SKIN

BRIEF ARTICLE

Kratom-Induced Photodistributed Hyperpigmentation: A Case Report

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ABSTRACT

Kratom, derived from the plant *Mitragyna speciosa*, is used recreationally and is increasingly being used in the United States to alleviate the symptoms of opioid withdrawal. A rare, but emerging side effect of long term kratom use is blue-gray hyperpigmentation of sun-exposed skin. We report a case of kratom-induced hyperpigmentation that expands on the limited number of reported cases in the literature. We describe a unique case of a 41-year-old male with kratom-induced hyperpigmentation with supporting clinical and histologic findings, highlighting the need to consider kratom in the differential diagnosis of photodistributed hyperpigmentation.

INTRODUCTION

Kratom, derived from the leaves of the plant *Mitragyna speciosa*, is traditionally used in Southeast Asia for its opioid-like effects. It is rapidly gaining popularity in the United States, particularly for self-treating opioid withdrawal. Blue-gray pigmentation in sun-exposed areas is a rare side effect of kratom use. The mechanism by which this occurs is poorly understood. Currently, only six known cases of kratom-induced hyperpigmentation have been reported in the United States.[1-6] We present a novel case of a 41-year-old Caucasian male who developed photodistributed blue-gray hyperpigmentation on his face, neck, arms, and hands after 5 years of kratom use. Currently, there is no known effective treatment for kratom induced hyperpigmentation.

CASE REPORT

A 41-year-old Caucasian man presented with progressive, asymptomatic, darkening of the skin on his face, arms, and hands over the past two years. On examination, he had diffuse, blue-gray pigmented patches on his face, posterior neck, extensor forearms, and dorsal hands (**Figures 1 and 2**). There was notable sparing of the submental area and knuckles.

He had a history of opioid use disorder that was successfully treated with suboxone fourteen years earlier. After developing back pain, the patient began taking kratom several years ago in increasingly higher doses. At presentation, he was ordering kratom online and taking 5-6 heaping spoonfuls of powder daily. Attempts to reduce intake led to withdrawal symptoms. He was referred to a detoxification clinic.

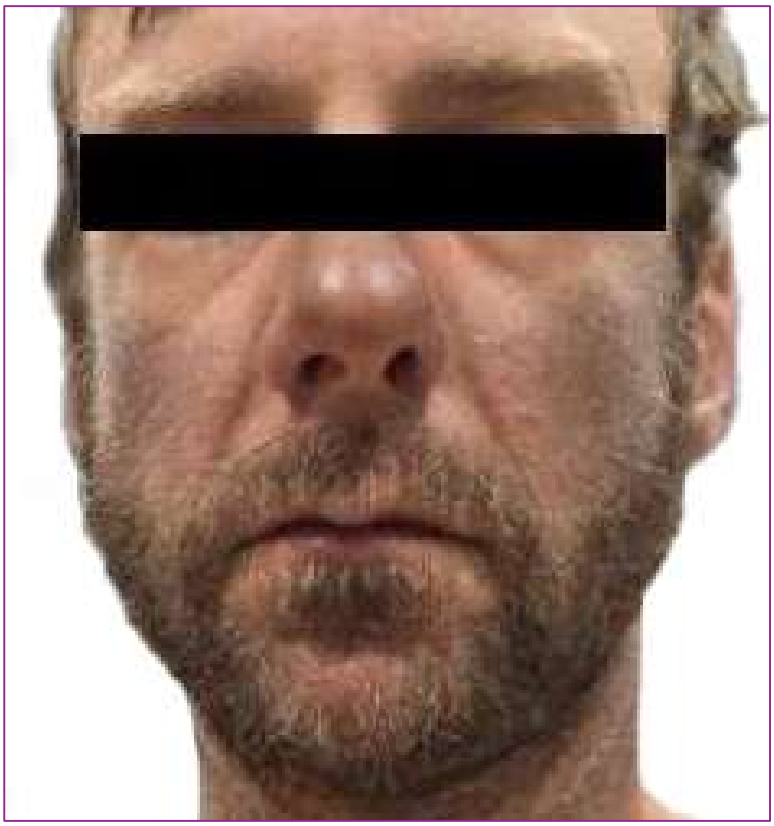

Figure 1. Blue-gray hyperpigmentation on the face

There was no history of any other potential pigment-inducing medications. His only other medications were escitalopram, nebivolol, and an albuterol inhaler.

Laboratory evaluation ruled out hemochromatosis and Addison's disease. Skin biopsy from an involved area on the right forearm demonstrated dense superficial dermal pigmentation with many melanophages. No melanocytic proliferation or significant inflammation was seen. Fontana-Masson stain was diffusely positive for melanin (**Figure 3**). Iron stain was negative.

DISCUSSION

Kratom is derived from *Mitragyna speciosa*, a plant in the Rubiaceae family native to Southeast Asia. It has been increasingly used in the United States due to its analgesic and opioid-like effects. It is widely available over-the-counter and online. It is most commonly used to self-manage the symptoms of opioid withdrawal, though it is also taken for pain relief, anxiety, increased energy, mood enhancement, and alleviation of posttraumatic stress disorder.[7] Kratom leaves are typically consumed as a brewed tea or as a powder added to beverages, but they can also be chewed, smoked, or ingested in capsule form. At low doses, kratom acts as a mild stimulant, while at higher doses, it produces sedative effects and pain relief that mimic opioids.[8]

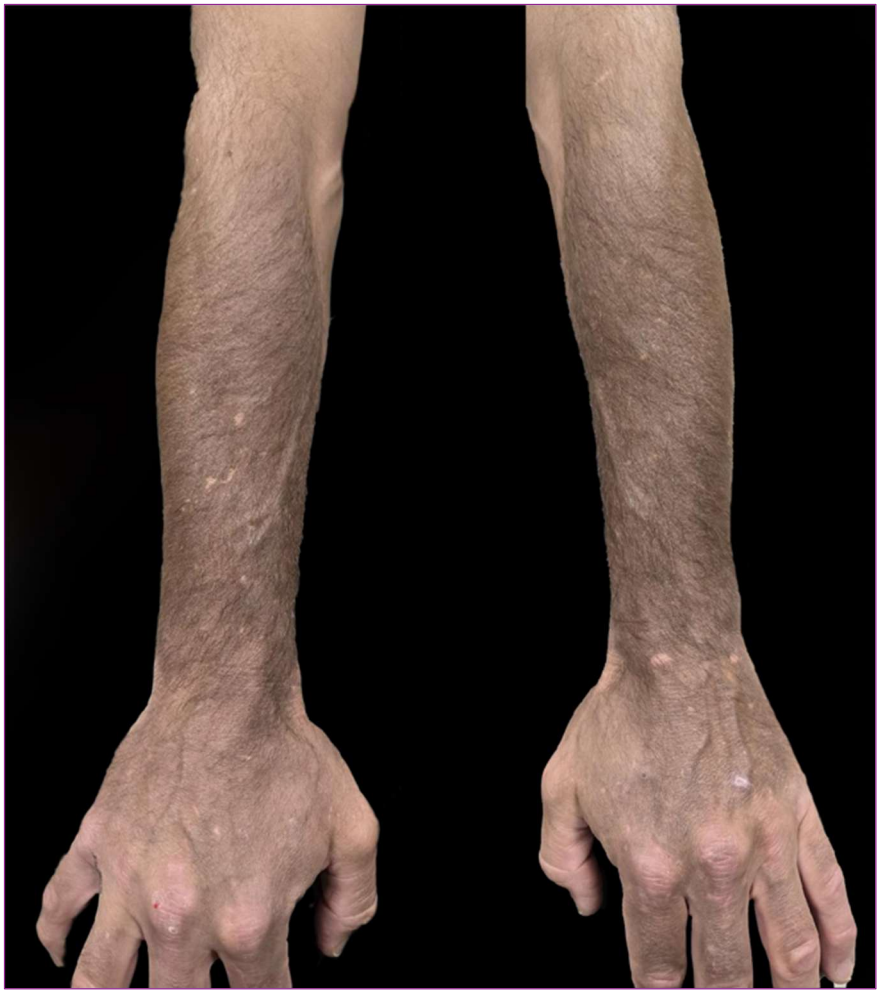

Figure 2. Kratom hyperpigmentation of the forearms and hands with sparing of the knuckles

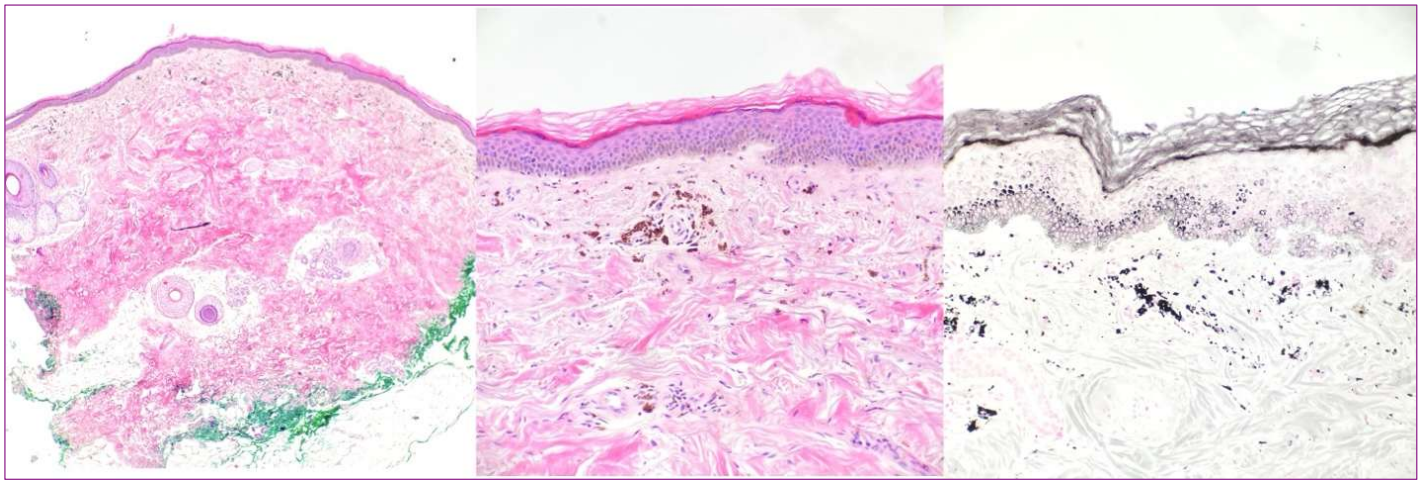

Figure 3. (A) Histology from punch biopsy of right forearm stained with hematoxylin and eosin. (B) Many melanophages in the absence of inflammation seen at 100X magnification. (C) Fontana-Masson stain diffusely positive for melanin at 100X magnification

Kratom is currently unregulated by the U.S. Food and Drug Administration and carries significant potential for toxicity. Reported adverse events include tachycardia, drowsiness, vomiting, confusion, hallucinations, seizures, respiratory depression, liver toxicity, coma, and cardiac arrest.[9] Its primary alkaloid, mitragynine, is metabolized in the liver by CYP3A4 to 7-hydroxymitragynine. Both compounds act as partial agonists on opioid mu receptors and also have dopaminergic activity, thereby exerting powerful effects on the central nervous system.[10] Due to its psychoactive, opioid-like effects, Kratom carries the risk for dependence and addiction, as seen in our patient.

To date, the Asian literature describes a limited number of cases of kratom-induced hyperpigmentation. In the United States, just six cases have been reported. Our case adds to the sparse number of reported cases in the U.S. literature. Similar to previously reported U.S. cases, our patient developed blue-gray discoloration in sun-exposed areas after chronic high-dose kratom use. In all documented western cases, pigmentation developed after an average of 5 years of sustained, high-dose kratom use, implying a threshold cumulative dose may be necessary before cutaneous findings emerge.[6] Notably, sparing of the knuckles, as in our patient, was also reported in two prior cases, suggesting this may be a helpful diagnostic clue.[3,6]

The mechanism by which kratom induces hyperpigmentation remains poorly understood. One proposed pathway involves mitragynine-mediated stimulation of melanocyte-stimulating peptide via opioid receptor binding, which may drive melanogenesis.[11] Ultraviolet exposure may also result in free radical formation of kratom and its metabolites, which in turn, may trigger melanogenic signaling cascades.[1] This theory would explain the predilection for sun-exposed areas in kratom-induced hyperpigmentation. Additionally, deposition of melanin-drug complexes, as supported by the Fontana-Masson positivity observed histologically, is similar to that seen in other drug-induced hyperpigmented rashes such as those caused by minocycline, amiodarone, imipramine, tricyclic antidepressants, phenothiazine, and antimalarial drugs and this may also contribute to the pathogenesis.

To date, no effective treatment for kratom-induced pigmentation has been reported. Q-switched laser therapy, which has shown efficacy for amiodarone-associated pigmentation, may be considered.[12] In the patient reported by Johnson et al., hyperpigmentation progressed despite treatment for three months with a compounded cream containing 12% hydroquinone, 6% kojic acid, 1% ascorbic acid, and 2% niacinamide.[2] Furthermore, cessation of kratom use has not led to resolution or improvement of pigmentation in the cases reported thus far.[4,6]

CONCLUSION

As kratom use rises in the United States, dermatologists should be aware of kratom as a potential etiology of photodistributed blue-gray pigmentation. Recognition of this rare side effect may prevent unnecessary testing. Further studies are needed to elucidate the mechanism by which the pigmentation forms and also to identify effective treatments.

Conflict of Interest Disclosures: None

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