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Case Report

Flame figures associated with eosinophilic dermatosis of hematologic malignancy: is it possible to distinguish the condition from eosinophilic cellulitis in patients with hematoproliferative disease?

Jianjun Qiao, Chang-E Sun, Weifang Zhu, Dingxian Zhu, Hong Fang

Department of Dermatology, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

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Abstract: Eosinophilic dermatosis of hematologic malignancy is a multifaceted dermatosis with a wide morphological spectrum, presenting as pruritic, erythematous, papular and occasionally vesicular, urticarial, nodular eruptions. Histopathologically eosinophil infiltration in the super and deep dermis was found. We reported a case of eosinophilic dermatosis of hematologic malignancy presented as urticarial and vesicular lesions in a patient with chronic lymphocytic leukemia. A skin biopsy revealed a prominent subepidermal blister and a diffuse infiltrate of eosinophils with flame figures in the dermis and subcutaneous tissue. Although flame figures associated with eosinophilic dermatosis of hematologic malignancy is rarely reported, we believe that it would not seem unusual to find them in this skin disease. Eosinophilic cellulitis, which share clinical and histological features with eosinophilic dermatosis of hematologic malignancy, has also been described as showing an association with hematoproliferative diseases. In order to clearly describe eosinophilic dermatosis in patients with hematologic malignancies, the terminology eosinophilic dermatosis of hematologic malignancy, instead of eosinophilic cellulitis, would be a more suitable term in patients with eosinophilic dermatosis.

Keywords: Eosinophilic dermatosis, hematologic malignancy, flame figures, chronic lymphocytic leukemia

Introduction

Eosinophilic dermatosis of hematologic malignancy or insect bite-like reaction is an infrequent dermatitis which has been described in association with hematoproliferative disorders, especially chronic lymphocytic leukemia [1-7]. This rare dermatosis often presents as pruritic, erythematous, papular and occasionally vesicular, urticarial, nodular eruptions [4-6, 8]. Here we describe a case of eosinophilic dermatosis of hematologic malignancy reaction presented as urticarial, vesicular lesions in a patient with chronic lymphocytic leukemia. A skin biopsy from the patient showed a prominent subepidermal blister and a severe diffuse infiltrate of eosinophils with flame figures in the dermis and subcutaneous tissue.

Case description

A 67-year-old female was admitted to our department with several episodes of recurrent pruritic eruptions of edematous plaques on the extremities, face and trunk for about nine months. During the process, several bullae, vesicles and papules occurred along with the edematous plaques. There was no preceding history of arthropod bites or drug administration. The patient had been clinically considered as insect bites reaction and bullous pemphigoid. But her cutaneous lesions failed to respond to either oral antihistamines or combination of minocycline and nicotinamide. The patient had been diagnosed with B-cell chronic lymphocytic leukemia 3 years before the cutaneous lesions occurred. The hematologic malig-

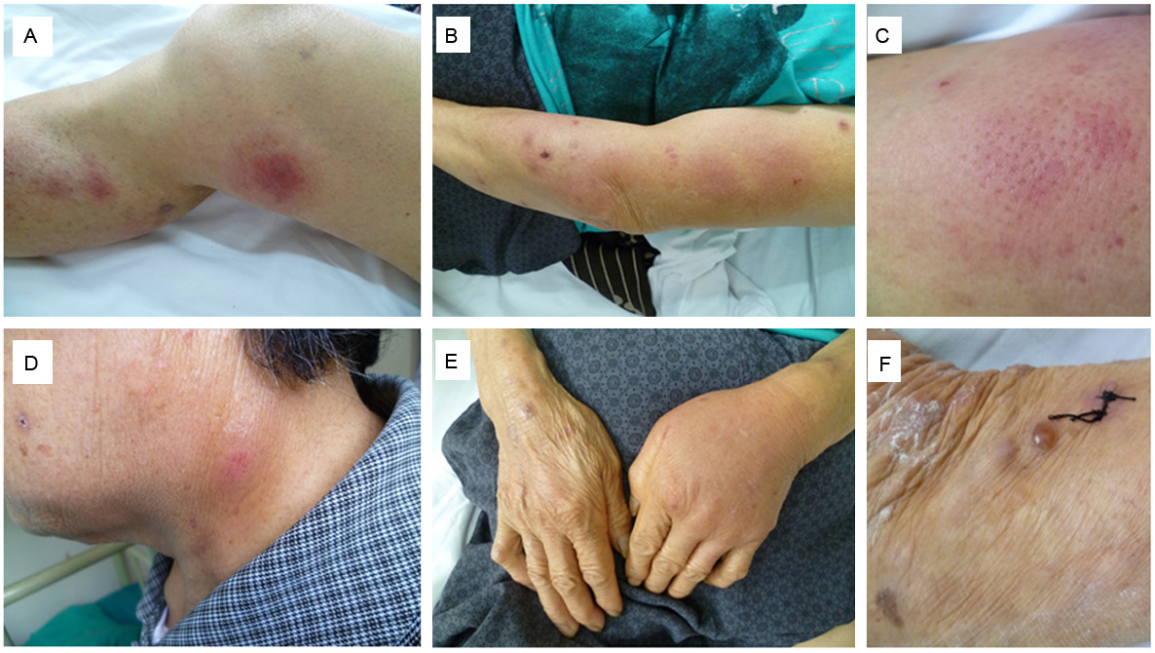

Figure 1. Generalized eruption on the extremities, trunk neck and face consisting of urticarial plaques (A-E), and vesicles (F).

nancy was stable and was not given any treatment.

Clinical examination of the skin revealed symmetrical generalized eruptions on the extremities, trunk neck and face consisting of urticarial plaques, vesicles, bullae, papules, and crust (**Figure 1A-F**). Physical examination revealed inguinal and cervical lymphadenopathy.

A skin biopsy from a vesicular lesion showed a prominent subepidermal blister and a severe diffuse infiltrate of eosinophils with florid flame figures in the dermis and subcutaneous tissue (**Figure 2A-C**). Direct immunofluorescence showed no findings of immunobullous diseases. The patient's laboratory tests were reviewed and a persistent eosinophilia ranging from 2.41×10^9/L to 5.34×10^9/L (normal: 0.05-0.5×10^9/L) was noted dating back to nine months ago.

Further investigations to determine the cause of the eosinophilia included negative parasites or eggs in the stools, a negative autoantibody screen including antineutrophil cytoplasmic antibodies and antinuclear antibody, and normal T-cell immunophenotyping on peripheral blood. Neither FIP1L1-PDGFRα fusion gene nor T cell receptor and immunoglobin gene rearrangement was detected on peripheral blood. Serum electrolytes were within normal limits. A bone marrow biopsy showed significant hyperplasia of small lymphocyte and eosinophil. Immunostain of the bone marrow revealed a B-cell chronic lymphocytic leukemia phenotype. Cytogenetic test showed the karyotype was normal, 46, XX.

The patient was diagnosed as eosinophilic dermatosis of hematologic malignancy based on the medical history, recurrent skin lesions, eosinophilia in peripheral blood, and histologic manifestation. The patient was given therapy with prednisone 60 mg per day. A remission of the eruptions and the itch were achieved within 10 days. Eosinophil count of peripheral blood was recovered to a normal value. The corticosteroid was subsequently tapered gradually. However the disease was flare-up when the prednisone was tapered to 16 mg per day.

Discussion

Eosinophilic dermatosis of hematologic malignancy was first described by Weed in 1965 [9]. It has been a debate whether this phenomenon is due to delayed hypersensitivity reaction to insect bites, particularly mosquitoes. However most patients with hematoproliferative disease

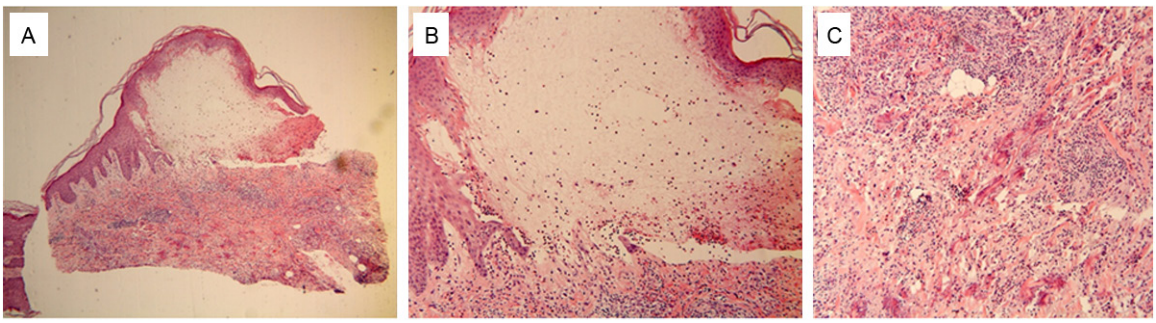

Figure 2. Histological findings of a vesicular eruption. A prominent subepidermal blister and a severe diffuse infiltrate of eosinophils with flame figures in the dermis and subcutaneous tissue (hematoxylin-eosin; original magnifications: A: ×40, B: ×100, C: ×400).

presenting with this reaction cannot recall any bite. Therefore, this condition was described with many terms such as (exaggerated) insect bite-like reaction, eosinophilic dermatosis of myeloproliferative disease, and exaggerated arthropod-bite reaction [5, 6, 8]. The disorder was proposed the following defining criteria [7]: (a) pruritic papules, nodules and/or vesiculobullous eruption refractory to conservative treatment; (b) eosinophil-rich lymphohistiocytic infiltrate in superficial and deep dermis; (c) excluding other causes of tissue eosinophilia and (d) preexisting diagnosis of a hematologic malignancy or dyscrasia or its subsequent development.

The clinical findings in patients with eosinophilic dermatosis of hematologic malignancy included recurring itchy papules, nodules, urticarial, vesicular and bullous lesions. Urticarial and vesicular lesions occur simultaneously in our patient. This may lead to clinically misdiagnosed as bullous pemphigoid.

Histologically the lesions were characterized by a superficial and deep-mixed inflammatory cell infiltrate containing eosinophils. Studies have shown an association between the type of the clinical manifestations (papule, vesicle, or panniculitis) and the depth of eosinophilic in filtration in the skin [2]. A heavy eosinophilic infiltration of the dermis may produce vesicobullous lesions that are seen clinically [10].

Flame figures were found in dermis in our patient. We postulate it would not seem unusual to find them in eosinophilic dermatosis of hematologic malignancy, although only one paper reported this phenomenon in this disease [8]. This figure consists of eosinophilic major basic protein deposited on collagen bundles and widespread degranulation of eosinophils. Although flame figures are not diagnostic of one clinical disorder, they are characteristic of some diseases [11]. They may be detected in other eosinophilic dermatosis associated with cutaneous eosinophilia such as eosinophilic cellulitis, bullous pemphigoid, eczema, prurigo, herpes gestationis, drug eruption, and scabies [12-14].

Eosinophilic cellulitis, also called Wells syndrome, is a rare inflammatory skin condition of unknown etiology that most commonly presents as pruritic, cellulitic-like plaques [15]. Eosinophilic cellulitis is often clinically preceded by a prodrome of itching or stinging followed by the development of annular or circinate erythematous-edematous plaques, but a wide variety of clinical pictures may present, including blistering, nodules, papulovesicular eruptions and excoriated papules [16-19]. The lesions spontaneously resolve over the course of several weeks. Eosinophilic cellulitis has also been described as showing an association with hematoproliferative diseases [20, 21]. Some authors considered eosinophilic dermatosis of hematologic malignancy and eosinophilic cellulitis in patients with hematologic disorders to be a same entity [7, 22]. There is an overlap in clinical and pathological features between eosinophilic dermatosis of hematologic malignancy and eosinophilic cellulitis: (a) Polymorphisms in the clinical features have been described in these two conditions [7, 19, 20]. (b) Both disorders are pathologically characterized by an eosinophilic infiltration, mainly in the dermis [1, 4, 19]. Very recently Farber et al. prefer the name eosinophilic dermatosis of hematologic malignancy rather than eosinophilic der-

matosis of myeloproliferative disease or insect bite-like reaction, because the new designation is a better descriptor of the pathologic process that encompasses the various hematologic malignancies associated with the eruption [1]. We believe this name is suitable for this condition in patients with hematologic malignancy. In order to clearly describe this condition in patients with hematologic malignancies, we also suggest that eosinophilic dermatosis of hematologic malignancy rather than eosinophilic cellulitis should be used in hematologic malignancy patients with this condition.

Although a variety of treatment modalities have been used for the condition, the results are still disappointing. Most frequently reported therapeutic modalities include topic and systemic corticosteroids, phototherapy, radiation, antihistamines, dapsone, interferon alpha, intravenous immunoglobulin and re-initiation of chemotherapy. Our patient achieved clinical remission with corticosteroid. It remains unclear whether eosinophilic dermatosis of hematologic malignancy has a prognostic implication for patients with hematologic malignancy.

Conclusion

In summary, we describe a patient with eosinophilic dermatosis of hematologic malignancy presenting as urticarial, vesicular lesions. Histopathologically it presented with diffuse infiltrate of eosinophils with flame figures in the dermis and subcutaneous tissue. We believe that the terminology eosinophilic dermatosis of hematologic malignancy is better than other names described in the literature for this condition in patients with hematologic malignancy.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hong Fang, Department of Dermatology, The First Affiliated Hospital, College of Medicine, Zhejiang University, No. 79, Qingchun Road, Hangzhou, 310003, Zhejiang Province, People's Republic of China. Phone: +86-571-87236385; Fax: +86-571-87236385; E-mail: fanghongzy@sina.com

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