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Hyperpigmentation

A case study

Keywords: hyperpigmentation

Case study

A man, 70 years of age, presented with a history of hyperpigmentation on his lower extremities. The rash was asymptomatic and the patient was uncertain how long it had been present. However, he recalled that it was definitely not present at his last appointment 10 months prior.

He had a past history of hypertension, hypercholesterolaemia, stroke and venous insufficiency. His usual medications were aspirin 81 mg/day and simvastatin 20 mg/day; he was also on hydrochlorothiazide/triamterene and gabapentin. In addition, a few months ago he was started on minocycline 100 mg/day orally by his urologist for prophylaxis of recurrent coagulase negative staphylococcal urinary tract infections in the setting of neurogenic bladder. The patient was quite pleased that he had experienced no recurrent urinary tract infections since starting minocycline.

Examination of his lower extremities revealed diffuse, macular dark bluish-black areas of discolouration. No crusting, ulceration, obvious haemosiderin deposition or oedema was present (*Figure 1, 2*).

Question 1

What is the likely diagnosis of this patient's hyperpigmentation?

Question 2

What is the differential diagnosis?

Question 3

What is the treatment of this condition?

Answer 1

The likely diagnosis is minocycline induced hyperpigmentation. This is supported by the temporal association of the discolouration developing after minocycline therapy and the characteristic bluish-black hue of the hyperpigmentation. Minocycline induced hyperpigmentation is classified into three types:

- type 1, which is the most common, develops in areas of previous inflammation and scarring and is often blue-black in colour

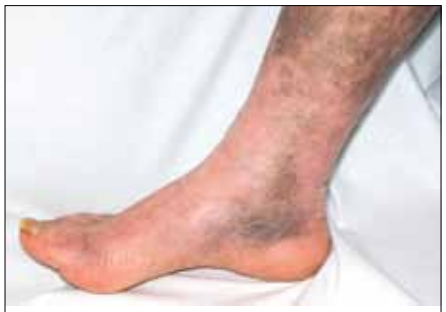

Figure 1. The medial aspect of the patient's right foot

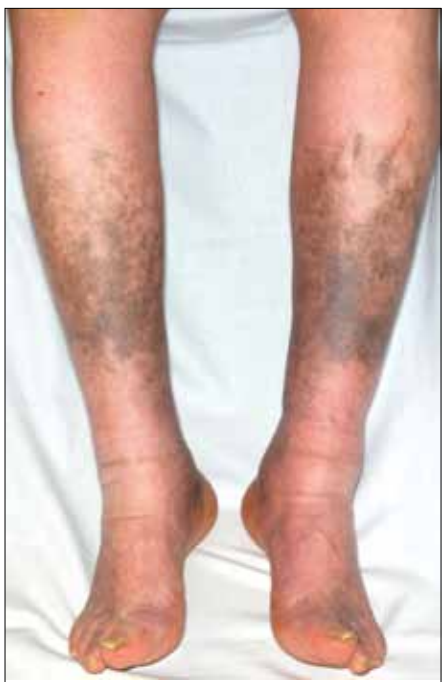

Figure 2. The patient's lower extremities

- type 2 consists of blue-grey pigmentation of previously normal skin and most commonly involves the legs, and
- type 3, the least common, consists of diffuse muddy-brown discolouration that is most prominent on sun exposed areas.

Skin histopathology differs between the three types of hyperpigmentation, suggesting different mechanisms may be responsible. The patient's rash is consistent with type 2 minocycline induced hyperpigmentation.[1]

Answer 2

Differential diagnosis includes:

- Schamberg disease (progressive pigmented purpuric dermatosis or purpura simplex). This is a pigmented purpuric dermatosis that affects the lower extremities and consists of irregularly shaped macules of orange-brown pigmentation that are often described as having a 'cayenne pepper' appearance. Aetiology is unknown. Hyperpigmentation can be asymptomatic or occasionally pruritic[2]
- venous stasis dermatitis. Venous stasis dermatitis may occur on the lower extremities of persons with venous insufficiency. Hyperpigmentation is generally reddish-brown in colour. Scaling, erythema and haemosiderin deposition are invariably present.[3] Although this patient has a history of venous stasis, his oedema has been well controlled. In addition, while haemosiderin deposition is present, the bluish-black discolouration (shown in *Figure 1, 2*) is not characteristic of venous stasis hyperpigmentation
- postinflammatory hyperpigmentation. This is a tan to dark brown hyperpigmentation that manifests in areas of previous inflammatory dermatoses or cutaneous thermal or other injury. Common dermatologic precipitants include acne, psoriasis, atopic, allergic or irritant contact dermatitis and cutaneous infections.[4]

Answer 3

Hyperpigmentation usually resolves with discontinuation of minocycline, although resolution may take months to years. Type 3 hyperpigmentation may be more likely than type 1 and 2 to persist, despite cessation of the medication.[5] For persistent hyperpigmentation, laser treatments can be used.[6] Biopsy is useful if the diagnosis is in question or confirmation of the type of hyperpigmentation is sought to guide treatment.

Discussion

Minocycline is a tetracycline class antibiotic that becomes black upon oxidation and can cause discolouration of the skin, nails, bulbar conjunctiva, oral mucosa, teeth, bones and the thyroid gland.[5] Black discolouration of breast milk due to minocycline use has also been reported.[7] Hyperpigmentation from minocycline often occurs after long term therapy with doses of 100 mg/day
or greater, although there is at least one case report of occurrence following only 20 days of minocycline use.[8]

Minocycline is frequently prescribed for treatment of acute infections, acne, and rosacea. Its anti-inflammatory effect may also be useful in rheumatoid arthritis and other inflammatory disorders. Interestingly, a higher incidence of minocycline induced hyperpigmentation may occur in patients being treated for autoimmune diseases. While a prospective trial of 300 patients on minocycline for acne treatment found the incidence of minocycline induced hyperpigmentation was 3.7%,[6] retrospective case series revealed incidences of 36% and 77% in patients treated for rheumatoid arthritis and immunobullous disease, respectively.[9,10] A retrospective review in patients treated for rheumatoid arthritis suggested that increasing age may be a risk factor for minocycline hyperpigmentation.[9] However, body weight, gender, prednisone use and aspirin use were not associated with an increased incidence of hyperpigmentation in the patient group studied.[9]

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Conflict of interest: none declared.

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