Pityriasis rosea-like eruption induced by omalizumab: a case report of a rare side effect

Lamia Alakrash[1], Lama Alzamil[2], Mohammed Aljughayman[1], Salman Almalki[3]

[1]Department of Dermatology, King Fahd Medical City, Riyadh Second Health Cluster, Riyadh, Saudi Arabia; [2]Department of Dermatology, College of Medicine, King Saud University, Riyadh, Saudi Arabia; [3]Department of Pathology, King Fahd Medical City, Riyadh Second Health Cluster, Riyadh, Saudi Arabia

Contributions: (I) Conception and design: L Alakrash, L Alzamil; (II) Administrative support: L Alakrash, S Almalki; (III) Provision of study materials or patients: L Alzamil, M Aljughayman; (IV) Collection and assembly of data: M Aljughayman; (V) Data analysis and interpretation: L Alzamil, S Almalki; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Mohammed Aljughayman, MD. Department of Dermatology, King Fahd Medical City, Riyadh Second Health Cluster, Makkah Almukarramah Rd., Riyadh 11525, Saudi Arabia. Email: mohammed.aljughayman1@gmail.com.

Background: Omalizumab is a monoclonal humanized antibody used as a third-line treatment for chronic spontaneous urticaria (CSU). While it has shown significant efficacy in controlling urticaria symptoms, it is also associated with various adverse effects. Cutaneous side effects of omalizumab have been reported, but the mechanisms underlying these reactions are not fully understood. This case report describes a patient who developed a maculopapular rash after receiving the 8th dose of omalizumab, which has not been previously reported.

Case Description: The patient in this case was a 46-year-old male with CSU who had been receiving omalizumab injections every four weeks. After the 8th dose, he developed a generalized itchy erythematous skin eruption six days after the injection. The rash progressively worsened over a two-week period. Interestingly, the patient had experienced a milder skin reaction after the 6th dose, which resolved on its own. A skin biopsy showed mild interstitial edema in the dermis with a mild perivascular infiltrate of lymphocytes and eosinophils, consistent with a drug-induced eruption. The patient was advised to hold the next dose of omalizumab and was managed with topical steroids. Significant improvement and resolution of the lesions were observed, and no recurrence or relapse was reported after the patient resumed omalizumab.

Conclusions: This case adds to the existing literature by reporting a pityriasis rosea-like eruption as an adverse reaction to omalizumab, which has not been extensively documented. The delayed onset and progressive nature of the rash after the 8th dose, as well as the milder previous reaction after the 6th dose, highlight the importance of considering omalizumab as a potential cause of various cutaneous reactions. Physicians should be vigilant in monitoring patients receiving omalizumab for any signs of skin eruptions or other adverse effects. Further research is needed to understand the mechanisms underlying cutaneous reactions to omalizumab and to establish guidelines for their management. This case emphasizes the need for ongoing attention to potential side effects or reactions in patients receiving omalizumab.

Keywords: Omalizumab; drug-eruption; maculopapular; adverse reaction; case report

Received: 19 May 2024; Accepted: 22 November 2024; Published online: 17 April 2025.

doi: 10.21037/acr-24-114

View this article at: https://dx.doi.org/10.21037/acr-24-114

Introduction

Omalizumab, a recombinant monoclonal humanized antibody against immunoglobulin E (IgE), is a Food and Drug Administration (FDA) approved drug for the treatment of chronic spontaneous urticaria (CSU). It is considered a third-line treatment for CSU and has

demonstrated significant efficacy and improvement in patients' quality of life. Additionally, omalizumab has been utilized off-label for various other conditions. However, this efficacy does come with certain drawbacks, as multiple adverse effects have been reported, including anaphylaxis, arthralgia, pharyngitis, and headache. On the other hand, serious adverse events such as malignancy, cardiovascular events and susceptibility to infections are a subject of controversy and concern (1). Several cutaneous side effects of omalizumab have been reported in the literature, and there are various theories regarding their origin. One possibility is the engagement of immunoglobulin G (IgG) receptors [Fc gamma receptors (FcγRs)] by immune complexes formed by omalizumab (2). Additionally, a component of the drug called polysorbate, has also been reported as a potential cause for these uncommon adverse reactions (3).

Herein, we present a case of pityriasis rosea (PR)-like eruption secondary to omalizumab that is different in terms of presentation and onset compared to what has been reported in the published literature. We present this case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-24-114/rc).

Case presentation

This is a 46-year-old male who has been under follow-up in the Dermatology department in our tertiary care hospital (King Fahd Medical City) as a case of CSU for 14 months. His medical history is unremarkable for any other illnesses. The patient had been receiving omalizumab injections with a dose of 300 mg every four weeks for the management of treatment-resistant CSU. Following the 8th dose of omalizumab, he suddenly developed a generalized itchy erythematous skin eruption that had started six days after the injection. The eruption was increasing progressively over a two-week period. The patient denied any upper respiratory tract symptoms or using over the counter drugs prior to developing the eruption. On examination, there were widespread erythematous blanchable discrete and confluent patches, papules, and plaques distributed on the chest, back, and upper extremities (*Figure 1A-1E*). There was no involvement of the face, scalp, mucous membranes, or nails. Interestingly, the patient had mentioned experiencing a similar but more subtle skin reaction following the administration of one of his previous doses; however, the reaction was subtle and localized therefore no action was taken by the patient and resolved spontaneously after a few days. The comprehensive laboratory analysis, including hepatic and renal function tests as well as a complete blood count, revealed no abnormalities, including a normal eosinophil count.

A skin punch biopsy was taken and sent for histopathological examination. The differential diagnosis included maculopapular drug eruption, viral exanthem, PR, prurigo pigmentosa, tinea corporis, mycosis fungoides, and pityriasis rubra pilaris. The pathology report showed focal parakeratosis, subacute spongiotic dermatitis, increased dermal eosinophils with vacuolar interface dermatitis, focal upper dermal extravasated red blood cells, and superficial perivascular lymphocytic infiltrate (*Figure 2*). These pathological findings were consistent with PR-like drug eruption.

At the time, the patient was instructed to hold his next dose of omalizumab and was managed with topical steroids. Afterwards the patient presented two weeks later for follow-up, and showed significant improvement as most of his lesions resolved with remaining post-inflammatory hyperpigmentation (*Figure 3*). The patient continued to hold omalizumab for a duration of 8 weeks for evaluation, then he was instructed to resume it. The patient tolerated the next doses without any reactions with full satisfaction.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the

Highlight box

Key findings

- This case reports a maculopapular rash as an adverse reaction to omalizumab, which has not been previously reported.

What is known and what is new?

- Previous case reports have described lichenoid-like eruption, urticaria, angioedema, pityriasis rosea, and amyopathic dermatomyositis as potential cutaneous reactions to omalizumab.
- The case highlights the importance of considering omalizumab as a potential cause of various cutaneous reactions and emphasizes the need for vigilance in monitoring patients for adverse effects.

What is the implication, and what should change now?

- The findings of this case report should prompt healthcare professionals to consider omalizumab as a potential cause when evaluating patients with maculopapular rashes after receiving the medication.
- Further research is needed to elucidate the exact mechanisms underlying cutaneous reactions to omalizumab and to establish comprehensive guidelines for their management.

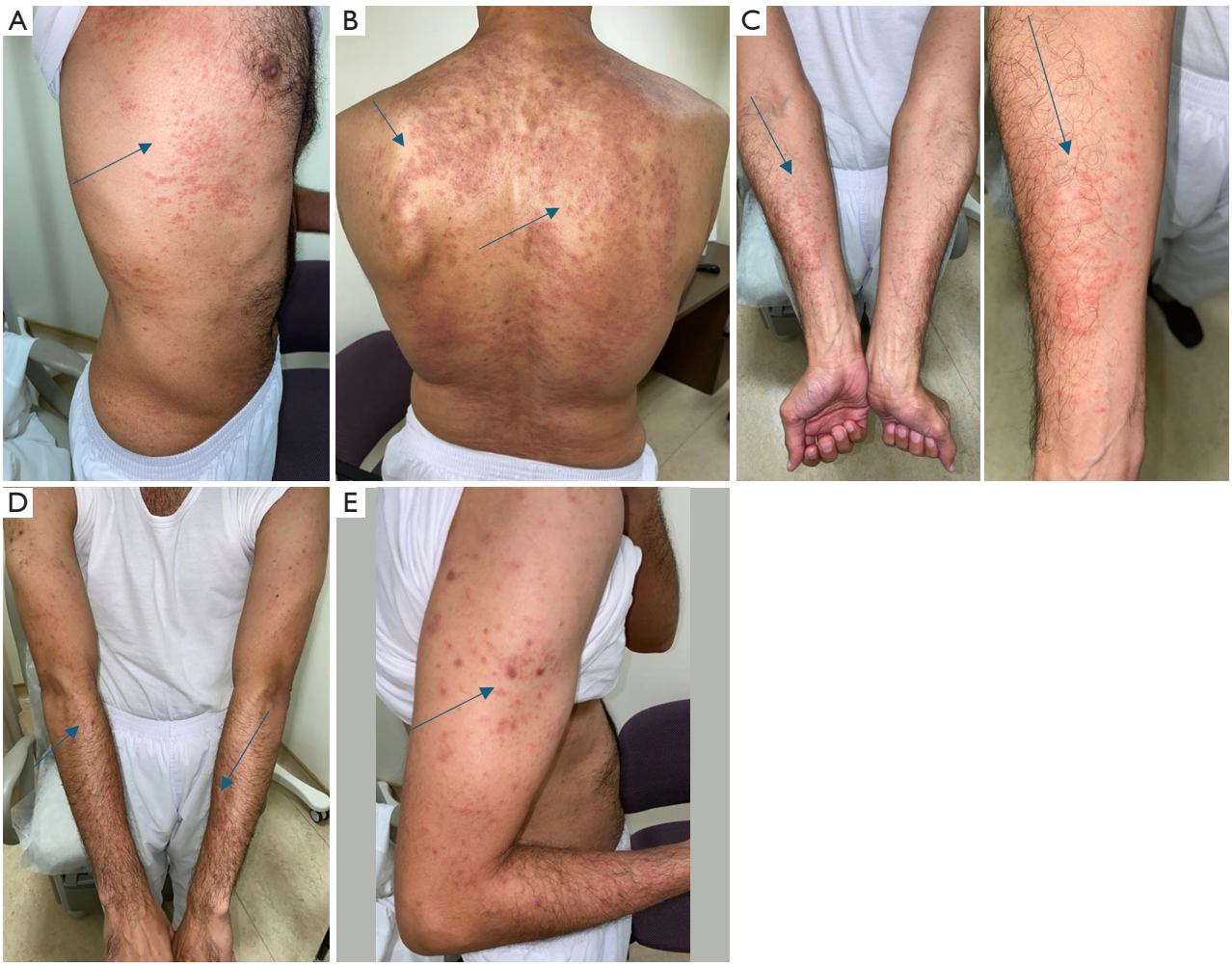

Figure 1 Multiple erythematous edematous papules and plaques on the chest (A), back (B), and arms (C-E). Arrows demonstrate the diffuse skin manifestations seen as erythematous papules and plaques.

Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Omalizumab has been reported to cause multiple cutaneous adverse reactions among patients. Nevertheless, none in the literature reported a PR-like drug eruption occurring in association with omalizumab. Our patient was receiving omalizumab for 7 months with no cutaneous reactions until he received the 8th dose. At the time, other possible causes for his eruption were excluded and omalizumab was the only known culprit. With cessation of the treatment and the use of topical steroids, the eruption subsided. Multiple case reports demonstrated the possibility of having various cutaneous reactions as adverse effects for omalizumab. One report described the appearance of a lichenoid-like eruption on the right arm and hand dorsum following intense sun exposure (4). Concluding that, omalizumab could have a role in photo-triggered reactions (4). Interestingly, in another study, a patient developed an urticarial eruption following the 4th dose of omalizumab (5), and with the continuous use this has led to an exaggeration of the urticaria as well as angioedema of the lips and tongue (5). In addition, a typical PR eruption was observed in two cases at the beginning of omalizumab treatment for CSU (6). Nevertheless, the authors believe that Omalizumab

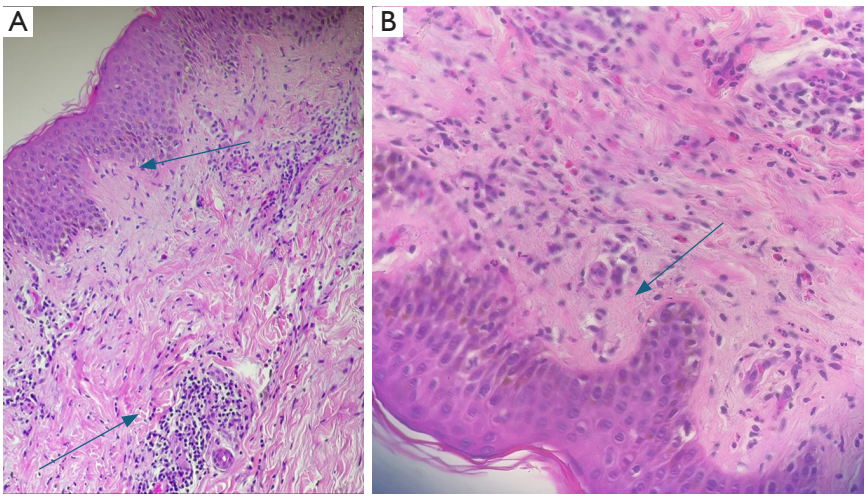

Figure 2 Mild interstitial edema in the dermis with mild perivascular infiltrate of lymphocytes and eosinophils. Neutrophils were seen within the vessel lumen but without evidence of vasculitis. Arrows demonstrate the interstitial edema along with perivascular infiltrate of lymphocytes. Neutrophils can be noted as well in the lumen of the vessels. Staining method: hematoxylin and eosin stain. Magnification: (A) ×20; (B) ×40.

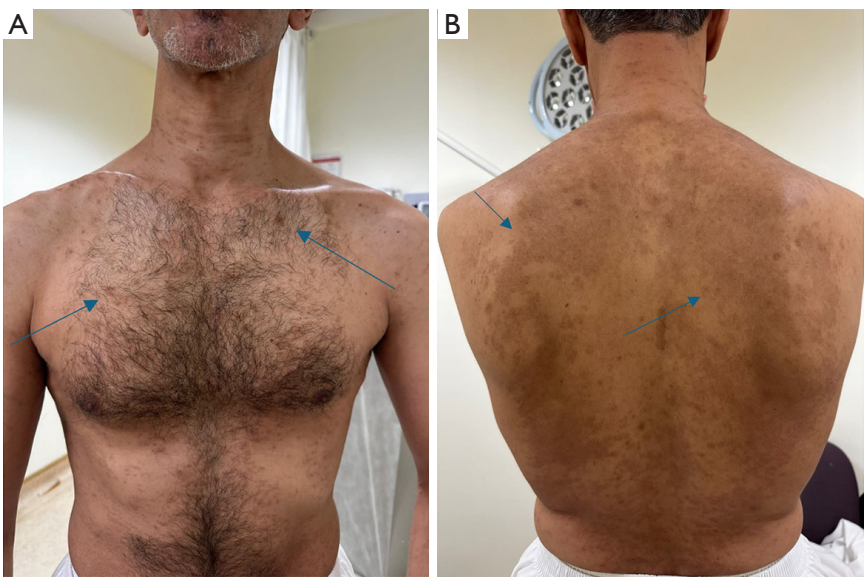

Figure 3 Well-defined hyperpigmented macules (A) and patches (B) at sites of resolved maculopapular rash. These images are published with the patient's consent. Arrows specify how the hyperpigmented macules and patches are distributed after resolving the resolved maculopapular rash.

treatment might have a role in HHV-6/7 reactivation and cutaneous cross-reactivity and PR onset.

Several theories were proposed to explain the reasons behind cutaneous eruptions occurring with the use of omalizumab. One explanation would be reacting to polysorbate, a component of omalizumab that is also present in some of the anticancer drugs and eye drops (7). Interestingly, unlike the intravenous doses containing polysorbate, adverse effects to polysorbate were not observed when the chemotherapeutic drug (free of polysorbate) was administered orally (8).

Another possible explanation is the activation of

the complement pathway related to IgG aggregates or recombinant DNA-derived humanized IgG1 (7). Improvement in one patient with the use of nonsteroidal anti-inflammatory drugs further strengthens this theory (9).

Our case describes the possibility of having a different form of Omalizumab-induced eruption.

Various forms of eruptions and multiple presentations have been reported with specific triggers noted in a number of articles. This illustrates the significance of keeping an open mind when dealing with patients receiving omalizumab. Furthermore, our case as well as other reported cutaneous reactions have been apparent after using multiple injections of the drug. This further shows the importance of life-long attention by physicians. The exact cause of the reported eruptions is still not clear and additional investigations needed to be done in order to reach a comprehensible understanding.

Conclusions

In conclusion, this case report highlights the importance of recognizing and monitoring cutaneous reactions to omalizumab, especially in patients with CSU. The emergence of a PR-like eruption following the 8th dose of omalizumab, a rare occurrence not extensively documented, suggests a potential association with this monoclonal antibody. The delayed onset and progression of the rash, coupled with a previous milder reaction after the 6th dose, emphasize the complexity of omalizumab-induced dermatologic responses. Vigilant observation for skin eruptions and other adverse effects is crucial in patients undergoing omalizumab therapy. Further investigations are essential to elucidate the underlying mechanisms of cutaneous reactions to omalizumab and establish comprehensive management strategies. This case serves as a significant reminder of the necessity for continued attention to potential adverse events in individuals undergoing omalizumab treatment.

Acknowledgments

The authors would like to thank the Research Center at King Fahd Medical City, Riyadh, for their valuable support in preparing this manuscript.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-24-114/rc

Peer Review File: Available at https://acr.amegroups.com/article/view/10.21037/acr-24-114/prf

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-24-114/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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doi: 10.21037/acr-24-114
Cite this article as: Alakrash L, Alzamil L, Aljughayman M, Almalki S. Pityriasis rosea-like eruption induced by omalizumab: a case report of a rare side effect. AME Case Rep 2025;9:65.