Bullous acral eruption related to secukinumab

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Abstract

Skin reactions related to secukinumab are uncommon. Although the initial phase 3 studies of this medication reported infection and urticaria as adverse cutaneous events, other cases of unique adverse events have since been reported. We are presenting a patient who developed an exuberant hand and foot reaction after starting secukinumab.

Keywords: drug reaction, adverse reaction, bullous, secukinumab, psoriasis, IL-17

Introduction

Secukinumab is a human monoclonal antibody targeting IL-17A and was the first biologic in this class to be FDA-approved for the treatment of moderate-to-severe psoriasis. Expected potential cutaneous side effects include infection and urticaria, though since becoming available commercially other cutaneous adverse effects have been published. Herein we report a case of a patient with a history of atopic dermatitis and psoriasis who developed a bullous acral eruption after starting secukinumab.

Case Synopsis

A 44-year-old woman with a history of atopic dermatitis and psoriasis on secukinumab presented with a new onset of a painful rash on her hands and feet. The patient had a longstanding history of atopic dermatitis since she was an infant that affected her face, trunk, extremities (including her hands and feet); in adulthood she developed a new rash on her scalp, trunk, elbows, and knees that was diagnosed as psoriasis in 2015. She tried multiple treatments for psoriasis, including topical steroids, narrow band UVB, adalimumab, and ustekinumab. Each therapy initially caused improvement but then efficacy would wane. In February 2018, the patient was started on secukinumab, receiving the loading dose of 300mg at day 0, followed by weekly 300mg injections over the subsequent four weeks. In the days following her fifth dose, the patient began experiencing a painful rash on her palms and soles. Other medications she was taking at that time included halobetasol ointment, fluocinonide gel, and tacrolimus ointment for her psoriasis and atopic dermatitis. In addition to these she was taking metformin, spironolactone, and norethindrone-ethinyl estradiol for PCOS and albuterol as needed for asthma. These medications were long-standing. She had also taken a course of doxycycline for a biopsy site infection, which she had tolerated in the past without incident. She denied any other new medications or supplements in the preceding

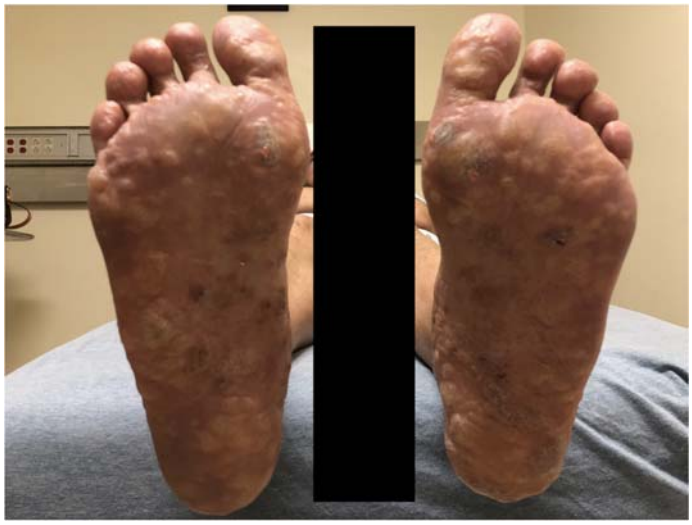

Figure 1: *Deep-seated tense vesicles coalescing into bullae on soles*

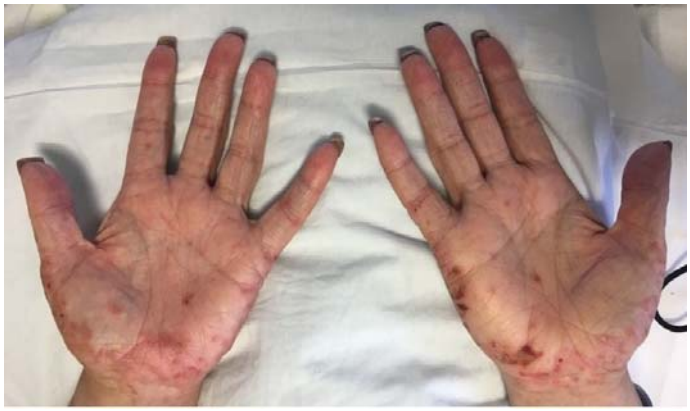

Figure 2*: Deep-seated tense vesicles on proximal palms*

months and was otherwise feeling well. Physical examination was notable for numerous deep-seated tense vesicles coalescing into bullae on her soles (**Figure 1**) and some on her proximal palms (**Figure 2**). Secukinumab was stopped and the patient was started on cyclosporine for possible flare of dyshidrotic eczema. Given the patient reported excruciating pain and inability to walk, she was admitted to the hospital for further care and pain control.

The differential diagnosis at the time of presentation included dyshidrotic eczema flare, eczema herpeticum, eczema coxsackium, and drug reaction. Infectious work up including bacterial and fungal tissue cultures, PCR for both HSV 1 and 2, Coxsackie A and B, and Parvovirus B19 serologies were negative.

Biopsy of a lesion on the patient's right foot showed spongiotic dermatitis with intra-epidermal vesicle formation, as well as a superficial and deep peri-vascular and interstitial inflammation with many eosinophils, most consistent with a hypersensitivity reaction (**Figures 3A**, **B)**. As secukinumab was the only new medication exposure started in the months prior to this eruption, it was favored to be the culprit medication for her reaction. The patient was started on cyclosporine 100mg twice daily during admission. She improved over the next few days while on cyclosporine and corticosteroid wet wraps. After two weeks, her dose of cyclosporine was decreased to 100mg daily for one month before transitioning to methotrexate 10mg weekly. She has remained off secukinumab since the eruption started, with no new bullous flares in the subsequent year. Her psoriasis and atopic dermatitis are currently well-controlled with methotrexate 15mg weekly and topical corticosteroids.

Case Discussion

Secukinumab is a human monoclonal antibody targeting IL-17A and the first biologic in this class to be FDA-approved for the treatment of psoriasis in 2015. IL-17A is expressed on keratinocytes, and higher levels of expression have been detected in psoriatic lesional skin compared to nonlesional skin [1]. Binding of IL-17A leads to expression of chemokines and subsequent recruitment of

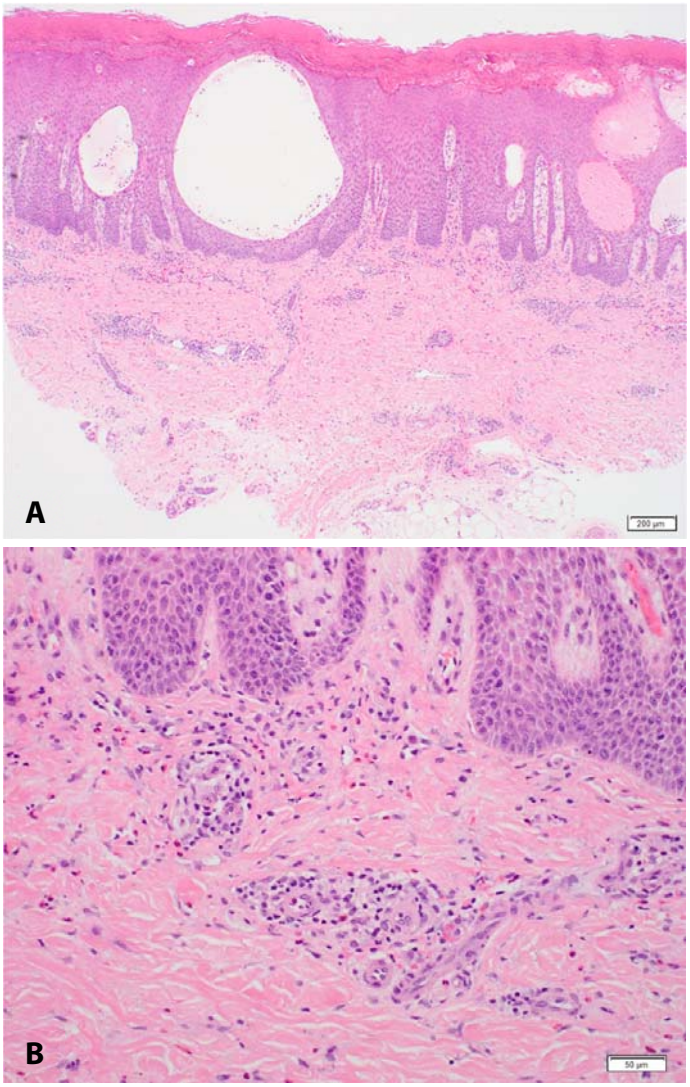

Figure 3*: **A)** Spongiotic dermatitis with intraepidermal vesicle formation, H&E, 40×. **B)** Superficial and deep perivascular and interstitial mixed inflammation, H&E, 200×.*

Table 1: *Adverse cutaneous events associated with secukinumab. Includes reports published through 2018.*

Adverse Cutaneous Events Associated With Secukinumab	
Event	Ref
Truncal pruritic and psoriasiform eruptions	[6-8]
Lichen planus/lichenoid reaction	[9-12]
Bullous pemphigoid	[13]
Subacute cutaneous lupus erythematosus	[14]
Severe mucositis	[15]
Granuloma annulare	[16]
Dermatophytosis	[17]
Recurrent angular cheilitis	[18]

Figure 3: ***A)*** *Spongiotic dermatitis with intraepidermal vesicle formation, H&E, 40×.* ***B)*** *Superficial and deep perivascular and interstitial mixed inflammation, H&E, 200×.*

inflammatory cells, resulting in the increased epidermal proliferation and skin barrier disruption seen in psoriasis [2]. Inhibition of this pathway leads to decreased inflammation and rapid improvement in skin disease, with a 50% reduction in PASI at three weeks; 70% of patients achieve PASI 90 at one year [3].

The recommended dose of secukinumab for plaque psoriasis includes a loading dose of 300mg at weeks 0, 1, 2, 3, and 4, followed by 300mg every four weeks [4]. It is recommended that patients be evaluated for tuberculosis (TB) prior to starting secukinumab and it should be used with caution in patients with chronic or recurrent infections or history of inflammatory bowel disease [4]. In addition to TB screening, guidelines published by the American Academy of Dermatology recommend additional screening with IL-17 inhibitors, including baseline complete blood count (CBC), complete metabolic panel (CMP), serologic testing for hepatitis B and C, as well as consideration of HIV testing if risk factors present [5]. Yearly testing for latent TB should be done for patients at high risk; otherwise, no further lab monitoring is recommended [5].

Reported skin related adverse events from phase 3 trials of secukinumab for psoriasis include oral herpes, urticaria, tinea pedis, oral candidiasis, and impetigo, though case reports of other cutaneous reactions have been reported (**Table 1**), [4, 6-18]. The Naranjo score is a tool that can help determine the likelihood that a medication in question is responsible for the adverse reaction, which in this case is three (**Table 2**), [19]. However, details specific to this patient's course make the score's interpretation imperfect, with a score of three indicating only possible causality. In this case,

Table 2: *Naranjo scale of patient. Her score of 3 suggests a possible causality. Factors specific to this case limit the utility.*

Naranjo Scale of Patient [Ref. 19]		Yes	No	Do Not Know	Score
1.	Are there previous conclusive reports of the reaction?	+1	0	0	0
2.	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3.	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4.	Did the adverse reaction reappear when the drug was readministered?	+2	-1	0	0
5.	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	-1
6.	Did the reaction reappear when a placebo was given?	-1	+1	0	0
7.	Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8.	Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	0
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
				Total Score:	3

secukinumab was only made publicly available in 2015 and so reports of reactions are limited. As the patient's reaction was severe and led to hospital admission, rechallenge of the medication was not done, particularly since multiple alternative treatments exist for psoriasis. No assay is available commercially to detect the medication in the blood and the toxicity level is not known. As the patient was completing her loading dose at the start of the reaction, we are unable to assess changes in the reaction with dose changes. She had never used this medication or other IL-17 inhibitors before, so previous exposure cannot be assessed. For these reasons, the score was not able to reach a definite likelihood score of 9. Although our patient had completed a one-week course of doxycycline 100mg twice daily in the two weeks prior to hospital admission, she had been on this medication before without issue. Doxycycline is also widely used with the most common skin-related adverse event being photosensitivity [20]. Therefore, given the timing of the administration of secukinumab weekly in the 5 weeks prior to this eruption, improvement with cessation of the medication, and a biopsy consistent with a hypersensitivity reaction, the most likely cause of reaction secondary to secukinumab is favored.

Conclusion

To our knowledge, this is the first reported case of a bullous acral eruption from secukinumab. As secukinumab may be started in patients with pre-existing palmar and plantar skin disease, we would like to spread awareness of this potential drug reaction that may occur so that the medication can be stopped in a timely manner.

Potential conflicts of interest

The authors declare no conflicts of interests.

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