Paraneoplastic Eosinophilic Dermatosis in a Case of Chronic Lymphocytic Leukemia

Abstract

Eosinophilic dermatosis of hematologic malignancy is a rare paraneoplastic manifestation particularly associated with chronic lymphocytic leukemia (CLL).Clinically, it presents as a peculiar polymorphic pruritic eruption with characteristic histological findings of superficial and deep dense perivascular infiltrate of lymphocytes and eosinophils without any vasculitis. Although it has been reported intermittently with different names, there is paucity of reports of this condition in Indian literature. Here, we report a patient of CLL having insect bite-like eruptions nonresponsive to conventional therapy and confirmed as eosinophilic dermatosis on histology. Patient was having eruptions well before the diagnosis of malignancy, and intensity as well as frequency increased as the disease progressed. Good control over the disease was achieved using chemotherapy and steroids. Thus, this case explains diagnostic and prognostic significance of eosinophilic dermatosis in CLL.

Keywords: *Chemotherapy and steroids, chronic lymphocytic leukemia, eosinophilic dermatosis*

Chetan D. Rajput, Balkrishna P. Nikam, Shailesh S. Malani

Department of Skin and VD, SBH Govt. Medical College, Dhule, Department of Skin and VD, Krishna Institute of Medical Sciences, Karad, Maharashtra, India

Introduction

Internal malignancies can present with various cutaneous manifestations. These include direct cutaneous lesions resulting from infiltration of the skin by malignant cells, specific cutaneous disorders such as paraneoplastic diseases, and nonspecific manifestations such as prurigo or infectious diseases. Paraneoplastic manifestations are caused by hormonal, neurological, hematological, or immunological disturbances. Eosinophilic dermatosis of hematologic malignancy is a rare paraneoplastic manifestation presenting as a peculiar eruption characterized by polymorphic lesions such as erythema, papules, vesicles, pustules, nodules, or urticarial plaques in patients with hematological malignancies.[1,2] We report a patient who had such eruptions well before the diagnosis of CLL, and was treated successfully with systemic steroids and chemotherapy.

Case Report

A 66-year-old female patient presented with intensely pruritic eruptions distributed over the face, neck, upper trunk, and extremities for 6 weeks. There was history of several episodes of similar cutaneous eruptions for the last 4–5 years. The patient was incidentally diagnosed with chronic lymphocytic leukemia (CLL) RAI stage I 3 years ago with hemoglobin (Hb) 11.2 g% total leukocyte count (TLC) 37,000 and platelet count 2,90,000 and was kept under observation. The intensity, frequency, and duration of pruritic eruptions increased over the last 6 months with involvement of different sites. She was treated many times with antiscabetics and topical steroids along with preventive measures against insect bite without any promising results, rather the condition worsened with each episode. Since 4 months, the patient was feeling fatigued easily and 2 weeks prior to presentation she received first cycle of chemotherapy with bendamustine and rituximab as leukemia was of stage III as per RAI staging with Hb 8.3 g% TLC 1,37,000, and platelet count 1,20,000. Human immunodeficiency virus immune assay was nonreactive however, the patient was found reactive for hepatitis B virus surface antigen (HBsAg), nonreactive for hepatitis B virus envelope antigen (HBeAg). Her alanine aminotransferase was110 IU/L and HBV DNA load was 14,181 copies/mL. Hence, as per the American association for the study of liver disease guidelines (AASLD), she was put on entecavir.

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Address for correspondence:
Dr. Chetan D. Rajput, Department of Skin and VD, SBH Govt. Medical College, Dhule - 424 002, Maharashtra, India.
E-mail: drchetanrajput@yahoo.com

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After the first cycle of chemotherapy, her general condition improved. There was axillary lymphadenopathy and hepatosplenomegaly. On cutaneous examination, multiple erythematous papules, edematous urticarial plaques and purpuric lesions of varying sizes were present over the face, neck, trunk, upper, and lower extremities [Figure 1a-d]. Initially, differential diagnoses considered were drug eruption, arthropod bite reaction, and Sweet's syndrome. Skin biopsy with hematoxylin and eosin stain found wedge-shaped moderately dense perivascular and interstitial infiltrate of many mature eosinophils intermixed with neutrophils in the superficial and mid-dermis with areas of leukocytoclasia without any evidence of vasculitis [Figure 2a and b]. Based on these findings, a diagnosis of eosinophilic dermatosis associated with CLL was made. Then patient was put on systemic steroids started as 30mg/day and tapered to a maintenance dose of 5mg/day. Simultaneously chemotherapy with bendamustine and rituximab was continued. Leukemia was in good control after four cycles of chemotherapy as the general condition of the patient improved and hematological investigations were normal (Hb –10.2 g%, TLC–8,200 and platelet count –2,25,000). Computed tomography (CT) scan showed decrease in the number of enlarged pretrachial, paratrachial and axillary lymph nodes. The size of the largest lymph node was reduced from the baseline size of 4.2 × 3.1 cm to 1.5 × 1.2 cm, and splenomegaly was reduced from 15 cm to 6 cm. Simultaneously, the intensity of pruritus decreased with significant reduction in the number and size of lesions during each eruption [Figure 3a-d]. New crops appeared less frequently and lesions persisted only for 1–2 days after four cycles of chemotherapy; the therapy was planned to complete six cycles.

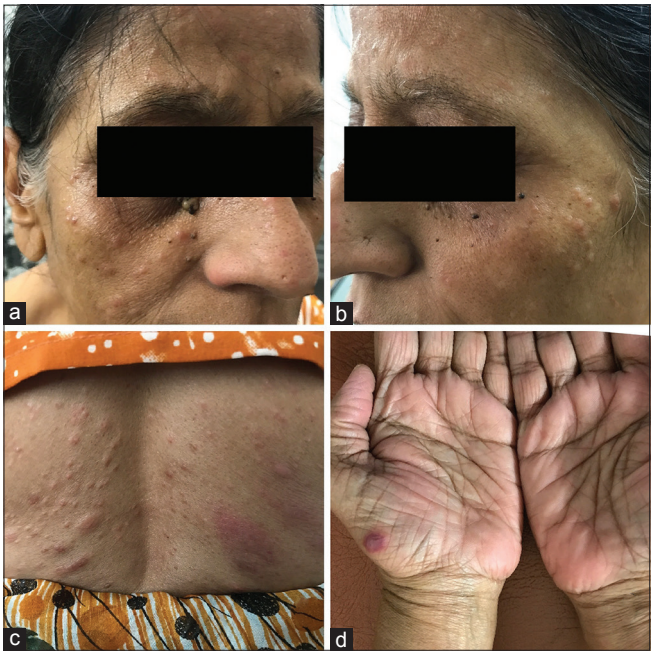

Figure 1: (a and b) Multiple erythematous papules over the face. (c) Multiple erythematous papules and edematous urticarial plaques over the back. (d) Purpuric lesion over the thenar aspect of right palm

Discussion

Weed (1965) first described peculiar polymorphic eruptions in CLL patients and termed it as exaggerated delayed hypersensitivity to mosquito bites.[3] Since then, this condition has been described intermittently in the literature with different names, such as insect bite-like reaction in hematologic neoplasm, eosinophilic dermatosis of myeloproliferative diseases, eosinophilic eruption of hematoproliferative diseases, eosinophilic folliculitis in association with chronic lymphocytic leukemia or eosinophilic panniculitis in chronic lymphocytic leukemia.[4,5] Although more commonly associated with CLL, other conditions include acute lymphoblastic leukemia, acute monocytic leukemia, large cell lymphoma, mantle cell lymphoma, multiple myeloma, and myelofibrosis.[6] Farber *et al*. preferred the term eosinophilic dermatosis of hematologic malignancy for covering these numerous hematologic malignancies associated with such cutaneous eruptions.[1]

Clinically, the disease can mimic papular urticaria, dermatitis herpetiformis, drug eruption, leukemia cutis, scabies, Sweet's syndrome, and early bullous pemphigoid.[1,2] However on histology, eosinophilic dermatosis shows characteristic superficial and deep dense perivascular infiltrate of lymphocytes and eosinophils without any vasculitis.[6] It is very difficult to differentiate it from insect bite reaction clinically as well as histologically, but central vesiculations and crusting is seen more commonly in insect bite. Moreover, absence of obvious history of insect bite, no response to conventional treatment and preventive measures against insect bite, and presence of hematological malignancy helps to differentiate it from insect bite reaction, confirming the diagnosis.

The exact pathogenesis of this disorder remains unclear. First it was considered that the patient had an abnormal response to insect bites, which supported by positive results of an intradermal test made with mosquito antigen.[3] However later, necessity of a bite to trigger the process could not be demonstrated.[7]

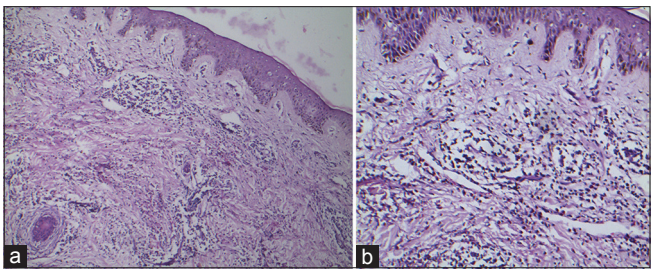

Figure 2: (a) Moderately dense perivascular and interstitial infiltrate of lymphocytes, eosinophils, and neutrophils with spongiosis in the superficial and mid-dermis. (Hand E staining, ×10). (b) Interstitial infiltrate of many mature eosinophils intermixed with neutrophilswith areas of leukocytoclasia without vasculitis (Hand E staining, ×40)

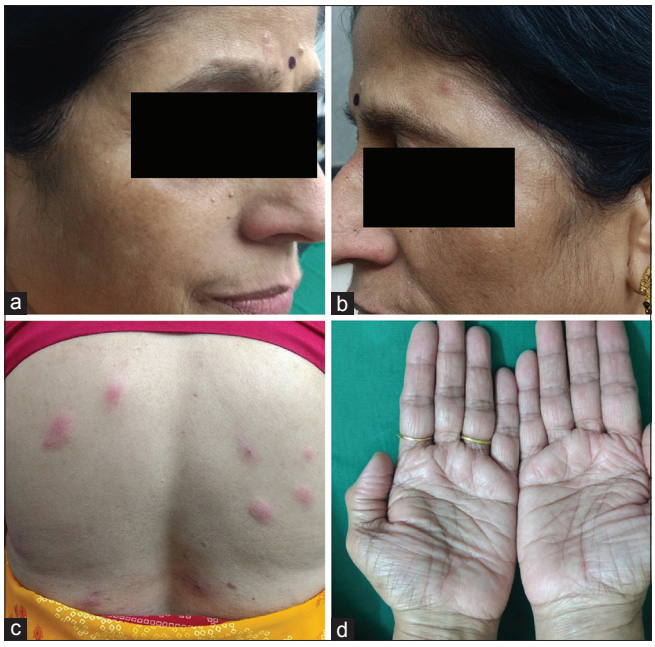

Figure 3: (a and b) Resolution of facial lesions after treatment. (c) Significant decrease in the number and size of lesions after treatment. (d) Clearance of palmar lesion after treatment

Eosinophilic eruptions can be seen in patients with congenital agammaglobulinemia and human immunodeficiency virus infection due to triggers such as insect bite, drug, or virus that can cause eosinophilic response as a result of altered immune processes with Th2 dominance.[4] In CLL, there is Th1dominancy in early stage but as the disease advances Th1 response decreases and Th2 response increases resulting in Th2 dominance. It has been suggested that increased Th2 response favors the suppression of apoptosis of malignant cells leading to deterioration of CLL.[8] Simultaneously, Th2 dominance causes excess production of interleukin 4 and 5, the major eosinophil-recruiting cytokine, resulting in eosinophilic infiltration of skin.[4] One more hypothesis suggests that tumor cells themselves deliver these cytokines.[9]

Eosinophilic dermatosis generally occurs in a patient after diagnosis of malignancies, but in our case the patient was having eruptions well before the diagnosis of malignancy. Further, the intensity went on increasing as the disease progressed. Leukemia and skin lesions were well controlled with chemotherapy and systemic steroids. Chemotherapy reduces leukemic cell burden causing normalization of altered immune responses that lead to control over eosinophilic dermatosis. Hence, patients aged older than 50 years with recurrent insect bite-like reaction not responding to conventional treatment should be evaluated for hematological malignancies and put on chemotherapy whenever needed.

Conclusion

This case of eosinophilic dermatosis in CLL has been reported due to paucity of data on this condition in Indian literature and to highlight the diagnostic and prognostic importance of this condition in a case of CLL.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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