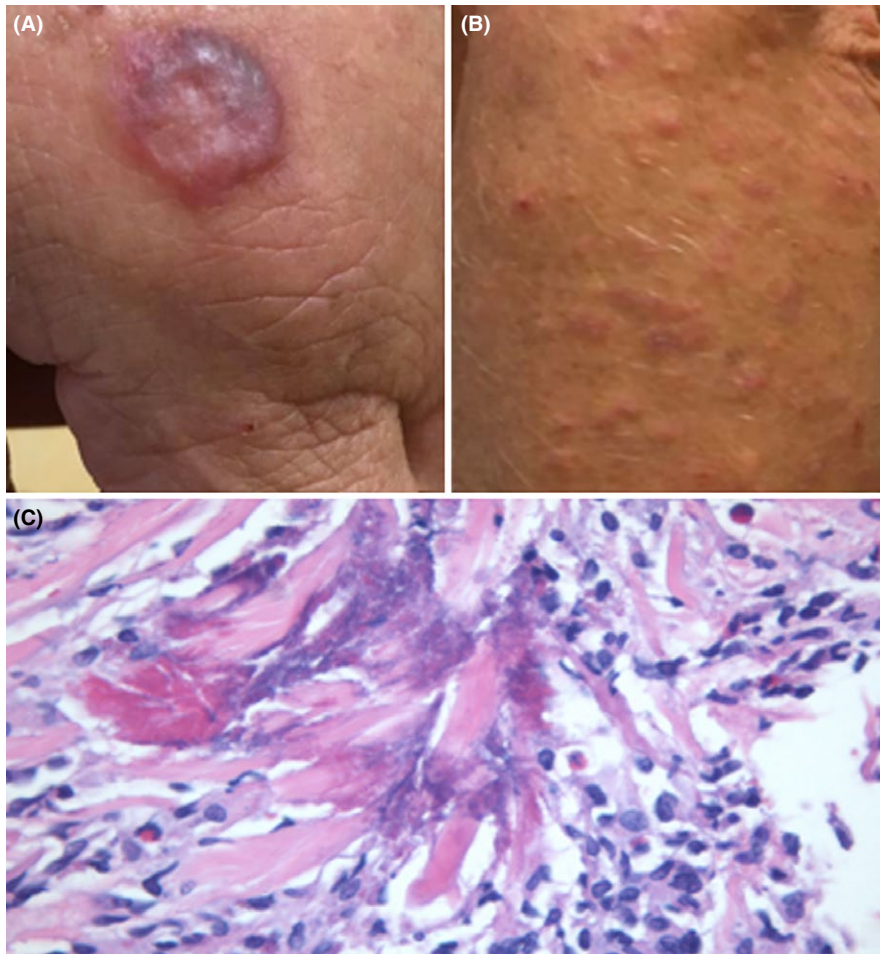


FIGURE 1 Gross (Panel A, B) and histologic (Panel C) findings in this patient with a malignancy associated with eosinophilic dermatosis due to arthropod exposure. Panel C demonstrates flame figures resulting from eosinophilic degranulation

3 | DISCUSSION

Eosinophilic dermatoses—which encompass Well’s syndrome and more broadly conditions with extensive eosinophil infiltration into cutaneous tissues related to an underlying disease process—have been observed in association with a variety of hematological malignancies, including chronic lymphocytic leukemia (CLL).^{1–6} Of note, CLL and SLL are viewed as the same disease process, but, in SLL, malignant cells are primarily limited to lymph nodes instead of the peripheral blood.

Flame figures—as seen in this case—represent eosinophil degranulation and were first reported in eosinophilic cellulitis (Well’s Syndrome).^{1–3,7} However, flame figures are not pathognomonic for Well’s syndrome and have since been observed in a variety of eosinophilic dermatoses, including arthropod bites, bullous pemphigoid, eczema, scabies infestations, hypereosinophilic syndromes, and drug reactions.^{2,3,8} This histopathology has also been observed among patients with hematological malignancies, owing to the high numbers of eosinophils seen in tissue specimens.^{1,2,5} In CLL, eruptions of pruritic papules and plaques that resemble arthropod bites, but without a

known patient exposure, have been reported on numerous occasions, leading to the development of the term “insect bite-like” in the clinical description of these cutaneous lesions.^{4,5} However, unlike the dermal leukemic infiltration seen in leukemia cutis, the infiltrate seen in an eosinophilic dermatosis is devoid of leukemic cells and is rich with a lymphohistiocytic and eosinophilic infiltrate.^{4–6} While rare, the increasing recognition of such cases has led to the classification of such cutaneous eruptions.⁶ Byrd et al described 2 unique disease archetypes seen in eosinophilic dermatosis of myeloproliferative disease. The first is characterized by an exuberant reaction to a known arthropod bite or exposure, and resolves spontaneously over the course of days to weeks. The second demonstrates a more subacute or chronic course that is resistant to conventional treatment, and was further classified as a unique entity known as eosinophilic dermatosis in myeloproliferative disease.⁶

In the case of CLL, the pathophysiology is yet to be fully understood; however, it is thought to occur as the result of a type IV delayed hypersensitivity reaction, as the cutaneous lesions are rich in T cells in addition to eosinophils, leading to the hypothesis that such a

reaction represents an exaggerated response to arthropod bites.^{2,4-6,8} This was illustrated in a case of 8 patients with CLL who developed significant dermal reactions from exposure to mosquito antigen versus control patients.⁹ It was postulated that in the setting of CLL, this exaggerated response may be due to an altered immune response secondary to an increased number of dermal lymphocytes.⁹

Similar to Wells Syndrome, conservative treatment of these lesions with topical steroids often yields disappointing results and requires systemic steroids at a dose of at least 40 mg/d, or in cases refractory to systemic steroids, treatment directed at the underlying malignancy.^{1,2,5,6,8,10} The patient was unable to recall any significant arthropod bites or exposures; however, given the history of spending a large portion of his time outdoors during the summer months prior to the development of his cutaneous lesions, an exaggerated arthropod response was determined to represent the most likely diagnosis. Ultimately, the patient underwent CLL-directed therapy with 6 months of the humanized, second-generation anti-CD20 monoclonal antibody obinutuzumab and had complete resolution of his adenopathy and skin lesions.

CONFLICT OF INTEREST

None declared.

AUTHORSHIP

CL, SS, and KW: were responsible for collection of case data and generation of the manuscript. CL: was responsible for the literature review.

ORCID

Curtis Lachowicz  <http://orcid.org/0000-0001-8506-0624>

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