SHORT COMMUNICATION

Multiple Nail Dystrophy Associated with Human Papillomavirus Type 29 (HPV-29)

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Nail-related diseases can be challenging to diagnose, and some of them have poorly understood causes. Human papillomavirus (HPV), which infects the epithelial cells of various organs, is also expected to impact nail diseases, but it is often overlooked as it is not routinely tested. The clinical phenotypes associated with HPV types are believed to stem from their distinct cytopathogenic effects (CPEs), which include macroscopic and microscopic features, pathological characteristics, and tissue tropism (1). However, detailed information on CPEs is lacking for most HPV genotypes, including HPV-29. Here, we report a unique case of HPV-29-associated nail dystrophy affecting multiple digits, unclassified under any known diseases, which may represent a new disease entity.

CASE REPORT

An immunocompetent woman in her 60s without underlying disease presented to our hospital with multiple nail changes affecting both hands and feet (**Fig. 1**a). She had been aware of these lesions for the past 15 years. Eight months earlier, she consulted a primary dermatologist and was treated with topical steroids, but the lesions remained. She presented with erythronychia, leukonychia, keratosis, longitudinal ridging, crumbling, splinter hemorrhage, and trailing lunulae in multiple nails upon

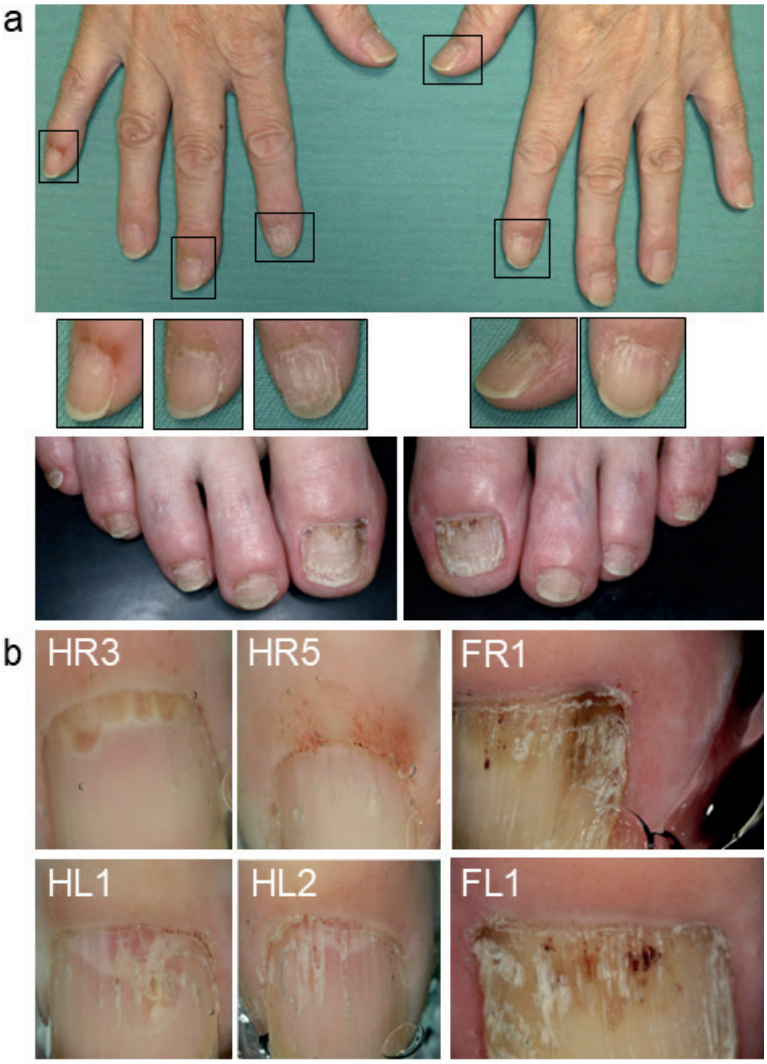

Fig. 1. Clinical presentation at the first visit. (a) Clinical manifestation on the hands and feet. (b) Representative dermoscopic images of the lesions. H=hand, F=foot, R=right, L=left, numbers=digit position.

visual examination, and with hypertrophy and hemorrhage of the eponychium upon dermoscopy (Fig. 1b). Tinea infection was not detected by direct microscopy, culture, or pathological examination. Histological analysis of the left hallux nail showed hypertrophy of the epithelium of the nail fold and nail matrix with papillomatous proliferation, elongation of the rete ridges with spongiosis, and perivascular lymphocytic infiltration along with eosinophils in the superficial dermis (**Fig. 2**). Given the suspicion of verruca vulgaris, we performed polymerase chain reaction (PCR) using consensus primers FAP59/64, which amplify a broad range of skin-associated HPV types from the L1 region (2). HPV-29 was detected by sequencing the PCR products from multiple lesions.

DISCUSSION

This case did not correspond to any of the following diseases: onychomatricoma is a rare tumor of the nail matrix, presenting as nail thickening, often with longitudinal yellowish discoloration. Known markers include the expression of CD34 or LEF-1 and loss of RB1 (3). This case showed nail thickening and color changes, but its occurrence in multiple lesions did not align with onychomatricoma. Furthermore, CD34 and LEF-1 were negative and RB1 was preserved (data not shown). Onychopapilloma is also a benign tumor of the nail bed and distal matrix, commonly considered a leading cause of localized longitudinal erythronychia. This tumor is thought to develop when the distal nail matrix prematurely differentiates into nail bed epithelium, leading to the formation of a hyperplastic nail bed (4). Some cases have a history of trauma, and a few have been associated with HPV infection. Several symptoms in our case resembled onychopapilloma, but it was atypical to find multiple lesions on both fingers and toes, displaying lateral spread and more prominent lesions at the proximal end. Verruca vulgaris may also be suggested by the detection of HPV. However, HPV infections associated with nails are predominantly periungual or subungual warts. Pure nail warts are extremely rare, and the few reported cases do not correspond to the clinical presentation observed in this case.

HPV-29 has an unclear clinical presentation due to the few reported cases. The first case involved a 40-year-old man with spotted hyperpigmented lesions (5). Our group reported the second case of a 60-year-old woman with hyperpigmented plaques on her lower legs (1). Based on recent DNA sequence analysis, HPV-29 is categorized in Alpha-PV species 2 (6), like HPV-3, which commonly causes flat warts. In contrast, periungual warts are more commonly associated with HPV type 2, categorized in Alpha-PV species 4.

In conclusion, this report describes a unique clinical, dermoscopic, and histopathological characterization of HPV-29-associated nail lesions. HPV-29 may have unique CPEs and constitute a distinct clinical entity of HPV-associated skin lesions, including unclassified multiple nail dystrophy.

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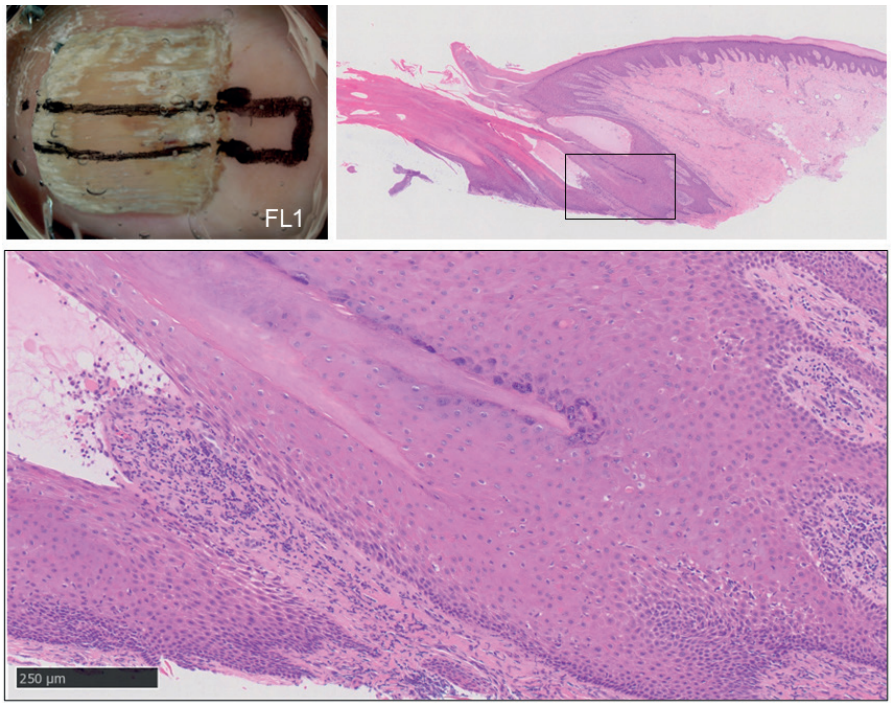

Fig. 2. Histopathological findings. Biopsy site (top left), low magnification of H&E-stained tissue histology slide (top right), and high magnification of the squared area (bottom). Scale bar: 250 µm.

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