SKIN

BRIEF ARTICLE

Multiple Injection Site Reactions after Treatment with Different Biologics for Psoriasis and Psoriatic Arthritis

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ABSTRACT

Psoriasis (PsO) is an autoimmune disease characterized by erythematous, pruritic, and scaly plaques that can be distributed throughout the body. The development of biologic treatments targeting an array of molecular pathways, including tumor necrosis factor-α and interleukins 12, 23, 17A, and 17F, has advanced treatment options for these patients. In this article, we report a unique case of a 35-year-old female with 11-year history of PsO and a new onset of guttate PsO following an episode of streptococcal pharyngitis. She was subsequently treated with guselkumab, bimekizumab, and ixekizumab, developing injection site reactions (ISR) to each biologic. The patient was suspected to be allergic to polysorbate-80 (PS-80), an aqueous medium used to stabilize biologics before administration. Notably, the patient had a negative response to PS-80 on allergy testing, and it remains unclear why the patient experienced ISR with certain medications and not others. Further research is needed to characterize ISR across the different biologics, particularly newer medications being utilized in clinical settings.

INTRODUCTION

Psoriasis (PsO) is an autoimmune disease characterized by erythematous, pruritic, and scaly plaques that can be distributed throughout the body.[1] Psoriatic arthritis (PsA) is a commonly associated condition, with approximately <10% to 40% of individuals with PsO developing this complication.[1] The prevalence of this condition is estimated to be 112 individuals per 100,000 globally.[2] Symptoms often manifest as joint pain, swelling, stiffness, and reduced range of motion. While both these diseases can be debilitating, the development of biologic treatments targeting an array of molecular pathways has advanced treatment options for these patients. Many of these biologics block different targets including tumor necrosis factor-α or interleukins (IL) 12, 23, 17A, and 17F.[3] As biologics are administered subcutaneously, injection site reactions are not uncommon. In this article, we report a unique case of a patient who experienced hypersensitivity reactions to multiple biologics for her PsO.

CASE REPORT

A 35-year-old female with a history of plaque PsO since age 11, presented to the dermatology clinic with a new onset of guttate

PsO following an episode of streptococcal pharyngitis. The patient experienced a severe flare up of her PsO and began treatment with light therapy and cyclosporin (CsA). The patient was treated with CsA for 4 months before starting guselkumab. After her first injection of guselkumab, she developed an erythematous injection site reaction (ISR) presumed to be cellulitis requiring hospitalization. Eight weeks later she was seen for a second severe ISR at which time it was suspected she may be allergic to an ingredient in the guselkumab injection (**Figure 1**). During this time, the patient also developed joint pain and was diagnosed with PsA. After multidisciplinary consultation with

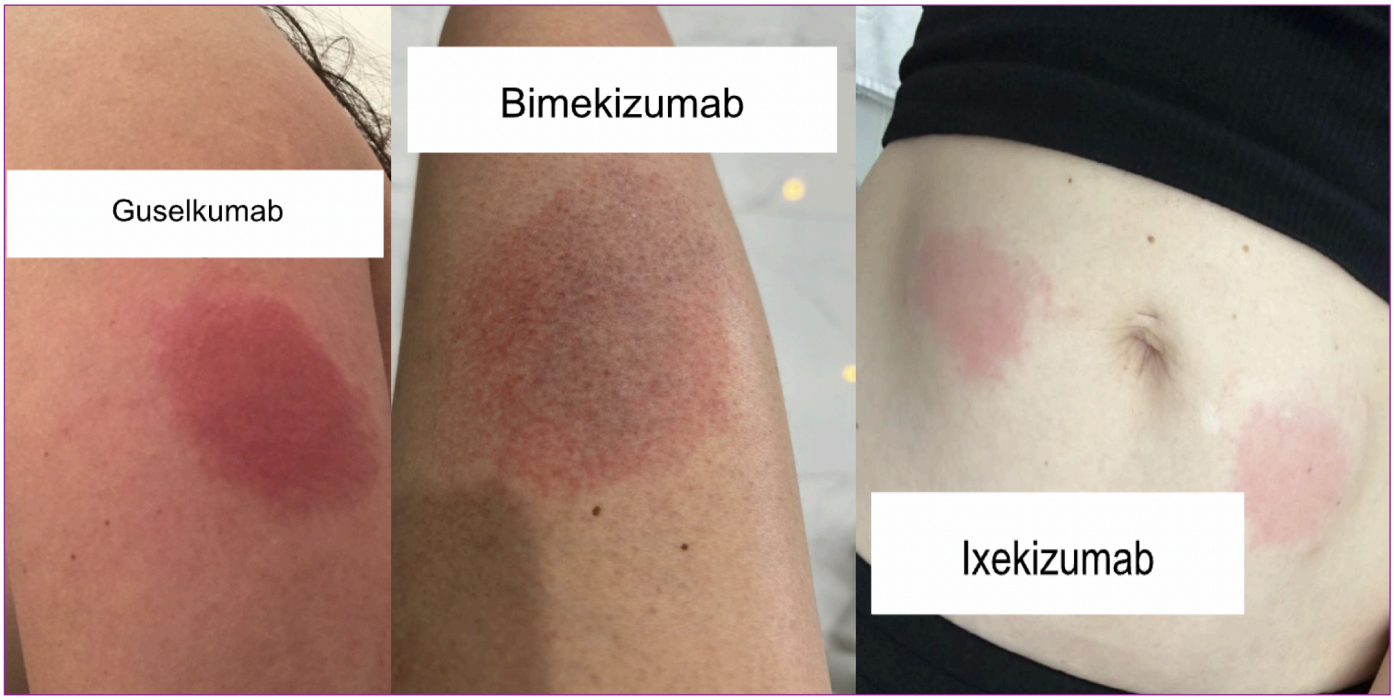

Figure 1. Injection site reaction to guselkumab, bimekizumab, and ixekizumab.

rheumatology, the patient was started on tofacitinib due to right sacroiliac joint pain, right shoulder joint pain, left knee pain, and preference for non-injectable medication. However, tofacitinib was discontinued after three months after she experienced multiple ear infections and folliculitis. She was then switched to secukinumab without developing ISR. Although the patient experienced mild improvement of her scalp PsO, it remained inadequately controlled along with her PsA. Upon becoming pregnant, the patient elected to discontinue secukinumab and begin treatment with certolizumab pegol.

Following the pregnancy, the patient resumed secukinumab 150 mg every two weeks while awaiting approval of bimekizumab. Once available, she started bimekizumab and experienced another ISR (**Figure 1**), despite the pretreatment of the injection site with steroids. She wished to explore other options and was prescribed ixekizumab. The patient experienced another ISR after the first injection of ixekizumab (**Figure 1**). Following the third ISR to a biologic, the patient was once again prescribed secukinumab. She is currently treated with 150 mg of secukinumab every 10 days with excellent treatment response.

DISCUSSION

Biologics have revolutionized the treatment of PsO and PsA, but they are not without side effects such as ISRs. Our patient developed ISRs to guselkumab, bimekizumab, and ixekizumab. all of which contain the ingredient polysorbate-80 (PS-80). PS-80 is a commonly utilized medium to stabilize the active medication until it is administered to the patient.[4] The ISR experienced by the patient can potentially be explained by degradation of polysorbates into free radicals and chemical byproducts via oxidation, leading to the development of protein aggregates, complement activation, and increased immunogenicity to the administered drug.[4] This may occur through suboptimal storage condition of the medications. Polysorbates are also known to cause type IV hypersensitivity reactions at the exposure site.[4] However, the patient did not have an ISR to secukinumab, which also contains PS-80. Notably, follow up drug allergy testing demonstrated positive reaction to guselkumab, bimekizumab, and ixekizumab and negative reactions to triamcinolone and cefazolin, both of which contain PS-80 and the latter of which was associated with immediate adverse symptoms (**Figure 2**).

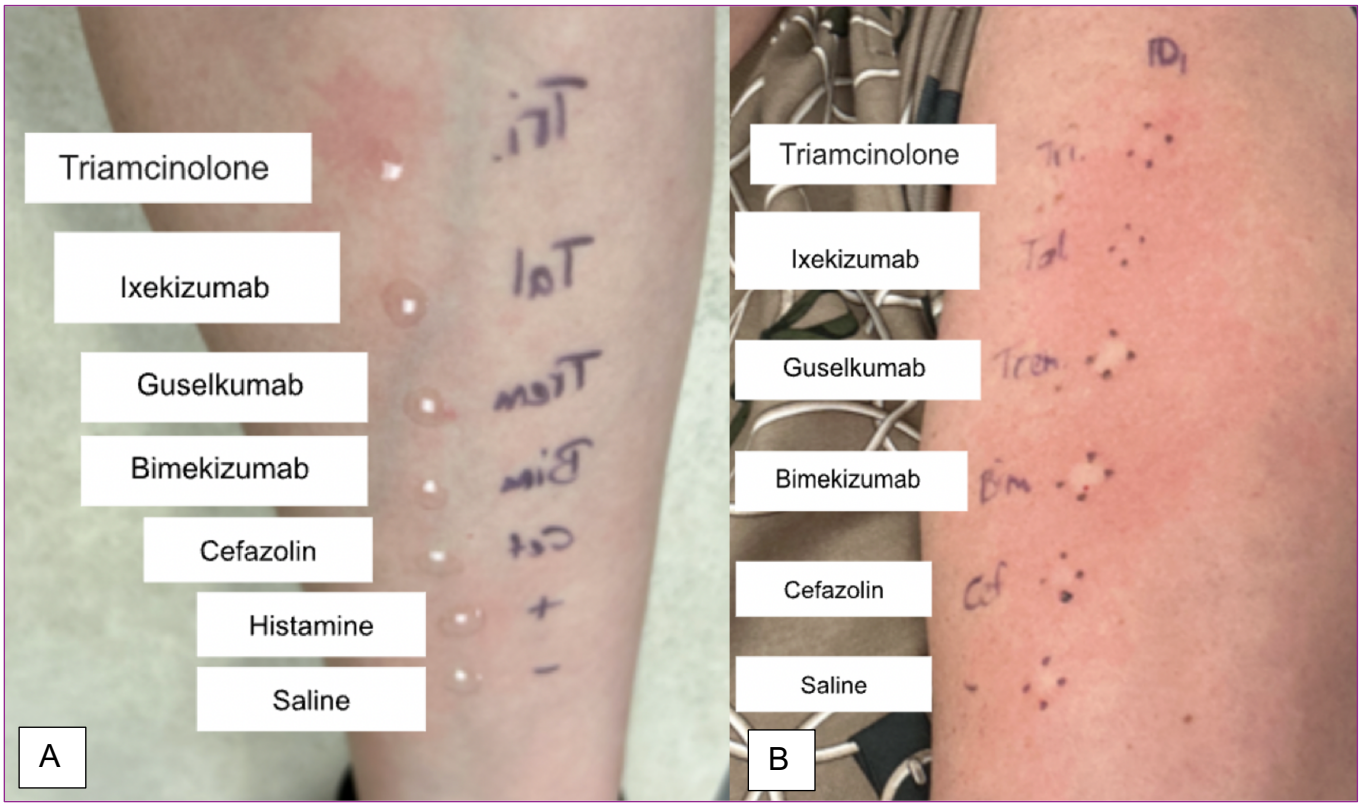

Figure 2. (A) Epicutaneous testing and (B) Intradermal testing**:** Patients' response to drug allergy testing for certain medicines containing Polysorbate – 80. Histamine served as the positive control and saline served as the negative control. From top to bottom, triamcinolone (40 mg/ml epicutaneous, 0.4 mg/ml intradermal), ixekizumab (80 mg/ml epicutaneous, 0.08 mg/ml intradermal), guselkumab (100 mg/ml epicutaneous, 0.1 mg/m intradermal), bimekizumab (160 mg/ml epicutaneous, 0.16 mg/ml intradermal), and cefazolin (100 mg/ml each).

Existing literature reports mixed findings regarding whether certain biologics are associated with increased rates of ISRs. A systematic review of 158 articles evaluating ISRs of phase 3 trials for biologics found ixekizumab to be associated with the highest prevalence of ISR and guselkumab and secukinumab to be associated with the lowest prevalence of ISR.[5] A smaller institutional retrospective cohort study found ixekizumab and guselkumab to be associated with the highest prevalence of ISR and secukinumab to be associated with the lowest prevalence of ISR.[6] Indeed, the prevalence of ISRs with the original formulation of ixekizumab led to the development of a new formulation.

In our patient, who had a negative response to PS-80 on allergy testing, it remains unclear why the patient experienced ISRs with certain medications and not others. Fortunately, the large assortment of available biologics allowed for trial and error to identify an appropriate medication regimen for this patient. Further research investigating the prevalence and causes of ISRs among available biologics, especially newer agents like bimekizumab, is needed.

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