International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Photodistributed Hyperpigmentation in a Chronic Kratom User

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Citation: *Suleman S, Khan R, Ioffe DOB, Chisholm C. Photodistributed Hyperpigmentation in a Chronic Kratom User. Int Clinc Med Case Rep Jour. 2023;2(15):1-5.*

Received Date: 30 August, 2023**; Accepted Date:** 03 September, 2023**; Published Date:** 05 September, 2023

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ABSTRACT

Kratom, a topical evergreen tree in the coffee family, originates from Southeast Asia and Papua New Guinea. It's traditionally used to manage pain, boost energy, and even as a substitute for opium. Kratom is commonly ingested orally, and historically, fresh leaves were chewed or brewed into tea. Its leaves, containing psychoactive compounds similar to opioids, are used both medicinally and recreationally. Modern commercial products include pastes, capsules, and powders. Kratom contains more than 40 alkaloids, mainly mitragynine and 7-hydroxymitragynine. They act as partial agonists at mu opioid receptors and antagonists at delta and kappa receptors; this dual property leads to varying CNS effects: stimulant-like at low doses, morphine-like sedation at high doses. In the U.S., there are no uses for kratom that are Food and Drug Administration (FDA) approved. There are warnings against its use due to potential side effects, including gastrointestinal disturbances, mental and neurologic effects, heart and lung problems, and liver problems. Amidst the many adverse effects, hyperpigmentation is commonly mentioned in the limited literature surrounding Kratom. There are currently only four case reports describing patients experiencing generalized hyperpigmentation on photodistributed areas after chronic kratom use. Here we present a case of a 32-year-old Caucasian male with a two-year history of slowly progressing skin discoloration on the hands, arms, neck and face and a long-standing history of kratom supplement use.

Keywords: Photodistributed; Chronic kratom; Hyperpigmentation

INTRODUCTION

Kratom, a topical evergreen tree in the coffee family, originates from Southeast Asia and Papua New Guinea. It's traditionally used to manage pain, boost energy, and even as a substitute for opium[1]. Its leaves, containing psychoactive compounds similar to opioids, are used both medicinally and recreationally[1,2]. In October 2016, an

anonymous online study surveyed 10,000 current Kratom users, providing a snapshot of its use in the United States. This occurred during a time of evolving legality, causing uncertainty among users. Most Kratom users are aged 31-50 and earn over $35,000. A majority have used Kratom for 1-5 years, a over 40% have talked about it with their healthcare provider[2].

Despite its pharmacology, little is known about Kratom's usage and health effects in the US. While available as a supplement for a decade, public attention surged due to a Centers for Disease Control and Prevention report on increased Kratom-related poison control calls from 2011 to 2015[2,3]. Research conducted prior to clinical trials revealed that kratom possses the capability to induce dependence and toxicity. Elevated kratom doses can result in symptoms including restlessness, high blood pressure, impaired breathing, and other effects[1]. Amidst the many adverse effects, hyperpigmentation is commonly mentioned in the limited literature surrounding Kratom[4]. There are currently only four case reports describing patients experiencing generalized hyperpigmentation on photodistributed areas after chronic kratom use[4,5].

CASE REPORT

A 32-year-old Caucasian male with past medical history of anxiety, recurrent kidney stones, and former smoker presents to the clinic with a two-year history of slowly progressing skin discoloration on his hands, arms, neck and face. He states these areas of discoloration are asymptomatic but have become more prominent over the last two years. He has been trying to avoid excessive sun exposure. He has had no prior treatments to these areas. His current medications include Adderall, baclofen, buspirone, and escitalopram. Upon further questioning, the patient reveals use of Kratom supplements over the last 4-5 years for pain control of his kidney stones as to avoid opioid use.

Clinical exam revealed blue-to-gray hyperpigmented patches over his hands, sparing his knuckles, arms, face, and neck **(Figure 1)**. A 4mm punch biopsy showed numerous melanophages in the superficial dermis with mild inflammatory cell infiltrate. No melanocytic proliferation is present. Deposits of refractile, perivascular intrahistiocytic brown pigment was confined to the level of the dermis **(Figure 2)**. Pigment deposition was positive for Fontana Masson stain and negative for Periodic Acid Schiff and Prussian Blue Iron stains **(Figure 3)**. Differential diagnosis included post-inflammatory pigment alteration, erythema dyschromicum perstans, lichen planus pigmentosus, and medication-related pigment deposition.

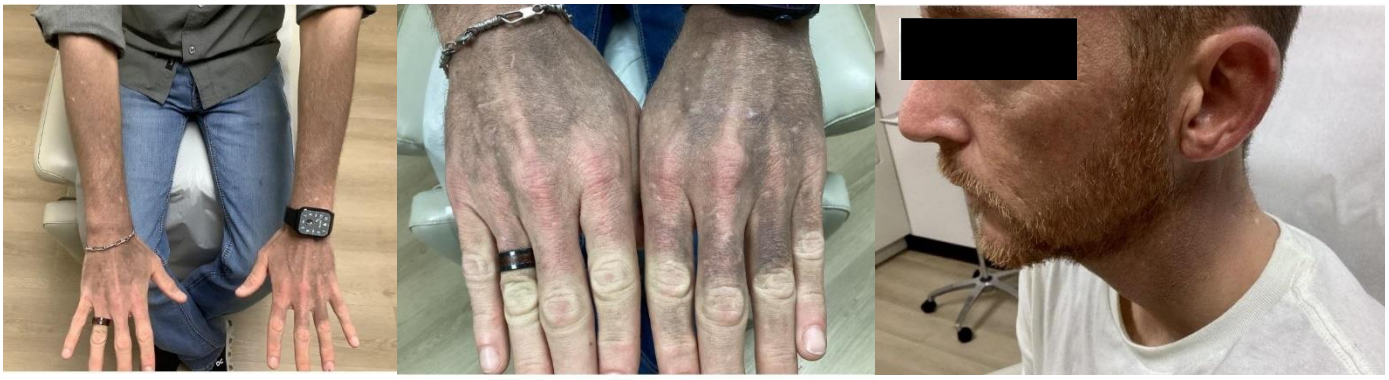

Figure 1: Hyperpigmented patches on patient's bilateral arms, hands (sparing knuckles), face and neck

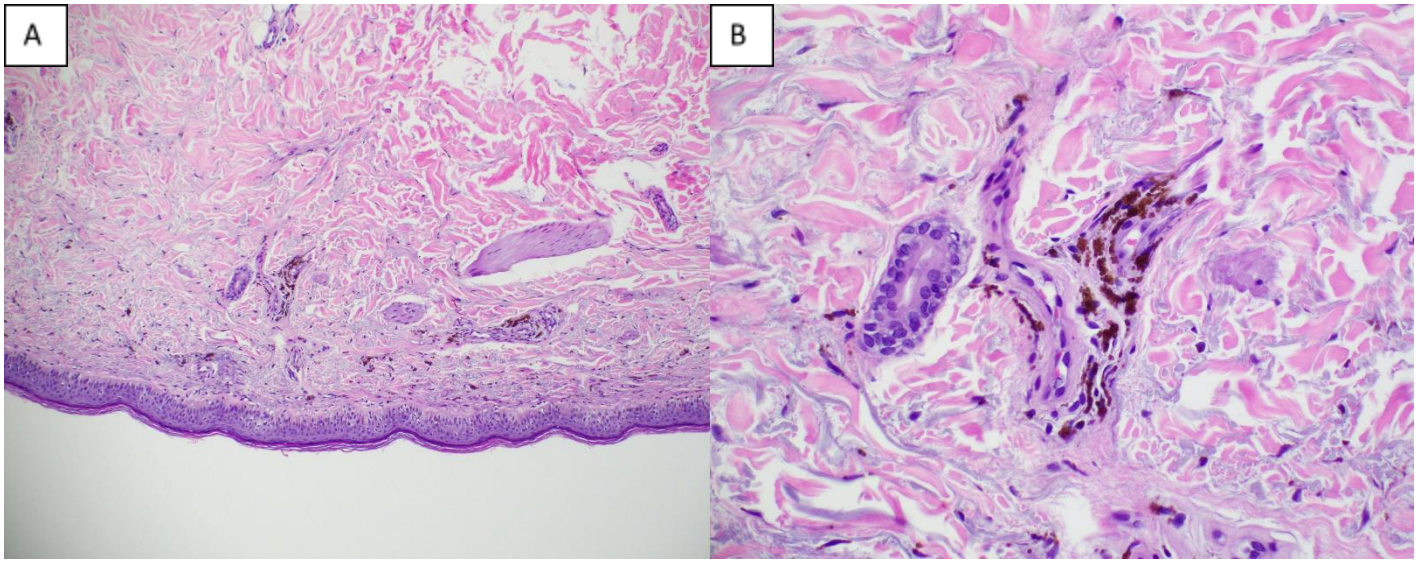

Figure 2: A) 10x magnification showing numerous melanophages in the superficial dermis with mild inflammatory cell infiltrate. No melanocytic proliferation is present.

B) 40x magnification showing deposits of refractile, perivascular intrahistiocytic brown pigment confined to the level of the dermis

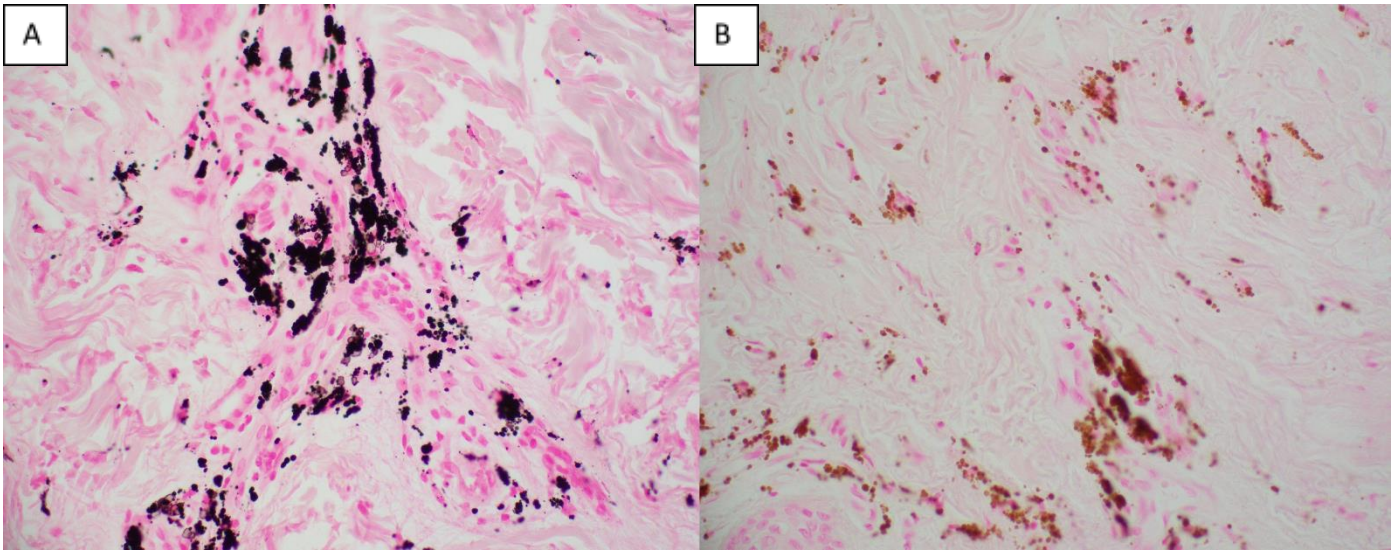

Figure 3: A) Pigment deposition positive for Fontana-Masson stain, B) Pigment deposition negative for Prussian Blue iron stain

The constellation of clinical findings, histopathological findings, similar clinicopathologic findings in two case reports on kratom hyperpigmentation, and history of chronic kratom intake in the absence of other culprit medications led to a diagnosis of kratom-induced photodistributed hyperpigmentation.

DISCUSSION

Kratom is commonly ingested orally, and historically, fresh leaves were chewed or brewed into tea. Modern commercial products include pastes, capsules, and powders. In the US, kratom extracts are primarily powders, often dissolved in fluid or taken with food[1]. Typically, 2-6g is recommended, depending on the Mitragyna strains and purposes[2]. Some users mix kratom into food or drinks, while active components are also found in vaping liquids[1]. Kratom contains more than 40 alkaloids, mainly mitragynine and 7-hydroxymitragynine. They act as partial agonists at mu opioid receptors and antagonists at delta and kappa receptors; this dual property leads to varying CNS effects: stimulant-like at low doses, morphine-like sedation at high doses. Limited clinical research exists, with just one randomized, double-blind trial among 18 identified studies. In this small Malaysian study, kratom raised pain threshold of users after an hour of kratom ingestion[1]. However, in the U.S., there are no uses

for kratom that are Food and Drug Administration (FDA) approved. The FDA has also warned against kratom's use due to potential side effects, including gastrointestinal disturbances, mental and neurologic effects, heart and lung problems, and liver problems[3]. Online blog posts have described user-reported skin discoloration. There have been only a handful of published case reports describing kratom-induced hyperpigmented lesions on photodistributed areas[4,5].

CONCLUSION

In general, our findings reveal an association that has not been previously extensively studied, linking long-term kratom consumption with the gradual development of skin hyperpigmentation primarily in sun-exposed areas of the body. The underlying mechanism for skin darkening in kratom users is not well understood. However, this observed adverse drug-related effect is important for clinicians to be aware of and recognize as a differential in photodistributed hyperpigmentation in patients.

Educating patients on this negative association can potentially motivate users to discontinue or decrease their consumption, which carries risks of being harmful to their overall health and habit-forming. As kratom use has been on the rise in the last decade, a thorough examination of its complete clinical safety profile and its essential components is necessary.

CONFLICTS OF INTEREST

This study does not have any conflict of interest.

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