

Minocycline induced hyperpigmentation in lepromatous patches: case report

Abstract

Minocycline is a tetracycline derivative that inhibits growth of *Mycobacterium leprae*, it is used as part of modified Multi Drug Therapy (MDT) in Hansen's disease. Pigmentation is a very common benign side effect of the drug and can be seen in inflammatory as well as non-inflammatory skin, sclera, teeth, gums, pinnae and scar tissue. We report a case of Hansen's disease (Borderline Lepromatous) with minocycline induced hyperpigmentation specifically over multiple lepromatous patches. Although clofazimine is more commonly responsible for pigmentation in Hansen's disease, there is paucity of data implicating minocycline as a cause. This patient presented with hyperpigmentation of leprosy patches both at sun exposed and protected sites. Histopathology of these patches revealed foamy histiocytes and numerous Acid Fast Bacilli (AFB) along with multiple melanophages unlike clofazimine pigmentation in which there is deposition of ceroid lipofuscin and not melanin. On stoppage of minocycline the pigmentation is gradually resolving.

Keywords: minocycline, pigmentation, lepromatous patch, melanin

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Key messages: Besides clofazimine, minocycline should also be considered as a cause of hyperpigmentation in lepromatous patches, however the histopathological features of the two are different.

Introduction

Minocycline is a tetracycline derivative that inhibits growth of *Mycobacterium leprae* and is used as a part of modified Multi Drug Therapy (MDT) in Hansen's disease. Pigmentation is a very common benign side effect of the drug and can be seen in inflammatory as well as non-inflammatory skin, sclera, teeth, gums, pinnae and scar tissue. We report a case of Hansen's disease (Borderline Lepromatous) with minocycline induced hyperpigmentation specifically over multiple lepromatous patches. Although clofazimine is more commonly responsible for pigmentation in Hansen's disease, there is paucity of data implicating minocycline as a cause.

Case history

A 22years old male patient of Hansen's disease (Borderline Lepromatous) symptomatic for last 01year presented with multiple erythematous and hypopigmented normoasthetic plaques and macules distributed over back and extremities (Figure 1) along with multiple thickened nerves.¹ A slit skin smear for AFB (L) was positive with a Bacteriological Index (BI) of 6+. Histopathological examination from a biopsy done from back revealed multiple foamy histiocytes with ZN stain for AFB (L) showing numerous leprae bacilli. He was started on MDT (MB) which consisted of Cap Rifampicin 600mg once a month, Cap Clofazimine 100mg on alternate days and Tab Dapsone 100mg once daily. He developed Dapsone induced haemolysis in 04months after initiation of MDT in the form of a raised reticulocyte count of 4% and Peripheral Blood Smear showed evidence of hemolysis. An unconjugated hyperbilirubinaemia also supported the diagnosis of dapsone induced hemolysis. Hence dapsone was stopped and patient was shifted to modify MDT in the form of Cap Minocycline 100mg once daily, Tab Ofloxacin 400mg once daily, Cap Clofazimine 100mg on alternate days. Cap Rifampicin 600mg once a month was continued due to high bacillary load. Patient developed hyperpigmentation over pre-existing patches of Hansen's macules affecting photo exposed as well as photo protected sites 03months after initiation of Minocycline²

(Figure 2). A skin biopsy was done from these hyperpigmented macules over back which was suggestive of increase in melanophages and mild increase in melanin with superficial dermis showing dilated blood vessels with perivascular chronic inflammatory infiltrate³ (Figure 3). ZN stain (Lepra) revealed multiple globi of Acid Fast Bacilli (Figure 4). Slit Skin Smear from the hyperpigmented macules continued to show a Bacteriological Index (BI) ranging from 3+ to 6+ at different sites.⁴ These histopathological findings were consistent with minocycline induced hyperpigmentation and are unlikely to be due to clofazimine.⁵



Figure 1 Lepromatous patches before administration of minocycline.

Discussion

Minocycline has been extensively used in various dermatological conditions including acne vulgaris, rosacea, vesico-bullous disorders like pemphigus vulgaris and pemphigus foliaceus.^{6,7} It also forms part of modified MDT since 1987, it acts by inhibiting the 30S ribosomal subunit of *Mycobacterium leprae* and it is combined with other drugs like rifampicin and fluoroquinolones.⁸ A very common side effect of

minocycline is cutaneous hyperpigmentation which can be because of multiple mechanisms. Type-1 hyperpigmentation is a blue-black pigmentation of inflamed skin, type 2 is discoloration of normal skin of the lower limbs which is usually blue-gray and type 3 is diffuse brownish discoloration. The type 1 & 2 is mainly due to iron containing minocycline metabolic products with melanosomes while type 3 is melanin deposition.⁴ Type 2 and 3 are related to duration of treatment directly and start appearing as early as 06weeks of initiation of therapy.⁴



Figure 2 Minocycline induced hyperpigmentation over lesions on back.

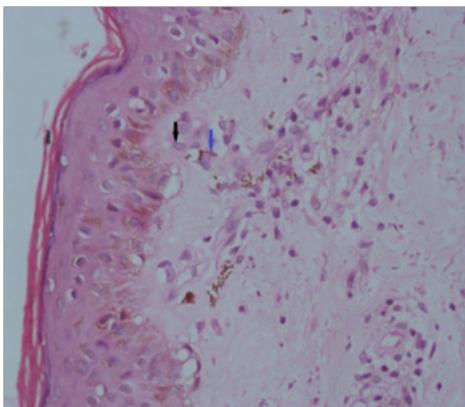


Figure 3 H&E stain 400 X Increase in melanin with superficial dermis showing dilated blood vessels with perivascular chronic inflammatory infiltrate.

Clofazimine also causes hyperpigmentation because of ceroid lipofuscinosis and usually developed within 02weeks of initiation of therapy and is a reddish brown diffuse pigmentation over both the inflammatory as well as normal skin. The histopathological findings show numerous macrophages with phagolysosomes containing lipids and clofazimine crystals.⁹ This case had type 1 hyperpigmentation induced by minocycline over face, ears, back and both forearms over both photo exposed and photo protected areas. These patches lacked features of xerosis or ichthyosis. Histopathological and microbiological evaluation confirmed infiltration of the hyperpigmented macules with leprae bacilli and melanin deposition. The unique presentation not only confirms that besides clofazimine, minocycline can also cause hyperpigmentation in Hansen's disease. The histopathology and microbiological picture of the pigmentation is very distinct and caused by entirely different mechanisms.

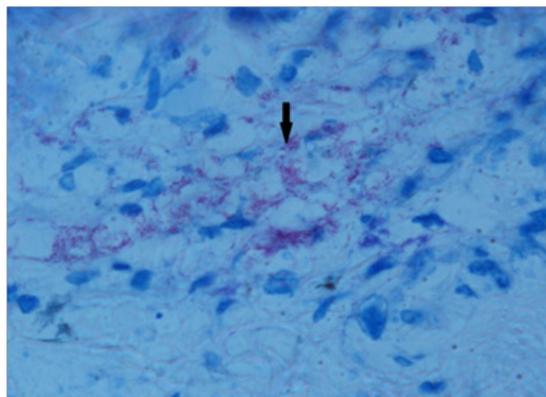


Figure 4 ZN stain 1000X with multiple globi of Acid Fast Bacilli.

Presentation at a meeting

None.

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None.

Conflicting interest

Authors declare that there is no conflict of interest.

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