Dermatologic manifestations of hydroxychloroquine therapy: A closer look at the nails

To the Editor: We commend Sharma et al[1] for their thorough review of the dermatologic manifestations of hydroxychloroquine therapy. The authors characterized adverse skin, hair, and nail events in a systematic review of 94 articles, analyzing 689 events. The top 3 most common adverse events were drug eruption or rash (358 cases), cutaneous hyperpigmentation (116 cases), and pruritus (62 cases). There were only 3 cases of hydroxychloroquine-associated nail adverse events. All patients presented with melanonychia, in 3 separate reports, with average cumulative dose of 230 g (range, 198-261 g).

We believe that a closer examination and more robust discussion of hydroxychloroquine-associated nail adverse events is necessary to explore both the true prevalence of these nail changes and salient clinical findings.

Giraldo et al[2] reported on a 48-year-old Ecuadorian woman with systemic lupus erythematosus (SLE) presenting with generalized blue-gray hyperpigmentation most prominent on the face and dorsal hands 12 months after starting hydroxychloroquine at 200 mg/day. She was also noted to have thin, longitudinal brown bands involving the left second and third, and right third fingernails. No biopsies with histopathology were performed on the skin or nails to confirm the diagnosis. In this case, although drug-induced longitudinal melanonychia is possible, given that the second and third fingernails were involved, lack of involvement of all 20 nails, the color and width of the bands, and her Fitzpatrick type IV skin, ethnic-type pigmentation due to melanocytic activation is certainly more likely.

Zhang et al[3] described a 55-year-old woman with SLE presenting with diffuse blue-gray melanonychia of her fingernails after 38 months of hydroxychloroquine treatment. She had no skin or mucosal pigmentation. No biopsy with histopathology was performed; however, given that she had Fitzpatrick skin type III, involvement of all 10 fingernails with diffuse blue-gray bands confirmed with dermoscopy, exclusion of other causes of melanonychia, and persistence of nail changes for 15 years, hydroxychloroquine-induced melanonychia is plausible.

Bahloul et al[4] performed a cross-sectional study of 41 patients treated with hydroxychloroquine for at least 6 months. The nails were examined in all patients, and there was only 1 case of melanonychia (2.4%). Although no details were given about this patient, the researchers noted that the melanonychia was not attributed to hydroxychloroquine.

The most common indication for hydroxychloroquine therapy in the systematic review was lupus erythematosus (72% of cases), including both SLE and discoid lupus erythematosus.[1] To further confound the precise association between hydroxychloroquine and its effect on the nails, in a retrospective study of 298 patients with SLE, diffuse melanonychia was observed in 37.4% at initial diagnosis and was more common in black compared to nonblack patients (odds ratio, 3.1 [95% confidence interval 1.3-7.3]). Patients with HIV and/or prior exposure to chloroquine, cyclophosphamide, and minocycline were excluded.[5]

Therefore, looking more closely at the hydroxychloroquine-associated nail adverse events described by Sharma et al,[1] we see that nail changes may be exceedingly rare: 1 case of melanonychia out of 689 total dermatologic adverse events (0.1%) at most. Because the histopathology of hydroxychloroquine melanonychia has not been characterized, further studies are needed to clarify whether it is causative or merely an association.

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