Blue-black hyperpigmented patches on the cheeks

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A 59-year-old, Black female presented with progressive darkening of her cheeks over several months. For several years, she had been self-treating discoloration on her bilateral cheeks with an over-the-counter skin brightening cream with topical 2% hydroquinone as an active ingredient. She then obtained a prescription for hydroquinone 8% cream and saw no lightening of the areas after 2 months of use. A skin examination revealed dark, blue-black, ill-defined patches with overlying scale bilaterally distributed on the upper medial cheeks.
Adjacent to the hyperpigmented patches were hypopigmented coalescing macules. A punch biopsy was performed, and representative sections are shown (Figs 2 and 3).

**Question 1: What is the best diagnosis?**

A. Discoid lupus  
B. Exogenous ochronosis  
C. Minocycline-induced hyperpigmentation  
D. Nevus of Ota  
E. Argyria

**Answers:**

A. Discoid lupus — Incorrect. Although patients with discoid lupus may present with hyperpigmented and hypopigmented scaly patches on the face, the histology would show follicular plugging, basilar vacuolization with dyskeratotic keratinocytes, superficial and deep perivascular and periaxial lymphocytic inflammation, dermal melanophages, and increased dermal mucin. A thickened basement membrane zone is occasionally conspicuous.

B. Exogenous ochronosis — Correct. This patient presented with blue-black discoloration of the face after long-term use of hydroquinone, an important risk factor for the development of exogenous ochronosis. Histology revealed numerous yellow-brown, “banana-shaped” pigment deposits throughout the papillary dermis, which is characteristic of this condition.

C. Minocycline-induced hyperpigmentation — Incorrect. Although type 1 minocycline-induced hyperpigmentation can present as blue-black macules on the face, histology is typified by the deposition of brown/black granules along elastic fibers and within perivascular macrophages and eccrine units in the papillary dermis and highlighted by a Perls Prussian blue stain.

D. Nevus of Ota — Incorrect. Although nevus of Ota can present with bluish-gray hyperpigmentation of the face, it is often unilateral in the distribution of the trigeminal nerve and involves the associated sclera of the eye approximately two-thirds of the time. Histopathology shows pigmented, spindle-shaped melanocytes throughout the dermis.

E. Argyria — Incorrect. Argyria is acquired after exposure to silver. Although patients present with gray or blue skin discoloration, histopathology showing brown/black silver granules in a linear fashion on the basal membrane of eccrine glands would be more specific to argyria. The silver deposits can be further highlighted by dark field microscopy.

**Question 2: Which enzyme is involved in the pathway of this condition?**

A. Tyrosinase  
B. Homogentisate oxidase  
C. Argininosuccinate synthetase  
D. Cystathionine β-synthase  
E. α-Galactosidase

**Answers:**

A. Tyrosinase — Incorrect. Tyrosinase is the rate-limiting enzyme involved in the production of melanin, and defects in this enzyme can lead to albinism. The cofactor for tyrosinase is copper, and, therefore, conditions in which copper levels are affected, such as Menkes disease, lead to pigmentary dilution.

B. Homogentisate oxidase — Correct. This patient’s hyperpigmentation is a result of the local competitive inhibition of homogentisic oxidase by hydroquinone. This leads to the accumulation of homogentisic acid in the skin.

C. Argininosuccinate synthetase — Incorrect. A deficiency of argininosuccinate synthetase causes a rare autosomal recessive disease called citrullinemia. This disease would cause the buildup of ammonia and other toxins in the blood.

D. Cystathionine β-synthase — Incorrect. Homocystinuria is caused by a deficiency of cystathionine β-synthase. A patient with this disease would typically present with symptoms such as the dislocation of the lens of the eye and osteoporosis.

E. α-Galactosidase — Incorrect. A mutation in the enzyme α-galactosidase leads to an X-linked lysosomal storage disorder called Fabry disease. A patient with this disease would present with cardiovascular and renal complications, angiokeratomas, and peripheral neuropathy.

**Question 3: What is the best treatment?**

A. Q-switched alexandrite laser treatment  
B. Intense pulsed light therapy
C. Pulsed dye laser treatment

D. Nd:YAG laser treatment

E. 20% trichloroacetic acid (TCA) peels

Answers:

A. Q-switched alexandrite laser treatment — Correct. Multiple sessions of Q-switched 755-nm alexandrite laser treatment can lead to successful lightening and decreased dermal pigmentation on histopathologic exam. To prevent scarring and dermal injury from lasers, the desired pulse duration for treating pigmented lesions within the dermis should be equal to or less than the thermal relaxation time of a dermal melanosome. Short-pulsed picosecond lasers generate less heat in both the dermis and epidermis and have a high specificity for targeting smaller cells, leading to a decreased risk of acquiring postinflammatory hyperpigmentation.

B. Intense pulsed light therapy — Incorrect. Although the Q-switched alexandrite laser is the best treatment option, intense pulsed light therapy can produce some improvement, especially due to its ability to alter the width of the pulse and wavelength according to the patient’s skin type.

C. Pulsed dye laser treatment — Incorrect. Pulsed dye laser treatment produces pulses of visible light at 585 or 595 nm with hemoglobin being the chromophore and, therefore, is best suited for vascular lesions.

D. Nd:YAG laser treatment — Incorrect. Although there are few reports of 1064-nm Q-switched Nd:YAG lasers reducing dyschromia seen in ochronosis, the results are only modestly successful compared to those of Q-switched alexandrite lasers after 4 sessions.

E. 20% TCA peels — Incorrect. 20% TCA peels are only superficial peels and do not penetrate below the epidermis. Theoretically, medium-to-deep peels would be better indicated for the treatment of ochronosis. 20% TCA peels are more appropriate for the treatment of melasma.

Abbreviation used:

TCA: trichloroacetic acid

Conflicts of interest
None disclosed.

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