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Delayed drug hypersensitivity reaction to secukinumab in a patient with hidradenitis suppurativa

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SUMMARY

A woman in her 30s presented to the dermatology clinic with widespread, pruritic, red papules and plaques involving the ears, trunk and extremities. The rash developed a few days after receiving her second injection of secukinumab, which was initiated for recalcitrant Hurley stage III hidradenitis suppurativa. Investigations revealed a psoriasiform drug hypersensitivity reaction secondary to secukinumab. In this report, we describe the clinical course, histopathological correlation and treatment of this rarely documented reaction.

BACKGROUND

Secukinumab is a human monoclonal antibody that binds to interleukin-17A (IL-17A), a proinflammatory cytokine that has been implicated in the pathogenesis of a wide range of disorders, including psoriasis and psoriatic arthritis. Recent evidence suggests that secukinumab may additionally serve as an effective therapy for patients with hidradenitis suppurativa (HS).[1] In the face of expanding clinical indications and increasing usage of this biologic therapy, adverse effects such as hypersensitivity skin reactions have been reported in a subset of treated patients.[2]

We report a case of a psoriasiform drug hypersensitivity reaction secondary to secukinumab that necessitated prompt discontinuation of the drug and treatment with a prolonged course of oral corticosteroids.

CASE PRESENTATION

A woman in her 30s presented with a widespread, pruritic, rash involving the ears, trunk and extremities of approximately 6 weeks' duration. The lesions first developed a few days after her second 300 mg weekly loading dose of secukinumab, which was originally initiated for recalcitrant Hurley stage III HS (figure 1).

Physical examination revealed numerous erythematous, scaly papules on the bilateral ears, upper chest, inframammary folds, bilateral upper extremities and abdomen (including umbilicus). Large, well-demarcated, erythematous, oedematous plaques were observed to involve the bilateral axillary folds symmetrically (figure 2). Her vital signs were stable, and she denied recent facial swelling or urticaria.

INVESTIGATIONS

A punch biopsy obtained from the right flank revealed psoriasiform epidermal hyperplasia with spongiosis, lymphocyte exocytosis and serous crusting with ample neutrophils in the stratum corneum. A dense superficial perivascular and interstitial infiltrate of lymphocytes with numerous eosinophils was also observed (figure 3). Periodic acid-Schiff stain was negative for fungal elements. In the context of the clinical findings, a diagnosis of a psoriasiform drug hypersensitivity reaction to secukinumab was made.

DIFFERENTIAL DIAGNOSIS

Given the notable involvement of skin folds and pathology displaying psoriasiform epidermal hyperplasia with spongiosis and prominent eosinophils, alternative diagnoses such as secukinumab-induced paradoxical psoriasiform eruption and symmetrical drug-related intertriginous and flexural exanthema were also considered. However, paradoxical psoriasiform eruption was deemed less likely considering the morphology of the lesions as well as the numerous eosinophils seen on histology. In addition, given that our patient did not exhibit gluteal or inguinal involvement, symmetrical drug-related intertriginous and flexural exanthema was felt to be inconsistent with the clinical presentation.

TREATMENT

Secukinumab was discontinued, and because the mean half-life of this biologic agent ranges from 22 to 31 days, an 8-week prednisone taper starting at 80 mg daily and incrementally decreased by 10 mg each week was initiated with resolution of the rash. Following completion of this prednisone taper, the patient experienced a mild recurrence of her original rash, which fully resolved without recurrence after an additional 4 weeks of prednisone was administered.

OUTCOME AND FOLLOW-UP

At 1 year following discontinuation of secukinumab, the patient's HS remains inadequately controlled after failing multiple other biologic, non-biologic and surgical treatments, including various antibiotic regimens, adalimumab, infliximab, certolizumab, apremilast, ustekinumab, spironolactone, metformin and surgical excision of numerous lesions involving the posterior neck, axillary folds, groin and buttocks.

Currently, her HS is partially controlled on high-dose, high-frequency infliximab infusions with imminent plans to initiate concurrent oral tofacitinib.

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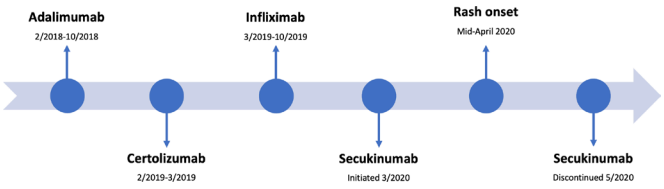

Figure 1 Visual timeline representing chronology of hypersensitivity reaction and prior medication use.

DISCUSSION

Secukinumab is a selective IL-17A inhibitor that is US Food and Drug Administration-approved for the treatment of plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. It is also increasingly being used in the off-label treatment of other inflammatory skin conditions, including HS. Secukinumab is typically well-tolerated and demonstrates a favourable safety profile with nasopharyngitis and upper respiratory infections listed as the most frequent side effects.

To our knowledge, we present the fifth documented case of a cutaneous delayed-type hypersensitivity reaction (type IV reaction) to secukinumab. Shibata *et al* described a 52-year-old woman with psoriatic arthritis who developed a papular eruption 3 days after the fourth dose of secukinumab. Skin biopsy confirmed a drug hypersensitivity eruption, and reintroduction of the medication prompted a relapse of the dermatitis.[3] Another report described a similar case in which a psoriasis patient developed a widespread papular eruption after the fourth dose of secukinumab. Skin biopsy exhibited 'focal parakeratosis, exocytosis of lymphocytes, rare apoptotic keratinocytes, and a perivascular infiltrate of lymphocytes and rare eosinophils in the upper dermis'.[4] The patient's condition gradually improved with systemic corticosteroids and discontinuation of the offending drug. In a third report, Wong and Chung described a 24-year-old woman with axial spondyloarthritis who developed a maculopapular eruption of the lower extremities in association with mild liver dysfunction after her 15th dose of secukinumab. No skin biopsy was performed. Her condition spontaneously normalised after discontinuation of secukinumab.[5]

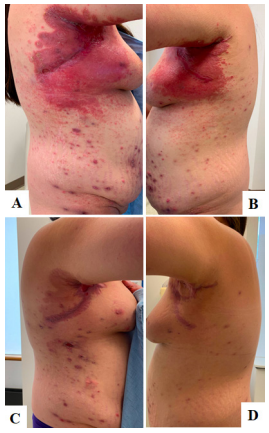

Figure 2 Clinical images of cutaneous delayed-type hypersensitivity (type IV) reaction to secukinumab. (A, B) Indurated, erythematous, scaly, crusted plaques with associated maceration on the bilateral axillary folds, as well as scattered erythematous papules and papulonodules on the abdomen and bilateral inframammary folds; taken 4 months after surgical excision of axillary hidradenitis suppurativa lesions and 6 weeks after initial onset of the eruption. (C, D) Resolution of the cutaneous hypersensitivity reaction 6 weeks after discontinuation of secukinumab and initiation of a prolonged prednisone taper.

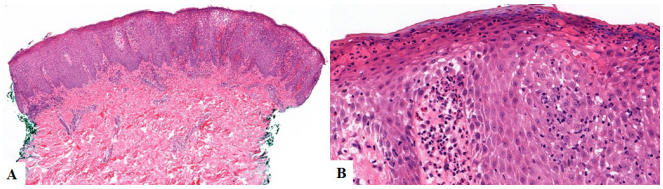

Figure 3 Histological images of cutaneous delayed-type hypersensitivity (type IV) reaction to secukinumab. Low-power (A) and high-power views (B) showing regular epidermal hyperplasia with spongiosis and serous crusting with ample neutrophils in the stratum corneum, as well as a superficial perivascular and interstitial infiltrate of lymphocytes and numerous eosinophils. Periodic acid-Schiff stain was negative for fungal elements (not shown).

Most recently, Darrigade *et al* described a case of a 51-year-old woman with psoriatic arthritis who, after the second administration of secukinumab, developed pruritic, erythematous skin lesions on the abdomen and breasts. A biopsy was not performed. However, patch testing revealed a positive reaction to secukinumab, and resolution was noted after 3 weeks of treatment with antihistamines and oral and topical corticosteroids.[6] Although patch testing was not performed in our case, confirmatory histopathology was obtained, which specifically implicates a psoriasiform pattern of drug hypersensitivity. Furthermore, the Naranjo algorithm scoring for our patient, a questionnaire designed to assess the probability of whether a suspected adverse drug reaction is due to the drug rather than alternative aetiologies, was seven and compatible with a probable adverse drug reaction to secukinumab.

Of note, there have also been reports describing pustular exacerbations of plaque psoriasis treated with secukinumab as well as secukinumab-induced new-onset psoriasiform eruptions involving the fingertips and nails.[7 8] Skin biopsies were not performed in these cases, which makes histological comparison to our case difficult. However, the decidedly different clinical features observed in these cases suggests that these represent entities distinct from the hypersensitivity reaction described by our group and others.

Furthermore, it is well known that HS and psoriasis are chronic inflammatory skin diseases that share common pathogenetic mechanisms involving tumour necrosis factor-alpha and IL-17. The two conditions have been known to co-occur, both on their own as well as part of syndromes, such as SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) and PsAPASH (psoriatic arthritis, pyoderma gangrenosum, acne and hidradenitis suppurativa). Despite the immunopathogenetic similarities

Learning points

- Secukinumab, a selective interleukin-17A inhibitor, has increasing off-label uses, including the treatment of hidradenitis suppurativa.
- Secukinumab may rarely cause delayed-type hypersensitivity reactions.
- The complex nature of adverse reactions to biologic agents, including secukinumab, illustrates the need for a high index of suspicion and prompt identification and response to prevent unfavourable outcomes.

and comorbid nature seen in HS and psoriasis, multiple factors, including characteristic clinical and histopathological features, timing of eruption and resolution with discontinuation of the offending drug, indicate that this patient experienced a type IV hypersensitivity reaction, not a co-occurrence of psoriasis.

Biologics, including monoclonal antibodies like secukinumab, have the potential to be immunogenic and can lead to the formation of antidrug antibodies that can precipitate undesirable effects, including decreased therapeutic efficacy or even drug hypersensitivity reactions. Secukinumab has been shown to be associated with a lower incidence of clinical immunogenicity in comparison to other biologics, such as adalimumab and infliximab.[9] Nevertheless, clinicians should be aware that secukinumab still carries the potential to trigger significant cutaneous eruptions that mandate timely drug discontinuation and potentially administration of corticosteroids for resolution.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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REFERENCES

1 Casseres RG, Prussick L, Zancanaro P, *et al*. Secukinumab in the treatment of moderate to severe hidradenitis suppurativa: results of an open-label trial. *J Am Acad Dermatol* 2020;82:1524–6.
2 Gülsen A, Wedi B, Jappe U. Hypersensitivity reactions to biologics (part I): allergy as an important differential diagnosis in complex immune-derived adverse events. *Allergo J Int* 2020;29:97–125.
3 Shibata M, Sawada Y, Yamaguchi T, *et al*. Drug eruption caused by secukinumab. *Eur J Dermatol* 2017;27:67–8.
4 Peigottu MF, Montesu MA. Adverse skin reaction to Secukinumab. *J Eur Acad Dermatol Venereol* 2017;31:e432–3.
5 Wong SCT, Chung HY. Secukinumab-induced delayed-type drug hypersensitivity reactions. *J Clin Rheumatol* 2020;26:e197–8.
6 Darrigade A-S, Dendooven E, Mangodt E, *et al*. Delayed-type hypersensitivity to secukinumab with tolerance to ixekizumab. *J Allergy Clin Immunol Pract* 2020;8:3626–8.
7 Sladden MJ, Sladden CS, Gulliver WPF. Secukinumab-induced psoriasiform eruption. *JAMA Dermatol* 2017;153:1194–5.
8 Dogra S, Bishnoi A, Narang T, *et al*. Secukinumab-induced paradoxical pustular psoriasis. *Clin Exp Dermatol* 2019;44:72–3.
9 Karle A, Spindeldreher S, Kolbinger F. Secukinumab, a novel anti-IL-17A antibody, shows low immunogenicity potential in human in vitro assays comparable to other marketed biotherapeutics with low clinical immunogenicity. *MAbs* 2016;8:536–50.