Nail Changes Following Valproate Therapy

Shrestha S,[1] Pandey A,[2] Pathak R[3]

[1]Department of Dermatology,
Rapti Province Hospital,
Dang, Tulsipur, Nepal
[2]Kathmandu University School of Medical Sciences,
Dhulikhel Hospital, Kathmandu University Hospital,
Dhulikhel, Kavre, Nepal.
[3]Department of Dermatology,
Pokhara Academy of Health Sciences,
Pokhara, Nepal.

Corresponding Author
Samir Shrestha
Department of Dermatology,
Rapti Province Hospital,
Dang, Tulsipur, Nepal.
E-mail: Shresthasambec731@gmail.com

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ABSTRACT

Valproic acid is a widely prescribed medication for seizure disorders, mood disorders, and migraines. The adverse effects involving nails following the use of sodium valproate are rare. The nail changes reported so far include onycholysis, onychomadesis, the roughness of the nail, brownish-yellow discoloration, and a transverse yellow band. These changes are independent of the age of the patients, dose, and duration of medication. The nail changes are reversible following the discontinuation of the medication.

KEY WORDS

Onycholysis, Onychomadesis, Nail discoloration, Valproic acid

INTRODUCTION

Valproic acid is a widely prescribed medication for seizure disorders, mood disorders, and migraines.[1] Cutaneous adverse effects of valproic acid have been well documented in the literature and include erythema multiforme, psoriasiform eruption with scalp involvement, cutaneous vasculitis, alopecia, diaphoresis, pruritus, petechiae, and photosensitivity. Acute hypersensitivity syndrome is less common with valproic acid compared to aromatic anticonvulsants such as carbamazepine and phenytoin.[2,3] The mucous membrane is rarely involved, which includes gingival and lip hyperpigmentation.[4]

Adverse effects on nails are rare, and there have only been a few cases reported so far.[5] Here we present a case of onycholysis following sodium valproate and briefly summarize other cases reported so far.

Onycholysis is the separation of the nail plate from the nail beds. The causes of onycholysis include systemic (thyroid disease, diabetes mellitus, anemia, peripheral vascular disease, multiple myeloma, bronchogenic carcinoma, multiple myeloma, scleroderma), dermatological (fungal infection, Reiter's syndrome, pemphigus vulgaris, hyperhidrosis, pellagra, syphilis, onychomycosis, contact dermatitis), local (trauma, infection, chemicals), drugs (bleomycin, vincristine, retinoids), and photo-onycholysis (porphyria, pseudo-porphyria, drugs like tetracycline and fluoroquinolones).[5-7]

CASE REPORTS

A 55-year-old man presented to our dermatology outpatient department with a year's history of asymptomatic nail changes. He had been taking valproic acid (500 mg, twice a day) for the last 2 years for a seizure disorder. He denied a history of chronic illnesses, use of other medications, trauma, recent weight loss, or dermatological diseases.

On examination, all fingers of his left hand and the 4th digit of his right hand showed roughness of the nail surface, brownish discoloration of the distal half of the nail, onycholysis, and longitudinal grooves. There was an absence of cuticles on a few of the nails (Fig. 1). Nail folds appeared to be normal. Mucocutaneous and hair examinations revealed no significant findings. There were no abnormalities detected on general or systemic examinations.

Figure 3. Showing onycholysis and brown discoloration of nails of 1st, 3rd, 4th and 5th fingers of left hand and 4th finger of right hand.

Basic lab tests, including the hemogram, liver function test, renal function test (RFT), and thyroid function test (TFT), were within the normal range. The potassium hydroxide (10% KOH) mount of nail scraping didn't reveal fungal hyphae. The serum zinc level was not assessed due to unavailability.

The patient was discontinued from sodium valproate and replaced by lamotrigine. After two months, a phone call was made for follow-up as the patient couldn't come due to a distant location. There was a complete resolution of the nail changes described previously.

DISCUSSION

Valproic acid is an antiepileptic medication that is frequently prescribed to treat seizures, obsessive-compulsive disorder, bipolar mood disorders, and migraines.[8] Common adverse effects include gastrointestinal discomfort, tremors, weight gain, hair loss, and rashes. Other rare adverse effects such as hepatic failure, pancreatitis, and platelet problems have also been observed.[2]

Although it is rare, anticonvulsant drugs such as Valproic acid have been associated with nail abnormalities such as hyperpigmentation, onycholysis, and onychomadesis.[9] Onycholysis secondary to valproic acid use has been reported a few times.[7,10,11] Onycholysis is believed to arise from a disruption of zinc metabolism caused by a combination of valproate-induced malabsorption and systemic zinc chelation.[12]

Nail changes from antiepileptics can occur anytime during treatment, regardless of dose, and have been reported to improve with drug discontinuation.[12] However, some patients require ongoing antiepileptic medicine, making treatment of nail disorders problematic in such cases.

Reconstruction of the nail matrix using a split toenail matrix graft has been reported for onycholysis with postoperative nail plate adherence without residual leukonychia.[8] In the same paper, the authors suggested surgical interventions, such as sterile matrix grafting, to treat onycholysis in those who need continued anticonvulsant medication.

The nail changes following sodium valproate use reported so far are summarized in table 1.

Table 1. Case Reports of nail changes following sodium valproate

Authors	Case (Age in years/ Sex)	Exposure (Dose/ Time)	Time of resolution after discontinuation of medication	Nail Changes
Solak et al.[5]	50/M	500 mg 2 years	1 month	Onycholysis The roughness of the nail Brownish-yellow discoloration
Grech et al.[7]	2/M	20 mg/ kg/day 13 weeks	2 weeks	Diffuse onycholysis
Buka et al.[13]	57/F	- 2 months	6-8 weeks	Transverse yellow band Progressed to complete nail discoloration
Poretti et al.[14]	3/M	20 mg/ kg/day 4 years	-	Onychomadesis
Icagasioglu et al.[15]	5/F	20 mg/ kg/day -	2 months	Onychomadesis
Jenerowicz et al.[11]	30/F	600 mg 3 years	-	Onycholysis Leukonychia
Biswal et al.[1]	22/M	1000 mg 2 months	1 month	Brownish-yellow discoloration
Current	55/M	1000 mg 2 years	2 months	Onycholysis

Nail changes are rare adverse effects following the use of sodium valproate. The changes reported so far include onycholysis, onychomadesis, the roughness of the nail, brownish-yellow discoloration, and a transverse yellow band. These changes are independent of the age of the patients, dose, and duration of medication. However, the changes are benign in nature and are reversible following the discontinuation of the medication.

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