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Case Report

Topical Minocycline Induced Bluish Black Hyperpigmentation in Acne Vulgaris Patient: The First Case Report of Topical Application

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Abstract

Minocycline induced hyperpigmentation is an aesthetically unsetting adverse drug event. Oral minocycline inducing hyperpigmentation is common course, keeping in line with this topical minocycline 4% was formulated. A moderately built woman diagnosed with acne was prescribed with topical minocycline 4% Gel and after 15 days of application she noticed dark patches on applied areas which progressed into macules. On examination, it was found that the topical minocycline has induced Type I (Bluish Black) Hyperpigmentation. To the best of clinician's knowledge, the drug was withdrawn and observed over a period of month. Post-withdrawal for 30-days the skin started to regain its original tone. Regardless of the fact that the topical formulation has been designed to reduce the drug contact with the systemic circulation and to decrease the side-effects, will the formulation succeed in providing the effective and safe therapy in acne patients?

Keywords: Topical Minocycline 4%, Hyperpigmentation, Type I, Bluish Black Pigmentation, Acne Vulgaris

INTRODUCTION

Minocycline induced hyperpigmentation is an aesthetically unsetting adverse drug event. Cutaneous discoloration is an established consequence of long-term minocycline treatment and was initially observed in sporadic cases in the 1970s.[1] Subsequently, minocycline-induced hyperpigmentation has been documented regularly due to the extensive use of drug in the treatment of acne.[2] The insoluble metabolite of minocycline chelates with iron in the tissues and accumulates in the dermis, which clinically manifests as bluish to mud-brown coloration.[3] The onset of skin hyperpigmentation may take from 2 weeks to 1 year following the minocycline therapy and generally occurs at cumulative doses of 50mg and 100mg/day.[4]

Minocycline is a second-generation, semisynthetic tetracycline that has exhibited effectiveness in treating moderate-to-severe acne. However, using minocycline in oral formulation has composed many adverse effects, especially skin pigmentation. Keeping in line with this, the topical minocycline 4% was developed for its antibacterial and anti-inflammatory activity combined with minimization of the systemic side effects associated with oral administration. In 2020, FDA approved the use of topical minocycline in moderate to severe acne patients above 9 years of age with once-a-day application for 12 weeks.[5]

There are reports on minocycline induced hyperpigmentation in oral formulation, but bluish black pigmentation was observed in topically applied minocycline in acne patients. The patient's presentation with topical minocycline-induced hyperpigmentation is discussed in detail below.

CASE HISTORY

A moderately built 28-year-old woman was diagnosed with moderate to severe acne vulgaris and was prescribed with Topical Minocycline 4% Gel. After 15 days of application of Topical Minocycline, she presented with complaints of dark patches on the applied areas, especially on the acne. The pigmentation first appeared as small tiny dots on the applied areas, which progressively developed into macules. The patient had no medical history and was not on any regular medications.

On physical examination, blue-black hyperpigmentation, commonly classified as Type I minocycline induced hyperpigmentation, was observed on the acne lesions (Figure 01).

Figure 1: Hyperpigmented areas on acne.

Figure 2: Post one month after drug withdrawal, Reduced bluish-black skin pigmentation.

To the best clinical knowledge of the treating physician, the topical application was withdrawn. After a month of discontinuing topical minocycline, the bluish-black pigmentation was reduced and gradually, the tone of skin was regained (Figure 02). There was no requirement of additional intervention for treating the pigmentation. Additionally, the patient was prescribed with topical clindamycin, a standard therapy, to continue the treatment for the acne.

DISCUSSION

Typically, there are three forms of hyperpigmentation caused by minocycline. The most prevalent sort, Type I, originates on the face and is characterized by blue-black discoloration in regions with prior inflammation and scarring. Type II is a blue-grey discoloration that affects apparently healthy skin which manifests mainly on the lower extremities, whereas Type III is the least frequent and manifests as muddy-brown pigmentation pre-eminently on sun-exposed skin. Recently, an additional type (Type IV) with the same characterization as Type III has been found, nevertheless it is not confined to sun-exposed skin.[6] The presented case belongs to Type I Minocycline induced hyperpigmentation.

It is approximated that around 10-20% of acquired hyperpigmentation are drug induced in nature.[7] The developmental process may vary from drug to drug, but could be explained by increased melanin production, formation of drug complexes and deposition on dermis.[8] These types of pigmentation are commonly encountered with non-steroidal anti-inflammatory drugs, amiodarone, tetracycline, silver and gold.[9] Adverse drug reactions are seemingly difficult to identify and the diagnosis depends on causal relationship between the event and drug. Naranjo's scale is commonly employed as one of the causality assessments scales.[10] The scoring for this case has been depicted in Table 01. In this instance, the Naranjo score was 7, suggesting that there was a "probable" chance of an adverse drug reaction. When determining causation, several challenges were encountered, including the inability to provide an answer or to apply certain criteria in this situation, mainly the severity of drug interactions when dose was increased or lowered or the reaction when drug was re-administered or when a placebo was administered. Despite all of these, a dermatologist's evaluation and experience offer a superior view at the scenario. (Table 1)

Table 1: Naranjo's scale for this case.

	Yes	No	Don't Know
Are there previous conclusive reports on this reaction?	+1		
Are there previous conclusive reports on this reaction?	+2		
Did the adverse drug reaction improve when the drug was discontinued or an antagonist was administered?	+1		
Did the adverse drug reaction reappear when the drug was readministered?			0
Are there alternative causes (other than the drug) that could on their own have caused the reaction?		+2	
Did the reaction reappear when a placebo was given?			0
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?			0
Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?			0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?		0	
Was the adverse event confirmed by any objective evidence?	+1		
Total	7*		

[*The score less than 2: "doubtful", 2 – 4: "possible", 5 – 8: "probable", and 9 or above: "definite".]

Acne being a facial ailment significantly impacts the social stigma of the patents, upon which hyperpigmentation can be more demeaning. Though there are multiple case-reports and well-documented literatures available for minocycline induced hyperpigmentation, as far as the author's knowledge, this is the first case report with "topical" minocycline induced hyperpigmentation. Regardless of the fact that the topical formulation has been designed to reduce the drug contact with the systemic circulation and to decrease the side-effects, will the formulation succeed in providing the effective and safe therapy in acne patients?

Topical minocycline induced hyperpigmentation is an alarmingly disfiguring consequences in dermatology. Keeping in view of the prescribing pattern of minocycline in the treatment of acne vulgaris, dermatologists should be wary of any noticeable skin discolorations.

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Conflicts of Interest: The authors do not have any conflicts of interests.

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