Onychomadesis: A rare adverse effect in early-period valproic acid therapy

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Abstract

Valproic acid is an effective, frequently used anticonvulsant drug. Typical adverse effects include weight gain, hair loss, and nausea. Hyperpigmentation, onycholysis, and onychomadesis are nail changes that can be seen after valproic acid use. Changes occur at the distal and proximal portions of the nail bed in onycholysis and onychomadesis, respectively. Onychomadesis is a very rare disease of childhood with the exception of systemic and genetic diseases. Here, we present a child aged 23 months, the youngest and the earliest isolated patient with onychomadesis, which occurred after valproic acid treatment and worried the family but resolved spontaneously. The improvement of this very rare adverse effect of antiepileptic drugs after cessation of valproic acid without treatment is emphasized. (Turk Pediatri Ars 2017; 52: 98-100)

Keywords: Adverse effect, epilepsy, onychomadesis, valproic acid

Introduction

Valproic acid is a commonly used drug to treat epilepsy. Onychomadesis is discontinuance of growth in the nail matrix from the proximal part of the nail and onset of separation of the nail from the nail bed. Onychomadesis is a very rare condition in children excluding systemic diseases and genetic diseases (1). In this case report, we found it appropriate to present a 23-month old patient who was diagnosed as having onychomadesis following treatment with valproic acid because of this rare adverse effect.

Case

Valproic acid treatment was initiated in a 23-month old male patient when a generalized spike wave pattern was observed on electroencephalogram that was performed because of a total number of three afebrile convulsions. Treatment was initiated with a dose of 10 mg/kg and the dose was increased to 20 mg/kg one

week later. Investigations revealed that complete blood count, serum calcium, phosphate, urea, creatinine, electrolytes, and liver function tests were normal. In the outpatient follow-up, metabolic screening tests and brain magnetic resonance imaging (MRI) were found as normal. The patient, who developed nail changes at the end of the third week of treatment, presented to our outpatient clinic once again. On physical examination, he had no finding expect for peeling and deformation in the nails in the right hand (Figure 1a). The nails in the left hand and in the feet were found as normal. The nail changes in the thumb and the third finger in the right hand were considered onychomadesis. The blood valproic acid level (60 µg/mL) and zinc level (14 µmol/L, normal: 10–20 µmol/L) were found within the normal limits. Fungal culture was negative. Valproic acid treatment was discontinued and phenobarbital treatment was initiated. Nail changes disappeared completely in the 6-week follow-up period. Verbal consent was obtained from the parents of the patient presented in this case report.

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Figure 1. a, b. Onychomadesis found in the third week of valproic acid treatment (a), Spontaneous recovery after valproic acid treatment was discontinued (b)

Discussion

Valproic acid is a commonly used drug to treat epilepsy. The most common adverse effects of valproic acid include hair loss, nausea, and weight gain. Acute liver failure, pancreatitis, hemorrhagic diathesis, and encephalopathy are serious adverse effects. Hair loss is most prominent in the first month of treatment and reversible after discontinuance of treatment. In addition, skin eruptions may be observed, albeit rarely (2). Onychomadesis is the onset of separation of the nail from the nail bed from the proximal part. Infections, systemic diseases, and trauma cause onychomadesis by leading to discontinuance of growth of the nail matrix, nail deformations, and horizontal lines on the nail (Beau's lines) (1). In our patient, nail changes started in the third week after drug treatment was initiated.

Nail changes, which may be observed following drug use, include hyperpigmentation, onycholysis, and onychomadesis. The changes start in the distal part of the nail in onycholysis and in the proximal part in onychomadesis (1). Two cases of nail changes that developed during valproic acid treatment have been reported to date. Nail changes started in the 13th week in a child aged 2 years who was reported by Grech et al. (3), and a diagnosis of diffuse onycholysis was made. Poretti et al. (4) documented child aged 3 years with onychomadesis involving only both big toes was found in the fourth year of treatment. Our patient is the youngest and the earliest reported (following drug use) patient among these case reports. The fact that the times of occurrence and the number of affected nails are different shows that the etiologic factors and pathophysiology are still incomprehensible. In the above-mentioned patients and in our patient, the investigations and follow-up re-

vealed no factors that could lead to these changes. In our case, it was observed that the nails started to recover two weeks after the drug was discontinued and completely recovered six weeks later (Figure 1b).

Infections (scarlet fever, hand-foot disease, fungal diseases), systemic diseases (Kawasaki disease, Stevens-Johnson syndrome) and drugs (chemotherapeutic drugs, antibiotics, retinoids) may lead to onychomadesis (5). Our patient had no history of systemic disease or drug use except for valproic acid treatment. Grech et al. (3) thought that there could be an association between the use of valproic acid and zinc metabolism, but emphasized that no correlation could be found in the studies conducted so far. Zinc levels were found as normal in our patient.

Onychomadesis is nail changes that develop in many systemic diseases and following drug use. Its pathology has not been elucidated fully. Here, we presented the youngest patient with isolated onychomadesis, which is observed very rarely, that occurred as a result of valproic acid treatment and caused anxiety in the family, but regressed spontaneously. We wished to emphasize that this adverse effect, which is observed very rarely with epileptic drugs, regressed spontaneously without treatment after valproic acid was discontinued.

Informed Consent: Verbal informed consent was obtained from patients' parents who participated in this case.

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