

**RAPID AND SUSTAINED RESPONSE TO SHORT-COURSE ORAL AZITHROMYCIN IN RECALCITRANT ERYTHEMA ANNULARE CENTRIFUGUM: A CASE REPORT****Mustafa Alperen Aydeniz^{1*}**¹Department of Dermatology and Venereology, Siirt Training and Research Hospital, Siirt, Turkey.

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***Corresponding Author: Mustafa Alperen Aydeniz**

Department of Dermatology and Venereology, Siirt Training and Research Hospital, Siirt, Turkey.

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ABSTRACT

Erythema annulare centrifugum (EAC) is an inflammatory dermatosis for which no standardized treatment approach has been established. We present a 36-year-old woman with recalcitrant EAC lesions persisting for one year who had failed to respond to previous topical and systemic corticosteroids and oral itraconazole. The patient was treated with oral azithromycin 500 mg/day for three days. Complete resolution of the lesions was observed by day 10, with no new lesions developing during the three-month follow-up period. This case highlights short-course oral azithromycin as a potential therapeutic option for recalcitrant EAC.

KEYWORDS: Azithromycin; erythema annulare centrifugum; macrolide; recalcitrant; treatment.**INTRODUCTION**

Erythema annulare centrifugum (EAC) is an inflammatory dermatosis characterized by annular erythematous lesions that expand peripherally. Classified among the reactive erythemas, EAC has been associated with various triggering factors, including infections, medications, systemic diseases, and malignancies.^[1] Clinically, EAC is classified into superficial and deep variants. Although lesions may persist for weeks or months, they generally resolve without scarring.^[2,3]

Elimination of an identifiable triggering factor is the primary approach to the management of EAC; however, no standardized treatment has been established. Successful outcomes with various treatments, including azithromycin, erythromycin, fluconazole, metronidazole, and doxycycline, have been reported in recalcitrant cases.^[3-8] Herein, we report a patient with recalcitrant EAC unresponsive to previous topical and systemic corticosteroids and oral antifungal therapy who achieved a rapid and sustained clinical response following a three-day course of oral azithromycin.

CASE REPORT

A 36-year-old woman with no known systemic disease presented to our clinic with a one-year history of annular skin lesions. She had previously received topical and systemic corticosteroids as well as oral itraconazole at different times, without clinical improvement. Dermatological examination revealed erythematous annular plaques with central clearing on both thighs (Fig. 1). Fine scaling was noted along the inner margin of the erythematous peripheral border. Based on the clinical findings, superficial EAC was suspected, and a skin biopsy was performed. Histopathological examination revealed orthokeratosis and focal parakeratosis, mild epidermal acanthosis and spongiosis, and a superficial dermal perivascular cuff-like lymphocytic infiltrate (Fig. 2). The histopathological findings, together with the clinical features, were consistent with superficial EAC. Evaluation for potential underlying diseases and triggering factors associated with EAC revealed no significant abnormalities on routine laboratory investigations. Internal medicine consultation identified no associated systemic pathology. The patient was treated with oral azithromycin 500 mg/day for three days. Complete clinical resolution of the lesions was observed by day 10 (Fig. 3). No new lesions developed during the three-month follow-up period.



Fig. 1: Erythematous annular plaque with central clearing on the right thigh, showing characteristic fine trailing scale along the inner margin of the peripheral erythematous border.

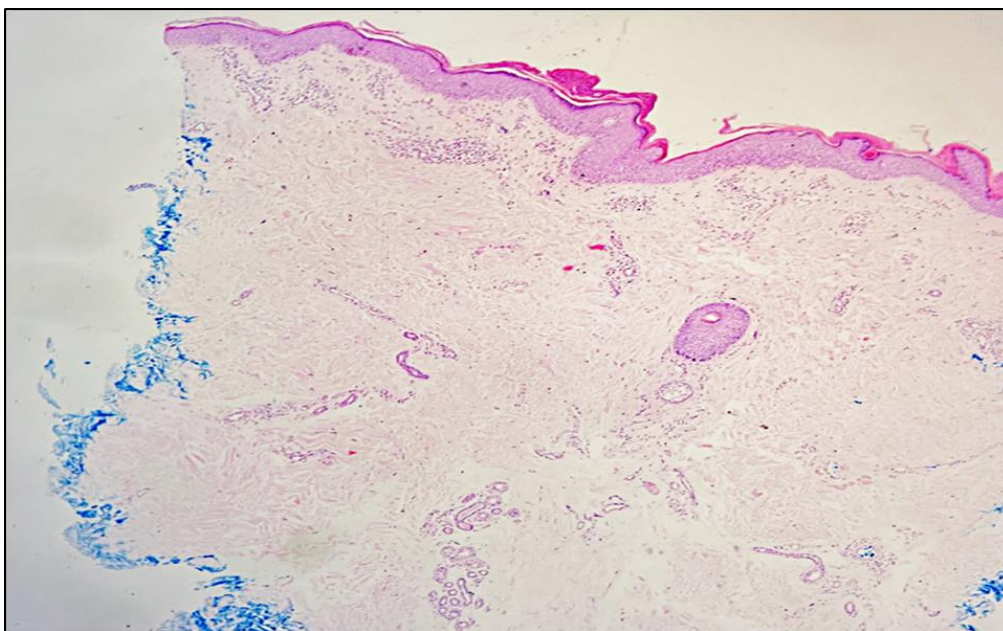


Fig. 2: Orthokeratosis and focal parakeratosis, mild epidermal acanthosis and spongiosis, with a superficial dermal perivascular cuff-like lymphocytic infiltrate (H&E, $\times 40$).



Fig. 3: Complete clinical resolution of the lesion on the right thigh by day 10 following a three-day course of oral azithromycin.

DISCUSSION

EAC is of uncertain pathogenesis; however, a cutaneous hypersensitivity reaction to various endogenous or exogenous antigenic stimuli is thought to play a role in its development.^[1] The incompletely understood etiopathogenesis and the inability to identify an underlying cause in a substantial proportion of cases have precluded the establishment of a standardized treatment approach for EAC. Identification and treatment of an underlying disease or triggering factor, when present, constitute the mainstay of management. Topical corticosteroids may be used for symptomatic lesions, while short courses of systemic corticosteroids may be considered in severe cases. In addition, successful outcomes with antifungal agents such as fluconazole and itraconazole, as well as antibiotics including metronidazole, doxycycline, erythromycin, and

azithromycin, have been reported, particularly in recalcitrant or idiopathic cases.^[3-8]

Azithromycin, a macrolide antibiotic, possesses immunomodulatory properties in addition to its antibacterial activity, including suppression of NF- κ B-mediated inflammatory responses and proinflammatory cytokine production, which may contribute to the clinical improvement observed in EAC.^[3] Accordingly, studies evaluating the efficacy of azithromycin in the treatment of EAC have been reported. In an open-label study published by Sardana et al. in 2018, 10 patients with idiopathic EAC received oral azithromycin 250 mg/day until clinical improvement was achieved. Histopathologically, three patients exhibited a superficial pattern, two a deep pattern, and five a mixed pattern; eight of the 10 patients responded to treatment. Patients with a superficial histopathological pattern showed an

earlier response to treatment, and no recurrence was reported during follow-up among those who responded.^[3] Similarly, in a case of recalcitrant superficial EAC reported by Gil-Lianes et al., complete clinical response was achieved within 15 days with oral azithromycin 250 mg/day. Treatment was continued for four months, and only mild flares were observed during the five-month follow-up period after discontinuation.^[9]

In a systematic review by Geng et al. evaluating 68 cases of EAC, complete response was reported in 19 of 21 patients (90.5%) who received oral antibiotic monotherapy; azithromycin was used in 11 patients, erythromycin in eight, and doxycycline in two. It has been proposed that azithromycin may exert its clinical effects by modulating the mTOR signaling pathway, thereby suppressing CD4+ T-cell proliferation and cytokine release.^[4] Recurrence was reported particularly in cases treated with erythromycin, whereas no recurrence was reported among patients who responded to azithromycin.^[3,4] In our case, recalcitrant superficial EAC lesions that had failed to respond to previous topical and systemic corticosteroids and oral itraconazole were treated with oral azithromycin 500 mg/day for only three days, resulting in complete clinical resolution by day 10. No new lesions developed during the three-month follow-up period. Considering that azithromycin has generally been administered at a dose of 250 mg/day until clinical response or for longer treatment periods in previous reports, the rapid and sustained response observed after only a three-day course in our patient is noteworthy. Nevertheless, as this observation is based on a single case, no definitive conclusions can be drawn regarding the efficacy of azithromycin or the optimal dose and duration of treatment.

CONCLUSION

In conclusion, previous reports on the use of azithromycin for EAC have generally employed a dose of 250 mg/day for treatment durations varying according to clinical response. In our case, recalcitrant superficial EAC lesions persisting for one year and unresponsive to previous treatments showed complete clinical resolution by day 10 following only a three-day course of oral azithromycin 500 mg/day, with no new lesions developing during the three-month follow-up period. This rapid and sustained response suggests that short-course oral azithromycin may represent a potential therapeutic option for recalcitrant EAC; however, larger studies are needed to determine its efficacy and the optimal dose and duration of treatment.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case and accompanying images.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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