SKIN

BRIEF ARTICLE

Treatment of Generalized Pustular Psoriasis with Bimekizumab

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ABSTRACT

Generalized pustular psoriasis (GPP) is a rare but serious subtype of pustular psoriasis. In the United States, the IL-36 inhibitor spesolimab is the only medication currently approved for GPP. We describe the longitudinal treatment of a patient with concomitant GPP, plaque psoriasis, and psoriatic arthritis. After almost a decade of recalcitrant disease and difficulty managing cardiovascular concerns, the patient was successfully treated with bimekizumab, a novel biologic targeting IL-17A/F. To our knowledge, this represents the first case of concomitant GPP and plaque psoriasis treated with this immunomodulator, offering additional treatment options for patients with this challenging disease.

INTRODUCTION

Generalized pustular psoriasis (GPP), a rare subtype of pustular psoriasis, presents with episodic, diffuse eruptions of sterile pustules often accompanied by systemic inflammation. GPP can be a life-threatening disorder, so prompt treatment is critical. Spesolimab – an IL-36 blocker – is the only treatment for GPP approved by the United States Food and Drug Administration (FDA). Herein, we report a patient with GPP, plaque psoriasis and psoriatic arthritis who had been successfully treated with infliximab until he developed severe heart failure. Comorbidities included morbid obesity. Insurance denied spesolimab. Eventually, the patient was effectively treated with the IL-17A/F blocker bimekizumab.

CASE REPORT

A 39-year-old man with a 20-year history of GPP, plaque psoriasis, and psoriatic arthritis was initially hospitalized in 2002 with a severe flare of pustular psoriasis. During this admission, he was febrile, tachycardic, edematous and erythrodermic and exhibited erythematous plaques with fluid-filled pustules across a body surface area (BSA) of over 90%. His prior regimen of intramuscular methotrexate 25 mg weekly, acitretin 75 mg daily, and corticosteroids (oral prednisone 20 mg daily with topical triamcinolone ointment) was changed to infliximab infusion, a TNF-α inhibitor, 5 mg/kg every 6 weeks after induction. He initially experienced significant improvement in symptoms with complete resolution of pustules and plaques, as well as a decrease in joint pain. His initial clinical course has been detailed in a previous publication.1 He later was briefly trialed on adalimumab, but failed treatment and was maintained primarily on infliximab. During the years of follow-up, he intermittently had recurrence of plaque and pustular psoriasis on his extremities, palmoplantar surfaces,

trunk, and gluteal cleft, necessitating an increase to infliximab 7mg/kg every 4-6 weeks in addition to short courses of methotrexate 20mg weekly and topical corticosteroids as adjuvants. A switch to IL-17 was later considered, but the patient refused, stating that he was fearful of the severity of his recurrent disease off infliximab. Therefore, he maintained treatment with infliximab, generally having plaques and/or pustules ranging from 5-30% BSA (**Figure 1**). His flares regularly occurred a few days prior to his next scheduled infusion dose.

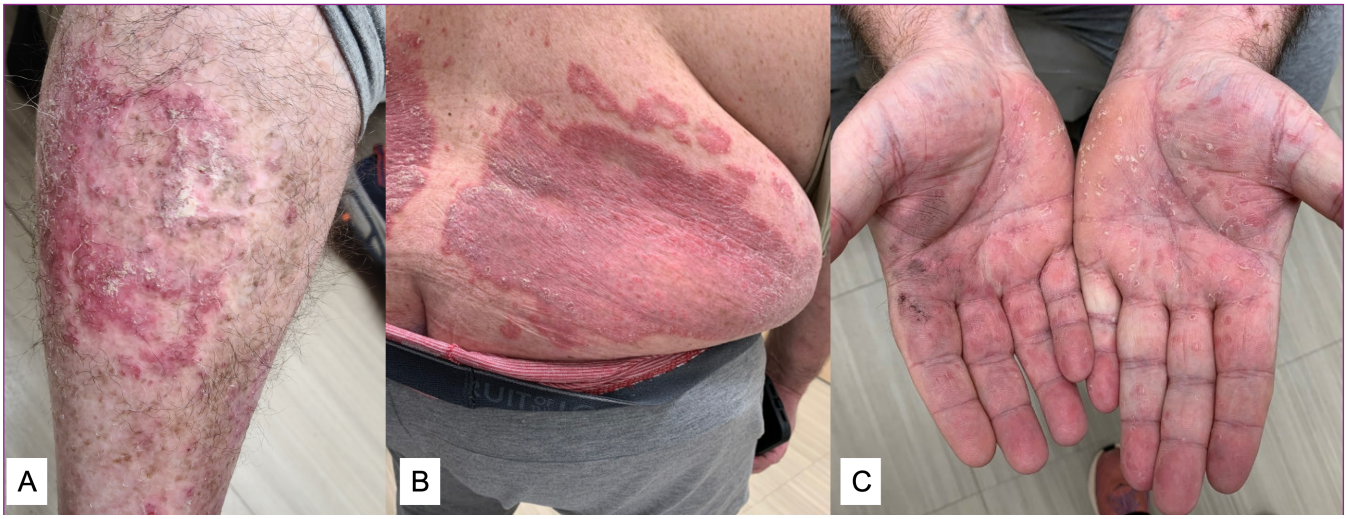

Figure 1. Recalcitrant plaques and pustules while the patient was on infliximab. Erythematous plaques with silvery scale on the left anterior shin (A) and lower bilateral back (B). Pustules and residual scale on an erythematous background of the bilateral hands (C).

After ten years of treatment, the patient developed class C congestive heart failure (CHF) with a left ventricular ejection fraction (LVEF) of 20-25%. Despite his attempts at lifestyle changes and medication management, his LVEF did not improve. Upon discussion with his cardiologist, infliximab was discontinued in April 2024, given that doses greater than 5mg/kg are relatively contraindicated in severe CHF. At the time of discontinuation, the patient had a BSA of approximately 10% and PASI score of 6.00 with pustules on both palmar and plantar surfaces and much of his trunk. Spesolimab was denied by his insurance. He was then started on bimekizumab 320mg every 4 weeks monotherapy with immediate improvement in both the psoriasis plaques and the pustular component and alleviation of joint manifestations. After 3 months on bimekizumab, the patient had a BSA of 0% and PASI of 0 with no pustules and no joint pain (**Figure 2**). He has been off methotrexate. Furthermore, his LVEF improved to 40% after stopping infliximab.

DISCUSSION

GPP, manifesting as diffuse plaques of pustules and systemic symptoms like fever and severe pain, has significant associated morbidity and mortality. Accumulation of neutrophils can cause acute formation of sterile pustules in the epidermis that can potentially lead to multiorgan damage, such as sepsis, acute renal failure and high output heart failure. The course of disease can be variable, with some patients experiencing

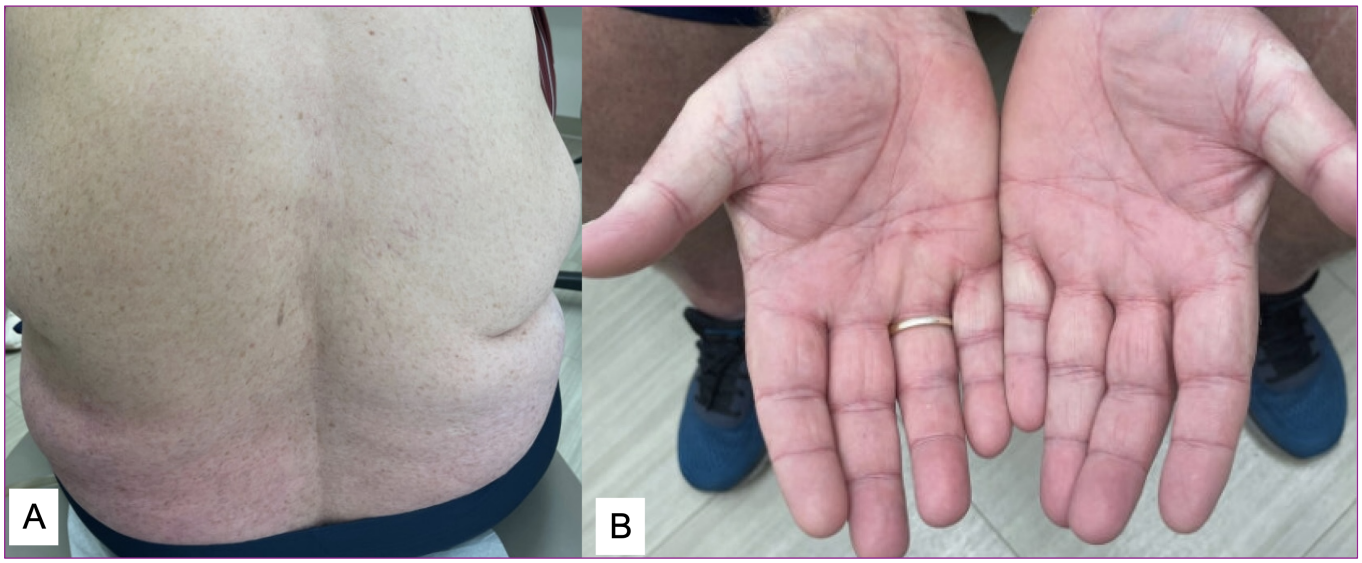

Figure 2. Complete resolution of plaque psoriasis lesions on the back (A) and pustules on the hands (B) at month 3 on bimekizumab.

either an acute form of extensive eruption or a more subacute/chronic form.[2]

Unlike in plaque psoriasis, the IL-36 pathway has been implicated in GPP. This allowed the development of biologics such as spesolimab that specifically target this pathway. Plaques of GPP, however, also show elevated levels of cytokines more classically associated with plaque psoriasis such IL-17A, albeit at lower levels.[3] Indeed, prior to spesolimab and other IL-36 inhibitors, many patients were treated with biologics approved for plaque psoriasis, including TNF-α inhibitors, IL-17/IL-17R inhibitors, and IL-23 inhibitors, with varying degrees of effectiveness.[4] This suggests that while GPP overall may be a disease process different from plaque psoriasis, there may be some overlap in pathogenesis. Furthermore, some studies suggest that up to 54% of patients with GPP have concomitant plaque psoriasis.[5] Those with both GPP and plaque psoriasis may have an increase in overall mortality compared to those with GPP alone, as well as a shorter period of treatment without relapse of disease.[2,6] The largest randomized controlled trial of the anti-IL-36R inhibitor spesolimab, though showing extremely promising results for patients with GPP, excluded patients with a history of psoriasis vulgaris.[7] These patients, similar to the one presented in the case report, thus may not have been captured in the most recent studies on GPP.

Bimekizumab is a monoclonal antibody targeted against IL-17A, IL-17F, and IL-17AF. Its unique property in comparison to older monoclonal antibodies affecting the IL-17 pathway is the additional inhibition of IL-17F and IL-17AF. Secukinumab and ixekizumab target only IL-17A, and brodalumab inhibits the IL-17A receptor. This property of bimekizumab has manifested in greater skin clearance for patients with plaque psoriasis compared to secukinumab as seen in a large randomized controlled trial.[8] Two prior case reports document the successful resolution of classic GPP with bimekizumab.[9,10] This biologic has also been used for other forms of pustular psoriasis, including palmoplantar psoriasis (PPP), acrodermatitis continua of Hallopeau, and palmoplantar plaque psoriasis with pustules.[11,12] The patient presented here not only successfully transitioned from infliximab

to bimekizumab, but also had complete resolution of his skin and joint disease, including lesions recalcitrant to years of treatment. Importantly, the improvement of his palmoplantar and intertriginous disease notably enhanced his reported quality of life.

To our knowledge, this is the first report of a patient with concomitant GPP and plaque psoriasis successfully treated with bimekizumab. This patient had improvement in both the plaque and pustule manifestation of his disease without adverse events or recurrence of disease as he was nearing his next dose. This biologic may offer another effective treatment option for GPP.

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