doi:10.36849/JDD.9489

Photodistributed Hyperpigmentation Associated With COVID-19 Vaccination

Rebecca Gibons BS,[a] Tanner Harding MD,[b] Erica Ginsburg MD,[b] Jessica Houpe MD,[b] Austinn Miller MD,[b] Imara Scott MD,[b] Michael Bernhardt MD[b]

[a]Florida State University College of Medicine, FL
[b]University of Central Florida/ HCA Florida Healthcare GME Consortium, FL

ABSTRACT

Background: Although drugs are a common cause of hyperpigmentation, the pathogenesis is unclear and varies based on the offending agent. Classic medications associated with hyperpigmentation secondary to increased melanin deposition include tetracyclines, prostaglandins, nicotine, and antimalarial medications. We report the case of a 70-year-old female who developed photodistributed hyperpigmentation due to increased melanin deposition following COVID-19 vaccination.

Case Report: A 70-year-old female presented with a one-year history of diffuse blue-grey hyperpigmentation in a photodistributed pattern. Eight months prior to onset, she received her third COVID-19 booster vaccine. The patient had never undergone therapy with medications classically implicated in the condition. A punch biopsy of the left cheek demonstrated brown pigment deposition with both superficial perivascular and deep focal interstitial and perivascular distribution. Fontana-Masson stain positivity in the setting of Prussian blue negativity was suggestive of increased melanin pigment deposition as the cause of her hyperpigmentation. Extensive laboratory workup was unremarkable.

Discussion: While the COVID-19 vaccine has been associated with a variety of cutaneous reactions, there is little evidence describing drug-induced hyperpigmentation after vaccination. Although we cannot definitively establish a causal relationship between the patient's COVID-19 vaccination and the development of her photoinduced hyperpigmentation, an in-office literature review suggested the correlation of these two events. The timing of the vaccine relative to the onset of pigmentary changes and the absence of other identifiable metabolic triggers elevate COVID-19 vaccination as a plausible offending agent. This report is intended to raise awareness of a rare but cosmetically disfiguring potential complication of COVID-19 vaccination.

J Drugs Dermatol. 2026;25(1):93-94. doi:10.36849/JDD.9489

INTRODUCTION

Up to twenty percent of all cases of acquired hyperpigmentation are postulated to be drug-induced. The incidence and pathogenesis of drug-induced hyperpigmentation are unclear and vary based on the offending medication.[1] Mechanisms postulated in the literature include drug-induced formation of special pigments, iron deposition through leakage of damaged dermal vessels, drug-induced melanin deposition, and the accumulation of the inciting medication with subsequent pigmentation secondary to chemical reaction induced by sun exposure.[1]

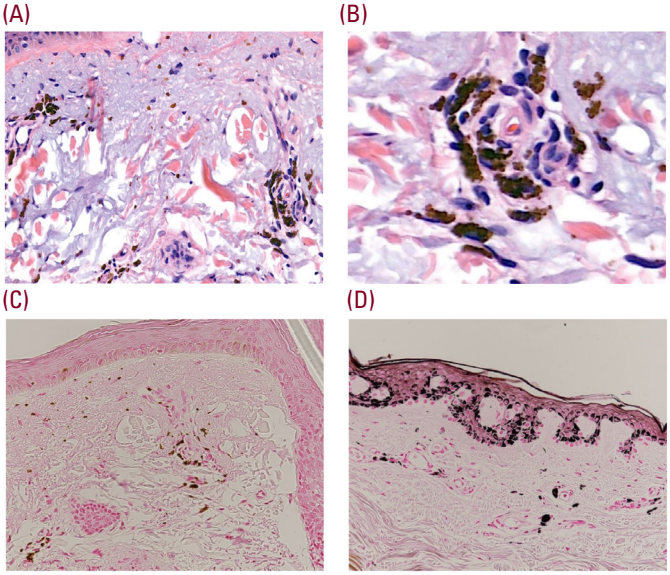
Classic medications associated with hyperpigmentation secondary to increased melanin deposition include tetracyclines, prostaglandins, phenothiazines, nicotine, amiodarone, cytotoxic agents, and antimalarial medications.[1,2] Many cutaneous reactions (including urticarial eruptions, eczematous dermatitides, and papulovesicular eruptions) have been associated with COVID-19 vaccination. We report the unique case of a 70-year-old female who developed photodistributed hyperpigmentation following COVID-19 vaccination.

CASE REPORT

A 70-year-old female presented to our clinic with a one-year history of diffuse blue-grey hyperpigmentation in a photodistributed pattern on the face, hands, and dorsal forearms (Figure 1).

FIGURE 1. Blue-grey dyspigmentation on sun-exposed skin.

FIGURE 2. Hematoxylin-eosin- superficial perivascular inflammation with pigment deposition, medium (A) and high (B) power. Pigment stained positive for Perls (iron) (C) and Fontana-Masson (melanin) in the superficial and mid-dermis (D).



Eight months prior to the onset of her hyperpigmentation, she received a third COVID-19 booster vaccine. The patient had never undergone therapy with amiodarone, tetracyclines (including minocycline), antimalarials, kratom, or gold. For several years prior to presentation, her only prescription medications included levothyroxine, lisinopril, and aspirin. She also took various vitamins and supplements (including vitamin D3, vitamin K2, biotin, vitamin E, grape seed, red wine, pine bark, bilberry, and citrus bioflavonoid complex). Prior to evaluation, the patient had undergone a skin biopsy of the dorsal hand, which was simply suggestive of postinflammatory hyperpigmentation (PIH). However, as her clinical presentation was at odds with her prior pathologic diagnosis, a repeat punch biopsy was performed on the left cheek. This demonstrated brown pigment deposition with both superficial perivascular and deep focal interstitial and perivascular distribution. Fontana-Masson stain positivity in the setting of Prussian blue negativity was suggestive of melanin-like pigment deposition (Figure 2). Extensive laboratory workup, including antinuclear antibody screen, complete blood count, complete metabolic panel, serum cortisol, and adrenocorticotropic studies, was unremarkable and unrevealing. She was referred for pico-laser treatment.

DISCUSSION

Although the patient regularly took numerous medications, vitamins, and herbal supplements, none have been associated with hyperpigmentation secondary to increased melanin deposition. Additionally, she had remained on a consistent medication regimen for years without alteration. However, as her blue-grey hyperpigmentation developed eight months following administration, COVID-19 vaccination remains a temporally plausible offending agent.

Lu et al report the case of a 27-year-old female who, one week following COVID-19 vaccination, developed dark brown macules and papules on the chest, which subsequently generalized and persisted for approximately one year.[3] This case differs in that the hyperpigmentation was not in a photodistributed pattern. Similar to our case, however, it was associated with melanin-like deposition. Pathology from repeat biopsy performed on our patient demonstrated findings consistent with increased melanin-like deposition, or at least exogenous pigment deposition from a medication with melanin-like chemical properties, to allow for Fontana-Masson positivity.

The two most common COVID-19 vaccines in the United States utilize modified messenger RNA (mRNA) to encode the SARS-CoV-2 spike protein with the intent of inducing an immune or inflammatory reaction.[4] The numerous cutaneous reactions associated with the COVID-19 vaccine may be secondary to a type IV or immune complex-mediated hypersensitivity reaction, with the antigen being the spike glycoprotein (or another substance in the vaccine). In individuals with a genetic predisposition, the vaccine may also enhance the immune system, triggering the development of inflammatory disorders such as psoriasis.[4]

COVID-19 vaccination has been associated with new-onset and worsening vitiligo, suggesting a possible immune-mediated cutaneous reaction.[5] Similar to drug-induced pigmentary changes, it is also possible that vaccination leads to an inflammatory response, yielding either increased melanin production or substances that result in pigmentation with sun exposure.

Although we cannot definitively establish a causal relationship between the patient's COVID-19 vaccination and the development of her photoinduced hyperpigmentation, the timing of the vaccine relative to the onset of pigmentary changes and the absence of other identifiable metabolic triggers elevate COVID-19 vaccination as a plausible offending agent. This report is intended to raise awareness of a rare but cosmetically disfiguring potential complication of COVID-19 vaccination.

DISCLOSURES

The authors have no conflicts of interest to declare.

REFERENCES

1. Dereure O. Drug-induced skin pigmentation. Epidemiology, diagnosis and treatment. *Am J Clin Dermatol.* 2001;2(4):253-62. doi: 10.2165/00128071-200102040-00006.
2. Krause W. Drug-induced hyperpigmentation: a systematic review. *J Dtsch Dermatol Ges.* 2013;11(7):644-51. doi: 10.1111/ddg.12042.
3. Lu J, Liu Y, Sun Y. Generalized and persistent skin pigmentation after COVID-19 vaccination. *J Eur Acad Dermatol Venereol.* 2022;36(12):e963-e964. doi: 10.1111/jdv.18379. Epub 2022 Jul 12.
4. Magro C, Crowson AN, Franks L, et al. The histologic and molecular correlates of COVID-19 vaccine-induced changes in the skin. *Clin Dermatol.* 2021;39(6):966-984. doi: 10.1016/j.clindermatol.2021.07.011. Epub 2021 Jul 25.
5. Tsai TF, Ng CY. COVID-19 vaccine-associated vitiligo: A cross-sectional study in a tertiary referral center and systematic review. *J Dermatol.* 2023 Aug;50(8):982-989.

AUTHOR CORRESPONDENCE

Rebecca Gibons BS

E-mail:..... rmg18bg@med.fsu.edu