Hydroxychloroquine-induced hyperpigmentation

Permalink
https://escholarship.org/uc/item/3d81x6mz

Journal
Dermatology Online Journal, 19(12)

Authors
Mir, Adnan
Boyd, Kevin P
Meehan, Shane A
et al.

Publication Date
2013

DOI
10.5070/D31912020723

Copyright Information
Copyright 2013 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at https://creativecommons.org/licenses/by-nc-nd/4.0/

Peer reviewed
Abstract

A 57-year-old woman with systemic lupus erythematosus and Sjögren syndrome presented with blue-grey hyperpigmentation of the face, upper back, and dorsal aspects of the feet after seven years of therapy with hydroxychloroquine. We present an unusual case of drug-induced hyperpigmentation.

Case synopsis

A 57-year-old woman presented to the Dermatology Faculty Group Practice at the Joan H. Tisch Center for Women’s Health with an acute eruption of cutaneous lupus erythematosis. She noticed incidentally that the skin on the dorsal aspects of her feet was darker than usual, but she could not tell how long this had been going on. Her feet had never been symptomatic.

Past medical history included systemic lupus erythematosus, Sjögren syndrome, hypothyroidism, and hyperglobulinemia. Medications included hydroxychloroquine for the past seven years, levothyroxine, cevimeline, fish oil, calcium carbonate, and vitamin D3.

Physical Examination: There was diffuse blue-grey discoloration, which was most noticeable on the face, upper back, and dorsal aspects of the feet.

Histopathology: A punch biopsy specimen was obtained from the upper back. Within the superficial dermis, there are yellow-brown, non-refractile and coarsely granular pigment deposits present within histiocytes and extracellularly. The pigment granules are highlighted by a Fontana-Masson stain.

Diagnosis: Hydroxychloroquine-induced hyperpigmentation

Discussion: We present the case of a patient presenting with diffuse blue-grey hyperpigmentation after long-term therapy with an antimalarial for systemic lupus erythematosus. Antimalarial-associated hyperpigmentation is a well-described phenomenon, which occurs in about 25% of patients on chloroquine, quinidine, hydroxychloroquine, and mefloquine [1, 2]. Most of these cases result from chloroquine use. In a study of 209 patients that were treated with chloroquine and hydroxychloroquine, which are the two most commonly used antimalarials for rheumatologic and dermatologic conditions, 35% of patients on chloroquine and 13% of
patients on hydroxychloroquine developed hyperpigmentation [2]. The results of this study suggest that gender and race are not relevant. Overall, only 12 cases of hydroxychloroquine-induced hyperpigmentation have been reported [2-11].

The lesions of hydroxychloroquine-induced hyperpigmentation are typically blue-grey macules that enlarge and become confluent over the affected body parts. The distribution of hyperpigmentation varies widely (Table). The head, neck, trunk, upper extremities, and lower extremities are each reportedly involved in roughly one-half of the cases. It is typically bilateral, although one case reports unilateral involvement of the temple [9]. There is no apparent predilection for sun-exposed sites. The hyperpigmentation begins in most patients after about four months of treatment with hydroxychloroquine. After discontinuation of the drug, there is a reduction in the level of hyperpigmentation, but it does not resolve completely.

The pathophysiology of this process is unclear. There are dermal melanin deposits in biopsy specimens, but unlike a fixed drug eruption, these are not preceded by an inflammatory phase and damage to the dermoepidermal junction. In vitro and in vivo studies have shown that antimalarial drugs can bind to melanin [12], but the importance of this binding and its role in eye toxicity and skin hyperpigmentation has not been thoroughly investigated.

**Table.** Distribution of hyperpigmentation in reported cases of hydroxychloroquine-induced hyperpigmentation

<table>
<thead>
<tr>
<th>Current report</th>
<th>Distribution of hyperpigmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho 2012</td>
<td>Neck, upper trunk, upper extremities</td>
</tr>
<tr>
<td>Skare 2011</td>
<td>Not reported</td>
</tr>
<tr>
<td>Jallouli 2010</td>
<td>Anterior legs</td>
</tr>
<tr>
<td>Morrison 2009</td>
<td>Shins, forearms, hands</td>
</tr>
<tr>
<td>Melikoglu 2008</td>
<td>Dorsal hands</td>
</tr>
<tr>
<td>Puri 2008</td>
<td>Upper back, shoulders</td>
</tr>
<tr>
<td>Puri 2008</td>
<td>Right temple</td>
</tr>
<tr>
<td>Rood 2008</td>
<td>Forearms</td>
</tr>
<tr>
<td>Amichai 2007</td>
<td>Lower extremities</td>
</tr>
<tr>
<td>Millard 2004</td>
<td>Face, neck, trunk, axillae, posterior thighs</td>
</tr>
<tr>
<td>True 2002</td>
<td>All extremities, torso, hairline</td>
</tr>
</tbody>
</table>

**References**