



Insight into the mechanisms of type III minocycline-induced pigmentation removal: A case of repeated immediate pigment clearing with the Q-switched 755-nm alexandrite laser over a 13-year period

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CASE REPORT

A 68-year-old man with rheumatoid arthritis presented for laser treatment of facial pigmentation (Fig 1, A). He had taken oral minocycline 100 mg 3 times weekly for 8 years (cumulative dose, 124.8 g) because of severe arthritic discomfort.

Physical examination showed patchy slate blue/grey hyperpigmentation of the face, gums, teeth, and nail beds, consistent with type III minocycline-induced pigmentation (MP).¹ There was no pigmentation of sun-protected areas.

Two different laser modalities were tested before treatment: Q-switched 755 nm (Qs755nm) alexandrite (3.4 J/cm² with 4-mm spot size, 4.8 J/cm² with 3-mm spot size) and Q-switched 1064 nm (Qs1064nm) neodymium:YAG (yttrium aluminum garnet) (4.8 J/cm² with 3-mm spot size, 3 J/cm² with 4-mm spot size). Qs755nm at 2.0 Hz/4-mm spot/3.4 J/cm² showed the most improvement, with immediate pigment clearing, and was used for full facial treatment (3450 pulses). This setting was also selected because it had the largest spot size with lowest fluence, thus limiting the number of pulses and treatment time required. As observed with the test treatment, pigment resolution occurred immediately on the same day after therapy.

There were no significant postoperative complications. Pigment resolution was maintained at

Abbreviations used:

FM: Fontana-Masson
MP: minocycline-induced pigmentation
Qs: Q-switched

13 months despite continued minocycline use, and the patient was highly satisfied (Fig 1, B).

The patient continued taking minocycline 100 mg 3 times weekly and re-presented 3 times over the next 13 years with facial hyperpigmentation (total cumulative dose of minocycline, 202.8 g). Each time, immediate pigment clearing was achieved with the Qs755nm alexandrite laser. Every visit concluded with a discussion that hyperpigmentation would recur with continued minocycline ingestion. At the time of this article's writing, he continues to take minocycline.

Histopathology

The pretreatment biopsy showed intracellular and extracellular type III MP in the dermis¹ (Fig 2, A), with notably no detectable change in the posttreatment biopsy (Fig 2, B).

However, in contrast to the pretreatment biopsy, the extracellular pigment in the posttreatment sample was no longer highlighted by Fontana-Masson (FM) stain, but intracellular pigment continued to

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Fig 1. **A**, The patient at initial presentation, with marked facial discoloration consistent with type III minocycline-induced pigmentation. No involvement of sun-protected areas was observed. **B**, At 13 months after the first treatment with the Q-switched 755-nm alexandrite laser, with maintenance of pigment resolution.

stain with FM (Fig 2, C and D). The change in melanin staining is consistent with the clinically observed reduction in pigment intensity.

DISCUSSION

Although minocycline is generally safe, cutaneous pigmentation is a common adverse effect.² Type III is the least common MP, involving sun-exposed areas and staining positively only for melanin. It is often unremitting or requires multiple treatments to achieve improvement.²

Although we are not the first to document successful Qs laser treatment of MP,³⁻⁵ our case is notable for the rapidity of pigment resolution repeated on multiple occasions over 13 years. In contrast to previous cases requiring multiple treatments,^{3,4} our patient experienced immediate and sustained cosmetic improvement after only 1 treatment. Although successful treatment of minocycline-related pigmentation has also been reported with newer picosecond lasers,^{6,7} these devices are more expensive and less accessible than the Qs alexandrite laser. Other reports have also described the treatment of minocycline-associated pigmentation with combination laser modalities.⁸ However, this is less convenient and more costly than using a single device such as the Qs alexandrite, as shown in our

case. Because our patient continued to take minocycline, he did experience re-pigmentation; however, each recurrence resolved immediately with 1 treatment using the Qs755nm alexandrite laser, showing its effectiveness in achieving MP clearing.

The findings of our case are reminiscent of immediate pigment darkening resulting from ferric oxide (red-brown) reduction to ferrous oxide (black).⁹ We term our outcome *immediate pigment lightening*, which may be another example of Q-switched laser alteration of dermal pigmentation through a physicochemical mechanism.

The pigment in our case may be an insoluble minocycline-cation coordination complex, with calcium or magnesium as central metal ions. Because tetracyclines are susceptible to heat and photodecomposition,¹⁰ a physicochemical process that disrupts these complexes could explain our findings. Specifically, the discrepancy between H&E and FM stains suggests that extracellular pigment is still present after treatment but in an altered chemical state, such that it can no longer absorb visible light.

CONCLUSIONS

To our knowledge, this is the first case to show immediate pigment lightening of type III MP repeated over multiple instances using only the

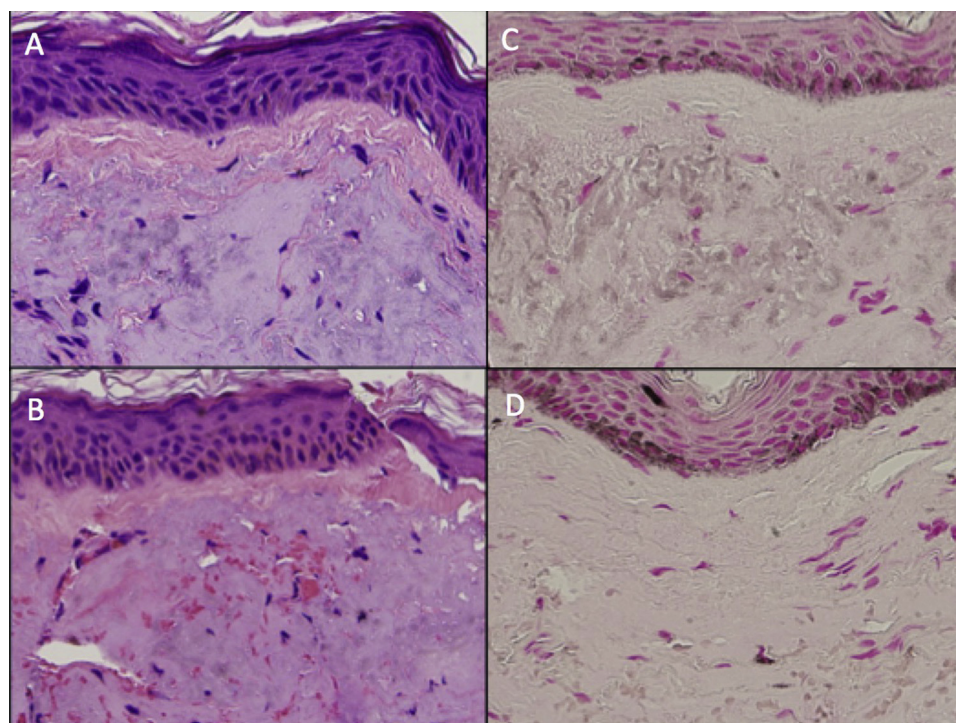


Fig 2. **A**, H&E stain of the pretreatment biopsy specimen showing intracellular and extracellular melanin, consistent with type III minocycline-induced pigmentation. **B**, H&E stain of the posttreatment biopsy specimen. No detectable pigmentary changes were noted compared with the pretreatment biopsy specimen. **C**, Pretreatment biopsy specimen showing both intracellular and extracellular pigment reactivity with Fontana-Masson stain. **D**, Fontana-Masson stain of the posttreatment biopsy specimen. The extracellular pigment was no longer reactive with the Fontana-Masson stain, whereas the intracellular pigment continued to stain positively. Original magnification, $\times 200$ for all images.

Qs755nm alexandrite laser. We propose that an insoluble minocycline-cation coordination complex with selective sensitivity to the Qs755nm alexandrite laser may be deposited within the dermis. Our case shows that the Qs755nm alexandrite laser may be a preferable treatment modality for type III MP, especially because it is a single device and may be more convenient and cost effective compared with other laser modalities or combination laser treatments. Further studies investigating the mechanisms of MP deposition and resolution are warranted to clarify our findings.

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