

Eosinophilic annular erythema: A striking clinical presentation with potential systemic implications



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INTRODUCTION

Eosinophilic annular erythema (EAE) is a rare eosinophilic dermatosis of unknown etiology. It was first described in an adult patient in 2000.¹ However, annular erythema of infancy, an entity characterized by the same clinical and histologic findings, was described in the pediatric population two decades earlier.² The hallmarks of EAE include recurrent annular or polycyclic erythematous lesions that are often pruritic and are commonly found on the trunk and proximal extremities. Histopathologically, EAE is defined by prominent dermal eosinophilia. Some investigators believe that EAE is a variant of, or exists on a spectrum with, Wells syndrome (WS).^{3,4} In this report, we describe a patient who presented with an erythematous polycyclic rash with associated tissue and peripheral hypereosinophilia. We also review systemic implications of hypereosinophilia.

CASE REPORT

A 49-year-old woman reported to our dermatology clinic with a chief complaint of truncal rash present for 2 weeks. Her medical history included asthma, seropositive rheumatoid arthritis treated with hydroxychloroquine, and hypereosinophilia (3400/ μ L) with negative flow cytometry evaluation 2 years before presentation. The patient stated that the rash began as a scablike lesion on her upper back that evolved into large, red circles covering the majority of her trunk. She denied any inciting event, including change in medications or arthropod bite or

Abbreviations used:

EAE: eosinophilic annular erythema
 HES: hypereosinophilic syndrome
 WS: Wells syndrome

sting. She reported severe pruritus associated with the rash that was not relieved by 1% hydrocortisone cream. She also reported occasional cough, which she associated with her asthma. She denied having fevers, chills, abdominal pain, nausea, vomiting, diarrhea, chest pain, oral involvement, palmoplantar involvement, recent travel, or close contacts with similar findings.

On physical examination, annular and polycyclic erythematous, nonscaly plaques with indurated raised borders were noted bilaterally on the trunk (Figs 1 and 2). A 4-mm punch biopsy specimen from an advancing border on the anterior trunk was obtained for hematoxylin and eosin evaluation and revealed a dense dermal infiltrate with numerous eosinophils (Figs 3 and 4). No flame figures were present. A complete blood count with differential showed continued and increased peripheral eosinophilia (8670/ μ L). Two examinations for ova and parasites performed on the patient's stool were negative. The patient was also negative for hepatitis B and hepatitis C. On the basis of her clinical, laboratory, and histologic findings, the patient received a diagnosis of EAE. She was referred to

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Fig 1. Annular and polycyclic erythematous, smooth plaque on the trunk.



Fig 2. Annular and polycyclic erythematous, smooth plaques with indurated raised borders on the trunk.

cardiology for assessment of cardiac damage secondary to hypereosinophilia and to hematology and oncology for workup for underlying neoplastic entities that may lead to hypereosinophilia. She was started on 12.5 mg of methotrexate weekly and 5 mg of prednisone daily. She chose to discontinue hydroxychloroquine. One month later when she was seen by oncology her eosinophil count had decreased to $1240/\mu\text{L}$ and her rash had improved. The oncologic workup included screening for BCR-ABL, Janus kinase 2, calreticulin, and myeloproliferative leukemia protein mutations, which were all

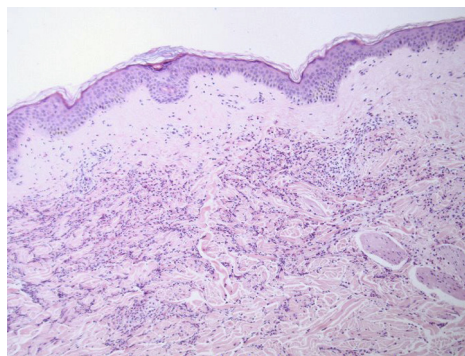


Fig 3. Results from biopsy showed a dense dermal infiltrate. (Hematoxylin-eosin stain; original magnification: $\times 10$.)

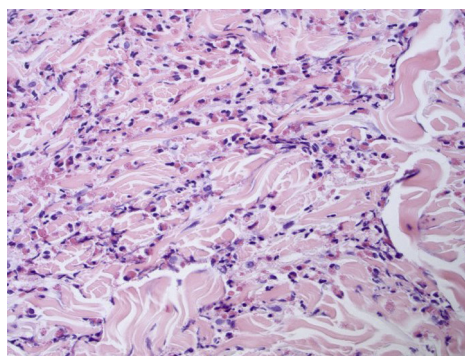


Fig 4. Higher power shows numerous eosinophils and an absence of flame figures. (Hematoxylin-eosin stain; original magnification: $\times 40$.)

negative. Tryptase level was also evaluated and found to be normal. The results of the chest x-ray and echocardiogram ordered by cardiology were unremarkable.

DISCUSSION

EAE is a rare condition characterized by recurrent erythematous annular plaques distributed on the trunk and upper extremities and tissue eosinophilia. Histopathology reveals a dense perivascular infiltrate of lymphocytes and abundant eosinophils.⁵ There is much debate in the literature about whether EAE is a distinct entity or potentially exists on a spectrum with WS. WS, also known as eosinophilic cellulitis, was originally described in 1979 as a recurrent granulomatous dermatitis with eosinophilia.³ It manifests clinically as well-defined, edematous, erythematous plaques that are often associated with a prodrome of pruritus or burning. Classically, “flame figures” composed of eosinophilic major basic protein and degenerated collagen are present histologically in WS and absent in EAE. However, a recent study showed that flame figures are often present in

longstanding cases of EAE.³ Furthermore, the peripheral eosinophil count is generally elevated in WS and was historically thought to be normal in EAE; however, cases of EAE with associated peripheral eosinophilia are also well documented.³

We agree that EAE and WS exist on a clinical spectrum. Any patient who presents with peripheral eosinophilia should be evaluated for underlying causes of eosinophilia, including, but not limited to, hypereosinophilic syndrome (HES) and infectious etiologies such as helminths and parasites. Hypereosinophilia is defined as >1500 cells/ μL in the peripheral blood on two examinations separated by at least 1 month or pathologic confirmation of tissue hypereosinophilia. HES is defined as hypereosinophilia with eosinophil-mediated organ damage that cannot be explained by another entity.⁶ In HES, eosinophilia-mediated damage commonly occurs in the skin, lungs, and gastrointestinal tract. Less commonly, patients can have life-threatening damage to the cardiovascular system and brain.⁷ The cutaneous findings reported in association with HES are broad but include polycyclic eruptions.^{7,8} Up to 37% of patients with HES have cutaneous findings.⁹ Therefore, an astute dermatologist must be aware of the possibility of underlying HES when faced with a patient with hypereosinophilia and cutaneous disease, including presentations consistent with EAE and WS. Thorough review of systems should focus on monitoring for the development of symptoms of the aforementioned organ systems. Initial studies to assess end-organ involvement include blood chemistry, electrocardiogram, echocardiogram, pulmonary function tests, chest radiograph and/or computed tomography, abdominal computed tomography, and tissue biopsies.⁷ HES is a heterogeneous disorder, and referral to other specialists is dictated by the patient's signs and symptoms. As many as 75% of cases of HES may be idiopathic; however, myeloproliferative causes of HES are well documented.⁷ Therefore, we refer all patients with unexplained hypereosinophilia to hematology and oncology.

The association of EAE with other systemic disorders has also been explored. Entities that have been reported in patients with a diagnosis of EAE include autoimmune thyroid disease, autoimmune hepatitis, autoimmune pancreatitis, chronic borreliosis, renal cell carcinoma, prostate carcinoma, chronic gastritis with *Helicobacter pylori* infection, diabetes mellitus, chronic hepatitis C infection, chronic kidney disease, eosinophilic granulomatosis with polyangiitis, and asthma.^{3,10-13} Interestingly, El-Khalawany et al³ observed that periods of proper

management of associated systemic diseases were associated with lower relapse rates and prolonged remission periods of EAE. No etiologic association between any of these disorders and EAE has been described. Although EAE can be self-limited, it is often resistant to treatment and recurrent. Individual case reports have documented response to systemic corticosteroids alone or in combination with hydroxychloroquine.³ Other therapies include dapsone, narrow-band UV B therapy, nicotinamide, indomethacin, cyclosporine, methotrexate, mycophenolate mofetil, mepolizumab, dupilumab, and suplatast tosilate.^{3,10} Our patient had complete resolution of rash and decreased eosinophilia count after initiation of 12.5 mg of methotrexate weekly and 5 mg of prednisone daily for 1 month. To date, the rash has not recurred. Our case report supports existing hypotheses that EAE and WS likely exist on a clinical spectrum and reviews important considerations when faced with a patient with cutaneous findings and peripheral hypereosinophilia.

Conflicts of interest

None disclosed.

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