Epithelial herpes simplex keratitis in a patient on treatment with secukinumab for psoriasis: An effect of interleukin-17 blockade?

Sir,

Herpes simplex virus is associated with a variety of ocular diseases, including epithelial and stromal keratitis.[1] Epithelial herpetic keratitis is the most common presentation of herpes virus infection of the anterior chamber of the eye.[2] Various studies conducted worldwide have demonstrated the role of interleukin-17 in the adaptive immune response mounted by the body against the herpes simplex virus and conferring protection against the viral infection.[3]

Several cases of severe mucocutaneous candidiasis have been documented in the literature in patients receiving secukinumab indicating the important role of interleukin -17 in mucosal immunity against various pathogens.

The role of interleukin-17A in the pathogenesis of psoriasis vulgaris is undisputed. At present, secukinumab is a commonly used interleukin-17A inhibitor for the treatment of moderate-to-severe chronic plaque-type psoriasis and psoriatic arthritis.

Here, we report a rare case of epithelial herpes simplex keratitis in a patient of chronic plaque psoriasis with psoriatic arthritis who received injection secukinumab for treatment.

A 35-year-old man, a known case of chronic plaque-type psoriasis for the past 15 years and psoriatic arthritis for three years, presented with a severe flare of both cutaneous and articular diseases of two months duration. He did not have any associated comorbidities. Cutaneous examination revealed numerous discrete well-demarcated papules and plaques with loosely adherent silvery scales distributed symmetrically on the extensor aspect of upper and lower extremities, trunk and scalp. Grattage test and Auspitz sign were positive. His psoriasis area and severity index score was 18.5. Multiple fingernails and toenails showed significant pitting and dystrophy. Musculoskeletal examination revealed the involvement of multiple small joints of the left hand and left shoulder. The tender joint count was three and the swollen joint count was two.

Throughout his illness, he had been treated with oral methotrexate at the dose of 15mg/week which he had taken intermittently over the past 15 years with a cumulative dose of 2.6 g. He had not taken methotrexate for the past two months. Since the patient was not responding to methotrexate and had recurrent disease flares including both cutaneous and articular disease, he was administered injection secukinumab after complete investigations for any risk factors including latent tuberculosis.

His complete blood hemogram and biochemical profile were within normal limits. Serology for hepatitis C and hepatitis B was negative. His chest X-ray and electrocardiography were normal. Since the patient was on long-term methotrexate, an IFN-γ release assay was done to rule out any latent tuberculosis focus.

After receiving four doses of injection secukinumab 300mg/week subcutaneously, his cutaneous lesions and joint pains resolved drastically. There was 75% reduction in the psoriasis area and severity index score, from 18.5 to 4.5. However, before administration of the fifth dose of injection secukinumab, he developed congestion and severe pain in his right eye. He also complained of blurring of vision, lacrimation and photophobia. However, there were no skin lesions. There was no history of similar eye complaints in the past. He was evaluated by an ophthalmologist. Slit-lamp examination following lissamine green staining revealed a characteristic dendritic ulcer with terminal bulbs, in the 7' O'clock position in the lower outer quadrant [Figures 1 and 2]. Corneal sensations were diminished. The hallmark of herpes simplex virus epithelial keratitis is the presence of linear, dichotomous dendritic lesions with terminal bulbs and staining with fluorescein. The presence of a characteristic clinical picture and diminished corneal sensations in our case were sufficient to arrive at a clinical diagnosis of herpes simplex virus epithelial keratitis.

How to cite this article: Sinha P, Dash M, Bhatkoti B, Krishnan L. Epithelial herpes simplex keratitis in a patient on treatment with secukinumab for psoriasis: An effect of interleukin-17 blockade? Indian J Dermatol Venereol Leprol 2022;88:225-7.

Received: May, 2021 **Accepted:** August, 2021 **EPub Ahead of Print:** November, 2021 **Published:** February, 2022

DOI: 10.25259/IJDVL_496_2021 **PMID:** 34877851

Injection secukinumab was withheld and he was started on topical 3% acyclovir five times a day, topical moxifloxacin eye drops four times a day along with topical lubricant eyedrops. No systemic antivirals were given and topicals were tapered off based on the clinical response.

For his psoriatic skin lesions, he was managed with topical steroids and emollients. His ocular symptoms resolved completely in about three weeks duration with no residual scarring [Figure 3]. The patient is currently on regular follow-up on topical therapy and is responding well to treatment.

The immunopathogenesis of psoriasis is mediated by the Th1 and Th17 cells and their respective cytokines. The interleukin 17 is one of the key Th17 type of cytokines and the role of interleukin-17A in the pathogenesis of psoriasis has been well established in the literature.[4] In the current era with an armamentarium of targeted therapies available for various diseases; secukinumab has carved a niche for itself as an effective modality of treatment in the management of psoriasis vulgaris.

Secukinumab has a relatively safer adverse effect profile as compared to other biologics such as TNF-α inhibitors with regard to latent tuberculosis activation, congestive heart failure and demyelination disorders. However, blockade of the interleukin-17A pathway reduces mucosal immunity.[5]

Interleukin-17 group of cytokines comprises of six types of cytokines: interleukin-17A to interleukin-17F and five types of receptors: interleukin-17 A R to interleukin-17 E R.[6] It is one of the major contributors in the pathogenesis of psoriasis. Aberrant keratinocyte hyperproliferation and differentiation in response to interleukin-17 leads to hyperkeratosis and acanthosis which results in the characteristic psoriatic lesions. It is also an important contributor to the body's defence against infectious pathogens as a part of local mucosal immunity; both innate and adaptive. It upregulates the expression of toll-like receptors in the mucosal epithelial cells and augments the release of antimicrobial peptides against pathogenic organisms.[6,7] It also plays a pivotal role in the release of various other pro-inflammatory cytokines with consequent chemotaxis of various inflammatory cells including neutrophils and macrophages.[6]

Secukinumab is a human immunoglobulin (Ig)G1 monoclonal antibody which selectively binds and neutralises interleukin-17A. It is indicated in patients with moderate-to-severe plaque-type psoriasis and psoriatic arthritis who are candidates for systemic therapy.[5] The reduced mucosal immunity due to blockade of the interleukin-17 pathway results in impaired mucosal defences.

Our patient developed severe epithelial herpes simplex keratitis. Most of the primary herpes simplex infections of

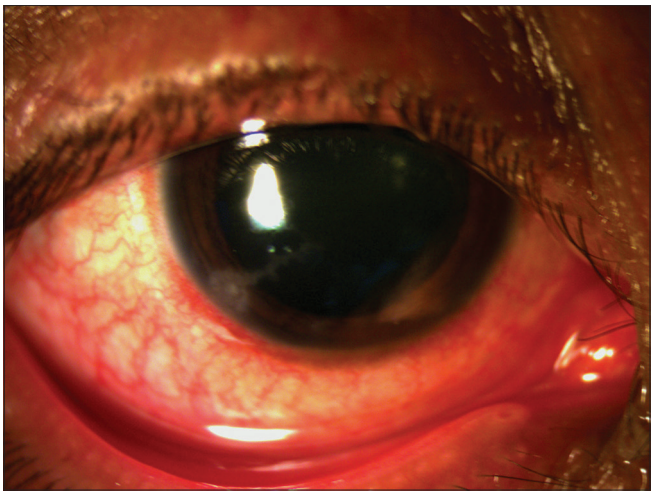

Figure 1: Physical examination of the right eye revealed severe conjunctival congestion. A whitish opaque dendritic lesion in the cornea at 7'o'clock position was observed

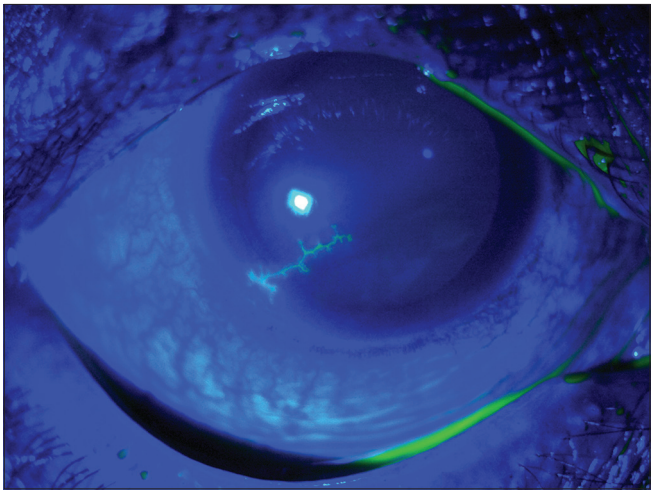

Figure 2: Slit-lamp examination of the right eye with lissamine green staining revealed a characteristic dendritic epithelial corneal ulcer with terminal bulbs

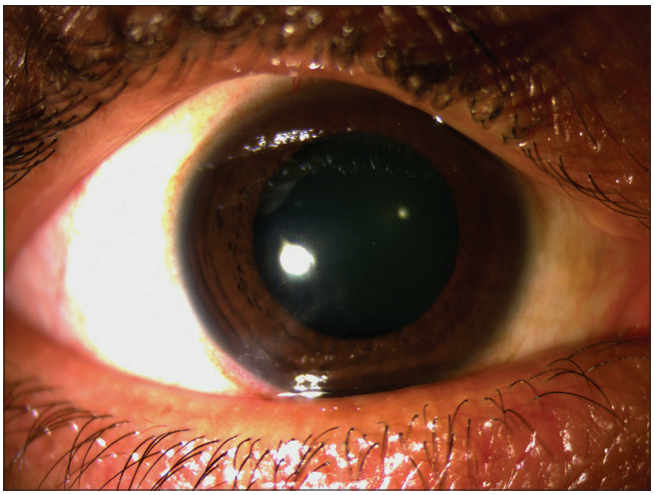

Figure 3: Grossly reduced conjunctival congestion and resolving corneal ulcer of the right eye two weeks after initiation of treatment

the eye are asymptomatic and self-limiting.[2] Following this, the virus attains latency and lies dormant in the dorsal root ganglion with occasional shedding and reactivation during an immunosuppressed state. Epithelial herpetic keratitis results from the direct invasion of the ocular tissue by the herpes simplex virus.

Corneal involvement due to the reactivation of the virus is a result of the delayed-type hypersensitivity reaction of the patient to the virus. This usually results in a stromal type of herpetic keratitis.[2]

An important observation from the previously reported cases of herpetic keratitis in the subset of patients who received organ transplantation and were on immunosuppressants is that the majority of these patients developed the stromal kind of viral keratitis.

We were unable to find any previous reports of herpes simplex keratitis occurring immediately following the administration of injection secukinumab and also that our patient developed primary herpes simplex keratitis of the epithelial type rather than the more frequently reported stromal type.

The corneal neovascularisation, thinning and scarring secondary to herpetic keratitis can result in blindness and early diagnosis and treatment can completely prevent this devastating complication. Hence, it is important to be aware of the possibility of this rare complication in patients on injection secukinumab.

Another important aspect in the management of this case is whether the patient can be readministered secukinumab. Acyclovir prophylaxis is generally recommended in recurrent stromal or mixed herpetic keratitis. There is no role of oral acyclovir in epithelial disease. Hence, keeping the above fact in mind, secukinumab should be avoided in this case.[8]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Preema Sinha, Mahashweta Dash, Bhupesh Bhatkoti[1], LekshmiPriya Krishnan

Department of Dermatology, Base Hospital, [1]Department of Ophthalmology, Command Hospital, Lucknow, Uttar Pradesh, India

Corresponding author:
Dr. Preema Sinha,
Department of Dermatology, Base Hospital, Lucknow, UttarPradesh, India. sinhapreema@gmail.com

References

1. Farooq AV, Shukla D. Herpes simplex epithelial and stromal keratitis: An epidemiologic update. Surv Ophthalmol 2012;57:448-62.
2. Azher TN, Yin XT, Tajfirouz D, Huang AJ, Stuart PM. Herpes simplex keratitis: Challenges in diagnosis and clinical management. Clin Ophthalmol 2017;11:185-91.
3. Rolinski J, Hus I. Immunological aspects of acute and recurrent herpes simplex keratitis. J Immunol Res 2014;2014:513-60.
4. Blauvelt A, Chiricozzi A. The immunologic role of IL-17 in psoriasis and psoriatic arthritis pathogenesis. Clin Rev Allergy Immunol 2018;55:379-90.
5. Frieder J, Kivelevitch D, Menter A. Secukinumab: A review of the anti-IL-17A biologic for the treatment of psoriasis. Ther Adv Chronic Dis 2018;9:5-21.
6. Song X, He X, Li X, Qian Y. The roles and functional mechanisms of interleukin-17 family cytokines in mucosal immunity. Cell Mol Immunol 2016;13:418-31.
7. Dubin PJ, Kolls JK. Th17 cytokines and mucosal immunity. Immunol Rev 2008;226:160-71.
8. Oral acyclovir for herpes simplex virus eye disease: Effect on prevention of epithelial keratitis and stromal keratitis. Herpetic eye disease study group. Arch Ophthalmol 2000;118:1030-6.