

# Treatment of Minocycline-Induced Cutaneous Hyperpigmentation With the Q-switched Alexandrite Laser

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Cutaneous pigmentation is a rare but well-described adverse effect associated with long-term minocycline hydrochloride therapy. Drug-induced skin pigmentation accounts for 10% to 20% of all cases of acquired hyperpigmentation. We describe a patient with substantial minocycline-induced hyperpigmentation. This adverse effect has been associated with non-dose-dependent, blue-gray circumscribed pigmentation of clinically normal skin and mucosa, which often persists despite discontinuation of therapy. We describe a patient with minocycline-induced hyperpigmentation who was successfully treated with a 755-nm Q-switched alexandrite laser. Laser treatment resulted in complete clinical clearance in the patient's hyperpigmentation. Side effects were limited to transient mild desquamation without dyspigmentation or scarring. The Q-switched alexandrite laser (755 nm) is an effective treatment of minocycline-induced hyperpigmentation. The improvement is progressive in successive sessions.

Cutaneous pigmentation is a well-described adverse effect associated with minocycline hydrochloride ingestion.<sup>1-5</sup> Cutaneous pigmentation from minocycline occurs with treatment over a prolonged period of time. Spontaneous fading of pigmentation after the discontinuation of minocycline has been reported to gradually occur over months<sup>1</sup> to years,<sup>6</sup> but it may not completely resolve.<sup>2,7,8</sup> We present a case of a man with noncircumscribed, ill-defined, hyperpigmented patches and plaques

limited to the vertex of the scalp, left forehead, left cheek, and left periorbital area who was effectively treated with the Q-switched alexandrite laser (755 nm).

## CASE REPORT

A 65-year-old white man was evaluated for treatment of noncircumscribed, ill-defined, hyperpigmented, coalesced, bluish gray patches and plaques localized to the vertex of the scalp, left forehead, left cheek, and left periorbital area (Figure 1). The patient experienced progressive pigmentation of his face over the last 15 years while taking minocycline at a dosage of 100 mg twice daily for rosacea.

His right cheek revealed only signs of UV damage and skin aging. Mild textural changes were present; the skin otherwise appeared normal. There was a bilateral bluish discoloration of the sclerae and left pinnae. There was no mucosal, dental, nail plate, or nail bed pigmentation. There was no inguinal lymphadenopathy. The patient had Fitzpatrick skin type II with a mild tan.

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He described playing golf and always driving the golf cart for many years, resulting in more sun exposure on the left side of the face. Furthermore, the patient consistently wore a baseball cap while playing golf. In comparison to the remainder of the parietal scalp, the cap had an opening in the back, causing UV exposure. The patient denied the use of photoprotective clothing and sunscreen.

He was treated with nonablative fractional resurfacing for 4 sessions prior to being seen in our clinic but reported no improvement. He experienced severe pain and discomfort with the treatments. After our initial consultation and evaluation, minocycline was discontinued. The patient also was using metronidazole gel, which was discontinued. Lisinopril treatment continued. After 2 consecutive months, we did not discern any spontaneous reduction in the discoloration of his skin and we did not observe any progressive darkening. The patient was in excellent health with no known drug allergies.

One month before initiating treatment, test spots were performed with the Q-switched alexandrite laser (755 nm) (Accolade, Cynosure, Inc). The patient was treated by one operator (M.K.). The patient tolerated all test spots without adverse sequelae and without the need for topical anesthesia or sedation. He cleansed the areas twice daily and applied sunscreen in the morning. The most prominent patches of the face were treated at monthly intervals for 13 visits with

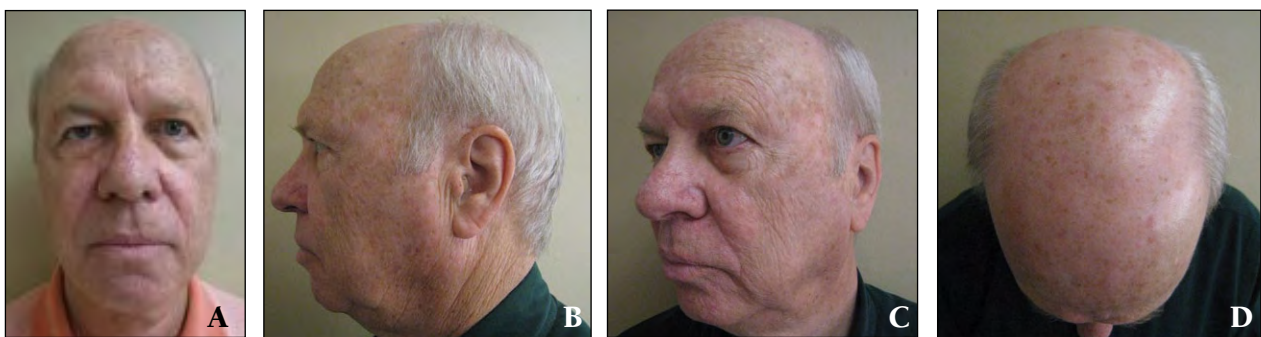
the Q-switched alexandrite laser (755 nm)(Figure 2). The skin was clear with resolution of the blue-gray patches and plaques in the vertex of the scalp, left forehead, left cheek, and left periorbital area. Side effects were limited to transient mild desquamation without dyspigmentation or scarring.

## COMMENT

Minocycline-induced cutaneous hyperpigmentation is a nonpainful cosmetic side effect that may dissipate slowly over months to years after discontinuation of the drug. The pathophysiology of minocycline-induced pigment is unknown. Hyperpigmentation may occur in 3 forms. Type I pigmentation presents as dose-dependent, blue-black pigmentation of scars. In type II pigmentation, non-dose-dependent, blue-gray pigmentation occurs within previously normal-appearing skin, especially the skin of the shins. In type III pigmentation, brownish discoloration of sun-exposed sites is observed. Histopathologically, types I and II demonstrate pigment granules in the dermis within macrophages concentrated around vasculature and also around eccrine coils in type II. The pigment demonstrates characteristic concomitant positivity with both Fontana-Masson silver and Perls Prussian blue stains and thus is fairly easy for the histopathologist to identify. The histopathologic findings in type III hyperpigmentation are less specific, consisting of increased melanin in



**Figure 1.** Hyperpigmentation from prolonged use of minocycline hydrochloride (front, A; left side, B; angled left side, C; scalp, D).



**Figure 2.** Resolution of hyperpigmentation after treatment with the Q-switched alexandrite laser (755 nm)(front, A; left side, B; angled left side, C; scalp, D).

basal keratinocytes with subjacent dermal melanophages without the presence of iron. Cases that stain for melanin and calcium have been described.<sup>9</sup> Because there are overlapping features, our case represents type II and type III minocycline pigmentation.

Minocycline is a semisynthetic derivative of tetracycline that was introduced in 1967.<sup>10</sup> It is the most lipophilic member of the tetracycline family.<sup>8</sup> Minocycline-induced pigmentation occurs when a quinone iminium ion and other reactive species polymerize to form black pigment and contribute to the production of autoantibodies.

Although not medically harmful, pigmentation is the most frequently observed cutaneous side effect of minocycline. Multiple organs and tissues may become involved. The thyroid gland has been reported as one of the more frequent sites of pigment deposition associated with minocycline ingestion.<sup>6,11-13</sup> Other reported sites of pigment deposition include the oral mucosa,<sup>14-17</sup> nails,<sup>4,5,15,18,19</sup> nail beds,<sup>6,20,21</sup> teeth,<sup>4,15,21-24</sup> bone,<sup>21,23,25</sup> sclerae,<sup>6,18</sup> substantia nigra,<sup>13</sup> atherosclerotic plaques,<sup>13</sup> and heart valves.<sup>16</sup>

Constituents of this pigment have included melanin, complexes containing iron and calcium,<sup>3-6,10,20</sup> and complexes of presumed minocycline moieties.<sup>2,4,5</sup> Unlike the other tetracyclines, minocycline complexes less with calcium but does chelate with iron.<sup>4</sup>

For all 3 clinical presentations of hyperpigmentation, pigmentation does not progress after discontinuation of minocycline.<sup>9-11,26</sup> Some reports have indicated that treatment with the Q-switched Nd:YAG laser (1064 nm) is not effective.<sup>23</sup> However, satisfactory results have been reported with the Q-switched alexandrite laser (755 nm).<sup>15-17</sup> On the basis of these reports, we decided to treat our patient with the Q-switched alexandrite laser (755 nm). Excellent results were achieved in the cosmetic clearing of the pigmentation.

## CONCLUSION

The treatment of minocycline-induced cutaneous pigmentation remains a clinical challenge. The use of lasers has revolutionized our therapeutic armamentarium. Minocycline-induced cutaneous hyperpigmentation can be safely and effectively cleared using the Q-switched alexandrite laser (755 nm) without any adverse sequelae.

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