Onychomadesis Following Cutaneous Vasculitis

Beau lines are transverse, band-like depressions extending from one lateral edge of the nail to the other and affecting all nails at corresponding levels (1). Onychomadesis is considered an extreme form of Beau line with subsequent separation of the proximal nail plate from the nail bed. Both fall along a spectrum of nail plate abnormalities that occur secondary to temporary nail matrix arrest (NMA). Various systemic and dermatologic conditions have been reported in association with onychomadesis (2-7) (Table 1). Nail changes can affect all or some of the nails and both the fingernails and toenails; however, fingernails are more frequently affected. The severity of the nail changes varies depending on the underlying cause, its duration, and environmental factors (8). We present a case of onychomadesis following cutaneous leukocytoclastic vasculitis (CLCV).

A 61-year-old woman presented to the Dermatology Clinic complaining of a purpuric rash that began on her lower extremities and rapidly progressed to her abdomen and upper extremities over the previous five days. Her medical history was remarkable for hypertension and diet-controlled diabetes mellitus. Her medications included enalapril, which she had been taking for the past four years. On three consecutive days before the skin eruption, the patient took oral diclofenac sodium for hip pain.

A clinical examination revealed non-blanching petechial rash on the legs, abdomen, and upper limbs up to the elbow (Figure 1, A) with leukocytoclastic vasculitis on biopsy (Figure 1, B). Direct immunofluorescence was negative.

Laboratory investigations revealed a white blood cell count of 14.5×10^9/L with a normal differential count, and a platelet count of 380×10^9/L. Westergren erythrocyte sedimentation rate was 65 mm/1st h, and C reactive protein was at 8.5 mg/dL. Antinuclear antibodies, rheumatoid factor, immune complexes, and cryoglobulinemia were negative, as were B and C hepatitis virus serological tests. Her renal, cardiac, pulmonary, and abdominal exams were normal. Diclofenac was discontinued due to a clinical suspicion of drug-induced cutaneous vasculitis. The rash resolved in 2 weeks without treatment, leaving post-inflammatory hyperpigmentation.

Table 1. Causes and associations of onychomadesis

Hand-foot-mouth disease (Coxsackie virus A)
Varicella
Fungal nail infection
Drugs (antineoplastic agents, azitromycin, retinoids, penicillin, valproic acid)
Local inflammation (trauma, acute paronychia, pyogenic granuloma)
Peripheral nerve injury (reflex sympathetic dystrophy)
Cutaneous T-cell lymphoma
Palmoplantar keratoderma
Lichen ruber planus
Severe systemic insult (fever, systemic diseases, renal failure, peritoneal dialysis, Kawasaki's disease, infection)
Bullous dermatoses (pemphigus, pemphigoid)
Cronkhite-Canada syndrome
Idiopathic familial onychomadesis

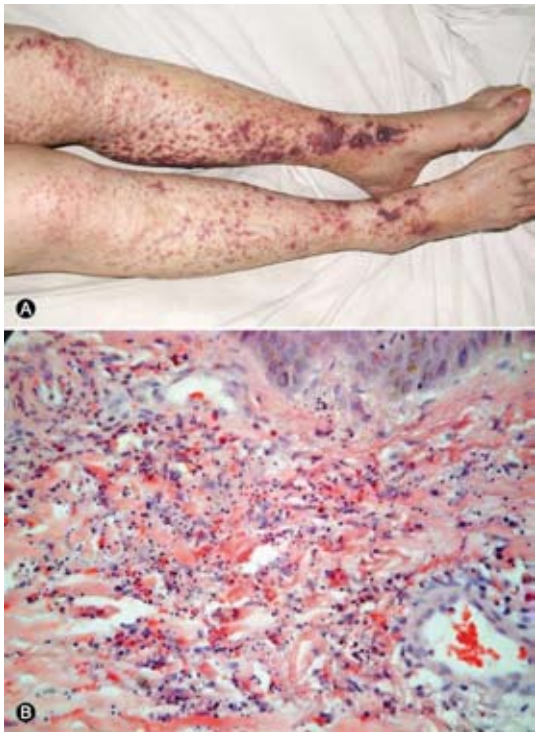

Figure 1. (A) Palpable purpura and hemorrhagic bullae on both lower extremities. (B) Leukocytoclastic vasculitis: endothelial swelling, leukocytoclasis, and extravasation of red blood cells (hematoxylin and eosin ×200).

Four weeks later, she presented with painless, palpable grooves on all 10 fingernails (Figure 2). The grooves were 3 to 4 mm in width, at a similar distance from the proximal nail fold. There were no signs of periungual inflammation. The patient denied any recent history of trauma, unusual activities, or chemical exposure. Routine serum biochemistry and hematology results were normal. Repeated potassium hydroxide preparations and fungal cultures of the nail clippings were negative. A diagnosis of Beau lines and onychomadesis was made. Nail changes were tolerable and did not require any specific treatment.

During the follow up, the Beau lines advanced with the linear growth of the nails and disappeared (Figure 3 and 4). Four fingernails developed complete nail shedding (onychomadesis). No toenail alterations were observed in this period. A complete recovery of the nail plate surface was observed after 4 months.

The nail matrix epithelium is formed by highly proliferating cells that differentiate and keratinize to produce the nail plate. The nail matrix epithelium is very susceptible to toxic noxae, and acute damage results in a defective nail plate formation. Nail matrix arrest is a term used to describe a temporary inhibition of the nail matrix proliferation that can present as Beau

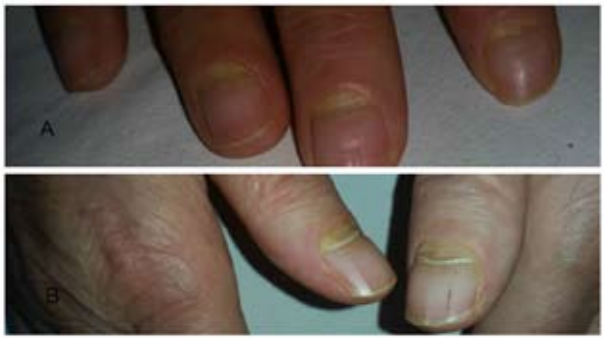

Figure 2. (A) Transverse deep grooves in the nail plate parallel to the lunula (Beau Lines) are present 7 weeks after onset of drug-induced leukocytoclastic vasculitis. (B) Onychomadesis affecting thumbnails on the same level. Note that the periungual tissue is normal.

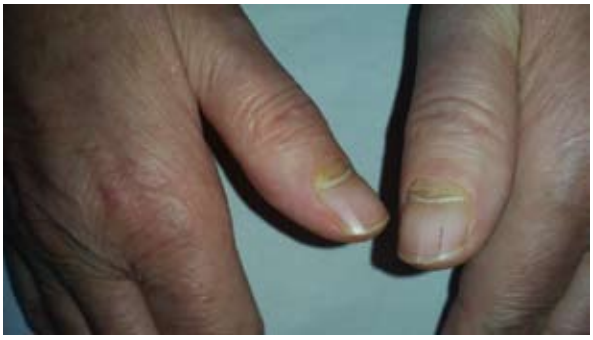

Figure 3. During the follow-up, the Beau lines advanced with the linear growth of the nails.

lines and onychomadesis (8). The width of Beau lines relates to the duration of the etiological agent. As the nail adheres firmly to the nail bed, the onychomadesis remains latent for several weeks before leading to temporary shedding (8,9).

There are several proposed etiological mechanisms for NMA. NMA associated with fever, severe infection, and major medical illnesses can be explained by an inflammation of the matrix, periungual tissues, or digital blood vessels (8); chemotherapy agents

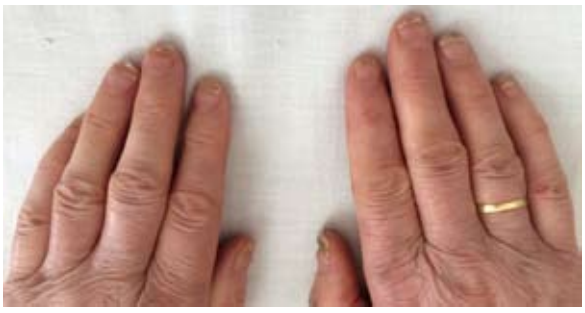

Figure 4. After 3 months of cutaneous vasculitis, recovery of the nail plate surface was almost complete.

temporary inhibit the mitotic activity in nail matrix (10); the detection of Coxackie virus in the shedding nail particle, following hand, foot, and mouth disease, suggests that the viral replication itself may directly damage the nail matrix (11). However, as nail changes are not unique, it may be difficult to incriminate a single etiological agent.

Our patient presented with an onset of Beau lines seven weeks after the initial CLCV lesions, which suggests that vasculitis might have acted as a trigger for NMA. As the fingers were not affected by CLCV, an indirect effect of vasculitis is more plausible.

Leukocytoclastic vasculitis is a small-vessel inflammatory disease mediated by a deposition of immune complexes. Thus, the circulating immune complexes may be involved in the damage of nail bed microvasculature.

Considering that the patient had been receiving enalapril and diclofenac, it is less likely that those drugs were involved in the pathogenesis of NMA. Enalapril was continued, and the nail changes were resolved while patient was still on enalapril. Furthermore, diclofenac is a widely prescribed drug and its association with NMA is yet to be described in literature.

We described a patient who developed Beau lines and onychomadesis following cutaneous leukocytoclastic vasculitis. This clinical observation can expand the spectrum of possible causes of nail matrix arrest.

References:

1. De Barber D. What do Beau's lines mean. Int J Dermatol 1996;134:542-7.
2. Tosti A, Piraccini BM, Camacho-Martinez F. Onychomadesis and pyogenic granuloma following cast immobilization. Arch Dermatol 2001;137:231-2.
3. Grover C, Vohra S. Onychomadesis with lichen planus: an under-recognized manifestation. Indian J Dermatol 2015;60:420.
4. Mehra A, Murphy RJ, Wilson BB. Idiopathic familial onychomadesis. J Am Acad Dermatol 2000;43:349-50.
5. Podder I, Das A, Gharami RC. Onychomadesis following varicella infection: is it a mere co-incidence? Indian J Dermatol 2015;60:626-7.
6. Aksentijevich I, Masters SL, Ferguson PJ, Dancey P, Frenkel J, van Royen-Kerkhoff A, *et al.* An autoinflammatory disease with deficiency of the interleukin-1-receptor antagonist. N Engl J Med 2009;360:2426-37.
7. Poretti A, Lips U, Belvedere M, Schmitt B. Onychomadesis: A rare side-effect of valproic acid medication? Pediatr Dermatol 2009;26:749-50.
8. Hardin J, Haber RM. Onychomadesis: literature review. Br J Dermatol 2015 Mar;172:592-6.
9. Braswell MA, Daniel CR 3rd, Brodell RT. Beau lines, onychomadesis, and retronychia: A unifying hypothesis. J Am Acad Dermatol 2015;73:849-55.
10. Piraccini BM, Iorizzo M, Starace M, Tosti A. Drug-induced nail diseases. Dermatol Clin 2006;24:387-91.
11. Bettoli V, Zauli S, Toni G, Virgili A. Onychomadesis following hand, foot, and mouth disease: a case report from Italy and review of the literature. Int J Dermatol. 2013;52:728-30.

Katerina Damevska[1], Gorgi Gocev[1], Nora Pollozahani[1], Suzana Nikolovska[1], Lence Neloska[2]

[1]University Clinic of Dermatology, St. Cyril and Methodius University, Skopje, Republic of Macedonia
[2]13th November Gerontology Institute, Skopje, Republic of Macedonia