Case Report

Complete Clearance of Pustular Psoriasis After A Single Dose of Risankizumab

Ashleigh E Hermann, DO[1]; Stephen E Weis, DO[2]

Author affiliations are listed at the end of this article.

Correspondence to:
Ashleigh Hermann, DO
1301 Throckmorton Street
Unit 1803
Fort Worth, TX 76102
(Ashleigh.beth1170@gmail.com)

Abstract

Introduction
Psoriasis is a chronic, multifactorial, inflammatory skin disease with several subtypes, including pustular psoriasis. Pustular psoriasis is characterized by pustules forming lakes of pus on the skin. Pro-inflammatory pathways, such as the interleukin (IL)-17/IL-23 axis, have been shown to play a significant role in the pathogenesis of psoriasis. Biologic therapies directed towards these pro-inflammatory pathways have effectively treated plaque psoriasis, but fewer treatments have shown similar efficacy for pustular psoriasis.

Case Presentation
We present a 45-year-old Black female who presented to the dermatology clinic with generalized pustular psoriasis affecting approximately 70% of her body surface area. She also noted joint stiffness and pain that was worse after inactivity. Her disease did not respond to previous treatment, which was using adalimumab for 6 months. She also had no response to a 3-month course of apremilast.

Two weeks after receiving her first dose of risankizumab, she had complete clearance of her pustular psoriasis, affecting 0% of her body surface area. She also noted significant improvement in her joint pain.

Conclusions
There is little data regarding the efficacy of IL-23 inhibitors in treating generalized pustular psoriasis. To date, our case is the only reported instance in the literature showing rapid clearance of pustular psoriasis after 1 injection of risankizumab. This case illustrates that IL-23 inhibitors play an essential role in the rapid clearance of pustular psoriasis.

Keywords
generalized pustular psoriasis; risankizumab; interleukin-23 (IL-23) inhibitors

Introduction
Psoriasis is a chronic, multifactorial, inflammatory skin disease with several subtypes. It can cause debilitating joint disease as well, known as psoriatic arthritis. Plaque psoriasis is the most common subtype, but there are also many other types of psoriasis. These types include guttate psoriasis, which occurs in 10% of patients, pustular, and erythrodermic—which occurs in fewer than 3% of patients with psoriasis.[1]

Pustular psoriasis is characterized by repeated flares of a sudden onset eruption of generalized sterile pustules, characteristically coalescing into lakes of pus. It is a debilitating skin disease, often with multisystem involvement. These skin findings have been associated with various systemic symptoms, including fever, myalgias, and arthralgias.[2,3] The most common laboratory findings include leukocytosis, elevated C-reactive protein serum levels, and liver function test abnormalities.[4,5] Pustular psoriasis has also been associated with hypocalcemia

and hypoparathyroidism.[6,7] Histopathologically, pustular psoriasis is characterized by pustules containing neutrophils in the epidermis with parakeratosis. Spongiform pustules of Kogoj and hyperplasia of suprapapillary vessels may also be present.[8]

Historically, pustular psoriasis was considered a variant of plaque psoriasis. However, recent research suggests these may be 2 genetically distinct conditions without a common pathophysiologic mechanism.[9] Biologics targeting the interleukin (IL)-17/IL-23 and tumor necrosis factor (TNF)-alpha pro-inflammatory pathways are beneficial in treating plaque psoriasis. There are a limited number of published reports with targeted immunotherapy for generalized pustular psoriasis.[10]

Case Description

A 45-year-old Black female presented to the dermatology clinic with generalized pustular psoriasis affecting approximately 70% of her body surface area (BSA) (**Figure 1A-C**). She also noted joint stiffness and pain that was worse after inactivity. She expressed a great deal of distress associated with her psoriasis. She was initially prescribed adalimumab, but after 6 months she showed no improvement in her psoriasis or psoriatic arthritis. Her physician then switched her to apremilast. She continued apremilast for 3 months without any improvement. The patient had been off apremilast for 3 months by the time she started risankizumab in the hope of achieving relief of all of her symptoms.

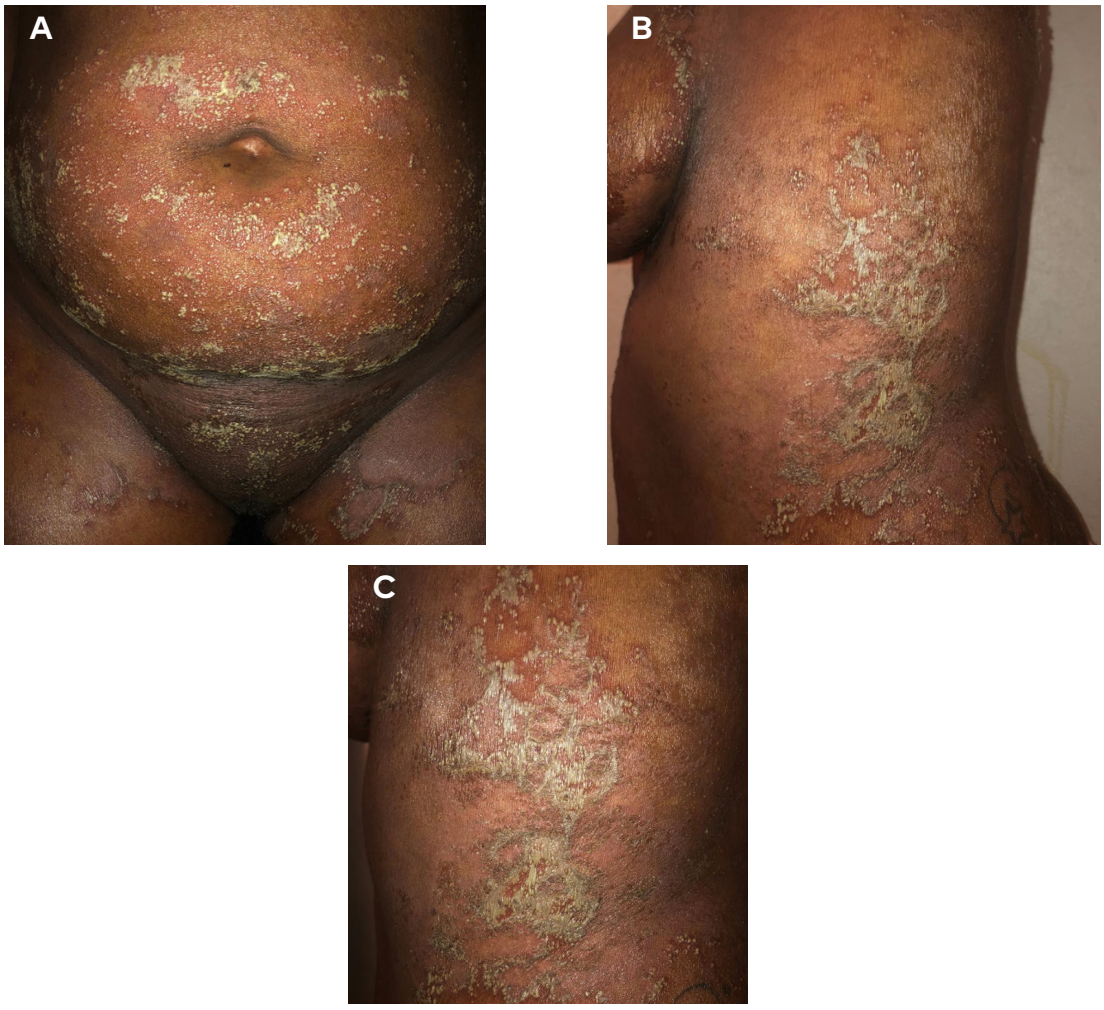

Figure 1. A. Multiple pustules on erythematous plaques coalesce to form "lakes of pus" on the abdomen, groin, and proximal extremities. **B.** Multiple pustules coalesce to form a large interconnecting plaque on the left lateral trunk and breast. **C.** An up-close view of the large plaque that consists of coalescing pustules forming a "lake of pus" on erythematous plaques.

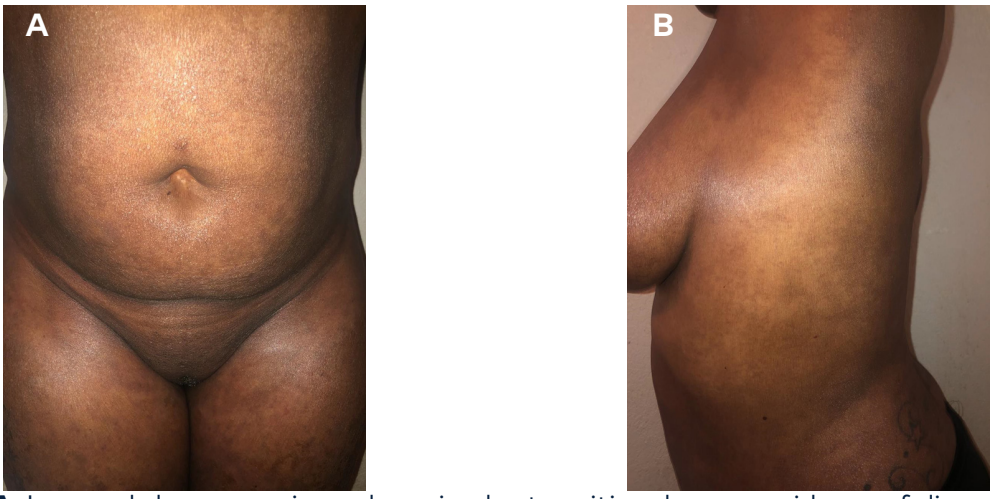

Figure 2. A. Lower abdomen, groin, and proximal extremities show no evidence of disease 2 weeks after a single injection with risankizumab. **B.** The left lateral trunk shows no evidence of disease 2 weeks after a single injection of risankizumab.

Two weeks after receiving her first dose of risankizumab, she had complete clearance of her pustular psoriasis, affecting 0% BSA (**Figure 2A-B**). She also noted significant improvement in her joint pain.

Discussion

Psoriasis is a chronic, multifactorial, inflammatory skin disease with several subtypes. Pustular psoriasis is characterized by repeated flares of a sudden onset eruption of generalized sterile pustules, characteristically coalescing into lakes of pus. Plaque psoriasis is characterized by well-demarcated erythematous plaques with a micaceous scale.

There have been various studies evaluating the cytokines involved in psoriasis. Plaque psoriasis occurs due to an upregulation of an inflammatory pathway in the skin. First, IL-23 is produced by keratinocytes and activated antigen-presenting cells. After it binds to its receptor IL-23R, it induces differentiation of T helper 17 cells that release cytokines in the IL-23/IL-17 axis, leading to psoriasis and psoriatic arthritis.[11] IL- 23 inhibitors effectively inhibit the cytokines involved in psoriasis downstream in the IL-23/IL-17 axis. Biologic treatments that inhibit these cytokines have been studied for plaque psoriasis, but fewer treatments have been shown to be efficacious for pustular psoriasis.

Generalized pustular psoriasis utilizes pathways both overlapping and separate from plaque psoriasis.[12] Pustular psoriasis is typically idiopathic but has also been found to be associated with 3 different gene mutations: IL-36-receptor antagonist (IL-36RN), caspase recruitment domain-containing protein 14 (CARD14), and adaptor protein complex 1 (AP1S3). IL36RN and CARD14 gene mutations increase expression of pro-inflammatory cytokines involved in the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) signaling pathway.[13,14] AP1S3 leads to the deregulation of the skin's innate immune response.[15] These pathways drive inflammation and induce a pustular skin eruption. A study performed by Johnston et al revealed the dominant cytokines isolated from pustular psoriasis lesions were IL-36 and IL-1 and also found elevated levels of IL-17 and TNF. The elevated levels of IL-17 were mostly unknown but postulated to be due to similarities in IL-1/17/36-induced gene sets driving a perceived IL-17A signature in the data.[12] Biologics targeting IL-17A have been used with success in treating generalized pustular psoriasis.[16-19]

There is little data regarding the efficacy of IL-23 inhibitors in the treatment of generalized pustular psoriasis. A randomized control trial revealed that ustekinumab (IL- 12/23 inhibitor) showed greater efficacy than anti-TNF-alpha agents in the treatment of pustular psoriasis.[20] There have been no studies to date showing the efficacy of the IL-23 inhibitor risankizumab in treating generalized pustular psoriasis. There has been 1 report of a patient on adalimumab with uncontrolled plaque psoriasis who was switched to risankizumab and subsequently

developed pustular psoriasis. This incident is in contrast to our patient. Our patient was previously treated with apremilast, then came off of it for approximately 3 months, and then started on risankizumab, which resulted in complete clearance of her pustular psoriasis after a single dose.[21] Our case is a unique instance in which the patient achieved complete clearance of generalized pustular psoriasis 2 weeks after receiving 1 dose of risankizumab.

The differential diagnosis includes SAPHO syndrome, characterized by synovitis, acne, pustular dermatoses, hyperostosis, and osteitis. This condition shares common features with psoriatic arthritis, though the main cutaneous manifestations of SAPHO include palmoplantar pustulosis, severe acne, and hidradenitis suppurativa. Also, this condition occurs with musculoskeletal manifestations, which typically include non-infectious osteitis, hyperostosis, and synovitis of the anterior chest wall, with the sternoclavicular junction being commonly affected, followed by the spine, sacroiliac joints, and peripheral non-erosive arthritis.[22] Acute generalized exanthematous pustulosis (AGEP) would also be on the differential with a diffuse pustular eruption. AGEP is a severe cutaneous adverse reaction characterized by the rapid development of nonfollicular, sterile pustules on an erythematous base. It is attributed to drugs in the majority of cases.[23] Our patient had an established diagnosis of pustular psoriasis with no recent history of new medications.

Conclusion

Psoriasis involves crosstalk between proinflammatory pathways that eventually lead to multisystem disease. Sustained activity of IL-1, IL-17, TNF, and IL-36 has been demonstrated in pustular psoriasis lesions, providing a rationale for treatment targeting these cytokines.[12] This case report illustrates that IL-23 inhibitors may also be effective in treating generalized pustular psoriasis. This case is unique due to the rapid clearance of pustular psoriasis only 2 weeks after 1 injection of risankizumab.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Dr Hermann is an employee of Medical City Fort Worth, a hospital affiliated with the journal's publisher.

Dr Weis is an employee of Medical City Weatherford, a hospital affiliated with the journal's publisher.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Author Affiliations

1. Medical City Fort Worth, Fort Worth, TX
2. Medical City Weatherford, Weatherford, TX

References

1. de Rie MA, Goedkoop AY, Bos JD. Overview of psoriasis. *Dermatol Ther*. 2004;17(5):341-349. doi:10.1111/j.1396-0296.2004.04037.x
2. Baker H, Ryan TJ. Generalized pustular psoriasis. A clinical and epidemiological study of 104 cases. *Br J Dermatol*. 1968;80(12):771-793. doi:10.1111/j.1365- 2133.1968.tb11947.x
3. Zelickson BD, Muller SA. Generalized pustular psoriasis. A review of 63 cases. *Arch Dermatol*. 1991;127(9):1339-1345. doi:10.1001/archderm.1991.01680080075005
4. Umezawa Y, Ozawa A, Kawasima T, et al. Therapeutic guidelines for the treatment of generalized pustular psoriasis (GPP) based on a proposed classification of disease severity. *Arch Dermatol Res*. 2003;295 Suppl 1:S43-S54. doi:10.1007/s00403-002-0371-6
5. Viguier M, Allez M, Zagdanski AM, et al. High frequency of cholestasis in generalized pustular psoriasis: evidence for neutrophilic involvement of the biliary tract. *Hepatology*. 2004;40(2):452-458. doi:10.1002/hep.20305
6. Lee Y, Nam YH, Lee JH, Park JK, Seo YJ. Hypocalcaemia-induced pustular psoriasis-like skin eruption. *Br J Dermatol*. 2005;152(3):591-593. doi:10.1111/j.1365-2133.2005.06460.x
7. Guerreiro de Moura CA, de Assis LH, Góes P, et al. A case of acute generalized pustular psoriasis of von Zumbusch triggered by hypocalcemia. *Case Rep Dermatol*. 2015;7(3):345-351. doi:10.1159/000442380
8. Iizuka H, Takahashi H, Ishida-Yamamoto A. Pathophysiology of generalized pustular psoriasis. *Arch Dermatol Res*. 2003;295 Suppl 1:S55-S59. doi:10.1007/s00403-002-0372-5

9. Setta-Kaffetzi N, Navarini AA, Patel VM, et al. Rare pathogenic variants in IL36RN underlie a spectrum of psoriasis-associated pustular phenotypes. *J Invest Dermatol*. 2013;133(5):1366-1369. doi:10.1038/jid.2012.490
10. Boehner A, Navarini AA, Eyerich K. Generalized pustular psoriasis—a model disease for specific targeted immunotherapy, systematic review. *Exp Dermatol*. 2018;27(10):1067-1077. doi:10.1111/exd.13699
11. Boutet MA, Nerviani A, Gallo Afflitto G, Pitzalis C. Role of the IL-23/IL-17 axis in psoriasis and psoriatic arthritis: the clinical importance of its divergence in skin and joints. *Int J Mol Sci*. 2018;19(2):530. doi:10.3390/ijms19020530
12. Johnston A, Xing X, Wolterink L, et al. IL-1 and IL-36 are dominant cytokines in generalized pustular psoriasis. *J Allergy Clin Immunol*. 2017;140(1):109-120. doi:10.1016/j.jaci.2016.08.056
13. Hoegler KM, John AM, Handler MZ, Schwartz RA. Generalized pustular psoriasis: a review and update on treatment. *J Eur Acad Dermatol Venereol*. 2018;32(10):1645-1651. doi:10.1111/jdv.14949
14. Marrakchi S, Guigue P, Renshaw BR, et al. Interleukin-36-receptor antagonist deficiency and generalized pustular psoriasis. *N Engl J Med*. 2011;365(7):620-628. doi:10.1056/NEJMoa1013068
15. Bachelez H. Pustular psoriasis: the dawn of a new era. *Acta Derm Venereol*. 2020;100(3):87–92. doi:10.2340/00015555-3388
16. Saeki H, Nakagawa H, Nakajo K, et al; Japanese Ixekizumab Study Group. Efficacy and safety of ixekizumab treatment for Japanese patients with moderate to severe plaque psoriasis, erythrodermic psoriasis and generalized pustular psoriasis: results from a 52-week, open-label, phase 3 study (UNCOVER-J). *J Dermatol*. 2017;44(4):355-362. doi:10.1111/1346-8138.13622
17. Imafuku S, Honma M, Okubo Y, et al. Efficacy and safety of secukinumab in patients with generalized pustular psoriasis: a 52-week analysis from phase III open-label multicenter Japanese study. *J Dermatol*. 2016;43(9):1011-1017. doi:10.1111/1346-8138.13306
18. Plachouri KM, Chourdakis V, Georgiou S. The role of IL-17 and IL-17 receptor inhibitors in the management of generalized pustular psoriasis. *Drugs Today (Barc)*. 2019;55(9):587-593. doi:10.1358/dot.2019.55.9.3020159
19. Ho PH, Tsai TF. Successful treatment of refractory juvenile generalized pustular psoriasis with secukinumab monotherapy: a case report and review of published work. *J Dermatol*. 2018;45(11):1353-1356. doi:10.1111/1346-8138.14636
20. Griffiths CE, Strober BE, van de Kerkhof P, et al; ACCEPT Study Group. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. *N Engl J Med*. 2010;362(2):118-128. doi:10.1056/NEJMoa0810652
21. McFeely O, Pender E, Victory L, Almutlaq H, Storan E. Risankizumab-induced paradoxical pustular psoriasis. *Clin Exp Dermatol*. 2022 Mar;47(3):616-617. doi: 10.1111/ced.15006
22. Furer V, Kishimoto M, Tsuji S, et al. The diagnosis and treatment of adult patients with SAPHO syndrome: controversies revealed in a multidisciplinary international survey of physicians. *Rheumatol Ther*. 2020 Dec;7(4):883-891. doi: 10.1007/s40744-020-00235-2
23. Szatkowski J, Schwartz RA. Acute generalized exanthematous pustulosis (AGEP): a review and update. *J Am Acad Dermatol*. 2015;73(5):843-848. doi:10.1016/j.jaad.2015.07.017