Eosinophilic Dermatosis of Hematologic Malignancy (EDHA): An Obscure Dermatologic Diagnosis Effectively Treated with Rituximab

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ABSTRACT

Eosinophilic dermatoses are a heterogeneous group of diseases, characterized by an eosinophil-rich infiltrate and/or degranulation of eosinophils. Eosinophilic dermatoses encompass a broad spectrum of diseases of different etiologies hallmarked by eosinophilic infiltration of the skin and/or mucous membranes, with or without associated blood eosinophilia.

Keywords: Eosinophilic; Dermatosis; Hematologic; Malignancy; Chronic lymphocytic leukemia; Recurrent pruritic skin disease; Arthropod bite-like reaction; Paraneoplastic; Medical dermatology; Oncology

INTRODUCTION

Eosinophilic Dermatosis of Hematologic Malignancy (EDHM) is an uncommon skin disorder which may be easily misdiagnosed. Careful evaluation of the skin and lymph nodes with prompt referral to an oncologist for evaluation will hasten the diagnosis and treatment of Chronic Lymphocytic Leukemia (CLL) or other hematologic malignancy. Treatment of the underlying disease will resolve the annoying, chronic, recurrent, pruritic and painful "persistent insect-bite-like reactions" now named EDHM. We report a case of EDHM, which resolved following quick recognition of the skin condition and subsequent treatment of CLL with rituximab.

CASE STUDY

A 47-year-old man presented with a two year history of pruritic skin lesions involving his face, scalp, arms and chest. Allergy, dermatology, rheumatology and general medical evaluations did not reveal an etiology for his symptoms which did not resolve with repeated courses of oral steroids and oral antihistamines. At the time of dermatologic consultation he had conjunctival injection, exuberant red papules and papulovesicles on his forehead, cheeks and neck (Figure 1). He had bilateral tonsillar enlargement without exudate and generalized lymphadenopathy (LAD). Skin biopsies showed histologic features resembling an arthropod bite reaction, characterized by a dense, superficial and deep, perivascular and periadnexal infiltrate composed of lymphocytes and several eosinophils (Figure 2). There was focal evidence of follicular mucinosis. Immunoperoxidase studies showed a predominantly T lymphocytic infiltrate in the dermis with CD3, CD5 and CD7 immunostains marking the majority of the cells with a high CD4 to CD8 ratio. T-cell receptor-beta gene rearrangement by fluorescent PCR was polyclonal. CD20 and CD79-A immunostains indicated the presence of only a minor B-lymphocyte component. Immunoglobulin heavy chain gene rearrangement by fluorescent PCR was clonal. A complete blood count showed a white blood cell count of 12 k/uL (neutrophils 26%, lymphocytes 58%, monocytes 10%, and eosinophils 6%), hemoglobin 15.4 g/dl and platelets 154 k/uL. Positron emission tomography/computed tomography (PET/CT) demonstrated cervical, thoracic and abdominopelvic lymphadenopathy (LAD) with splenomegaly (13.8 cm) all exhibiting low SUV scores. Flow cytometry showed predominantly CD20+, CD5+ and CD23+ lymphoid cells consistent with CLL. Treatment with rituximab led to complete resolution of the LAD and skin rash and return to normal of his CBC and flow cytometry. He has remained clear of both cutaneous and hematologic disease for greater than three years.

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RESULTS AND DISCUSSION

The diagnostic terms of “exaggerated delayed hypersensitivity reaction to mosquito bites” or “insect bite like reaction” were replaced by Eosinophilic Dermatitis of Hematologic Malignancy (EDHM) when the association was first recognized. Philip Cohen in a comprehensive review of 208 cases has proposed a new nomenclature (acronym) for EDHM: Hematologic-related malignancy-induced eosinophilic dermatosis (He Remained) [1,2]. Various hematologic malignancies including acute monocytic leukemia, acute lymphoblastic leukemia, B-cell non-Hodgkin lymphomas, myelofibrosis and Chronic Lymphocytic Leukemia (CLL) have all been reported with EDHM. CLL as in this case is the most common hematologic malignancy associated with EDHM, although EDHM is a rare cutaneous eruption seen in CLL [3]. More common are the fleeting exaggerated large pruritic red reactions to routine insect bites that patients with CLL get during the spring and summer in contrast to the persistent EDHM.

Byrd JA, et al proposed the criteria for EDHM: (1) pruritic papules, nodules and or vesiculo-bullous eruption refractory to standard treatment, (2) histopathology revealing eosinophil rich superficial and deep dermal lympho-histiocytic infiltrate, (3) exclusion of other causes of tissue eosinophilia and (4) diagnosis of hematologic malignancy [4].

The histopathology of EDHM may be difficult to interpret because of the reactive T-cells and lack of leukemic cells, the presence of follicular mucinosis and eosinophilic folliculitis. The latter may be confused with HIV associated eosinophilic folliculitis. The immunoglobulin heavy chain clonal rearrangement in the skin biopsy suggests that the sparse number of leukemic B-cells play a pathogenic role in EDHM [5].

The dermatologist often encounters the diagnostic dilemma of patients with unexplained painful or pruritic red papules and papulovesicles, with a skin biopsy report “consistent with arthropod bite reaction”. In the summer there are ample potential causes for “bug bites”. When the lesions persist or wax and wane over prolonged periods alternative diagnoses need be considered such as scabies, urticarial stage of bullous pemphigoid, Wells syndrome or drug hypersensitivity reaction. The complete skin examination should include palpation of lymph nodes and if generalized lymphadenopathy is discovered at the time of the skin eruption, then the diagnosis of EDHM should be immediately considered. LAD is one of the most common preceding findings of CLL [6]. In a group of patients with CLL and EDHM (median age 64.8 years old, range 33-69 years old) 54% had LAD and 27% had splenomegaly at the time of the skin rash [7]. The recognition of either lymphadenopathy or splenomegaly by the dermatologist should expedite the referral to an oncologist for evaluation and treatment. Our patient was 47-year-old at the time of presentation of his CLL, much younger than the median age at diagnosis (64-70 years) of CLL [6]. Also present on physical examination, the bilateral tonsillar enlargement was possibly a rare first sign of his CLL [8]. Moreover, treatment of the CLL, as in our case, should lead to prompt resolution of the otherwise refractory skin disease.

CONCLUSION

EDHM should be included in the list of paraneoplastic dermatoses often pointing to CLL as the most common cause. Treatment of the underlying hematologic condition will usually resolve the paraneoplastic skin disease.

CONFLICT OF INTEREST

There is no conflict of interest to be reported by any of the authors.

REFERENCES

