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Eosinophilic annular erythema: four additional cases and a review of the literature on therapeutic options

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Abstract

Eosinophilic annular erythema (EAE) is a rare, benign dermatosis characterized by recurrent erythematous-urticarial plaques and tissue eosinophilia. Its cause is unknown, though it may involve hypersensitivity to an unidentified antigen. EAE typically follows a chronic, relapsing course, affecting the trunk and extremities. Treatment guidelines are lacking, and therapy responses vary. This study presents four new cases and reviews current treatment options. Four patients with EAE, aged 20 to 72, were treated at Galliera Hospital (Genova, Italy). They exhibited erythematous, annular lesions on the trunk or extremities with variable pruritus. Histology confirmed eosinophilic inflammation without flame figures. Previous systemic steroid treatments provided partial improvement but resulted in relapse. Topical clobetasol improved symptoms in two of three patients, while systemic methylprednisolone also showed benefit. However, one patient on topical clobetasol and another on systemic methylprednisolone were lost to follow-up. A search in PubMed until July 2024 identified English-language articles with histologically confirmed EAE and clear treatment outcomes. Antimalarial drugs, dapsone, and corticosteroids were the most frequently prescribed non-biological therapies leading to disease control. Other effective treatments in individual cases included nicotinamide, doxycycline, and narrow-band ultraviolet-B (UV-B) phototherapy. Biological drugs such as dupilumab, benralizumab, and mepolizumab showed promising results. The treatment of EAE remains challenging, with many cases resistant to antimalarials, dapsone, and corticosteroids. Further research is necessary to identify more effective treatments. Targeting T-helper 2 (Th2)-type cytokines with specific antibodies may offer a promising approach for refractory EAE, potentially providing a rapid and sustained clinical response.

Introduction

Eosinophilic annular erythema (EAE) is a rare, benign dermatosis characterized by recurrent annular and figurate erythematous-urticarial plaques associated with tissue eosinophilia. The disease typically follows a chronic, relapsing-remitting course.[1,2] Lesions are typically pruritic and develop in a centrifugal growth pattern, primarily affecting the trunk and the extremities.[1] Histologically, EAE is characterized by a dense superficial and deep perivascular lymphohistiocytic infiltrate rich in eosinophils, in the absence of “flame figures” (eosinophilic major basic protein and degenerated collagen).[2,3] Some authors consider EAE a subtype of Wells syndrome (WS, or eosinophilic cellulitis) with a more superficial eosinophilic infiltrate.[2] However, others dispute this classification due to differences in clinical presentation, histopathology, and disease course. WS often manifests as burning, painful, erythematous nodules or plaques resembling cellulitis, while EAE presents with a pruritic annular rash with central pigmentation and elevated borders.[2,4] Histologically, both conditions

show eosinophilic infiltration, but EAE often lacks the characteristic “flame figures” that are a hallmark of WS, especially in early lesions – though these may occasionally appear in well-developed or long-standing cases.[2,5,6] Additionally, WS is usually self-limiting and responds well to corticosteroids, while EAE tends to follow a chronic course with frequent relapses and resistance to treatment.[2,4] The etiology and pathogenesis of EAE remain unclear, but it is hypothesized to represent a hypersensitivity reaction to an unidentified antigen, such as an allergic stimulus or insect bites.[5,7] EAE has been associated with various diseases, including autoimmune disorders, borreliosis, *Helicobacter pylori* infection, chronic hepatitis C, diabetes, and kidney disease. There are also a few reports of EAE developing in association with internal malignancy, such as thymoma, metastatic prostate adenocarcinoma, breast cancer, cervical cancer, and renal cancer.[8] Many annular dermatoses should be considered in the differential diagnosis of annular eosinophilic erythema. These include secondary syphilis, which may present with atypical, itchy, psoriasiform plaques; erythema annulare centrifugum, characterized by annular patches with trailing scale often linked to infections or medications; granuloma annulare, presenting as nonscaly plaques with firm borders, typically on the extremities; erythema migrans, an early sign of Lyme disease, presenting as an annular erythematous macule with central clearing; erythema gyratum repens, often paraneoplastic, featuring concentric erythematous bands with a wood-grain appearance; pityriasis rosea, which presents with multiple scaly, annular lesions and is usually self-limiting; subacute cutaneous lupus erythematosus, which can manifest as annular or papulosquamous lesions on sun-exposed areas; and lichen planus, presenting with pruritic, violaceous, polygonal papules that may occasionally form annular patterns.[9-12] Generally, EAE is resistant to multiple treatments and is characterized by a chronic relapsing and remitting course. Rarely, the disease can be self-limited and could resolve with no treatment.[1,5,7] To date, there are no established treatment guidelines for EAE, with only a few cases responding to various drugs. Furthermore, there are reports of relapse of the condition after discontinuation of these therapies.[13] Given the scarcity of literature and the absence of consensus guidelines, we aim to contribute to a better understanding of therapeutic options for eosinophilic annular erythema. To this end, we present four additional cases of EAE diagnosed at the Dermatology Unit of Galliera Hospital (Genoa, Italy), accompanied by a comprehensive literature review with particular focus on treatment options and their reported efficacy.

Case Series

Four patients were observed at the Dermatology Unit of Galliera Hospital between 2017 and 2023, all exhibiting shared clinical and histopathological features of EAE. The patients included two men and two women, ranging in age from 20 to 72 years (mean age 35.5 years). Three of the patients had

no comorbidities and were not on any medication, while one was under treatment having a history of cardiovascular disease, bipolar disorder, and depression. Clinically, all patients presented with an erythematous rash with an annular or polycyclic pattern involving the trunk or the extremities (Figure 1). Pruritus was an inconstant and variable feature. The lesions followed a chronic-remitting course, with a duration ranging from 1 to 7 years (mean duration 4 years). Prior to admission, all patients had been treated with systemic steroids, resulting in only partial improvement and subsequent relapse during the tapering of steroids. In all cases, histological examination revealed both superficial and deep perivascular and interstitial lymphocytic inflammation with numerous eosinophils. There were no flame figures, plasma cells, or evidence of vasculitis (Figure 2). All patients underwent abdominal ultrasonography and laboratory tests, including complete blood count with differential, liver and renal function tests, hepatitis serology, blood glucose, antinuclear antibodies, and prostate-specific antigen test in men, all of which returned normal results. Considering the clinical presentation, chronic-remitting course, and histological findings, the patients were diagnosed with EAE. Treatment was initiated with topical steroids for three patients and systemic steroids for one. The therapeutic response was assessed clinically, focusing on lesion size reduction, improvement in erythema, and relief of pruritus. Among the patients treated with topical clobetasol, two showed improvement in both the rash and pruritus, with stable disease after 1 year of follow-up. The third patient also demonstrated clinical improvement; however, this patient was lost to follow-up. The fourth patient was treated with systemic methylprednisolone at a dose of 16 mg/day, which was gradually tapered over several weeks. This patient likewise showed improvement but was subsequently lost to follow-up. It is important to note that follow-up duration varied among patients, and two were lost to follow-up, thereby limiting the assessment of long-term treatment efficacy. Patient characteristics and treatment regimens are summarized in Table 1.

Review of the literature

Although EAE is generally regarded as a benign condition with a favorable prognosis, the relapsing and remitting cycles, along with patients' discomfort, justifies a therapeutic intervention. Currently, there are no established treatment guidelines for this condition in the literature. Several therapeutic approaches have been reported, including oral corticosteroids, indomethacin, doxycycline, hydroxychloroquine, methotrexate, dapsone, nicotinamide, or narrowband ultraviolet-B (UV-B) phototherapy.[8] Furthermore, there are reports on the use of biological drugs that target the T-helper 2 (Th2)-type cytokines, such as dupilumab, mepolizumab, and benralizumab.[13] To review the therapeutic options for EAE, a PubMed search was conducted using the key words "Eosinophilic Annular Erythema" and "EAE", screening all published data up to July 2024 (Figure 3). Additionally,

potentially relevant papers were identified by manually checking the references of the included literature. All selected articles underwent a full-text assessment to determine their eligibility. Inclusion criteria comprised English-written articles presenting cases compatible with EAE with histological confirmation (eosinophil infiltration, absence of "flame figures"), that showed improvement or successful treatment, with subsequent disease control and no recurrence at follow-up. Additionally, inclusion criteria required cases to provide precise reports of the dosage of the drugs successfully used in the treatment of EAE. Exclusion criteria applied to cases that, despite being clinically compatible with EAE, had incompatible histological findings (such as the presence of "flame figures"). Cases were also excluded if the treatment outcomes could not be clearly established for individual patients or if the precise dosages of the effective drugs were not reliably reported.

After applying the selection criteria, 21 publications were identified that met the inclusion and exclusion standards, encompassing a total of 21 cases of EAE. Among the selected cases, 13 patients were women (61.9%) and 8 were men (38.1%). Ages ranged from 8 to 83 years, with a mean age of 50.7 years. The rash was pruritic in 17 out of 21 patients (81%). The duration from onset to admission varied from 2 weeks to over 9 years, with a mean duration of 32.6 months.

Our analysis revealed that antimalarial drugs, specifically hydroxychloroquine and chloroquine, were the most frequently prescribed treatments, used in 6 (28%) out of 21 cases. Hydroxychloroquine was employed in 4 cases. In two cases, a dosage of 200 mg twice daily resulted in complete resolution – one case after 10 weeks and the other after 1 month, the latter also receiving topical steroids; no recurrence was observed after 1 year and 16 months of follow-up, respectively.[14,15] Another case achieved resolution with a 6-month treatment at a dosage of 6.5 mg/kg/day, with no relapse noted after 6 months of follow-up.[16] Lastly, one patient with a long-standing course of the disease showed improvement and disease control after a three-year treatment with varying dosages of 200 to 400 mg/day.[17] Chloroquine was administered in 3 cases. In two instances, a dosage of 250 mg/day led to resolution. In the first case, chloroquine was initially administered at 4 mg/kg/day for 10 days before being reduced to 250 mg/day for 10 weeks; in the second case, it was prescribed for 1 month. Follow-up data indicated no recurrence after 2 years and 9 months, respectively.[18,19] In another case, a patient was treated with prednisone (0.5 mg/kg/day) and chloroquine (4 mg/kg/day). Prednisone was tapered and discontinued after 2 months, while chloroquine was maintained for 1 year, leading to complete resolution and no relapse.[20]

Dapsone led to resolution in 3 (14%) out of 21 cases. In two cases, the drug resulted in complete resolution of the rash, administered at dosages of 25 mg/day for 3 weeks and 100 mg/day for 4 weeks. In the first case, no relapse was observed after 8 months of follow-up; in the second case, the disease remained in clinical remission after 5 months on 75 mg/day of dapsone.[21,22] In another case, complete

clearance was achieved after 1 week of treatment with dapsone at 100 mg/day, which was then maintained at the same dosage for 1 year. However, attempts to reduce the dosage led to early relapse.[23]

Regarding Dupilumab, it was effectively used in 3 (14%) out of 21 cases at a dosage of 600 mg subcutaneously on day 0, followed by 300 mg subcutaneously every 2 weeks.[24-26] In all three cases, a dramatic response was observed after the second injection, with complete resolution of the rash. At the time of publication, all three patients were still receiving treatment with 300 mg subcutaneously every 2 weeks, with no recurrence reported.

Both topical and systemic corticosteroids alone controlled EAE in 2 (10%) out of 21 cases. In one case, the application of betamethasone dipropionate ointment for 1 month led to the resolution of the rash, although no follow-up data are available for this case.[27] In another case, a complete response was achieved with intravenous methylprednisolone administered at a dosage of 10 mg/kg/day for 3 days, followed by 0.5 mg/kg/day for 2 months. No recurrence was observed after 2 months of follow-up.[28]

Benralizumab administration resulted in a complete response in 2 (10%) out of 21 cases. The treatment regimen involved 30 mg subcutaneously every 4 weeks for the first 3 doses, followed by 30 mg every 8 weeks.[13,29] In one case, rapid and complete resolution occurred during the induction phase, with minimal lesions appearing just before the next scheduled dose [13]. No follow-up data were available for the other case.[29]

Mepolizumab was prescribed in 1 (5%) out of 21 cases at a dosage of 100 mg subcutaneously every 4 weeks for 3 doses, leading to almost complete resolution of the rash 1 month after the third injection. No relapse was observed at 6 months of follow-up, although some residual skin changes on the lower legs persisted.[8]

Nicotinamide was effective in 1 (5%) out of 21 cases, administered at a dosage of 900 mg/day for 1 year, with no recurrences observed after 1 year of follow-up.[30]

Doxycycline, used in 1 (5%) out of 21 cases, led to significant improvement at a dosage of 100 mg BID for 3 months, with resolution of the rash reported after 1 year of follow-up. Notably, the condition flared during a period of drug cessation while awaiting a refill.[31]

Narrow-band ultraviolet B phototherapy, applied in 1 (5%) out of 21 cases, achieved complete resolution of EAE after eight sessions, with no recurrence observed 9 months after completing the light treatment.[4]

It is worth noting that there have been reports of improvement with other treatments such as indomethacin (25 mg three times per day for 4 weeks), methotrexate (10 mg/week for 2 weeks), and mycophenolate mofetil (500 mg twice daily, then 500 mg/day for 10 weeks). In particular,

indomethacin led to a striking response. However, due to the emergence of side effects, these treatments were discontinued, and no follow-up data are available. Therefore, these treatments were not included in the analysis.[17,32]

Additionally, we highlight a case of EAE with an unusual localization on the palms and soles, which coexisted with thymoma. Although this association may be coincidental, thymectomy led to complete resolution of the rash, suggesting a potential role of thymoma in the pathogenesis of EAE in this instance. Since no medical treatment was used to resolve the rash in this case, the article was not included in the analysis.[33] Data on the patients and their respective treatments are shown in Table 2.

Discussion

Due to its rarity, there are only 49 articles on EAE currently available in the literature, with no clinical trials or randomized controlled studies. As a result, the analysis relies exclusively on anecdotal case reports and small case series. Moreover, more than half of the available reports (55%) were incomplete and had to be excluded from our review. These limitations highlight not only the gaps in current knowledge but also the need for more structured research efforts. In particular, the development of multicenter collaborative studies would be essential to collect standardized clinical data, better understand treatment responses, and ultimately guide evidence-based management of EAE. In the absence of formal treatment guidelines for EAE, it is not possible to categorize therapies into clear first-line, second-line, or experimental approaches. However, certain medications have been used more frequently and reported in a greater number of cases, suggesting they may be more effective.

According to our detailed analysis, antimalarial drugs (28%), dapsone (14%), and corticosteroids (10%) were the most frequently prescribed non-biological therapies. The literature suggests that when antimalarials are effective, they can lead to significant improvement within 2 to 4 weeks.[8] However, our analysis indicates that these treatments may need to be continued for several months or even years to achieve disease control.[16,17,20] Dapsone therapy appears to lead to a faster resolution of the rash, typically within 1 to 4 weeks; nevertheless, maintenance therapy may be necessary to prevent relapses.[23] Topical and systemic corticosteroids controlled the rash within 4 to 8 weeks.[27,28] It has been observed that, in refractory patients, a combination of systemic corticosteroids and hydroxychloroquine was associated with an 88% rate of complete clinical response.[6] Despite these therapeutic options, many cases resistant to antimalarials, dapsone, and corticosteroids have been reported.[1-3,18,24] In addition, there are accounts of the condition recurring after these therapies are discontinued.[13]

Although further studies are needed to consolidate these observations, biological drugs that target the Th2-type cytokines such as dupilumab, benralizumab, and mepolizumab appear to be promising options for treating EAE. When prescribed, these biologics have led to rapid and complete resolution of both the rash and symptoms. To date, there are no reports of EAE being unresponsive to these therapies. Specifically, dupilumab has shown an impressive response, with significant improvement observed after the second injection (approximately 2 weeks after initiation).[24-26] Benralizumab and mepolizumab also demonstrated effective responses, though slightly slower. For benralizumab, limited lesions appeared as the next dose approached, while with mepolizumab, some residual skin changes on the lower legs persisted, but no relapse was reported.[8,13]

The pathogenesis of EAE is not fully understood, but dysregulated tissue eosinophilia is considered a crucial factor. Interleukin 5 (IL-5), produced by Th2 lymphocytes, mast cells, natural killer cells, and eosinophils themselves, plays a significant role. IL-5 induces the migration of eosinophils from the bone marrow into the bloodstream. Along with Th2-derived cytokines IL-4 and IL-13, IL-5 promotes eosinophil activation and tissue recruitment. By binding to IL-5Rα, IL-5 activates Janus kinase 2 (JAK2)/signal transducer and activator of transcription 5 (STAT5) and rat sarcoma/mitogen-activated protein kinase (RAS/MAPK) pathways, which are involved in eosinophil growth, survival, and degranulation.[13,34] The biological drugs mentioned specifically interfere with eosinophilic activation through various mechanisms, supporting the hypothesis that dermal eosinophil infiltration in EAE may result from immune dysregulation. Dupilumab, prescribed for patients with atopic dermatitis, is a dual inhibitor of IL-4 and IL-13. Mepolizumab inhibits IL-5, while benralizumab targets IL-5Rα; both are primarily prescribed for the treatment of severe eosinophilic asthma.[35] However, mepolizumab has also shown effectiveness in eosinophilic pustular folliculitis, severe eosinophilic granulomatosis with polyangiitis, and eosinophilic fasciitis.[36-38] Currently, there is no long-term follow-up data on the use of these drugs in EAE, nor information on relapse if treatment is suspended. According to the literature, these therapies have proven to be safe and well-tolerated in the context of long-term use, which may be necessary given the course of EAE.[39-41] While further research is needed, antibodies targeting the Th2-type cytokines could be an effective therapy for patients with recalcitrant EAE and potentially serve as a first-line treatment, leading to a rapid clinical response that is sustained over time.

Conclusions

EAE remains a rare and poorly understood dermatologic condition, with no established treatment guidelines and limited evidence derived mainly from anecdotal case reports and small case series. In our experience, topical and systemic corticosteroids provided partial improvement, although long-

term efficacy could not be definitively assessed due to the variable duration of follow-up and loss of two patients to follow-up. Our review of the literature highlights antimalarial drugs, dapsone, and corticosteroids as the most frequently used non-biologic therapies, although treatment resistance and disease recurrence after discontinuation are common. In contrast, biologic agents targeting Th2-type cytokines, such as dupilumab, benralizumab, and mepolizumab, have shown promising results, with rapid and sustained resolution of symptoms in reported cases, and appear to be safe for long-term use. Nonetheless, the current body of literature is subject to significant limitations, most notably the predominance of anecdotal reports and a likely publication bias favoring cases with successful treatment outcomes. These factors may lead to an overestimation of therapeutic efficacy and reduce the generalizability of the available evidence. Given the rarity of EAE and the lack of controlled studies, future research should prioritize prospective, multicenter investigations designed to systematically assess treatment effectiveness, clarify the role of biologic therapies, and establish standardized clinical endpoints for evaluating therapeutic response.

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Figure 1. A) Erythemaous annular polycyclic plaques on the trunk of a 20-year-old man (Case 1); **B**) right arm of a 72-year-old man (Case 2); **C**) trunk of a 23-year-old woman (Case 3); **D**) right knee of a 27-year-old woman (Case 4).

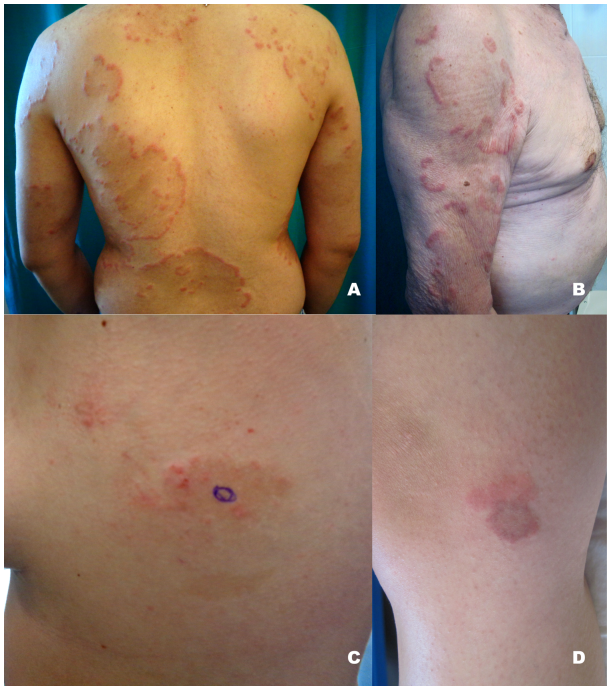

Figure 2. A) Superficial and deep mainly perivascular infiltrate under uninvolved epidermis (Case 1; HE, 40x); **B**) lymphocytic infiltrate with eosinophils (Case 1; HE, 400x); **C**) superficial and deep mainly perivascular infiltrate under normal epidermis (Case 4; HE, 40x); **D**) heavy lymphocytic infiltrate with eosinophils (Case 4; HE, 400x); **E**) superficial and deep and interstitial infiltrate (Case 2; HE, 40x); **F**) intraepidermal pustules with serum, lymphocutes and eosinophils (Case 2; HE, 400x).

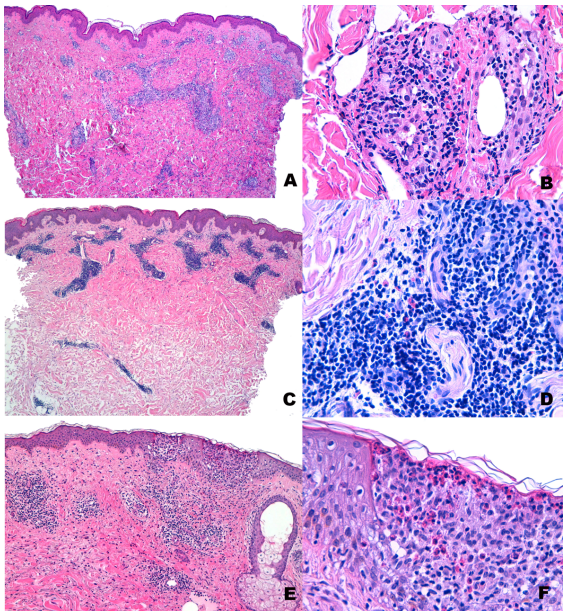

Figure 3. PRISMA flow diagram.

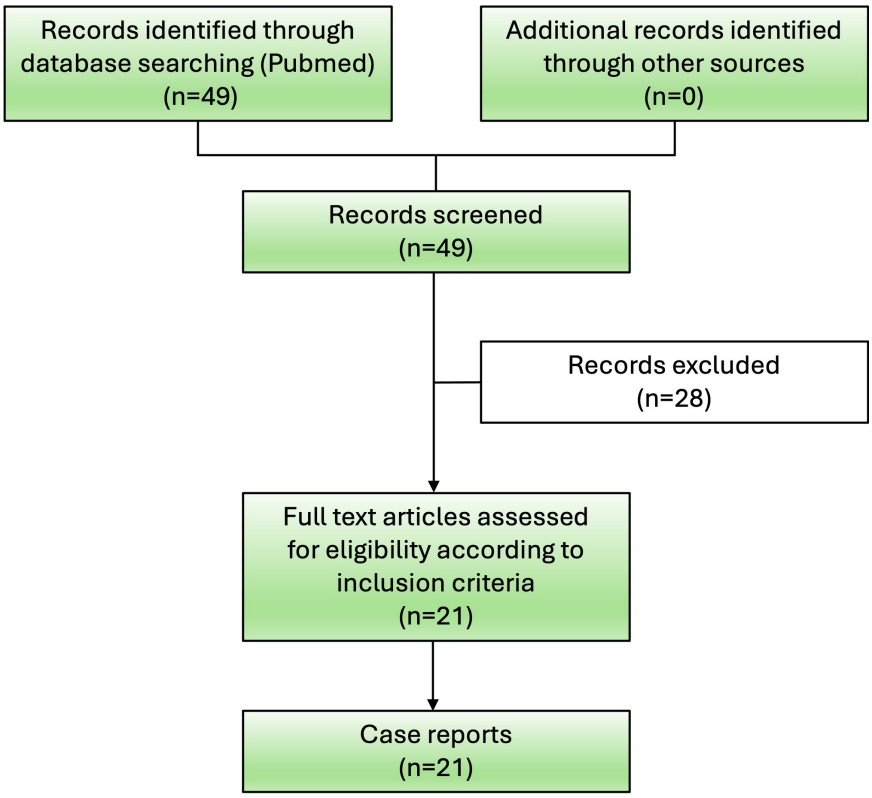

Table 1. Cases of EAE observed at the Dermatology Unit of Galliera Hospital (Genova, Italy).

Patient	**Age (years); sex**	**Localization**	**Time from onset to admission**	**Comorbidities and medications**	**Additional information**	**Management**	**Evolution**
Case 1	20; M	Trunk, arms	1 year	-	-	Topical clobetasol 1 application/day	Lost at follow-up
Case 2	72; M	Arms, legs	3 years	Pantoprazole, trazodone, low-dose aspirin, clopidogrel, dibase, ezetimibe, rosuvastatin, quetiapine	-	Methylprednisolone 16 mg, slowly tapered	Lost at follow-up
Case 3	23; W	Trunk	1 year	-	-	Topical clobetasol 1 application/day	Stable disease after 1 year of follow-up
Case 4	27; W	Right knee	7 years	-	-	Topical clobetasol 1 application/day	Stable disease after 1 year of follow-up

W, woman; M, man.

Table 2. Cases of EAE and relative therapeutic regimens that led to improvement or resolution of the rash, with control over the disease.

Author, year	Age (years); sex	Localization	Time from onset to admission	Comorbidities and medications	Additional information	Management	Outcome	Evolution
Alharbi *et al.*, 2017[18]	60; W	Face, trunk, extremities	6 months	-	-	Dapsone 100 mg/day	Resolution after 1 week	Under maintenance with dapsone 100 mg/daily for 1 year
Bolado *et al.*, 2023[8]	83; W	Face, neck, trunk, extremities	8 years	Macular hole	-	Benralizumab 30 mg s.c., q4wk for the first 3 doses, then q8wk	Resolution	Under maintenance with benralizumab, limited lesions arise when the next dose time approached
Chaabani *et al.*, 2020[10]	28; M	Trunk, then buttocks, upper and lower limbs	3 months	-	-	Hydroxychloroquine 200 mg BID x 1 month + topical steroids	Resolution	No relapse after 1 year of follow-up
Eljazouly *et al.*, 2022[11]	31; M	Trunk, limbs, glutes	2 weeks	-	-	Hydroxychloroquine 6.5 mg/kg/day x 6 months	Resolution	No relapse after 6 months of follow up
Gordon *et al.*, 2018[19]	14; W	Lower extremities, then arms, trunk, forehead	-	-	-	Dupilumab 600 mg s.c. for induction, then 300 mg every 2 weeks	Resolution	Under maintenance with dupilumab with no relapse
Howes *et al.*, 2008[12]	52; W	Trunk, limbs	3 years	Lethargy, arthralgia	-	Hydroxychloroquine 200-400 mg/day x 3 years	Improvement	Disease flares if hydroxychloroquine is suspended
Ikutama *et al.*, 2023[22]	82; M	Trunk, thighs	2 weeks	Transient hypothyroidism	-	Betamethasone dipropionate ointment x 1 month	Resolution	No relapse
Kahofer *et al.*, 2000[13]	62; W	Trunk, extremities	9 years	Thyroiditis, chronic tonsillitis; thyrostatic treatment 10 years before admission	*Borrelia burgdorferi* IgG+++	Chloroquine 250 mg/day x 1 month	Resolution	No relapse after 9 months of follow-up

Karatas *et al.*, 2017[9]	69; W	Trunk, neck, extremities	12 months	Autoimmune thyroiditis; levothyroxine sodium	-	Hydroxychloroquine 200 mg BID x 10 weeks	Resolution	No relapse after 16 months of follow-up
Kim *et al.*, 2017[23]	73; M	Trunk	-	Chronic kidney disease, asthma, Churg-Strauss disease		Intravenous methylprednisolone 10 mg/kg x 3 days, then 0.5 mg/kg x 2 months	Resolution	No relapse after 2 months of follow-up
Lachance *et al.*, 2023[16]	57; W	Left thigh, then trunk, arms and legs	1 month	Mitral prolapse operated; aspirin, citalopram, bupropion	-	Dapsone 100 mg/day x 4 weeks	Resolution	Under maintenance with dapsone 75 mg/day, no relapse after 5 months of follow-up
Ljubojevic *et al.*, 2018[14]	59; M	Back, glutes, extremities	1 month	-	-	Chloroquine 4 mg/kg/day x 10 days, then 250 mg day x 10 weeks	Resolution	No relapse after 2 years of follow-up
Maione *et al.*, 2020[21]	56; W	Trunk, limbs	7 years	-	-	Dupilumab 600 mg s.c. for induction, then 300 mg every 2 weeks	Resolution	Under maintenance with dupilumab, with no relapse after 6 months of follow-up
Manriquez *et al.*, 2014[17]	29; W	Trunk, proximal extremities	12 months	Type I diabetes mellitus, chronic kidney disease	-	Dapsone 25 mg/day x 3 weeks	Resolution	No relapse after 8 months of follow-up
Masaki *et al.*, 2021[24]	56; W	Back	-	Asthma, eosinophilic chronic rhinosinusitis	Angioedema and asthma attack presented along with the rash	Benralizumab 30 mg s.c., q4wk for the first 3 doses, then q8wk	Resolution	Data not available
Mebazaa *et al.*, 2009[15]	30; W	Trunk, limbs	-	-	-	Prednisone x 2 months + chloroquine 4 mg/kg/day x 1 year	Resolution	No relapse after 1 year of follow-up
Ogawa *et*	65; M	Trunk, extremities	-	Autoimmune	-	Nicotinamide p.o. 900 mg/day x 1 year	Resolution	No relapse after 1 year of follow-up

al., 2016[25]				pancreatitis, diabetes mellitus				
Okazaki *et al.*, 2024[20]	47; W	Trunk, extremities	4 years	-	-	Dupilumab 600 mg s.c. for induction, then 300 mg every 2 weeks	Resolution	Under maintenance with dupilumab, with no relapse after 4 months of follow-up
Thomas *et al.*, 2015[27]	8; M	Face	4 months	-	*Borrelia burgdorferi* IgG+	NB-UVB x 8 session	Resolution	No relapse after 9 months of follow-up
Young *et al.*, 2023[26]	39; M	Back, buttocks, genitals	Over 9 years	-	*Borrelia burgdorferi* IgM+ 8 years before presentation	Doxycycline 100 mg BID x 3 months	Resolution	Resolution after 1 year of follow-up. The rash flared during a period of drug cessation
Żychowska *et al.*, 2020[7]	65; W	Extremities	2 months	-	-	Mepolizumab 100 mg s.c. q4wk for 3 times	Resolution	No relapse after 6 months from the 3rd dose

W, woman; M, man; s.c., subcutaneous; q4wk, every 4 weeks; q8wk, every 8 weeks; BID, *bis in die* (twice daily); p.o., *per os* (orally); NB-UVB, narrowband ultraviolet-B.