CASE REPORT

Nail Hyperpigmentation Following Valproic Acid Use: A Rare Case Report

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Abstract

Aim and background: Valproic acid (N-dipropylacetic acid) is a widely accepted anticonvulsant. Apart from its use in seizure treatment, it is also prescribed for various psychiatric disorders like bipolar disorder. The common side effects include gastrointestinal distress, tremors, weight gain, transient alopecia, exanthemas, and low platelets. Very few cases have been reported of nail and nail bed hyperpigmentation. We aim to report and highlight a case of hyperpigmentation of fingernails and toenails of both the upper limb and lower limb following use of valproic acid.

Case description: A 22-year-old male presented with acute manic symptoms characterized by overtalkativeness, tall claims, being irritable, and aggression. He was hospitalized in view of being unmanageable at home. All the baseline investigations were within the normal range. The patient tested negative for HIV, hepatitis, and syphilis. Oral second generation antipsychotic, tablet riseperidone (4 mg/day) and valproic acid (1gm/day) was prescribed. The patient showed significant improvement with the above treatment and was discharged after 20 days of hospitalization. During the first follow-up, after a period of 4 weeks following discharge, tablet risperidone was gradually tapered-off in view of improvement of symptoms. On the second follow-up after 2-months duration, he reported a "brownish-yellow discoloration of all finer nails and toenails". The patient had no other systemic disease and denied any other concomitant drug use or misuse. The potassium hydroxide (KOH) study was negative for any fungal infection, and the histopathological report was negative for any pigment incontinence melanophages/increased melanocytes. Discontinuation of valproic acid for about a month resulted in the clearing of brownish-yellow pigmentation.

Conclusion: Valproic acid rarely causes nail and nail bed discoloration due to deposition of a drug (drug metabolite) or deposition of iron following blood vessel damage. These proinflammatory changes can be reversed if identified earlier with subsequent stoppage of valproic acid.

Clinical significance: To provide prompt management, both general practitioners and specialists must be aware that medications may cause hyperpigmentation.

Keywords: Hyperpigmentation, Nail, Valproic acid.

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Introduction

Valproic acid (N-dipropylacetic acid) is a widely accepted anticonvulsant. It is used among patients with different kinds of seizures as monotherapy or adjunctive therapy. It is also prescribed for various psychiatric disorders like bipolar disorder, schizophrenia, schizoaffective disorder, post-traumatic stress disorder, etc. It is also used as prophylaxis for migraine.[1] The common side effects include gastrointestinal distress, tremors, weight gain, transient alopecia, exanthemas, and low platelets. Other rare side effects include hepatic failure, pancreatitis, and hyperammonemic encephalopathy.[2]

Valproic acid therapy during pregnancy has been implicated to cause various malformations, including a 20-fold increase in neural tube defects, cleft lip and palate, and cardiovascular abnormalities.[3]

Very few cases have been reported of nail and nail bed hyperpigmentation. We report a case of hyperpigmentation of fingernails and toenails of both the upper limb and lower limb (Figs 1 and 2).

Case Description

A 22-year-old male presented with acute manic symptoms characterized by overtalkativeness, tall claims, being irritable, and aggression. He was hospitalized in view of being unmanageable at home. All the baseline investigations, including hemogram, liver function test (LFT), renal function test (RFT), and thyroid function test (TFT), were within the normal range. The patient tested negative for HIV, hepatitis, and syphilis. Initially, he was started on injectable sedatives (Inj. haloperidol and Inj. lorazepam) in view of aggression for the first 2 days. Oral second-generation antipsychotic tablet risperidone (4 mg/day) along with tablet valproic acid (1000 mg/day) was started. He was later considered to undergo modified electroconvulsive therapy due to persistent aggression, and a total of five sessions were administered. The patient showed significant improvement with the above treatment and was discharged after 20 days of hospitalization. During the first follow-up after a period of 4 weeks following discharge, there was a significant improvement in

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Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

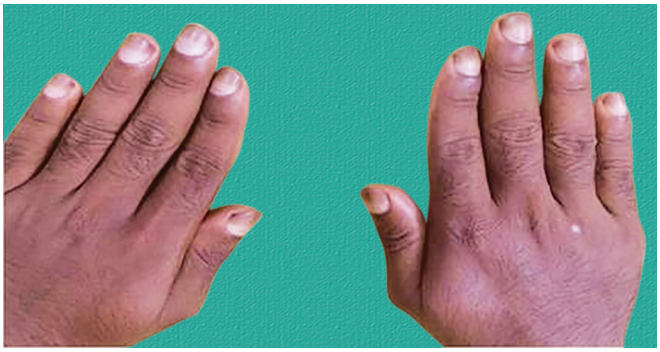

Fig. 1: Hyperpigmentation of fingernails

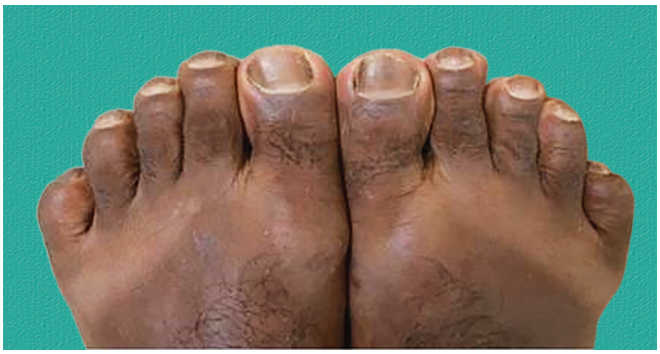

Fig. 2: Hyperpigmentation of toenails

manic symptoms and no adverse effects were reported. Tablet risperidone was gradually tapered off during the first follow-up. On the second follow-up after 2-months duration, he reported a "brownish-yellow discoloration of all finer nails and toenails".

The patient had no other systemic disease and denied any other concomitant drug use or misuse. He was referred to the dermatology department, where a detailed physical examination revealed a brownish-yellow discoloration of all fingernails and toenails. Basic laboratory tests that included hemogram, LFT, RFT, and TFT were all within normal range. He has advised KOH nail clipping and distal nail bed biopsy. The KOH study was negative for any fungal infection, and the histopathological report was negative for any pigment incontinence melanophages/increased melanocytes. Discontinuation of valproic acid for about a month resulted in the clearing of brownish-yellow pigmentation.

Discussion

Anticonvulsants, including valproic acid use, have been associated with a range of adverse effects from common to those that are rare. Various hair, skin, and nail changes are reported, the most common being alopecia and hair color change.[4] Various nail changes include hyperpigmentation,[5] yellow nail pigmentation, and onychodystrophy.[6] Onychomadesis and onycholysis are types of nail dystrophy in which separation of the nail plate from the proximal nail fold with the shedding of the nail plate,[7] separation of the nail from the nail bed takes place, respectively, have been reported with valproic acid use. One case of lip and gingival hyperpigmentation has been reported.[8] Our findings are similar to findings of Johnson and Goldsmith's findings of hyperpigmentation of nails following valproic acid use. The mechanism of causing hyperpigmentation following valproic acid use in our case was found to be due to deposition of a drug (drug metabolite) and deposition of iron following blood vessel damage.

Conclusion

Valproic acid rarely causes nail and nail bed discoloration. These pro-inflammatory changes can be reversed if identified earlier with subsequent stoppage of valproic acid.

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