

### Minocycline-Induced Hyperpigmentation of the Tongue

**M**inocycline hydrochloride is an important and effective treatment for acne vulgaris. While relatively few adverse effects have been documented, minocycline has been associated with cutaneous and mucosal hyperpigmentation in addition to hyperpigmentation of the teeth, sclera, bone, heart, and thyroid.<sup>1</sup> We report a case of a woman who, while taking minocycline, developed discrete hyperpigmentation of the tongue. Only 2 cases of lingual hyperpig-



**Figure 1.** Slate-gray, discrete, hyperpigmented patches on the tongue after 16 weeks of minocycline hydrochloride treatment.

mentation associated with minocycline therapy have been reported.<sup>2</sup> Herein, we describe a case of minocycline-induced hyperpigmentation of the tongue with resolution following the discontinuation of therapy.

**Report of a Case.** The patient was a 23-year-old African-American woman with an 11-year history of acne vulgaris; she was otherwise in good health and denied taking any medications. She began therapy with clindamycin lotion twice daily, adapalene gel every night, and 50 mg of minocycline hydrochloride by mouth twice daily. Three weeks later, because of limited improvement in her acne, the dose was increased to 100 mg. Four months after starting this regimen, the patient noted the sudden appearance of dark spots on her tongue. Findings of examination revealed 4 discrete, slate-gray hyperpigmented patches on the dorsal and lateral aspects of the tongue (**Figure 1**). Hyperpigmentation was not present elsewhere in the oral cavity or on the cutaneous surface. She denied any pain or swelling. A diagnosis of minocycline hyperpigmentation was made, and the drug treatment was discontinued. The patient refused a biopsy of the tongue. Examination findings 6 weeks following the discontinuation of minocycline treatment revealed almost complete resolution of the hyperpigmented patches (**Figure 2**). Treatment with clindamycin lotion and adapalene gel had been maintained throughout the patient's course.



**Figure 2.** Almost complete resolution of hyperpigmentation 6 weeks following discontinuation of minocycline hydrochloride therapy.

**Comment.** Minocycline is a semisynthetic tetracycline used to treat acne vulgaris. It is a broad-spectrum antibiotic that is well absorbed and highly lipid soluble. This lipophilicity facilitates penetration into all the body's tissues and accounts for high levels of the drug in the brain, thyroid, fat, maxillary sinus, bile, and liver. Minocycline is found in saliva at 30% to 65% of serum concentrations after oral administration.<sup>1</sup>

Three types of minocycline-induced cutaneous hyperpigmentation have been described. Type 1 is commonly seen on the face at sites of inflamed, scarred, or previously traumatized skin. Histologically, iron-containing compounds are present in the dermis, which may represent hemosiderin or iron chelates of minocycline. Type 2 is characterized by circumscribed hyperpigmented macules or a more diffuse hyperpigmentation occurring distant from sites of inflammation, particularly on the lower extremities. Deposition of melanin and iron occur in the dermis. Type 3 is associated with muddy-brown hyperpigmentation in areas of sun exposure. Melanin deposits occur in the epidermis and papillary dermis; however, no iron deposits are present.<sup>3,4</sup> There have been reported cases of minocycline-associated hyperpigmentation of the lips and acquired pseudomongolian spot, which histologically resemble a resolving fixed drug eruption. These cases may possibly represent a fourth type of minocycline-induced cutaneous hyperpigmentation.<sup>4,5</sup>

The differential diagnosis of oral hyperpigmentation is quite extensive. Isolated tongue hyperpigmentation is rare and has been associated with endogenous causes such as melanoma, oral melanosis, physiologic melanin pigmentation, pigmented fungiform papillae of the tongue, black hairy tongue, and as a normal variant. Exogenous causes include antimicrobials, chemotherapeutic agents, methyldopa, tricyclic antidepressants, and amalgam tattoo.<sup>2</sup>

Oral hyperpigmentation as a result of minocycline therapy is an infrequently reported adverse effect of long-term minocycline use.<sup>1</sup> In our patient, the

hyperpigmentation of the tongue resolved promptly following discontinuation of minocycline treatment. Previously reported were 2 women with acquired hyperpigmentation of their tongue that occurred after initiation of minocycline therapy.<sup>2</sup> They had taken oral minocycline for approximately 4 weeks to 4 months before the onset of lingual pigmentation. One patient had partial resolution of the pigmentation 3 months following the discontinuation of therapy. The clinical course of the other patient is unknown. It is of utmost importance to affected patients that cutaneous pigmentation usually resolves with the cessation of minocycline treatment.<sup>4</sup> This observation is supported by our findings.

Oral hyperpigmentation can arise from a multitude of exogenous and endogenous causes. This striking adverse effect of minocycline is important to consider in the differential diagnosis of localized hyperpigmentation of the tongue.

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