Onychomadesis: A New Side Effect of Sodium Valproate Therapy in Children?

Onikomadesis: Çocuklarda Sodyum Valproat Tedavisinin Yeni Bir Yan Etkisi mi?

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ABSTRACT

Valproic acid has been widely used for the treatment of epilepsy. Although usually well-tolerated, it has been associated with some side effects. Nail abnormalities are rare side effects of valproic acid. Onychomadesis refers to a complete nail separation from the nail bed, beginning at the proximal portion. We report the case of a 5-year-old female who developed onychomadesis of the fingernails after initiation of valproic acid monotherapy at a therapeutic dose for prophylaxis of convulsions— an association that has not been previously reported. We suggest that the toxic side effects of valproic acid may rarely include onychomadesis in childhood and interrupting the drug intake is essential in the treatment of onychomadesis. (Archives of Neuropsychiatry 2011; 48: 79-81)

Key words: Valproic acid, VPA, side effect, onychomadesis, epilepsy

ÖZET


Anahtar kelimeler: Valproik asit, VPA, yan etki, onikomadesis, epilepsı

Introduction

Onychomadesis describes complete nail shedding from the proximal portion. It is consecutive to a nail matrix arrest and can affect both fingernails and toenails. It is a rare disorder in children. Except for serious generalized diseases or inherited forms, most cases are considered to be idiopathic. Nail matrix arrest has been associated with a variety of drug exposures and systemic illnesses, including infections, and may result in a variety of changes, including transverse ridging (Beau's lines) and nail shedding (onychomadesis) (1,2).

Valproic acid (VPA) has been widely used for the treatment of epilepsy. Although usually well-tolerated, it has been associated with some side effects, of which, nail abnormalities are rare ones (3).

We report the case of a 5-year-old female who developed onychomadesis of the fingernails after initiation of VPA monotherapy at a therapeutic dose for prophylaxis of convulsions. To the best of our knowledge, such an association has not been previously reported.

Case Report

A previously well, 5-year-old female had developed recurrent short-lived episodes of unconsciousness and drop attacks while walking since two month.

Full blood count, serum calcium, phosphate, urea, creatinine, electrolytes and liver function tests were normal.

Electroencephalogram (EEG) demonstrated normal background activity during the wakeful state and bilateral
intermittent focal spikes throughout anterior temporal and central regions during sleep recording. She was diagnosed with localization-related epilepsy. VPA was initiated at a dose of 10 mg/kg/day followed by a maintenance dose of 20 mg/kg/day. No further seizures occurred for the next 3 weeks. The patient developed alopecia, palmar and plantar rash, and desquamation of the distal phalanges of the fingers and toes after three weeks of treatment. Subsequently, onychomadesis of the fingernails occurred (Figure 1, 2); the toenails were not involved. No other medication was taken. Fungal culture was negative, and serum concentration of valproic acid was normal (50 µg/mL). Serum zinc level was not measured. Because of the favourable course of epilepsy, VPA was replaced by carbamazepine. Normal nail growth was observed 3 weeks after stopping VPA and entirely normal nails 2 month later.

**Discussion**

According to Piraccini and et al. a drug should always be suspected when these signs affect all nails at the same distance from the proximal nail fold. A drug intake of 2 to 3 weeks before the appearance of the nail symptom should be considered, as a fingernail takes about 40 days to emerge from the proximal nail fold (4).

Anticonvulsants such as carbamazepine, hydantoin, trimethadione, and VPA, if taken during pregnancy, may be responsible for fingernail and toenail hypoplasia in the newborn (3). Nail hyperpigmentation, onycholysis, and onychomadesis also may be seen in adults receiving these drugs (5,6).

VPA-associated onychomadesis in a child have been previously reported only once (7). In that brief report, after four years of treatment with VPA, a 7-year-old boy developed onychomadesis of both thumbnails and two toenails. The serum zinc level was normal. The nails recovered normally after VPA was stopped. The authors speculated that the association of treatment with VPA and onychomadesis in their patient seems to be possible and they cannot confirm any involvement of zinc metabolism.

Czajkowski et al. reported a 54-year-old man with Stevens-Johnson syndrome induced by carbamazepine. The reported patient had prodromal symptoms like fever, headache and polyarthralgia 3 days before the occurrence of muco-cutaneous lesions in addition to nail changes including onychomadesis (6).

Grech and Vella reported a 2-year-old male with onycholysis, which is a distal separation of the nails from the nail bed. In this case report, after thirteen weeks of VPA treatment for prophylaxis of febrile convulsions, the patient developed diffuse onycholysis of the fingernails and toenails. Recovery of the nails was observed 2 weeks after stopping VPA, and entirely normal nails - 4 weeks later (8). In our patient, three weeks after the initiation of VPA therapy, onychomadesis subsequently appeared after alopecia and skin rash with desquamation.

Side effect of drugs in the nail are usually the outcome of acute toxicity to the nail epithelia and not related to drug dosage (4,5).

Primary or secondary zinc deficiency can cause a wide variety of cutaneous manifestations, and such findings of secondary zinc deficiency due to VPA therapy have been reported in 2 adult patients (9). On the other hand, although serum zinc levels in epileptic children were found to be decreased, there was no difference in nail samples from patients and controls (10). Therefore, zinc replacement treatment may be considered unnecessary.

In the present case, a toxic side effect of VPA therapy on the nails was assumed because: onychomadesis rapidly appeared three weeks after VPA therapy; the patient had no another etiological factor such as Stevens-Johnson syndrome, scarlet fever, hand-foot-mouth disease, local causes of onychomadesis including fungal infections, eczema or trauma; and had not received another drug. This opinion was supported by the rapid recovery of nails after stopping VPA. Due to ethical considerations, the patient was not rechallenged with VPA.

We suggest that the toxic side effect of VPA may rarely include onychomadesis in childhood and interrupting the drug intake is essential in the treatment of onychomadesis.
References