5-2019

Yellow Nail Syndrome

Angela J. Jiang
Henry Ford Health System

Jesse Veenstra
Henry Ford Health System

Alison Boucher
Henry Ford Health System

Discoid Lupus Erythematosus with Hydroxychloroquine-Induced Hyperpigmentation

Olabola Awosika, MD, MS, Bhavnit K. Bhatia, MD, and Jungho Kwon, MD

Department of Dermatology, Henry Ford Health System, Detroit, MI

History

- A 65-year-old African American female presented for follow-up of an 8-year history of biopsy proven discoid lupus erythematosus (DLE) of the bilateral upper eyelids.
- She had significant re-pigmentation of the eyelids on hydroxychloroquine 200 mg once daily, tacrolimus 0.1% ointment, and daily SPF 50 sunscreen.
- However, in the last year, she noted progressive hyperpigmentation over the face, neck, and chest.

Examination

- On the bilateral eyelids, there were ill-defined hypopigmented macules with areas of significant re-pigmentation.
- On the face, neck, and upper chest, there were confluent, dark brown to gray, hyperpigmented patches in a photo-distributed pattern.

Histopathology

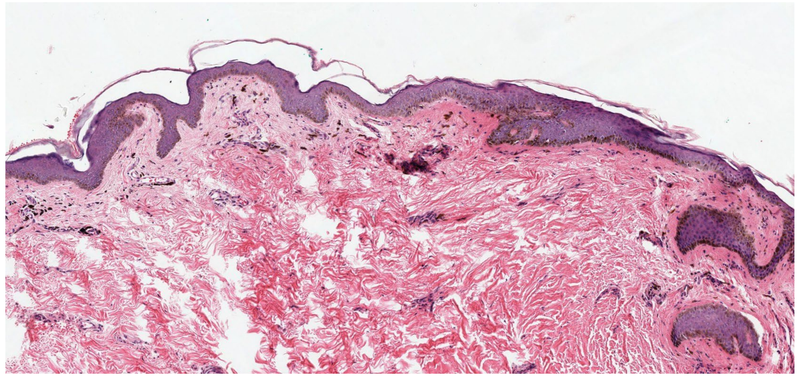

Figure 1: Pathology specimen revealing brown coarsely granular pigment deposits within histiocytes and extracellularly, along the epidermal basal layer and throughout the superficial dermis.

Clinical Photos

Figure 2. A) Bilateral upper eyelids with hypopigmented macules and significant repigmentation. Gray to brown confluent hyperpigmented patches are also noted on the face, neck, and upper chest. **B)** 7 months after discontinuing hydroxychloroquine and starting heliocare and strict photoprotection, there is decrease in hyperpigmentation.

Course and Therapy

- Punch biopsy was taken of the neck and showed the following:
  - –Hematoxylin and eosin stain demonstrated histiocytic and extracellular brown coarse granular pigment deposits along the epidermal basal layer and superficial dermis.
  - –Fontana-Masson stain highlighted these granules, supporting the presence of melanin.
  - –A Perl's iron stain for hemosiderin was negative.
  - –These changes were consistent with drug induced pigmentary alteration secondary to hydroxychloroquine.
- At the time of presentation for worsening hyperpigmentation, the patient had been on hydroxychloroquine for 3 years with stabilization of her DLE.
- After biopsy confirmation that her pigmentation was likely induced by hydroxychloroquine, it was discontinued.
- The patient was then started on strict photoprotection with daily use of broad spectrum sunscreen and heliocare daily, with slow improvement of hyperpigmentation over the past year.
- The patient was also started on tacrolimus 0.1% ointment daily the superior eyelids, to alternate with triamcinolone 0.1% ointment or hydrocortisone 2.5% ointment daily for flares of DLE.

Discussion

- One of the most common side effects of antimalarial medications is cutaneous hyperpigmentation.
- The prevalence of this side effect in DLE is unknown, but it can occur in up to 25% of patients with systemic lupus erythematosus. The majority of cases are due to chloroquine, although there have been reports with use of hydroxychloroquine.
- Onset of antimalarial-induced pigmentation commonly occurs after 4 months of use, ranging from 3 months to 22 years for hydroxychloroquine induced-pigmentation.
- Risk factors may include skin phototypes V or VI, concomitant use of oral anticoagulants or antiplatelet agents, and sun exposure.
- Discoloration due to chloroquine or hydroxychloroquine will appear as slate-gray to blue-black patches, with predominance for the anterior shins. Other common sites include the face, forearms, hard palate, gingivae, or the nail beds.
- Histopathology of antimalarial-induced pigmentation demonstrates yellow to brown pigmented granules throughout the dermis in macrophages and fibroblasts.
- Special stains, such as the Fontana-Mason and Perl's staining, will display the presence of melanin and hemosiderin, respectively, within the dermis. Biopsies of hydroxychloroquine-induced pigmentation may only demonstrate presence of melanin and not hemosiderin.
- There is no consensus on treatment for pigmentation induced by antimalarials. Discontinuing use of antimalarial medications will reduce pigmentation. However, the hyperpigmentation typically does not completely resolve.

References

1. Bahloul E, Jallouli M, Garbara S, et al. Hydroxychloroquine-induced hyperpigmentation in systemic diseases: prevalence, clinical features and risk factors: a cross-sectional study of 41 cases. Lupus. 2017;26:1304-8.
2. Jallouli M, Frances C, Piette JC, et al. Hydroxychloroquine-induced pigmentation in patients with systemic lupus erythematosus: a case-control study. JAMA Dermatol. 2013;149(8):935-40.