

Images in Allergy

Fixed Drug Eruption of the Tongue Due to Trimethoprim-Sulfamethoxazole

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A 21-year-old woman with a history of recurrent urinary tract infections was treated with trimethoprim-sulfamethoxazole (SMX/TMP) and 24 hours later developed a painful, large, pseudomembranous ulcer on the left posterior dorsal aspect of her tongue, with an adjacent yellowish-white patch (Figure 1). She had no other mucosal or cutaneous involvement. She reported 2 previous episodes of tongue lesions after receiving SMX/TMP. Each episode occurred within 1 to 3 days of taking the drug and lasted 2 to 4 weeks. Topical antifungal therapy was ineffective. Two 4-mm lesional punch biopsies of the tongue were obtained. An anterior biopsy showed ulcerated epithelium with intercellular edema and exocytosis, and an underlying inflammatory infiltrate (Figure 2). A posterior biopsy demonstrated hyperkeratotic, acanthotic mucosal epithelium. The provisional diagnosis was fixed drug eruption (FDE) of the tongue, and the patient was advised to avoid SMX/TMP and other sulfonamide antibiotics. Figure 3 shows the healing tongue 3 weeks after discontinuation of SMX/TMP. With avoidance, she has had no more recurrent tongue lesions.

FDE, which represents approximately 2% to 3% of cutaneous drug reactions in adults, is characterized by recurrent cutaneous and/or mucosal lesions at the same site with readministration of the drug. FDE is likely a T-cell-mediated, delayed-type hypersensitivity reaction involving CD8+ T cells. Frequent culprits are nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, including SMX/TMP. Oral mucosal lesions may occur alone or accompanied by skin and/or genital lesions. Oral lesions are usually aphthous-like, bullous/erosive, or erythematous.¹ The prevalence of oral FDE varies by study. In a study of 450 patients with FDE, the tongue was affected in only 13 cases (2.9%) and the oral mucosa (excluding lips) in only 17 cases (3.8%).² However, Özkaya¹ found oral mucosal lesions (excluding lips) in 61 of 176 (35%) cases of FDE. Only 9 of 61 (15%) had isolated oral mucosal involvement. In this study, solitary bullous/erosive lesions of the dorsal tongue were almost exclusively induced by SMX/TMP.

Correct diagnosis of oral FDE is challenging because it may appear similar to other conditions, including herpes simplex virus infection, oral candidiasis, erythema multiforme, or autoimmune



FIGURE 1. Large pseudomembranous ulcer on the left posterior dorsal aspect of the tongue, with an adjacent yellowish-white patch and multiple small vesicular lesions.

blistering diseases such as pemphigus vulgaris and Behçet's disease. FDE is usually a clinical diagnosis based on a characteristic history, and an oral provocation challenge is the reference

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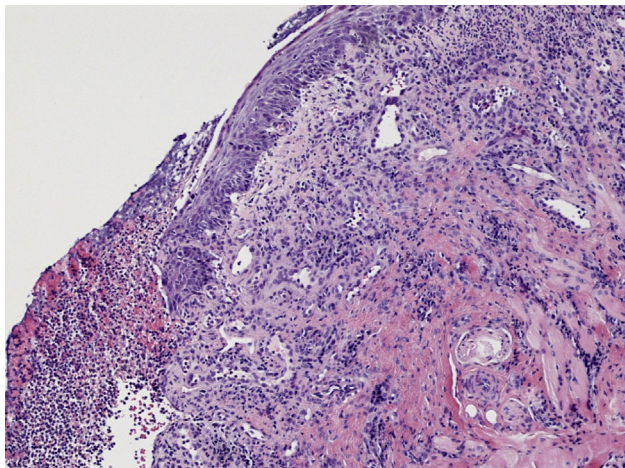


FIGURE 2. The anterior tongue revealed ulcerated stratified squamous epithelium exhibiting intercellular edema and exocytosis. The underlying stroma was edematous and contained a diffuse infiltrate of lymphocytes, plasma cells, and neutrophils.

standard for diagnosis. Otherwise, patch testing with the drug has been reported to yield a diagnosis in many cases,^{E1,E2} although there is no established standardized method for patch testing. Our case was limited by not performing a confirmatory test. However, the patient's history of recurrent oral lesions on 3 occasions after receiving SMX/TMP was sufficiently convincing, and a challenge would have exposed the patient to a risk of symptom recurrence.

The management of FDE primarily involves drug discontinuation and avoidance. Limited data suggests some cross-reactivity in FDE among sulfonamide antibiotics^{E3} and NSAIDs.^{E4} Therefore, avoidance of similar drugs may be warranted.

Recognizing unusual presentations of adverse drug reactions is an important skill for the allergist. A high index of suspicion for



FIGURE 3. Lesional healing of the tongue 3 weeks after discontinuation of trimethoprim-sulfamethoxazole.

oral FDE must be maintained when a patient presents with recurrent isolated oral lesions.

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