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Minocycline-Induced Blue-Gray Discoloration

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To the Editor,

Drug-induced hyperpigmentation has commonly been described as the consequence of an increased deposition of melanin in the epidermis and/or in the dermis of the photo-exposed skin [1, 2].

A 61-year-old Italian man was referred from the cardiology unit for a blue-gray discoloration of his face of 3 years' duration. He had been followed up for 14 years following a cardiac transplantation and was under immunosuppressive treatment with numerous drugs, including cyclosporine, azathioprine, and everolimus. Other medications included aspirin, allopurinol, simvastatin, and bisoprolol.

At the time of our consultation, we observed a prominent blue-gray discoloration characterized by symmetric patches localized on the temporal, preauricular and periorbital skin (Fig. 1), while the trunk, limbs, and the mucosae were spared. Routine blood tests and other recent investigations excluded the most common causes of hyperpigmentation, including Addison disease, hyperthyroidism or malignancy. A skin biopsy from the pigmented skin showing prominent solar elastosis, epidermal thinning, and focal hyperpigmentation of the basal layer was not helpful for a diagnosis. A more detailed medical history revealed that the patient had been taking minocycline 100 mg every other day for nearly 10 years. In fact, he had observed an improvement of a folliculitis of his trunk after minocycline prescription from his physician; he had therefore continued to take the drug autonomously. Minocycline intake was immediately stopped and a diagnosis of minocycline-induced pigmentation was made. At 2 years of follow-up, the face discoloration was still present, although less prominent (Fig. 2). The patient refused any surgical procedure, such as laser treatment or skin bleaching agents.

Disorders of pigmentation are usually due to the deposition of melanin and an increase in active melanocytes. The clinical features are characterized by blue-black or blue-gray diffuse or pitted pigmentation primarily of the face, extremities and other photo-exposed areas. Various exogenous factors can be involved, including inflammation and injury (postinflammatory hyperpigmentation). Differential diagnosis includes various dermatoses of unknown etiology, such as erythema dyschromicum perstans or ashy dermatosis, lichen planus pigmentosus and melasma or argyria,

Fig. 1. Diffuse blue-gray discoloration over the face.

Fig. 2. The patient today, showing mild improvement after discontinuation.

which is caused by an inappropriate or accidental exposure to silver compounds [1, 3].

On the other hand, acquired hyperpigmentation of the skin or mucosae is also a frequent adverse effect of numerous treatments. The most common drugs are chemotherapeutic agents, anti-acne antibiotics (tetracycline and minocycline), oral contraceptives, hydroxychloroquine, clofazimine, and amiodarone [1, 2, 4–7].

Our patient was an allograft recipient under immunosuppressive treatment; our main concern was therefore the risk of a malignancy transformation or other long-term post-transplant complications. Only a detailed medical history did reveal his self-treatment with minocycline leading to the final diagnosis.

Long-term minocycline treatment is prescribed in patients affected by acne/folliculitis, as well as in patients with rheumatic disorders, because of the benefits described in rheumatoid arthritis and osteoarthritis [4–7]. Numerous studies on the efficacy and safety of minocycline as an antimicrobial drug have been reported, although there are possible side effects after a long-term treatment. Two decades ago, an English study demonstrated that hyperpigmentation occurs after a minimum treatment duration of 8 months and a cumulative dosage over 70 g, concluding that minocycline up to 200 mg/day is safe [4]. The reason why hyperpigmentation is frequently seen with minocycline, but much less with other tetracyclines like doxycycline remains uncertain. Nevertheless, this adverse reaction is rarely seen in younger patients affected by acne, but usually in elderly people, with chronic disorders. This is likely the consequence of the cumulative dosage of minocycline, since patients with acne routinely take 50 or 100 mg daily, while the prescription for arthritis is 200 mg daily [5–7].

Three distinct types of minocycline-induced hyperpigmentation have been described: type I characterized by blue-gray spots on facial acne and scars, type II showing dark patches on the legs;

both types have similar histologic features characterized by iron and melanin dermal deposition. However, our patient was affected by type III, showing hyperpigmentation of the sun-exposed areas, characterized by nonspecific melanin deposition in the basal layer at histological staining. This type is more resistant to treatment and persists indefinitely, especially in patients undergoing a long-term treatment [5–7].

Statement of Ethics

The authors have no ethical conflicts to disclose. A written consent was obtained from the patient.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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