

Immediate Hypersensitivity Reactions to Biologic Therapies in Psoriasis and Hidradenitis Suppurativa

Giulia Jardim Criado

Centro Universitário Lusiada

Andreia Castanheiro Castanheiro Costa

Centro Universitário FMABC

Roberta Fachini Jardim Criado

`roberta.criado@fmabc.br`

Centro Universitário FMABC

Case Report

Keywords: Biologic agents, Immediate hypersensitivity, Drug allergy, Intradermal testing, Skin testing, Urticaria

Posted Date: October 14th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11089717/v1>

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Additional Declarations: No competing interests reported.

Abstract

Biologic therapies targeting TNF- α , IL-17, and IL-23 have revolutionized treatment for psoriasis and hidradenitis suppurativa. Hypersensitivity reactions to these agents represent clinical challenges and may necessitate treatment discontinuation or desensitization.

We describe three patients who developed recurrent urticarial reactions after repeated exposure to biological agents and underwent allergic evaluation. In these three patients, the reactions became more extensive after subsequent administration in contrast to the local or nonspecific reactions previously described with these biologic agents. Intradermal tests (IDTs) showed positive immediate reactions without delayed responses. The positive IDTs provided sufficient support to avoid suspected culprit agents, and the culprit biologics were discontinued and replaced with agents that targeted different pathways without any reaction, demonstrating that an allergy evaluation may help guide therapeutic decision-making. The urticarial reactions resolved completely, and no further hypersensitivity reactions occurred. These cases highlight the importance of recognizing that recurrent urticaria after biological administration could be a real drug reaction.

Introduction

Psoriasis and hidradenitis suppurativa are chronic inflammatory skin disorders, in which dysregulated immune responses type 1 and Type 3 play a central role. Targeting tumor necrosis factor- α (TNF- α), interleukin (IL)-17, and IL-23 pathways have revolutionized the treatment for moderate to severe psoriasis and hidradenitis suppurativa.^{1,2}

As the use of biological agents has increased, hypersensitivity reactions have become a relevant clinical concern. These reactions may range from localized cutaneous manifestations to severe systemic reactions and may have different underlying mechanisms.^{3–5} Distinguishing immediate hypersensitivity from other adverse events is important because continued exposure to a culprit agent may carry a risk of more severe reactions, and alternative biological therapies may remain available.^{3,4}

We describe three patients with psoriasis or hidradenitis suppurativa who developed recurrent urticarial reactions during biologic therapy and underwent allergic evaluation, including skin testing, (Skin prick test Intradermal test) and provocation when necessary. These cases illustrate the diagnostic value of intradermal testing and the feasibility of subsequent treatment with a biological agent targeting a different pathway.

Patients and Methods

This case series was conducted at a specialized allergic outpatient clinic in Brazil. Patients with psoriasis or hidradenitis suppurativa who developed mild-to-moderate urticarial reactions during biological therapy characterized by recurrence and progressive worsening after subsequent injections without systemic involvement or anaphylaxis were evaluated for suspected immediate hypersensitivity.

Following ethical approval, written informed consent was obtained from all participants for the diagnostic procedures and case Reports. Suspected culprit biological treatment was discontinued. Before skin testing, the patients underwent a 7-day washout of H1-antihistamines. Skin prick testing (SPT) and intradermal testing (IDT) were performed under medical supervision using normal saline as a negative control and histamine as a positive control. Concentrations and dilutions were selected according to the EAACI/ENDA position paper and previously published data.^{3,4,5}

In each patient, intradermal test was positive, and the re-exposure to the suspected culprit biological agent was not considered clinically justified because the positivity of intradermal test. Patients were subsequently switched to biologic agents with different mechanisms of action, followed by complete resolution of symptoms.

Results

All three patients developed recurrent immediate urticarial reactions during treatment with biological agents. The clinical and allergic characteristics of the patients are summarized in **Table 1**.

Case 1

A 30-year-old woman with methotrexate-resistant psoriasis vulgaris started the treatment with secukinumab. After 12 weeks of treatment, the patient developed recurrent urticarial lesions. Lesions initially appeared at the injection site and subsequently spread to other areas of the body after each administration. Individual lesions resolved within 2–24 hours without residual hyperpigmentation or purpura. The SPT to secukinumab was negative, whereas IDT at 5 mg/mL (1:10 dilution) produced a positive reaction at 20 min, with no delayed response. The secukinumab was replaced with risankizumab, an IL-23 inhibitor with complete disappearing of urticaria and total control of the disease. The patient did not experience further hypersensitivity reactions. (Fig. 1)

Case 2

An 18-year-old man with Hurley stage II hidradenitis suppurativa developed generalized urticaria, intense pruritus, and injection-site edema after six weeks of treatment with adalimumab, a fully human monoclonal antibody TNF- α inhibiting TNF-mediated inflammatory pathways

Individual wheals appeared after 1–4 h after the injection, changed location every 2–4 hours and resolved spontaneously within 2–3 days. The SPT to adalimumab at 40 mg/mL was negative, whereas IDT at 4 mg/mL (1:10 dilution) as described by Broyles et al.³ produced a positive reaction after 20 minutes, without a delayed response. The treatment was changed to secukinumab, with clinical improvement and no recurrence of urticaria.

Case 3

A 21-year-old woman with psoriasis vulgaris received bimekizumab, an IgG1κ monoclonal antibody that targets IL-17A and IL-17F. After four weeks of treatment, following the second dose, the patient developed progressive local erythema and edema that subsequently evolved into generalized erythema and urticaria. The wheals were transient, migrated, and resolved within 3 hours. The SPT with the undiluted drug was negative. IDT at 1:100 dilution (1.6 mg/mL) produced a positive reaction at 20 min, with no late-phase response. Bimekizumab was replaced with risankizumab, resulting in the complete clearance of psoriasis without further reactions. (Fig. 3)

After the tests, all three patients yielded a score of 7 on the Naranjo algorithm, supporting a probable causal association between the biological agent and reported adverse events.

Discussion

These three cases showed a consistent pattern of recurrent urticaria associated with biological administration. Although the reactions were clinically mild and not accompanied by systemic manifestations, they became more extensive or pronounced after subsequent doses. Recurrent or progressively worsening symptoms after repeated exposure should encourage allergy assessment rather than automatically attributing them to local irritation or a nonspecific adverse event, particularly because further exposure to the culprit agent may be associated with more severe hypersensitivity reactions.^{3,4} This distinction is clinically relevant because the identification of a possible hypersensitivity mechanism may influence the therapeutic strategy, particularly the decision between discontinuing the culprit biologic, switching to an alternative agent, or considering desensitization when continued treatment is clinically necessary.³ The clinical presentation in our patients differs from the local and nonspecific reactions more commonly described with subcutaneous TNF-α inhibitors and Bimekizumab. Several features support an immediate hypersensitive reaction. The lesions occurred in close temporal relation to administration, recurred and worsened after subsequent doses, resolved rapidly, and did not cause purpura or residual skin changes.

The skin testing provided additional evidence. In this context, an allergic evaluation was performed to better characterize the reaction and assess the likelihood of an immune-mediated mechanism.^{3,4} Skin prick tests (SPTs) were negative in all three patients, whereas intradermal tests (IDTs) showed positive reactions at 20 min, with no delayed component.³⁻⁵ In the setting of a compatible immediate reaction, a positive IDT supports the diagnosis of immediate hypersensitivity to the suspected biological agent.^{3,4} Therefore, drug provocation was not considered clinically justified.³⁻⁵

Lasheras-Pérez et al.⁶ described a case of localized immediate hypersensitivity to bimekizumab, presenting as erythematous-edematous, pruritic wheals at the injection sites within 2 hours of administration.⁶ Allergy evaluation, including intradermal testing and basophil activation testing, supported the diagnosis of an immediate hypersensitivity reaction to bimekizumab similar as our case.⁶

The interpretation of skin testing should consider the lack of standardized and validated protocols for most biological agents. In this series, concentrations and dilutions were selected based on available guidance and previously published experience.³⁻⁶

A direct, non-immunologic mast cell activation mechanism, including MRGPRX2 mediated pseudo allergy, was considered unlikely to be allergic. All three reactions occurred after repeated exposure rather than after the first administration and became progressively more evident with subsequent doses. This temporal pattern is less characteristic of a mechanism that does not require prior immunological sensitization.^{7,8}

An important therapeutic observation was that all three patients tolerated a subsequent biologic directed via a different pathway. Resolution of hypersensitivity symptoms after withdrawal of the culprit agent, together with continued control of the underlying disease, indicates that a reaction to one biologic does not necessarily imply intolerance to biologic treatment. When the culprit agent is indispensable and no suitable alternative is available, desensitization may be considered.

Our case highlights the potential value of an allergic evaluation in patients presenting cutaneous reactions to biologic agents, particularly when the clinical phenotype is unclear and a decision regarding treatment continuation, switching, or desensitization is required. Rasmussen et al⁷. Recently, showed the importance of allergy evaluation in patients with suspected hypersensitivity to biologic agents used for inflammatory disorders. In their cohort, non-immediate urticaria and/or angioedema represented the most frequent non-immediate phenotype, and the authors emphasized that allergy evaluation may help distinguish true hypersensitivity from concomitant cutaneous conditions and guide subsequent management.⁷ In our cases, however, alternative diagnoses, including chronic spontaneous urticaria and cutaneous vasculitis, were excluded, supporting the interpretation of the transient, migratory lesions as being temporally associated with biologic exposure. In the present case, switching to another biologic provided effective disease control without recurrence of hypersensitivity.⁷⁻⁹

The main limitation of this study is the small number of patients. In addition, standardized skin testing protocols are not available for most biological agents.^{3,4,7} Nevertheless, all three patients showed a consistent clinical pattern, positive immediate IDT responses, and complete resolution after withdrawal of suspected culprit agents.³⁻⁹ The favorable outcomes after the introduction of alternative biologics provide a practical message for clinicians managing suspected hypersensitivity during the treatment of chronic inflammatory skin disease. Although desensitization has been recommended when continued treatment with the culprit biologic is necessary, or essential switching to an alternative biologic with a different mechanism of action may provide a simpler therapeutic approach^{7,8} In our patients, the replacement resulted in clinical improvement without the need for prolonged desensitization protocols.

Conclusion

Recurrent or progressively worsening urticaria after biologic administration warrants allergy evaluation.^{3,4} In these patients, the compatible clinical pattern and positive intradermal tests supported the diagnosis of immediate hypersensitivity, allowed avoidance of re-exposure to the suspected culprit drug, thereby reducing the risk of recurrent hypersensitivity reactions.^{3–9} Switching to biologics with different mechanisms of action permitted continued control of the underlying inflammatory disease, without recurrence of hypersensitivity.^{7,8}

Declarations

Ethical Approval: For this original article, formal approval by the local Ethics Committee of the research proposed for publication is available (CAAE 76588023100000082). Written informed consent was obtained from all participants for the diagnostic procedures and publication of cases.

Conflict of Interest Statement: The authors declare no conflict of interest related to this study.

Funding Sources: No funding was received for this study.

Data Availability Statement: Data supporting the findings of this case series are not publicly available because they contain patient-level clinical information. Additional information may be available from the corresponding author upon reasonable request, subject to applicable ethical and privacy restrictions.

Author contribution: **GJC:** Data curation, writing, and editing of the original manuscript; **ACC:** Data curation and editing of the original manuscript; **RFJC:** Conceptualization, methodology, supervision, review, and editing of the manuscript.

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Tables

Table 1 . Skin testing methods for biologic hypersensitivity

CASE	Biologic agent	Test performed	Concentration	Result	Methodological reference
1	Secukinumab	SPT	Adapted protocol	Negative	Barbaud A,et al <i>Allergy.</i> 2023;78(10):2415-2439.
1	Secukinumab	IDT	Progressive dilutions	Positive	Barbaud A,et al <i>Allergy.</i> 2023;78(10):2415-2439.
2	Adalimumab	SPT	40 mg/mL	Negative	Broyles AD, et al <i>J Allergy Clin Immunol Pract.</i> 2020;8(9S):S16-S116
2	Adalimumab	IDT	4 mg/mL	Positive	Broyles AD, et al <i>J Allergy Clin Immunol Pract.</i> 2020;8(9S):S16-S116
3	Bimekizumab	IDT	1:100 dilution	Positive	Lasheras-Pérez MA, et al. <i>Contact Dermatitis.</i> 2025;92(6):488–489. +Institutional protocol
	All agents	Negative control	Normal saline (0.9%)	Negative	Standard practice

Figures

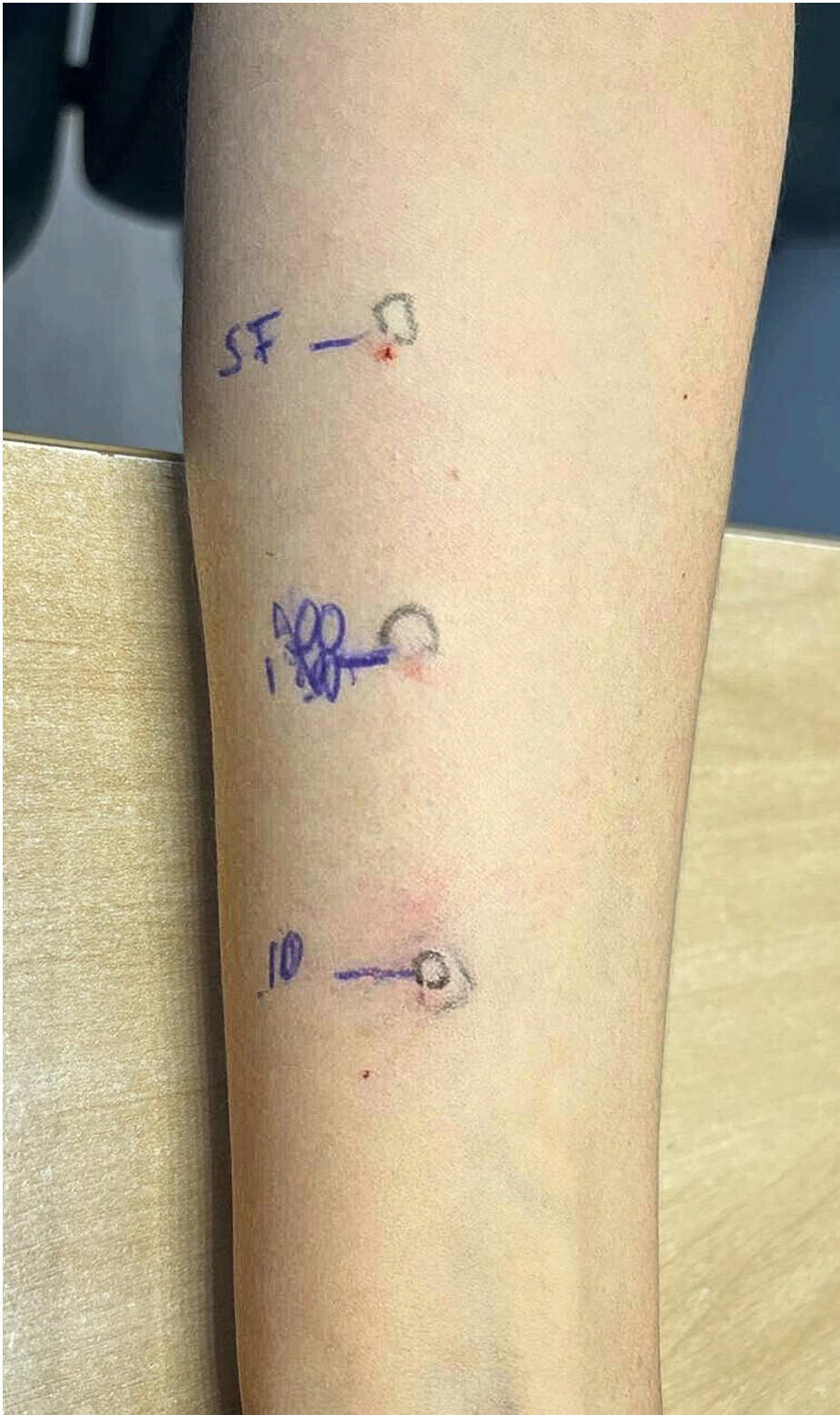


Figure 1

Positive intradermal test to secukinumab at 5 mg/mL (1:10 dilution) at 20 minutes.



Figure 2

Positive intradermal test to bimekizumab at a 1:100 dilution (1.6 mg/mL) at 20 minutes.