Eosinophilic Annular Erythema with Benign Prognosis: A Case Report and Literature Review

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ABSTRACT:
Eosinophilic annular erythema (EAE) is a rare eosinophilic dermatosis with a chronic recurrent course of disease. EAE might be a disease spectrum of Wells syndrome or a distinctive entity[1]. We reported an EAE case with typical clinical morphology and histological findings but a rather benign clinical course. The investigations showed relatively high blood eosinophils. While most articles mentioned EAE with clinical chronicity and recurrence, there are a few reports of spontaneous resolution. Our case supports the evidence of a benign clinical course, suggesting that clinicians consider initiating less aggressive treatment in similar cases.
Key words: Eosinophilic annular erythema, Figurate erythema, Eosinophilic dermatosis, Wells syndrome

Introduction

Eosinophilic annular erythema (EAE), first described in 1981, is a rare disease that manifests as annular, erythematous papules and plaques. The lesion commonly occurs on the trunk and the extremities[2]. Typical histology includes dense perivascular infiltration with abundant eosinophils and the absent of flame figures. The disease entity was discussed whether a distinctive disorder or a variant of Wells syndrome. The disease is mostly chronic, recurrent and relapsing course[3]. The first-line treatments are antimalarial drugs and systemic corticosteroids[4].

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Case report

A 52-year-old healthy Thai female presented with progressively itchy erythematous arcuate plaques on her left flank for 6 days. Physical examination revealed two arcuate erythematous plaques on the left flank (Figure 1). Initial laboratory investigations showed a normal complete blood count without eosinophilia (eosinophils 8.1%, absolute eosinophil counts 460 cells/μL) and no parasite were found in the stool exam. The differential diagnoses included erythema annular centrifugum, EAE, Wells syndrome, granuloma annulare and creeping eruption. A skin biopsy was performed. Histology revealed dense perivascular and peri-eccrine infiltrate with lymphocytes and abundant eosinophils in a coat-sleeved pattern with slight extravasated erythrocytes (Figure 2). The diagnosis of EAE was made. Direct immunofluorescence was not performed in this case due to the nature of the lesions, which were fixed, gradually progressing, and localized to the trunk. A comprehensive examination did not reveal erythema or wheals elsewhere. Therefore, direct or indirect immunofluorescence was planned in the event of extended lesions, relapse, or recurrence. The patient was initially prescribed oral albendazole 400 mg/day for 3 days for treatment of creeping eruption without clinical improvement. Clinical progression post-treatment was observed, despite completing the 3-day course of oral albendazole (400 mg/day), indicating the treatment's ineffectiveness. Topical clobetasol cream was initiated twice daily. The lesions had completely resolved after 2 weeks of topical treatment with no reappearance in 2 years and leaving hyperpigmented patches. To identify potential underlying conditions associated with EAE, history taking and physical examination were performed, revealing no symptoms or risk factors for systemic autoimmune diseases or chronic infections, such as HBV, HCV, or HIV. The patient's physical examination was unremarkable aside from the skin lesions. Basic laboratory investigations, including a complete blood count and blood chemistry (renal and liver function, fasting blood sugar, and lipid profile), were within normal limits. Due to the lack of clinical indicators for systemic involvement and its self-limitation nature, extensive laboratory investigations were not pursued, consistent with the patient's benign clinical presentation.

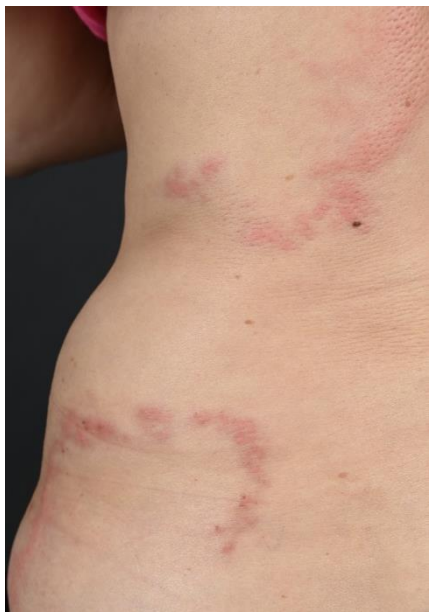

Figure 1 Two arcuate erythematous papules and plaques on the left flank

Discussion

In 1981, Peterson and Jarratt reported the first EAE as annular erythema of infancy. The first case of EAE in adults successfully treated with chloroquine was reported by Kahofer *et al*.[3]. The diagnosis was clinical and typical histopathological features, including perivascular infiltration with numerous eosinophils in the dermis. The clinical morphology of EAE presented with annular erythematous plaques with centrifugal progression, central clearing, commonly, on trunk and proximal extremities[2,4]. The lesions usually persist from days to months. Its clinical

course is mostly chronic and recurrent. Although most cases required medication, spontaneously resolving was also reported[5]. The etiology and pathogenesis of EAE is unclear. The disease entity was discussed whether it is a distinctive disorder or a variant of Wells syndrome. Histological finding of EAE includes superficial, deep perivascular and interstitial infiltration with numerous eosinophils without flame figure. However, there are reports of flame figure finding in chronological tissue biopsies from late EAE lesions[2,6]. These support that EAE and Wells syndrome share characteristics in the same spectrum of eosinophilic dermatosis.

Chronic inflammatory disease, chronic infection, and malignancies are found associated with EAE including chronic renal disease and diabetes mellitus, hepatitis C infection, chronic gastritis with Helicobacter pylori, eosinophilic granulomatosis with polyangiitis, autoimmune thyroid disease, malignant solid tumor[1,4].

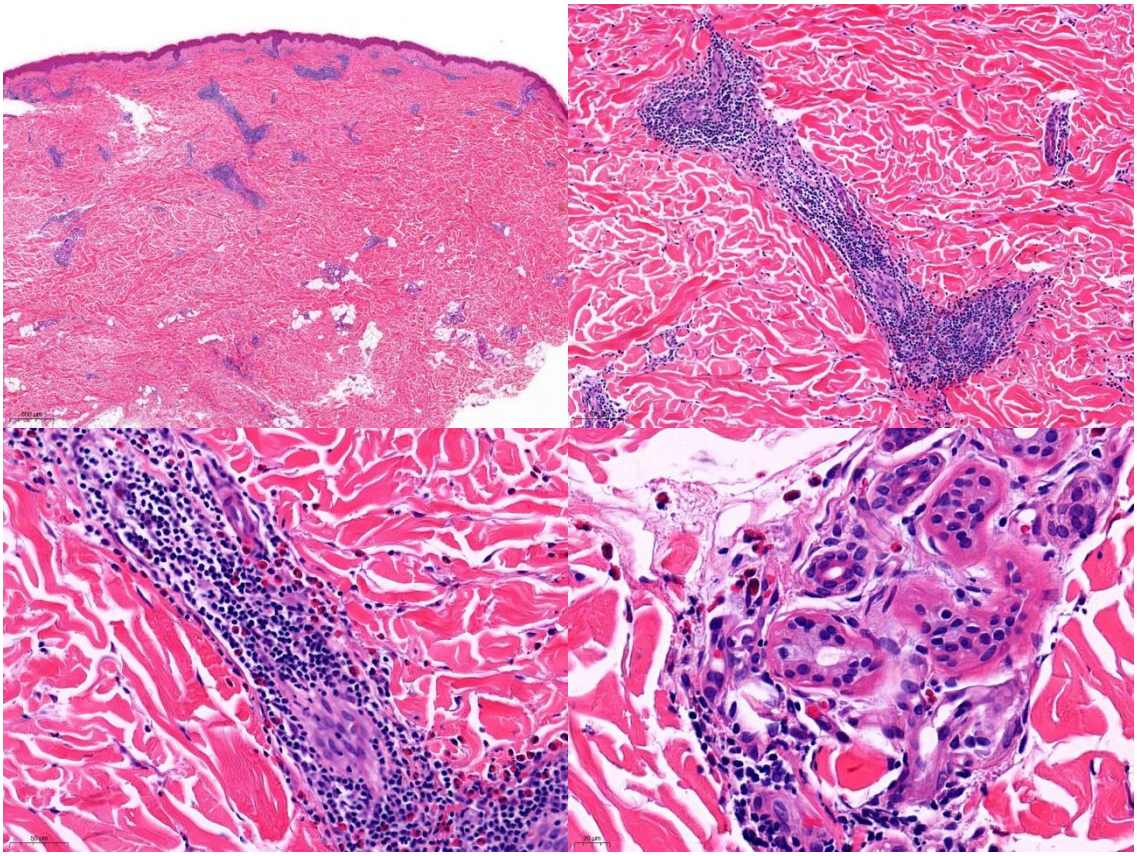

Figure 2. The H&E section revealed dense superficial and deep perivascular and peri-eccrine infiltrate with lymphocytes with abundant eosinophils in a coat-sleeved pattern with slight extravasated erythrocytes.

Table 1 Clinical presentation, histology and treatment outcome of reported eosinophilic annular erythema

Authors (year of publication)	Morphology	Peripheral eosinophilia	Histology	Treatment response	Key point
Rongioletti et al (2011)[2]	Annular erythema	Not available	**Early lesions:** - Dense infiltrate with lymphocytes and abundant eosinophils - Absence of flame figures **Well-developed lesions:** - Presence of flame figures - Presence of granulomatous infiltrate	Response to oral indomethacin, prednisone, or HCQ	The first report of flame figures from repeated biopsy of EAE
El-Khalawany (2013)[6]	Annular erythema with slightly atrophied center in long-standing lesion	Yes; high in the advance stage of disease	**Early lesions:** - Moderate dermal infiltrate with eosinophilic degranulation - Absence of flame figures **Well-developed lesions:** - More interstitial distribution - More eosinophilic degranulation - Presence of flame figures in some cases **Long-standing lesions:** - Dense diffuse dermal infiltrate - Presence of flame figures in all cases - Presence of granulomatous infiltration	No effective treatment achieved a permanent cure and relapse in all cases	EAE is a spectrum of WS, which has a chronic course, treatment resistance, and common relapse. Close monitoring and reevaluation are needed for the diagnosis.
Heras et al. (2017)[1]	Annular erythema	No	- Eosinophilic dermal, mainly perivascular, infiltrate - Absence of flame figures	Response to topical corticosteroid but recurrence	The absence of peripheral eosinophilia and good pharmacological response of EAE are differentiating characters to WS.
Dacy et al (2021)[5]	Annular erythema	No	- Perivascular and interstitial infiltrate with numerous eosinophils - Absence of flame figures - No evidence of vasculitis	Response to prednisolone and HCQ, with chronic relapsing-remitting course	Most cases require treatment. However, spontaneous resolution can be observed in 4 to 12 months.
Gray et al (2021)[7]	Annular erythema	Yes	- Dense dermal infiltration with numerous eosinophils - Absence of flame figures	Complete resolution with MTX and prednisolone	EAE is often resistant to treatment and recurrent. But spontaneous resolution can be observed.
Lachance et al (2023)[8]	Annular erythema or Urticarial vasculitis-like lesion	Yes	- Eosinophilic spongiotic dermatitis with intraepidermal vesicles - Absence of flame figures - No evidence of vasculitis	Complete remission with dapsone	Extensive lesions and peripheral eosinophilia can predict a failure of systemic prednisolone as a monotherapy.
Present study	Annular erythema	No	- Perivascular and peri-eccrine infiltrate with abundant eosinophils in a coat-sleeved pattern - Absence of flame figure - No evidence of vasculitis	Complete response to topical corticosteroid	EAE might be a spectrum of Wells syndrome with milder symptoms, subtle tissue eosinophilia, no flame figures, and no peripheral eosinophilia. Initial less aggressive treatment should be considered.

EAE = Eosinophilic annular erythema; WS = Wells syndrome; MTX = Methotrexate; HCQ = Hydroxychloroquine

Table 1 presents a summary of previously reported cases of EAE, including their clinical characteristics, treatments, and outcomes.[1, 2, 5-8] Drugs of choice for EAE treatments are topical corticosteroids, systemic corticosteroids, and antimalarial drugs. Other treatments include dapsone, indomethacin, nicotinamide, methotrexate, mepolizumab, dupilumab, baricitinib, and phototherapy[4]. Clinical relapse commonly occurs after discontinuing medications. EAE can spontaneously resolve in 4 to 12 months therefore, the initial therapy should not be aggressive[9].

In our reported case, the diagnosis was made by clinical annular erythema, the absence of blood eosinophilia, and key histologic findings of dense perivascular infiltration with numerous eosinophils without flame figures. Interestingly, our case had relatively high blood eosinophil without definite eosinophilia[10], since the calculated circulating eosinophil did not reach 500/mm^2. In this circumstance, we suggest that EAE might be a spectrum of Wells syndrome with milder symptoms, subtle tissue eosinophilia, no flame figures, and no peripheral eosinophilia. The case represented an EAE with benign prognosis and complete resolution.

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