Recalcitrant annular pustular psoriasis associated with psoriatic arthritis successfully treated with secukinumab

María Herrero-Moyano, MD, Tania Marusia Capusan, MD, Constanza Martínez-Mera, MD, Mar Llamas-Velasco, PhD, and Esteban Daudén, PhD
Madrid, Spain

Key words: acitretin; annular pustular psoriasis; generalized pustular psoriasis; interleukin-17A; neutrophils; psoriatic arthritis; pustular psoriasis; secukinumab.

INTRODUCTION

Pustular psoriasis is a well-known form of psoriasis, the main variants of which are acute generalized pustular psoriasis (GPP), including GPP of pregnancy, annular pustular psoriasis (APP), acrodermatitis continua of Hallopeau (ACH), and palmoplantar pustulosis (PPP). APP is a rare entity that presents as recurring annular or figurate erythematous plaques with peripheral pustules and scales that expand centrifugally.

Secukinumab is a novel human monoclonal antibody that inhibits interleukin (IL)-17A. Secukinumab was recently approved for the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis. We present the first report to our knowledge of an APP case successfully treated with secukinumab.

Abbreviations used:

ACH:	acrodermatitis continua of Hallopeau
APP:	annular pustular psoriasis
DLQI:	Dermatology Life Quality Index
GPP:	generalized pustular psoriasis
IL:	interleukin
PPP:	palmoplantar pustulosis
BSA:	body surface area
PPASI:	Pustular Psoriasis Area and Severity Index
VAS:	Visual Analog Scale

CASE

A 29-year-old white woman presented with a 22-year history of severe pustular eruptions arising on erythematous skin. Most of the pustular eruptions had annular morphology although occasionally showed generalized pustular flares. During this time, dyslipidemia and psoriatic spondyloarthropathy were diagnosed. She had a body mass index of 25.22. Up to 5 biopsy specimens of the cutaneous lesions were taken and analyzed, which showed histopathologic findings indicative of pustular psoriasis. A mutation analysis of the IL-36 receptor antagonist gene was performed with negative results. The patient was treated with acitretin (0.5-1 mg/kg/d), ciclosporin, methotrexate, and psoralen and ultraviolet A monotherapy, achieving only a partial response, particularly with acitretin. Treatment with infliximab in combination with acitretin was started in October 2007. This treatment failed to control the disease, and infliximab was changed to adalimumab, achieving an almost complete response.[1] The patient remained under this combination therapy for 19 months, but unfortunately, she lost the response. Because of the severity of the annular pustular flares, ustekinumab, etanercept, and golimumab were tried successively, always in combination with acitretin (up to 50 mg/d), although the response of psoriasis was very poor. In March 2016, treatment with secukinumab was started (300 mg at baseline, 1, 2, 3, and 4 weeks, and monthly

From the Dermatology Department, Hospital Universitario de La Princesa.

Funding sources: None.

Conflicts of interest: Dr Daudén has been an advisory board member and consultant and has received grants, research support, and speaker's honoraria or has participated in clinical trials for Abbott, Astellas, Biogen, Centocor Ortho Biotech, Galderma, Glaxo, Janssen-Cilag, Leo Pharma, Merck-Serono, Novartis, Pfizer, Schering-Plough, Stiefel, Wyeth Pharmaceuticals, and 3M Pharmaceuticals. Dr Llamas-Velasco has participated in clinical trials or received speaker's honoraria for Abbvie, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Lilly, and Pfizer. Drs Herrero-Moyano and Capusan have no conflicts to disclose.

Correspondence to: María Herrero-Moyano, MD, Hospital Universitario de La Princesa, Servicio de Dermatología, Calle Diego de León 62, 28028 Madrid, Spain. E-mail: mariaherreromoyano@gmail.com.

JAAD Case Reports 2018;4:842-4.
2352-5126

https://doi.org/10.1016/j.jdcr.2018.03.016

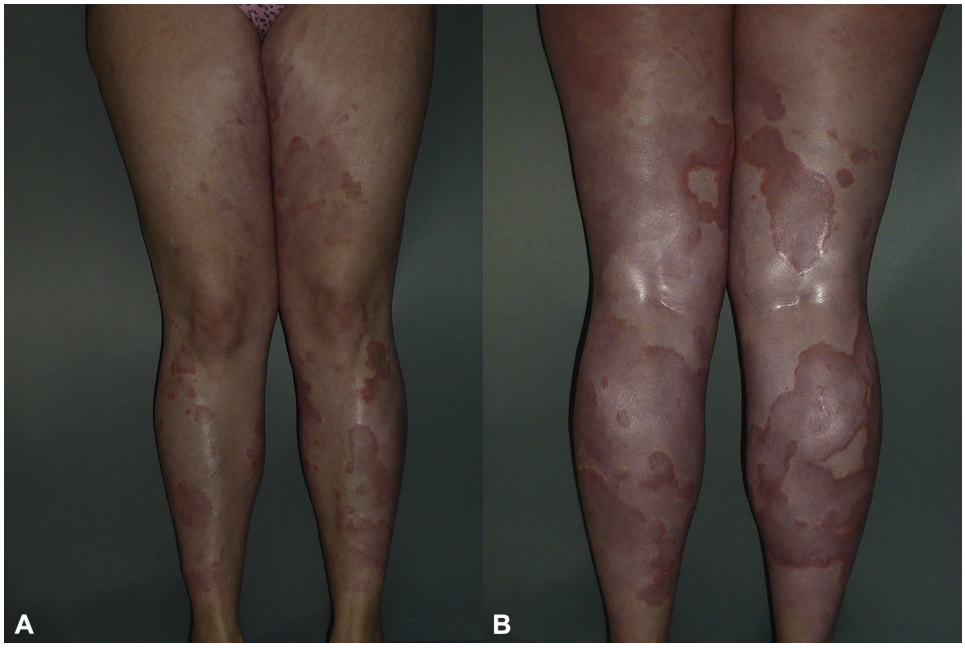

Fig 1. Annular pustular lesions before treatment.

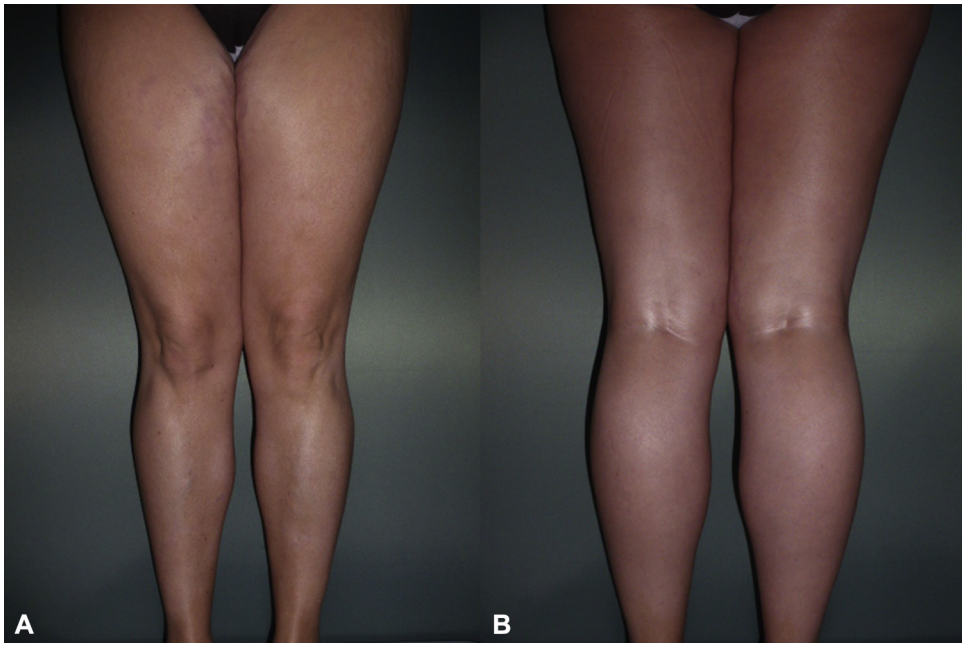

Fig 2. Lesions 3 months after treatment with secukinumab.

afterward) in combination with acitretin (35 mg/d). At baseline, she presented severe annular pustular lesions, particularly on the trunk and upper and lower extremities: Pustular Psoriasis Area and Severity Index (PPASI), 15; body surface area (BSA), 15%; Patient Global Psoriasis Assessment, 7; Euroqol, 50; Dermatology Life Quality Index (DLQI), 12; and arthritis Visual Analog Scale (VAS), 6 (Fig 1). She presented a dramatic improvement (at 1 month: PPASI, 1; BSA, 1%; Patient Global Psoriasis Assessment, 1; Euroqol, 80; DLQI, 6; and arthritis VAS, 4), and at 3 months the patient had a complete clearing of the pustular psoriasis (Fig 2). To date, after 20 months of continuous treatment, the patient remains cleared despite tapering of acitretin to 10 mg/d (PPASI, 0; DLQI, 2). Only the joint symptomatology remains (arthritis VAS, 3). No adverse events were reported.

Table I. Published reports on the use of secukinumab in different variants of pustular psoriasis

Case reports	Clinical variant	No. of patients	Comedication	Overall response
Böhner et al,[2] 2016	GPP	1	No	GPPASI from 48-8 and BSA from 80-10 at wk 7
Imafuku et al,[8] 2016	GPP	12	Cyclosporine (4 pts), etretinate (3 pts, 10-40 mg/d), methotrexate (1 pt), and prednisolone (1 pt)	At wk 52: PASI 75, 72.7%; PASI 90, 63.6%; and PASI 100, 27.3%
Polesie et al,[3] 2017	GPP	1	No	Clear at wk 3
Mugheddu et al,[4] 2017	GPP	1	No	PASI 75 was achieved at wk 4, PASI 90 at wk 8, and complete remission at wk 12, maintained at wk 24.
Yeung et al,[7] 2016	PPP	1	No	Complete resolution of pustules at wk 3
Baron et al,[5] 2017	ACH	1	No	Clearance of pustules at 5 d
Muggli et al,[6] 2017	ACH	1	No	Complete resolution at 6 wk
Our case	APP	1	Acitretin (35 mg/d)	Complete resolution at 3 mo, maintained after 20 mo

GPPASI, Generalized pustular PASI; *PASI*, Psoriasis Area and Severity Index; *pt*, patient.

DISCUSSION

Annular pustular psoriasis is a rare form of psoriasis excluded from clinical trials. In a review of the literature about the treatment of pustular psoriasis with secukinumab, we found 3 case reports of GPP,[2-4] 2 case reports of ACH,[5,6] 1 of PPP,[7] all responding well to this drug, although the effectiveness evaluation system is very variable (Table I). We also found a Japanese 52-week, open-label, phase III, multicenter, single-arm study on patients with GPP (APP was an exclusion criteria), in which the treatment succeeded in 10 (83.3%) of 12 patients.[8] It has been suggested that IL-17A plays a role in the migration of neutrophils to psoriatic lesions, thereby explaining how inhibition of this cytokine may contribute to the improvement of pustular psoriasis.[9] There are no publications to our knowledge reporting the treatment of APP with secukinumab.

We emphasize the rapid and complete response to standard doses achieved in our patient, who suffered from a severe APP unresponsive to other conventional and biological therapies. We consider that the role of acitretin in the response of our patient was limited, as it achieved only a partial response when used as monotherapy, and it has been used at high doses (35-50 mg/d) in combination with different biological drugs since 2007 with low success rates.

Further studies are warranted to evaluate the effectiveness and safety of secukinumab in patients with severe APP.

The authors thank Manuel Gomez Gutierrez for copy editing the manuscript.

REFERENCES

1. Gallo E, Llamas-Velasco M, Daudén E, García-Diez A. Refractory generalized pustular psoriasis responsive to a combination of adalimumab and acitretin. *Int J Dermatol*. 2013;52(12):1610-1611.
2. Böhner A, Roenneberg S, Eyerich K, Eberlein B, Biedermann T. Acute generalized pustular psoriasis treated with the IL-17A antibody secukinumab. *JAMA Dermatol*. 2016;152(4):482-484.
3. Polesie S, Lidholm AG. Secukinumab in the treatment of generalized pustular psoriasis - a case report. *Acta Derm Venereol*. 2017;97(1):124-125.
4. Mugheddu C, Atzori L, Lappi A, et al. Successful secukinumab treatment of generalized pustular psoriasis and erythrodermic psoriasis. *J Eur Acad Dermatol Venereol*. 2017;31(9):e420-e421.
5. Baron JA. Acrodermatitis of Hallopeau and erosive oral mucositis successfully treated with secukinumab. *JAAD Case Rep*. 2017;3(3):215-218.
6. Muggli D, Maul JT, Anzengruber F, et al. Secukinumab for acrodermatitis continua of Hallopeau. *JAMA Dermatol*. 2017;153(4):336-337.
7. Yeung J, Valbuena V. Successful use of secukinumab in pustular psoriasis. *JAAD Case Rep*. 2016;2(6):470-472.
8. 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.
9. Nograles KE, Zaba LC, Guttman-Yassky E, et al. Th17 cytokines interleukin (IL)-17 and IL-22 modulate distinct inflammatory and keratinocyte-response pathways. *Br J Dermatol*. 2008;159(5):1092-1102.