Herpetiform aphthous ulcerations induced by secukinumab: Report of 2 cases

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Key words: acute gingivostomatitis; aphthous; herpetiform; interleukin-17 blocker; psoriasis; secukinumab.

INTRODUCTION

The anti–interleukin (IL)-17A antibody secukinumab is used for moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. It has an excellent safety profile and its side effects are well described.[1] Nevertheless, many patients treated with secukinumab in real life are needed to detect exceedingly rare side effects. Here, we report 2 cases of acute gingivostomatitis that developed on introduction of secukinumab.

CASE REPORT

A 35-year-old woman presented with an 8-year history of SAPHO (synovitis, acne, pustulosis, hyperostosis, osteomyelitis) syndrome. The patient was treated with various regimens, including salazopyrin, methotrexate, and infliximab with poor control of her osteoarticular manifestations. She was started on secukinumab, 300 mg (standard dosing for plaque psoriasis). Five weeks later, after the induction phase, the patient experienced a first episode of painful gingivostomatitis. She had 2 recurrences 2 and 6 months later, respectively, causing discomfort and weight loss and lasting 3 weeks. She had no other gastrointestinal symptoms or signs. On examination, she presented with painful herpetiform ulcerations of the soft palate, a white-coated tongue, and swollen and erythematous papillae (Fig 1, *A*). Histologic studies showed an acanthotic epithelial mucosa with spongiosis, exocytosis, and numerous neutrophils associated with a dense lymphohistiocytic infiltrate (Fig 1, *B*). Periodic acid–Schiff staining was negative. Herpes simplex virus (HSV) 1 and 2 polymerase chain reaction and immunohistochemistry on the biopsy repeatedly remained negative. Several mycologic cultures excluded infections with *Candida* species. The clinical evolution was favorable within 3 weeks with betamethasone mouthwash and reduction of the secukinumab dose to 150 mg.

Abbreviations used:

HSV: Herpes simplex virus
IL: interleukin

A 37-year-old woman had a 14-year-history of plaque psoriasis. Her personal and familial histories were unremarkable, with no evidence of inflammatory bowel diseases. She had been treated with methotrexate, etanercept, and adalimumab, with incomplete control of her psoriasis. Therefore, treatment with secukinumab, 300 mg, was initiated. At the end of the induction phase, she experienced a painful stomatitis with swollen lips, herpetiform ulcerations, and whitish deposits on the tongue (Fig 2). There were no other gastrointestinal manifestations. Search of HSV1 and HSV2 infection by polymerase chain reaction and mycologic cultures for *Candida* species yielded negative results. The lesions completely resolved within 3 weeks after discontinuation of secukinumab and replacement with ustekinumab.

Causality between secukinumab treatment and gingivostomatitis in our patients was assessed using the French method[2] and yielded plausible causality based on the chronological development, the recovery after cessation of secukinumab, the exclusion of

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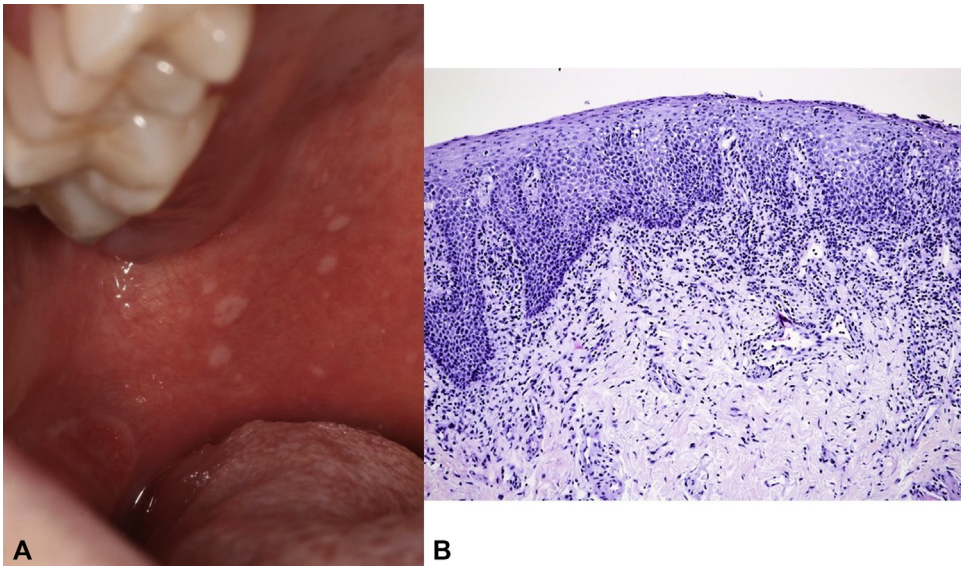

Fig 1. A, A 35-year-old woman presented with painful herpetiform ulcerations of the soft palate, a white-coated tongue, and swollen and erythematous papillae. **B**, Histologic studies show an acanthotic epithelial mucosa with spongiosis, exocytosis, and numerous neutrophils, associated with a dense lympho-histiocytic infiltrate.

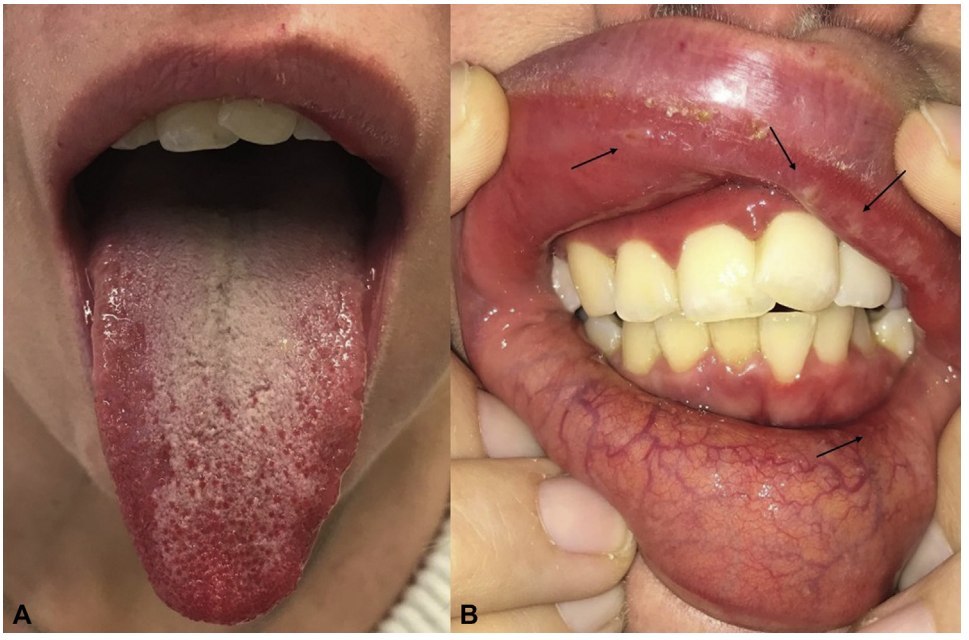

Fig 2. A 37-year-old woman presented with whitish deposits on the tongue (**A**), swollen lips, and herpetiform ulcerations of the lips and gums (**B**).

alternative causative drugs, the absence of infection, and the absence of other inflammatory disease.

DISCUSSION

In the literature, the occurrence of non-*Candida* gingivostomatitis after IL-17 blockers is only anecdotally reported. Mouth ulcerations were seen in 2 patients in a phase-2 secukinumab trial, but no clinical details were provided.[3] Further, a case of a patient with spondylarthrosis who had recurrent oral ulcers after secukinumab treatment developed inflammatory bowel disease 1 month after the start of secukinumab.[4] After the second injection of secukinumab, this patient experienced periodic occurrence of endobuccal aphthoid lesions, appearing 2 to 3 days after each injection. Finally, a case of severe

mucositis appearing 1 week after initiation of secukinumab was described in a 62-year-old man.[5] In this case, secukinumab discontinuation resulted in substantial improvement. In our 2 cases, clinical course as well as extensive laboratory workup reasonably ruled out other inflammatory diseases potentially affecting the oral mucosa, such as lichen planus, autoimmune bullous diseases, or erythema multiforme.[5]

Why oral aphthous ulcers developed after secukinumab used remains unclear. Secukinumab is associated with the development of mucocutaneous candidiasis, as the IL-17 pathway is crucial for antifungal defense.[6] Yet, IL-17 blockers may also affect the oral microbiome in way that is not detectable by mycologic cultures and may thus favor the development of an inflammatory stomatitis.

Taken together, acute herpetiform aphthous ulcerations may represent a rare complication of secukinumab treatment. The clinical outcome is favorable after reduction or cessation of secukinumab. With increasing use of IL-17 blockers, clinicians should be familiar with this rare but striking and bothersome side effect.

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