Oral lichenoid reaction in a psoriatic patient treated with secukinumab: A drug-related rather than a class-related adverse event?

Tania Marusia Capusan, MD,[a] María Herrero-Moyano, MD,[a] Constanza Romina Martínez-Mera, MD,[a] Al Walid Freih-Fraih, MD,[b] and Esteban Dauden, PhD[a]
Madrid, Spain

Key words: anti–interleukin-17A; oral lichenoid reaction; psoriasis; secukinumab.

INTRODUCTION

Secukinumab (SEK), a fully human anti–interleukin (IL)-17A monoclonal antibody, is effective in the treatment of psoriasis. Although it has a favorable safety profile, 2 cases of associated oral lichen planus (OLP)/lichenoid mucositis have been recently described.[1,2]

Abbreviations used:

EBV: Epstein-Barr virus
IL: interleukin
OLP: oral lichen planus
SEK: secukinumab

CASE REPORT

A 45-year-old man with severe chronic plaque psoriasis was first seen in May 2006. Associated diseases included diabetes, dyslipidemia, chronic liver disease, and pancreatitis. He received unsuccessful treatments with acitretin, psoralen and ultraviolet A, ciclosporin, methotrexate, infliximab, ustekinumab, adalimumab, etanercept, and golimumab. In December 2015, SEK treatment at standard doses was started. After a good initial response, the effectiveness decreased progressively. After 8 months, the patient had painful ulcerative lesions surrounded by a whitish discoloration of the mucosa on both sides and the back of the tongue (Fig 1). There was no history of injuries, dental procedures, any oral disease, or new drug use. Culture from the ulcers was positive for *Candida albicans* and negative for herpes simplex virus. A microarray study of the ulcers was positive for Epstein-Barr virus (EBV).

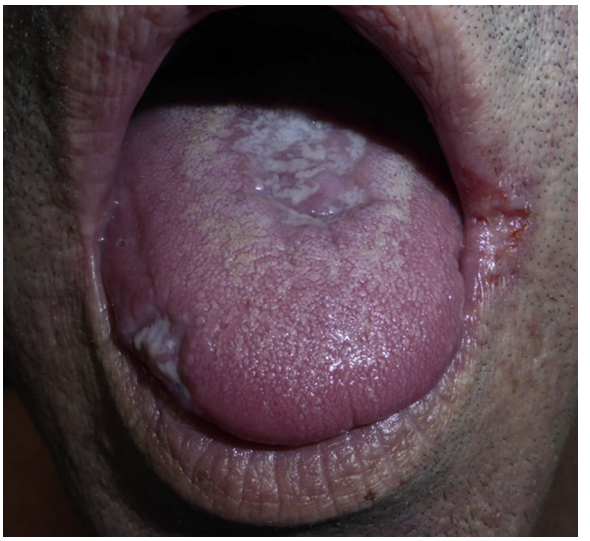

Fig 1. Superficial erosions and lichenoid lesions are present on the right anterolateral and dorsum of the tongue.

From the Departments of Dermatology[a] and Pathology,[b] Hospital Universitario La Princesa, Instituto de Investigación Sanitaria Princesa.

Funding sources: None.

Conflicts of interest: Prof. Esteban Dauden has the following conflict of interests: Advisory Board member, consultant, grants, research support, participation in clinical trials, honorarium for speaking, and research support with the following pharmaceutical companies: Abbvie/Abbott, Amgen, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, MSD-Schering-Plough, Celgene and Lilly. The rest of the authors have no conflicts to disclose.

Correspondence to: Tania Marusia Capusan, MD, Hospital Universitario de La Princesa, Servicio de Dermatología, Calle Diego de León 62, 28006 Madrid, Spain. E-mail: taniamarusiacapusan@gmail.com.

JAAD Case Reports 2018;4:521-3.
2352-5126

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https://doi.org/10.1016/j.jdcr.2018.04.015

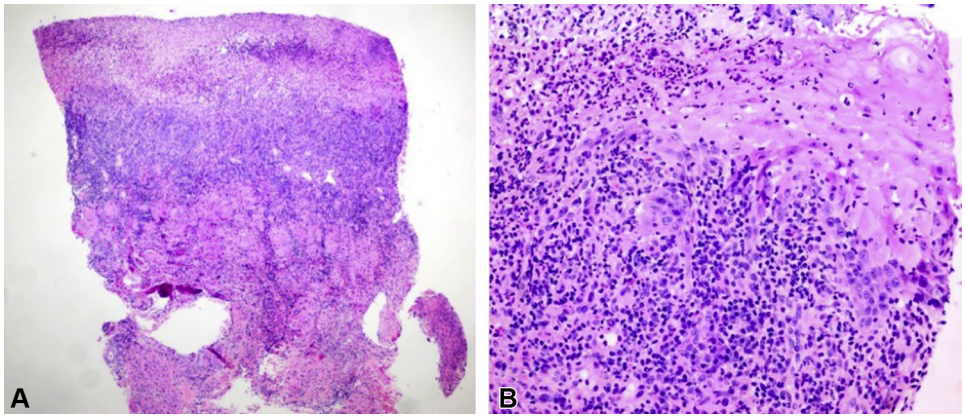

Fig 2. A, Extensive epithelial erosion with neutrophilic and lichenoid infiltrate in the superficial corium obscuring the dermoepidermal junction. **B**, Effacement of the epithelium with superficial lichenoid infiltrate and neutrophilic exudate at the edge of the erosion as well as small foci of hydropic degeneration with rete ridges elongation. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×4; **B**, ×20.)

Two biopsies found ulcerative lichenoid mucositis with scarce pseudohyphae on the surface (Fig 2). Direct immunofluorescence was negative. Immunohistochemical study in the biopsy tissue was negative for both EBV latent membrane protein 1 and EBV-encoded small RNA. Amplification of EBV DNA by real-time polymerase chain reaction was undetectable in peripheral blood. Serum anti–desmoglein-1 and -3, anti-BP180 and anti-BP230 antibodies were not detected. The patient was treated with intralesional corticosteroids and oral itraconazole. The lesions improved but persisted. After 12 months, SEK was discontinued and changed to apremilast. After a short course of treatment, psoriasis remained refractory, although ulcerative oral lesions clearly improved and completely disappeared 8 weeks after SEK withdrawal.

Finally, the patient was treated with the humanized anti–IL-17A monoclonal antibody, ixekizumab, achieving clearance of psoriasis. After 1 month, the patient had whitish plaques but not ulcers. Biopsy and cultures found oral candidiasis without lichenoid inflammation. The lesions resolved with fluconazole, and there was no recurrence during the last 9 months with ixekizumab.

DISCUSSION

Two psoriatic patients with oral lesions presumably induced by SEK have been described. The first patient had an ulcerative lichenoid mucositis on the lower lip a few days after starting treatment. The lesions were considered a possible anti–IL-17 drug-related class effect presenting as a lichenoid drug eruption rather than a true OLP. SEK discontinuation led to improvement of the lesions.[1] The second patient had a painful whitish plaque on the buccal mucosa 5 months after SEK. In this case, an OLP associated with candidiasis was diagnosed.[2]

Although the etiology of OLP remains uncertain, sometimes viral and *Candida* infections have been reported associated with its development.[3] Similarly, some drugs, including tumor necrosis factor–α inhibitors, have been associated with the induction of oral lichen planuslike reactions.[4] In addition, *Candida* infections are a well-known consequence of impaired IL-17 immunity[5,6] and therefore a moderately frequent adverse effect of IL-17 inhibitors. In our patient, the clinical and histopathologic characteristics of the lesions led us to consider the diagnosis of lichenoid inflammation, although we are unable to determine whether they represent a true OLP or a lichenoid eruption. The chronological association with the initiation of SEK, the persistence of the lesions throughout the therapy, the complete healing of the ulcers after SEK discontinuation, and the absence of other causes that could justify the lesions, suggest an etiologic role of SEK in their development. Although it cannot be ruled out, we consider unlikely that either *C albicans* or EBV play a role. The fact that the ulcerative lesions did not appear during treatment with ixekizumab supports that they may be a drug-related, rather than a class-related adverse event.

The authors are grateful to Manuel Gomez Gutierrez for copyediting the manuscript.

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