

## Gray-blue discoloration of the proximal nail beds



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**Key words:** blue nails; minocycline; nail; nail bed; pigmentation; side effect.



## CASE PRESENTATION

A 58-year-old Caucasian woman presented with asymptomatic gray-blue discoloration of the proximal nail beds of her fingernails (Fig 1). She described 5 years of gradually worsening gray-blue perioral macules coalescing into patches and on examination was observed to also have diffuse gray-blue discoloration of the bilateral auricular helices and sclerae. Her past medical history was significant for smoking, nephrolithiasis, acne vulgaris and hidradenitis suppurativa. The patient declined biopsy or treatment.

### Question 1: What is the most likely diagnosis?

- A. Normal variant
- B. Argyria
- C. Minocycline-induced pigmentation
- D. Wilson disease (hepatolenticular degeneration)
- E. B12 deficiency

### Answers:

**A.** Normal variant – Incorrect. Although blue lunula can be observed in otherwise healthy black individuals,<sup>1</sup> it would not be considered normal variant in a patient of this skin type. The gray-blue discoloration also extends into the nail bed, beyond the lunula, in this case.

**B.** Argyria – Incorrect. Argyria is in the differential diagnosis for blue lunula. This patient did not have a history of silver supplementation or other exposure.

**C.** Minocycline-induced pigmentation – Correct. Given the patient's past medical history of acne and hidradenitis suppurativa, for which tetracycline antibiotics are frequently utilized, and blue-gray pigmentation of her skin, sclera (Fig 2), helices (Fig 3), and nail beds, this is the correct diagnosis. She took minocycline 100 mg daily by mouth for 25 years.

**D.** Wilson disease (hepatolenticular degeneration) – Incorrect. Wilson disease, an autosomal recessive disorder of copper metabolism, is in the differential for a patient with blue lunula; however, the color does not extend into the nail bed as in this case.

Wilson disease also presents with cirrhosis, hyperpigmentation, and pruritus.<sup>1</sup>

**E.** B12 deficiency – Incorrect. Blue or blue-black discoloration of the nails can be observed in the setting of vitamin B12 deficiency,<sup>2</sup> however this is diffuse and secondary to melanocyte activation as opposed to depositional etiology as in this case.

### Question 2: What type(s) of minocycline hyperpigmentation is known to increase in incidence with higher cumulative dose?

**A.** Type I: blue-black macules in areas of acne scarring or inflammation on the face

**B.** Type II: blue-gray macules or diffuse discoloration at sites distant from inflammation

**C.** Type III: diffuse muddy-brown discoloration on sun-exposed skin

**D.** Type IV: blue-gray macules in areas of scarring on the back

**E.** Types II and III

### Answers:

**A.** Type I: blue-black macules in areas of acne scarring or inflammation on the face – Incorrect. Type I does not appear to be related to cumulative dose or duration.<sup>3</sup> This typically resolves several months after minocycline is discontinued.

**B.** Type II: blue-gray macules or diffuse discoloration at sites distant from inflammation – Incorrect. Although true, this is not the best answer. This

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patient best classifies as Type II, given involvement of the nails, sclera, and cartilage. This typically resolves months after minocycline is discontinued.<sup>3</sup>

**C.** Type III: diffuse muddy-brown discoloration on sun-exposed skin — Incorrect. Although true, this is not the best answer. In contrast to types I and II, this pigmentary change persists indefinitely.<sup>3</sup>

**D.** Type IV: blue-gray macules in areas of scarring on the back — Incorrect. In this more recently reported entity, the patients were on shorter courses of minocycline with low cumulative dose, similar to Type I.<sup>3</sup>

**E.** Types II and III — Correct. Both Types II and III are associated with prolonged or high dose minocycline intake, with previous reports noting between 70 to 100 g of cumulative dose as a risk factor.<sup>3,4</sup>

**Question 3: Which of the following is most likely to be the initial location of minocycline pigmentation?**

- A.** Nails
- B.** Mandible
- C.** Cartilage
- D.** Axillae
- E.** Sclera

**Answers:**

**A.** Nails — Correct. Minocycline pigmentation usually occurs after prolonged treatment; however, it is not always dose dependent. There are reports of nail pigmentation presenting as early as 8 weeks into a minocycline course,<sup>5</sup> therefore it has been suggested that nail bed discoloration may be the first location of pigmentation.

**B.** Mandible — Incorrect. There are reports that 10% of patients taking minocycline between 100 and 200 mg/day for greater than 1 year had intraoral bone pigmentation and 20% had this finding after taking minocycline for 4 years.<sup>4</sup> Blue or blue-black discoloration of the bone can be seen through the semi-translucent maxillary and mandibular anterior alveolar mucosa.

**C.** Cartilage — Incorrect. Cartilage pigmentation has been reported in patients taking minocycline for over 1 year.<sup>4</sup>

**D.** Axillae — Incorrect. Type I minocycline pigmentation involves the face, Type III minocycline pigmentation involves sun-exposed skin, and Type IV minocycline pigmentation involves the back. Intertriginous areas are typically uninvolved.

**E.** Sclera — Incorrect. Scleral pigmentation is seen in patients taking minocycline for years. Of note, it has been observed that almost all patients with scleral pigmentation also have pigmentation of the nails.<sup>4</sup>

**Conflicts of interest**

None disclosed.

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