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Photo Vignette

Onychomadesis following childhood hand-foot-mouth disease in two pairs of siblings- a familial predisposition?

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Abstract

Onychomadesis is presented in four patients as a result of hand-foot-mouth disease.

INTRODUCTION

Nail matrix arrest is commonly seen following a variety of systemic illnesses or drug exposures. Short-term slowing down of nail formation or partial nail matrix arrest causes transverse ridging of the nail plate (Beau's lines), whereas longer-term nail growth cessation or complete nail matrix arrest leads to nail shedding from the proximal portion (onychomadesis) [1]. Hand-foot-mouth disease (HFMD) is a common self-limiting childhood viral illness and has been reported as a possible cause of onychomadesis [2]. We describe two pairs of siblings whose history and clinical course also supported the same observation.

CASE REPORTS

Cases 1 and 2

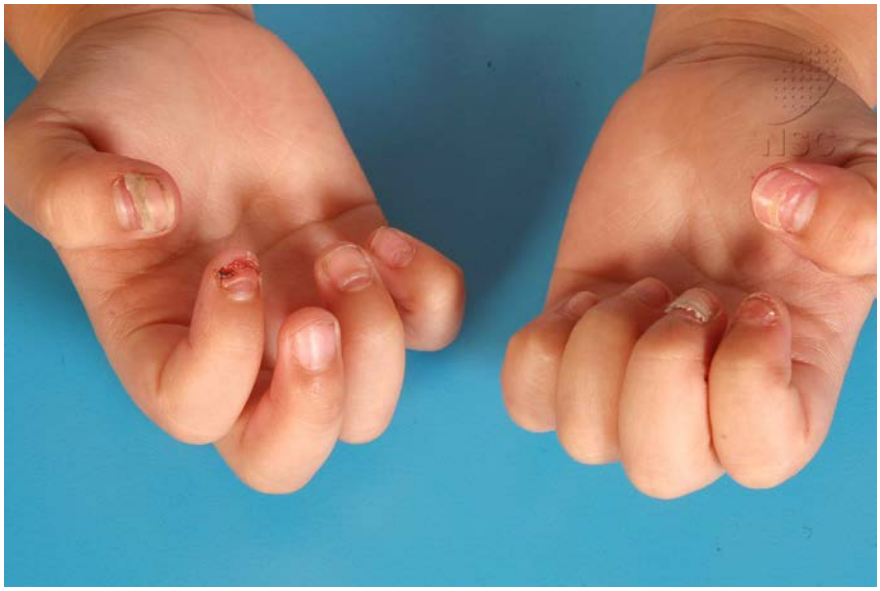

Figure 1. Prominent Beau's lines and onychomadesis of the fingers 6 weeks following HFMD (3-year old girl).

Case Synopsis

A 3-year old girl presented with lines and proximal shedding of fingernails and toenails 6 weeks after she was diagnosed with HFMD. She initially presented with high fever with vesicular lesions on the hands and feet, which had since resolved. Clinically there were Beau's lines and onychomadesis over some of the fingernails and toenails (Figure 1). Her 13-year old brother also first developed fever with a palmoplantar vesicular eruption consistent with the diagnosis of HFMD at the same time. His condition also ran a mild course with resolution of the fever and rash, but 4 weeks later he exhibited similar proximal nail shedding and Beau's lines over his fingernails and toenails like his sister (Figure 2). Both children were otherwise healthy with no significant past medical history. In both cases, there was no drug history and no history of prior trauma or injury to the nails. There were no hair or dental abnormalities observed and no clinical features of paronychia or onychomycosis.

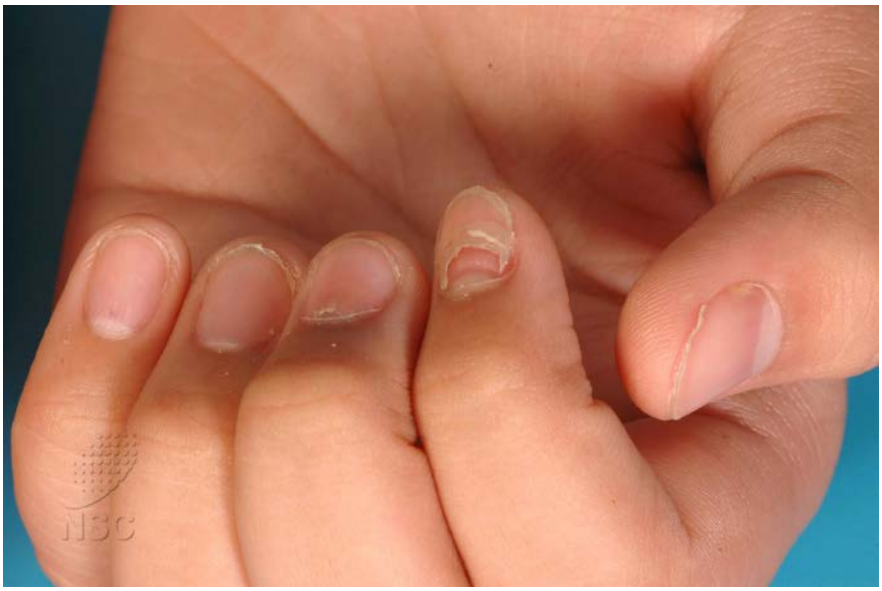

Figure 2. Proximal nail fold shedding of the finger 4 weeks after HFMD (13-year old brother of 3-year old girl).

Cases 3 and 4

A 4-year old girl first developed HFMD with a self-limiting episode of fever and palmoplantar vesicular lesions. Approximately 4 weeks later she presented with Beau's lines over the proximal nail cuticle of both thumbs and left middle finger (Figure 3). The toenails were not affected. There were no abnormal hair or dental features, neither was there paronychia or onychomycosis clinically. The mother reported that the patient's 2-year old sister also developed similar nail changes after recovering from an episode of HFMD at the same time. Both children had no past medical or drug history. There was also no history of preceding nail trauma or injury.

Figure 3. Proximal nail fold shedding of the finger 4 weeks following HFMD (4-year old girl). Her 2-year old sister also developed similar nail

changes 4 weeks after HFMD contracted at the same time.

DISCUSSION

Hand-foot-mouth disease (HFMD) is a common self-limiting childhood viral illness characterized by fever followed by palmoplantar vesicular eruption with erosive stomatitis. The condition generally runs a relatively benign course and HFMD epidemics have primarily been associated with coxsackievirus A16 (CV-A16) and enterovirus 71 (EV-71) infections [3]. Onychomadesis is not commonly observed in mild childhood viral illnesses. There are few reports on the association between nail matrix arrest and enteroviral infections. The relationship between HFMD and onychomadesis was first recognized a decade ago [2] and recent HFMD outbreaks in Europe saw an increased frequency of HFMD-related onychomadesis cases [4,5].

HFMD continues to be an important public health problem in Singapore, with the annual incidence rate per 100,000 population escalating from 125.5 in 2001 to 435.9 in 2007 [6]. The peak of the HFMD epidemic saw a total of 30,878 cases reported in 2010, an increase of 78.7% from 17,278 cases reported in 2009 (20,687 cases were reported in 2011) [7]. Despite the large numbers of HFMD cases seen in Singapore the past decade there were no previous reports of HFMD-related nail changes. The epidemiological study of HFMD cases seen in Singapore from 2001-2007 also failed to report any HFMD-related nail matrix changes [6].

Nail matrix arrest is well recognized in the setting of severe physiological stress such as fever, infection, systemic disease or drug exposure. However, the exact mechanism of nail changes remains elusive [1]. The mechanism of nail matrix arrest in HFMD is unclear. All our patients had a history of physician-diagnosed HFMD and were generally well except for prodromal low-grade fever and self-limiting palmoplantar vesicular lesions. The strong temporal association between the two and the absence of intermediate pathologies suggest the causal relationship. Previous reports also showed similar latency period of 3-9 weeks [2,4,5]. It is difficult to attribute fever or the mild viral illness as the cause of the nail matrix arrest. HFMD is generally a benign disease with very few fatalities reported in a previous HFMD epidemic in Singapore [8]. In this series, all the patients analyzed were documented to have fever, although there was no mention of any HFMD-related nail changes [8].

The true incidence of HFMD-related onychomadesis and Beau's lines may be under-reported, because mild cases are probably overlooked. Current reports of nail matrix arrest in children with a clinical history of HFMD are sparse and limited mainly to non-Asian patients on the European continent [2,4,5]. Perhaps this might point towards a potential genetic or environmental susceptibility. Our report is unusual in that two pairs of siblings with similar HFMD-related nail changes occurred at around the same time. This might support a potential familial predisposition or point to the possibility of a similar strain of enterovirus that may have a higher likelihood of causing nail matrix arrest.

The possibility of different enterovirus strains and virulence causing nail matrix arrest has been explored. Onychomadesis was the hallmark of the Finland 2008 HFMD outbreak, of which coxsackieviruses A6 (CV-A6) and coxsackievirus A10 (CV-A10) were identified as culprits, although the incidence of nail matrix changes was not reported [4]. Analysis of an outbreak of 221 onychomadesis cases in Valencia, Spain revealed a high frequency (61%) of HFMD among the onychomadesis cases, of which CV-A10 was identified as the most common culprit [5]. It is postulated that virus replication damages the nail matrix, resulting in temporary nail dystrophy. Enterovirus 71 (EV-71) has been identified more frequently in the HFMD epidemics of Southeast Asia and Australia in recent years [9]. In Singapore the predominant cause of HFMD epidemics remains EV-71 and CV-A16 infections.

We view the postulate proposed by Davia et al [5] that the virus may cause nail matrix arrest by direct action on the nail matrix as a plausible explanation for the resultant Beau’s lines and onychomadesis seen post-HFMD. Possibly, virally-induced cytopathic destruction of the nail matrix keratinocytes may occur, although there is no evidence to date that it does. Biopsy of the nail matrix when onychomadesis has been established would be unlikely to yield any results as the nail matrix would have recovered by then. Because we have not seen features of proximal nail fold paronychia or hand dermatitis in these children with onychomadesis post-HFMD, it is very unlikely that the intense hygiene measures and frequent hand-washing initiated after HFMD outbreaks at preschool centers were the cause of the nail changes seen. HFMD is predominantly a disease of childhood. Therefore, another explanation could be that HFMD exerts a more severe impact on the general condition of small children and the consequent nail growth arrest is more prolonged and complete to result in onychomadesis.

CONCLUSION

Although the temporal association between HFMD and onychomadesis from nail matrix arrest is increasingly recognized, the mechanism of nail changes remains elusive. The significance and extent of this association and the identification of different

enterovirus serotypes in future HFMD epidemics requires further evaluation.

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