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Eczematous reactions in patients with plaque psoriasis receiving biological therapy: an observational study

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Abstract. – OBJECTIVE: The use of biologic agents, mainly tumor necrosis factor (TNF)-α and interleukin (IL)-17A inhibitors, was associated with cutaneous side effects, but the factors associated with eczematous reactions occurring during biologic treatments are not completely known.

PATIENTS AND METHODS: An observational, retrospective, multicentre Italian study evaluated the clinical features and the management of eczematous eruptions in 54 patients with chronic plaque psoriasis who developed eczema after treatment with biological agents (anti-IL-17 or 23).

RESULTS: Many of these patients had personal and family history of atopy. Eczematous reactions developed between a few days and 3 years after initiation of the biologic drug. The highest proportion of cases associated with eczematous reactions during biologic treatments was seen in patients on anti-IL-17 agents, including brodalumab. We observed that eczema rapidly remitted without relapse in all patients who switched to anti-IL-23 agents. Among our cases, fast responders to psoriasis therapy seem to have more persistent eczematous reactions.

CONCLUSIONS: Patients with psoriasis and a history of atopic dermatitis should be treated with an IL-23 inhibitor due to its efficacy in psoriasis and the rarely reported eczematous reaction.

Key Words:
Plaque psoriasis, Eczematous reaction, Anti-IL-17 agent, IL-23 inhibitor.

Introduction

Plaque psoriasis is a chronic, immune-mediated inflammatory skin disease that requires repeated prolonged periods of either topical or systemic treatment[1]. Although biologic agents are important systemic tools for the treatment of psoriasis, their use was associated with cutaneous side effects, mainly in subjects receiving tumor necrosis factor (TNF)-α and interleukin (IL)-17A inhibitors[2].

Several types of eruption were described in this setting, including atopic dermatitis and eczematous reactions, dyshidrotic dermatitis, nummular dermatitis, stasis dermatitis, seborrheic dermatitis, eyelid dermatitis, and papular dermatitis[2]. A systematic review by Al-Janabi et al[3] found 24 studies reporting 92 patients with chronic plaque psoriasis who had developed eczema while on treatment with biologic agents. These subjects represented 1.0-12.1% of patients in the studies included in the review. The involved agents were

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adalimumab, etanercept, infliximab, ixekizumab, secukinumab, or ustekinumab; common factors in patients were a prior history of atopy, eosinophilia, and elevated level of serum immunoglobulin. Additionally, eruptions associated with anti-IL-23 and anti-IL-12/23 agents were reported by Reyn et al[4] and by Mufti et al[2] in a more recent meta-analysis on this subject.

Psoriasis is primarily driven by cytokines from type 17 T helper (Th17) cells, with type 1 T helper (Th1) cells playing a smaller role. In contrast, atopic eczema is mainly driven by type 2 (Th2) or type 22 (Th22) T helper cells. Anti-psoriatic treatments that inhibit TNF-α or IL-17 can suppress the Th1 and/or Th17 pathways, potentially causing an imbalance in T helper cell populations, which may trigger dermatitis onset[5].

As further understanding of the factors associated with eczematous reactions occurring during biologic treatments for psoriasis is necessary, we report here the results of an observational, retrospective, multicentre Italian study that evaluated the clinical features and the management of eczematous eruptions in patients with chronic plaque psoriasis treated with biological agents especially anti-IL-17 or -23.

Patients and Methods

Ten dermatological centers in Italy participated in this study. Patients with chronic plaque psoriasis who had developed an eczematous eruption while treated with a biologic agent (anti-IL-17 or -23) between January 2022 and December 2022 were included in the study. All treatments were chosen based on the researcher's judgment and were used according to the current regulations.

Investigators obtained demographic and medical history before starting treatment with the culprit biological agent. The investigators clinically diagnosed the eczematous eruption at control visits.

Patients were considered super responders (SRs) if they achieved psoriasis area severity index (PASI) = 0 at weeks 12 and 24. They were considered non-SRs if they did not achieve PASI = 0 at weeks 12 and 24[6].

The study was notified to the Ethics Committee of S. Martino-IRCCS Policlinic Hospital, Genova, Italy (Ospedale Policlinico San Martino-IRCCS, Genova, Italy; study number 63/2024; protocol: Pubb_Pso_Burlando; Study ID: 00429). The study was performed in accordance with the revised version of the Declaration of Helsinki. All patients signed an informed consent form for the publication of clinical data.

Statistical Analysis

Data were summarized by descriptive analysis. Means and standard deviations (SDs) were calculated for continuous variables, while absolute values and frequency (percentage) were calculated for categorical variables. All analyses were performed with IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Overall, 54 patients were included, of whom 32 (59%) were males and 22 (41%) females. The mean age was 52.5±7.2 years in the overall population, 54.2±6.4 years in males and 47.7±9.1 in females. The mean time since diagnosis of psoriasis was 19.3±11.5 years in the overall population, 21.8±12.3 years in males, and 14.7±6.3 years in females.

A total of 24 (44%) patients reported a family history of atopic diseases, 16 (30%) had atopic diseases, and 11 (20%) had previously been affected with eczema.

Prior to the biologic treatment related to eczema development, 18 (34%) patients had received cyclosporin A, 3 (5.5%) systemic steroids, 4 (7.4%) UVB phototherapy, 20 (37.0%) methotrexate, 2 (3.7%) apremilast, 2 (3.7%) isotretinoin, 2 (3.7%) infliximab, 16 (29.6%) adalimumab, 13 (24.0%) etanercept, 1 (1.8%) guselkumab, 12 (22.2%) utekimumab, 3 (5.5%) ixekizumab, and 3 (5.5%) secukinumab. Indeed, 24 (44.4%) patients had received two previous treatments, 15 (27.7%) one treatment, 8 (14.8%) three treatments, 4 (7.4%) five treatments, and 3 (5.5%) patients had received more than five treatments.

Eczema developed in 24 (44.4%) patients receiving ixekizumab, 24 (44.4%) on secukinumab, 2 (3.7%) on risankizumab and 4 (7.4%) on brodalumab.

The dermatitis was observed after a mean time of 26.6 weeks (range, 0-150 weeks) since initiation of the involved biologic treatment. Eczema was generalized in 21 (39.0%) patients, atopic dermatitis-like in 20 (37.0%) and psoriasiform in 13 (24.0%) patients.

After the development of eczema, 11 (20.3%) patients continued the same biologic treatment, adding topical treatments. The majority of pa-

tients (40 out of 54, 74.0%) switched to a different systemic treatment for plaque psoriasis. Seven patients (12.9%) transitioned to tildrakizumab, guselkumab, or ustekinumab, five (9.2%) to brodalumab, four (7.4%) to risankizumab, four (7.4%) to upadacitinib, two (3.7%) to ixekizumab, and one (1.8%) each to golimumab, infliximab, etanercept, or adalimumab. Finally, 4 (7.4%) patients with severe eczema switched to dupilumab to treat it.

The patients were followed up after the switch for a mean time of 12.37 months (range, 1-102 months). During this follow-up period, 50 (92.6%) of patients had no eczema relapse; eczema relapsed in 2 (3.7%) patients who switched to guselkumab. The two (3.7%) patients who switched to dupilumab had relapsed psoriasis and, therefore, further switched to upatacitinib.

The eczema persisted for a mean time of 6.3 weeks (range, 1-26 weeks) in the whole population. Among the patients who were considered SR for psoriasis treatment, eczema persisted for a mean time of 8.5 weeks and for a mean time of 5 weeks in non-SR.

Discussion

This multicenter retrospective study on 54 patients with psoriasis who developed eczema eruption while treated with a biologic agent showed that this reaction may occur within a wide range of time (from a few days to 3 years). A similar observation was reported in the systematic review by Mufti et al[2] that included subjects with any type of condition. We also observed that many patients with psoriasis who developed eczema reactions during biologic treatments had a personal and family history of atopy. This observation in subjects with psoriasis may stand with results from the meta-analysis by Mufti et al[2] on patients with other diseases. In our cohort, most reactions occurred during therapy with an anti-IL-17 antibody, which is in agreement with a previous report from our group[7].

Interestingly, two patients treated with brodalumab had an eczema reaction. Brodalumab, which targets the IL-17 receptor, has been proposed as an alternative treatment option for psoriasis patients who develop dermatitis or paradoxical psoriasis while receiving biologic therapy. However, several cases of brodalumab-induced eczematous reactions have been later reported[8]. Interestingly, these patients obtained complete eczema clearance after switching to the anti-IL-23 risankizumab. Only two patients on risankizumab (an anti-IL-23) had eczema, and two patients who switched from an anti-IL-17 agent to guselkumab (an anti-IL-23) had another relapse, but they had suffered from atopic dermatitis in childhood. The highest proportion of cases associated with eczematous reactions during biological treatments was seen in patients on anti-IL-17 agents. The mechanism behind eczematous reactions during biological treatments is not well understood. However, it is believed that the imbalance of different antigen-specific T-cell subsets induced by biologics may be the basis for the development of dermatitis[7]. Better knowledge of these mechanisms is necessary to design a preventive strategy. Among our cases, fast responders to psoriasis therapy seem to have more persistent eczematous reactions, but this observation needs confirmation in a more extensive study. Accordingly, we observed that eczema rapidly remitted without relapse in all patients switched to anti-IL-23 agents.

Four out of 50 patients who experienced an eczematous relapse moved to upadacitinib, an oral selective inhibitor of JAK-1 approved for atopic dermatitis as well as for psoriatic arthritis[9]. Research on eczematous psoriasis is expanding, and it is being successfully treated with this JAK inhibitor[10]. Given its safety profile, it appears to be a suitable treatment option for patients under 65 years old[9].

Conclusions

In conclusion, patients with psoriasis but with a history of atopic dermatitis should be treated with an IL-23 inhibitor due to its efficacy in psoriasis and the rarely reported eczematous reaction. Patients with a history of or current atopic disease who develop an eczematous reaction while on an anti-IL-23 should move to an anti-JAK, especially if they are younger than 65 years old and have no comorbidities.

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Conflicts of Interest

Martina Burlando served as a speaker or advisory board member for Almirall, Abbvie, Amgen, Eli Lilly, Janssen, Novartis, and UCB.
Matteo Megna served as a speaker or advisory board member for Almirall, Abbvie, Eli Lilly, Janssen, and UCB.
Giacomo Caldarola served as a speaker or advisory board member for Almirall, Abbvie, Amgen, Eli Lilly, Novartis, and UCB.
Nicoletta Bernardini served as a speaker or advisory board member for Almirall, Abbvie, Eli Lilly, and Novartis.
Claudia Giofré served as a speaker or advisory board member for Almirall, Abbvie, Amgen, and Eli Lilly.
Paolo Gisondi served as a speaker or advisory board member for Almirall, Abbvie, Amgen, Eli Lilly, Janssen, Novartis, and UCB.
Clara De Simone served as a speaker or advisory board member for Almirall, Abbvie, Amgen, Eli Lilly, Janssen, Novartis, Sanofi, and UCB.
Emanuele Cozzani served as a speaker or advisory board member for Almirall, Abbvie, and Eli Lilly.

AI Disclosure

No form of generative artificial intelligence was used for writing the manuscript.

Availability of Data and Materials

Available from the corresponding author upon reasonable request.

Authors' Contributions

Study conception and design: Martina Burlando, Emanuele Cozzani; collection and interpretation of data: Martina Burlando, Matteo Megna Giacomo Caldarola, Nicoletta Bernardini, Claudia Giofré, Paolo Gisondi, Clara De Simone; statistical analysis: Martina Burlando; manuscript drafting: Martina Burlando; manuscript editing: Martina Burlando; approval to submit: Emanuele Cozzani.

Ethics Approval

The study was notified to the Ethics Committee of S. Martino-IRCCS Policlinic Hospital, Genova, Italy (Ospedale Policlinico San Martino-IRCCS, Genova, Italy; study number 63/2024; protocol: Pubb_Pso_Burlando; Study ID: 00429).

Informed Consent

Participants signed consent to publish anonymous data.

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