

## Classical Hand, Foot and Mouth Disease Replaced by Atypical Hand, Foot and Mouth Disease

Regina FÖLSTER-HOLST, Section Editor of ActaDV

Department of Dermatology, Venereology and Allergy, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Rosalind-Franklin-Straße 7, DE-24105 Kiel, Germany. E-mail: rfoelsterholst@dermatology.uni-kiel.de

I have worked as a clinical paediatric dermatologist for over 30 years, but I am still learning. The best example is of atypical hand, foot and mouth disease (HFMD), which has replaced the classical form in recent years. Like the classical form of HFMD, associated with Coxsackie A16 (CV-A16) in Europe and with Enterovirus A71 (EV-A71) in the Asia-Pacific region, the atypical form of HFMD is one of the viral exanthemas in which the viruses can be identified from different body fluids, including cutaneous vesicles.

In the last 5–6 years I have not seen any cases of CV-A16-mediated classical HFMD; however, I have seen many children and adults with the CV-A6-mediated atypical form. While the classical form of HFMD is clinically characterized by oval greyish vesicles with a red halo, located on the hands and feet, as well as by oral vesicles and erosions, the atypical form has more polymorphic lesions, which are much more extensive and lead to widespread exanthema. Another clinical distinguishing feature is the higher level of impairment of the patient's general condition in the atypical form. While patients with the classical form of HFMD do relatively well, with the exception of oral pain, which is particularly noticeable while eating, most patients with the atypical form also experience flu-like symptoms, including fever.

For at least 10 years the atypical form of HFMD has been reported worldwide.

In the current issue of *Acta Dermato-Venereologica* Horsten et al. (1) describe an outbreak of atypical HFMD in 23 children and adults who presented between June 2014 and January 2016 in a hospital in Southern Denmark. The diverse referral diagnoses from dermatologists (eczema herpeticum, vasculitis, Stevens-Johnson syndrome, syphilis) reflect the need for clinicians to be informed of the atypical clinical presentation of CV-A6-associated HFMD. I have had the same experience in

consulting for children's skin diseases in Kiel, Germany, where referral diagnoses have also included impetigo contagiosa, chickenpox, tinea and atopic dermatitis.

Recently the same Danish research group described an adult woman developing a generalized rash with multiple papulovesicular and pustular lesions, including in the palmoplantar and perioral region (2). The clinical appearance was in line with CV-A6-associated atypical HFMD. However, in this case, PCR analysis of a stool sample revealed another enterovirus, Echovirus 3. The researchers mention that echoviruses are rare causes of vesicular rashes. Other authors have pointed out that there are further enteroviruses associated with HFMD, including the Coxsackie viruses CV-A10, CV-B3, CV-B5 and the Echovirus 30 (3, 4). Due to severe complications, such as aseptic meningitis and myocarditis, the authors recommend the development of vaccines against these infections (3, 4).

Clinical trials of a formalin-inactivated EV-A71 vaccine have been completed in Asian countries, but there is no protection against other viruses associated with HFMD (3). The development of a globally representative multivalent HFMD vaccine is therefore recommended.

### REFERENCES

1. Horsten HH, Kemp M, Fischer TK, Lindahl KH, Bygum A. Atypical hand, foot, and mouth disease caused by coxsackievirus A6 in Denmark: a diagnostic mimicker. *Acta Derm Venereol* 2018; 98: 350–354.
2. Høgsberg T, Bygum A. Disseminated vesicular rash in an immunocompetent adult woman: a quiz. Atypical hand, foot, and mouth disease caused by echovirus 3. *Acta Derm Venereol* 2018; 98: 163–164.
3. Aswathyraj S, Arunkumar G, Alidjinou EK, Hober D. Hand, foot and mouth disease (HFMD): emerging epidemiology and the need for a vaccine strategy. *Med Microbiol Immunol* 2016; 205: 397–407.
4. Klein M, Chong P. Is a multivalent hand, foot, and mouth disease vaccine feasible? *Hum Vaccin Immunother* 2015; 11: 2688–2704.