Paradoxical psoriatic arthritis flare with the initiation of brodalumab and guselkumab

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Key words: biologics; brodalumab; guselkumab; paradoxical reaction; psoriasis; psoriatic arthritis.

INTRODUCTION

Paradoxical plaque psoriasis reactions have been reported with biologics, primarily with the use of anti-tumor necrosis factor (TNF) agents. Brodalumab (Siliq, Valeant Pharmaceuticals), a human monoclonal antibody against interleukin (IL)-17 receptor A (IL17RA), has been proven to be effective against psoriasis and psoriatic arthritis (PsA).[1] Guselkumab (Tremfya, Janssen Biotech), an interleukin 23 blocker, has also been proven to be effective in treating moderate to severe psoriasis and PsA.[2] Guselkumab has been recently approved by the United States Food and Drug Administration to treat PsA. Both of these biologics contend as alternative options after the failure of a first-line biologic agent, as well as potential first-line treatment options in biologic-naïve patients.

We report an unusual case of severe and worsening arthritis in long-standing psoriasis and PsA patient within days of starting brodalumab and subsequently within days of beginning guselkumab despite a significant clearing of plaque psoriasis.

Abbreviations used:

IL:	interleukin
psA:	psoriatic arthritis
TNF:	tumor necrosis factor

CASE DESCRIPTION

A 47-year-old white man with a long-standing history of PsA and worsening plaque psoriasis was previously treated with tofacitinib (Xeljanz, Pfizer) for 8 months with intermittent prednisone tapers. His PsA had been managed in the past by rheumatology using methotrexate, etanercept, adalimumab, and secukinumab, with limited success. The patient achieved control of arthritis, which usually affected his bilateral knees and lumbar spine, with tofacitinib monotherapy. Previous treatments with phototherapy, methotrexate, and anti-TNF biologics were insufficient in controlling the patient's plaque psoriasis. The presenting body surface area was 60%, with the patient having a body mass index of 50.3, making topical regimens an impractical approach. The patient was referred to dermatology to manage his persistent plaque psoriasis in conjunction with his rheumatologic care (tofacitinib).

To better control the cutaneous manifestations, alternative classes of biologics, acitretin, and apremilast, were discussed. 210 mg brodalumab subcutaneous injection trial was chosen, keeping in mind the patient's risk factors, and was administered in conjunction with tofacitinib. The patient noticed significant cutaneous improvement within days. However, on day seven, the patient contacted the office with knee pain, shoulder pain, and walking difficulties. No rechallenge of brodalumab was given. The patient continued to see improvement in his plaque psoriasis for two weeks after his initial injection. Three weeks following the administration of brodalumab, the patient returned with the resolution of joint pain and a return of plaque psoriasis (Figs 1 and 2). His psoriatic guttate lesions were pruritic and consisted of severe plaque elevation and a dusky-to-deep erythema with the predominance of thick tenacious scale, which was typical of his usual cutaneous flares. An in-office administration of 100 mg guselkumab subcutaneous injection was started, which improved the patient's plaque psoriasis within days.

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Funding sources: None.

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JAAD Case Reports 2021;10:47-9.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.01.014

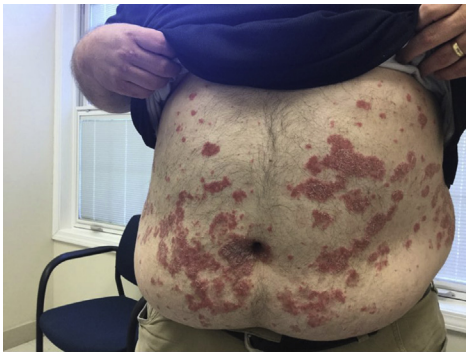

Fig 1. Image of the anterior aspect of the body, showing extensive involvement of the abdomen during the patient's plaque psoriasis flare, which occurred between stopping brodalumab and starting guselkumab. This flare was similar to his previous cutaneous flares before initiating brodalumab.

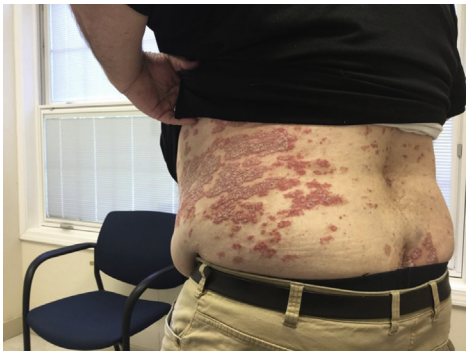

Fig 2. Image of the posterior aspect of the body, showing extensive involvement of the back during the patient's plaque psoriasis flare, which occurred between stopping brodalumab and starting guselkumab. This flare was similar to his previous cutaneous flares before initiating brodalumab.

However, one week after starting guselkumab, the patient was hospitalized with a PsA flare involving significant right knee pain. During the hospitalization, fluid was drained from the affected knee showing elevated white blood cell levels. X-ray imaging of his knee revealed arthritic changes with suprapatellar effusion. Synovial fluid and blood cultures showed no growth. The hospitalization lasted for 5 days, with increasing leukocytosis each day. The patient was discharged while on a prednisone taper. Guselkumab was discontinued. Two weeks after the hospitalization, the patient noticed sustained swelling of the right calf, which was due to a ruptured popliteal cyst as a result of inflammation from his PsA flare, shown by a venous duplex scan performed shortly after his discharge. As a result, the patient underwent a repeat arthrocentesis for symptomatic relief and received another course of steroids. The patient is ambulating appropriately and is doing well.

DISCUSSION

Paradoxical reactions have been described in the literature for biologics such as anti-TNF alpha agents, ustekinumab, secukinumab, and ixekizumab.[3] It has been hypothesized that joint inflammation in paradoxical psoriatic reactions occurs due to a cytokine imbalance caused by the biologic agent.[4] It has also been theorized that there is a lower efficacy of certain biologics in the joints than in the skin, causing an appearance of subclinical arthritis, which usually manifests as an absence of skin lesions with the appearance of joint inflammation, as seen in our patient.[4]

Paradoxical reactions caused by newer biologics are unusual. Only one case of a paradoxical reaction to brodalumab has been published, manifesting as *de novo* psoriatic alopecia, which was effectively managed with guselkumab.[5] This paradoxical case of alopecia exhibited rapid improvement upon initiation of brodalumab and a subsequent paradoxical reaction shortly after the resolution of initial symptoms, similar to our patient. In contrast to our patient, this patient experienced a resolution of his reaction with the initiation of guselkumab, while guselkumab appeared to trigger a psoriatic flare in our patient. A new-onset PsA paradoxical reaction has also been reported with ustekinumab, an anti-IL12/IL23 antibody.[6] However, in both of the aforementioned case reports, a *de novo* reaction was seen, which is different from our patient who exhibited a worsening of previously controlled arthritis due to underlying PsA. Similar reactions have been outlined in patients who developed PsA while receiving biologic treatment for plaque psoriasis.[7] The authors hypothesized that biologics might not be sufficient to prevent joint manifestations in some patients.[7] Additionally, patients unresponsive to anti-psoriatic therapies may develop uncontrolled inflammation, leading to articular involvement, as in to our patient, who had uncontrolled psoriasis before beginning brodalumab and guselkumab.[7] Although the exacerbation of the underlying disease is possible, a paradoxical reaction appears consistent given the timeline of the joint effusions with the initiation of both biologics in the context of previously controlled arthritis (through tofacitinib). A worsening of arthritic disease with these agents has not been reported in the setting of a dramatic improvement of cutaneous features.

In summary, we report a previously undescribed case of a severe paradoxical PsA flare in the setting of

psoriasis improvement with the start of both brodalumab and guselkumab injections. Although paradoxical reactions have been described for biologic agents in the past, this case highlights a possible adverse reaction associated with the initiation of both brodalumab and guselkumab.

Conflicts of interest

None disclosed.

REFERENCES

1. Mease PJ, Genovese MC, Greenwald MW, et al. Brodalumab, an anti-IL17RA monoclonal antibody, in psoriatic arthritis. *N Engl J Med*. 2014;370:2295-2306.
2. Deodhar A, Gottlieb AB, Boehncke WH, et al. Efficacy and safety of guselkumab in patients with active psoriatic arthritis: a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet*. 2018;391:2213-2224.
3. Puig L. Paradoxical reactions: anti-tumor necrosis factor alpha agents, ustekinumab, secukinumab, ixekizumab, and others. *Curr Probl Dermatol*. 2018;53:49-63.
4. Munera-Campos M, Ballesca F, Carrascosa J. Paradoxical reactions to biologic therapy in psoriasis: a review of the literature. *Actas Dermosifiliogr*. 2018;109:791-800.
5. Hosokawa Y, Hamada T, Ashida H, Ikeda M. Effective treatment with guselkumab for psoriatic alopecia as paradoxical reaction. *J Dermatol*. 2019;46:e302-e303.
6. Čarija A, Ivić I, Marasović-Krstulović D, Puizina-Ivić N. Paradoxical psoriatic arthritis in a patient with psoriasis treated with ustekinumab. *Rheumatology (Oxford)*. 2015;54:2114-2116.
7. Napolitano M, Balato N, Caso F, et al. Paradoxical onset of psoriatic arthritis during treatment with biologic agents for plaque psoriasis: a combined dermatology and rheumatology clinical study. *Clin Exp Rheumatol*. 2017;35:137-140.