



Case Report

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Hydroxychloroquine-Induced Hyperpigmentation: A Case Report

Mona Talaschian¹ , Anahita Sadeghi² , Sara Pakzad³

1. Department of Internal Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
2. Digestive Diseases Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
3. Department of Medical-Surgical Nursing, School Nursing & Midwifery, Tehran University of Medical Sciences, Tehran, Iran.



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Running Title: Hyperpigmentation as a Side Effect of Hydroxychloroquine

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Hyperpigmentation; Drug side effect; Rheumatoid arthritis**ABSTRACT**

Antimalarial agents, including chloroquine and hydroxychloroquine, have been used for the treatment of various rheumatoid diseases and skin diseases because of their anti-inflammatory and immune-modulating properties. Cutaneous adverse effects such as exacerbation of psoriasis, pruritus, and hyperpigmentation have been reported as side-effects of antimalarial drugs. In this case, we report a middle-aged man with a history of rheumatoid arthritis who was treated with non-steroidal anti-inflammatory drugs and hydroxychloroquine. He complained of hyperpigmentation of the face after one year of initiating the hydroxychloroquine. It was discontinued and methotrexate was started. Skin biopsy was confirmed drug reaction. After more than 10 years of follow up, his skin discoloration had not been improved.

Introduction

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because of their anti-inflammatory and immune-modulating properties. Cutaneous adverse effects such as exacerbation of psoriasis, pruritus, and hyperpigmentation have been reported with treatments using those drugs. Clinically, patients on these medications present with yellow-brown to slate-gray patches [1, 2].

*** Corresponding Author:****Mona Talaschian, MSc.****Address:** Department of Internal Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.**E-mail:** dr.talaschian@gmail.com



Figure 1. Extensive facial hyperpigmentation because of the side effects of hydroxychloroquine in a patient with chronic rheumatoid arthritis

The hyperpigmentation tends to be localized and less distinctive than that with other antimalarial drugs. The patients aged between 28 and 92 years, who had received daily doses of 400 mg of hydroxychloroquine, developed hyperpigmentation after 7 to 36 months [3].

Case Presentation

A 47-year-old man was presented with a history of rheumatoid arthritis for 20 years. He was treated with non-steroidal anti-inflammatory drugs and hydroxychloroquine. He complained of hyperpigmentation of the face after one year of initiating the hydroxychloroquine. The brown hyperpigmentation expanded over most of his face (Figure 1). The Patient lacked any other constitutional symptoms. Skin biopsy was confirmed drug reaction and due to cutaneous side effects of hydroxychloroquine. Laboratory investigations, including hemoglobin, total leukocyte count, differential blood count, platelets, were within the normal range. He was treated with methotrexate, etanercept, and betamethasone 5 mg twice a day. Also, hydroxychloroquine was discontinued. Over more than 10 years of follow up, his skin discoloration had not been improved.

Discussion

Hyperpigmentation because of antimalarial drugs has been reported since 1945. However, hydroxychloroquine-associated hyperpigmentation seems to be less common than that with other antimalarial drugs and it may happen from 3 months to 22 years following the initiation of therapy [2]. In this case, a middle-aged man with a history of rheumatoid arthritis, who was treated with non-steroidal anti-inflammatory drugs and hy-

droxychloroquine developed hyperpigmentation of the face after one year of drug therapy.

The drug was discontinued and methotrexate was started but his skin discoloration was not improved over more than 10 years follow up. The mechanism of hyperpigmentation as a side effect of hydroxychloroquine is unknown but some recent studies demonstrated the deposited of melanin pigment, hemosiderin, or both in the lesional skin [4, 5]. Hydroxychloroquine accumulates in melanin-rich tissues and triggers a phototoxic reaction. Hemosiderin deposits in the dermis secondary to extravasation of red blood cells through damaged vessels and pigment changes associated with using hydroxychloroquine can result in a limited-degree of morbidity [6, 7].

One of the largest studies was conducted with the biopsy of patients with hyperpigmentation and showed that all biopsies contained melanin and hemosiderin [8]. A case reported in 2014 was a middle-aged woman with rheumatoid arthritis under the treatment with low-dose prednisolone and immune therapy. Seventeen months later the patient was referred to the dermatology outpatient clinic with a 4-month history of an asymptomatic, progressive, and distinct gray-brown macular pigmentation. After a biopsy, hydroxychloroquine was suggested as the cause of hyperpigmentation. Ten months after discontinuation of hydroxychloroquine, partial regression of the hyperpigmentation was noticed [9]. The treatment consisted of discontinuing hydroxychloroquine, which resulted in the gradual decrease in hyperpigmentation of lesions within several months [4, 5]. Thus decreasing the dose or discontinuing the treatment improves skin symptoms [1].

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed about the purpose of the research and its implementation stages; they were also assured about the confidentiality of their information; moreover, they were free to leave the study whenever they wished, and if desired, the research results would be available to them.

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Conflict of interest

The authors declared no conflict of interest.

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