



## Hand, Foot and Mouth Disease

### Case Reports of Familial Child to Immunocompetent Adult Transmission

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#### Abstract

*Hand, foot and mouth disease (HFMD) is a highly contagious viral infection characterized by typical maculopapular or vesicular eruptions on the hands, feet and in the oral cavity. It affects predominantly children and/or immunocompromised adults. It usually follows a benign and self-limiting course. However, HFMD cases with severe or lethal complications such as encephalitis, meningitis, pulmonary edema and myocarditis have also been reported, mostly in children, but also in adults<sup>1</sup>. We present three cases of familial transmission of HFMD with typical features, benign course and complete recovery among otherwise healthy immunocompetent adults.*

**Keywords-** *Hand, foot, and mouth disease, coxsackie virus A16, viremia.*

#### Introduction

Hand, foot, and mouth disease (HFMD) is an acute viral and a highly contagious infectious disease with a distinct clinical presentation of oral and cutaneous lesions. It is predominantly a childhood or immunodeficiency-associated disease due to their high sensitivity to the enterovirus 71 (EV71) and coxsackievirus A16 (CVA16). Very few cases have been reported in immunocompetent adults so far<sup>2</sup>. HFMD rarely appears as an epidemic infectious disease. It is associated with climate changes, usually occurring in spring and summer. It is mainly caused by coxsackievirus A16 (CVA16), but other strains such as A5, A6, A7, A9, A10, B2, B5 and human enterovirus 71 have also been isolated<sup>3</sup>. The main

routes of transmission are person-to-person (through oral-pharyngeal secretions or by direct vesicle contact), via contaminated water (fecal-oral route) and via contaminated objects. The incubation period is short, ranging from 2 to 7 days. It starts as non-specific symptoms, but there may be mild fever and catarrhal manifestations. The initial viral implantation is in the oral cavity and ileum, spreading to the regional lymph nodes within 24 hours. Viremia occurs after 72 hours, followed by secondary infection and viral seeding in areas such as the oral mucosa, hands and feet. On the seventh day, there is an increase in antibody levels and the disease begins to disappear. Oral lesions are the first clinical signs of the disease and sometimes the only sign. Skin

manifestations occur concurrently or shortly after the oral lesions and consist of multiple erythematous macular, popular or vesicular lesions on the hands and feet. A study in Japan suggests the possibility that the HFMD could also cause opsoclonus-myoclonus (jerky eye movements in all directions) as a possible viral or autoimmune response, other studies reports cases of retinopathy and vision loss in this entity. The diagnosis is by observing the clinical signs of the disease, such as fever and the characteristic lesions on the hands, feet and mouth. Confirmation of diagnosis is carried out by isolating the virus responsible for the disease, or by identifying virus-neutralizing antibodies in patient serum<sup>4</sup>. Pain may be treated with standard doses of acetaminophen or ibuprofen. Direct analgesia may be applied to the oral cavity through mouthwashes or sprays. In addition plenty of fluids, avoidance of spicy and acidic foods and foods that require a lot of chewing also helps. Intravenous immunoglobulin and milrinone have shown some efficacy in a few reports. Pleconaril is an uncoating inhibitor that shows promise in enterovirus 71-associated infections. Amantadine and quinacrine, both translation inhibitors and ribavirin, a replication inhibitor, are also being investigated as treatment options.<sup>5</sup> In most cases, the prognosis is good moving toward spontaneous healing within 7–10 days without sequelae, scabs or scars. However, there have been reports of onychomadesis associated with the disease, in addition to neurological disorders such as meningitis (EV-4), Guillain–Barre syndrome, meningoencephalitis, as well as paralytic polio, myoclonus and somnolence, mainly caused by the sub genotype C4aEV71, in children under 5 years (the main risk group in the population). Most of these patients have low levels of vitamin A, associated with reduced immunity and they are therefore more susceptible to a more severe manifestation of the disease. Delays in access to health services lead to an increased likelihood of a more severe form of the disease<sup>4</sup>.

### Case Report

**Case 1:** A 26-year-old female student with no significant past medical history or any new recent medications presented in the month of August with a two-day history of non-itchy, painful erythematous papular skin lesions. She reported a history of fever and sore throat three days before the onset of cutaneous symptoms. She reported close contact while caring for her four-year-old niece who was diagnosed with HFMD one week ago. She denied any similar lesions in the past. Physical examination of the patient revealed tender, erythematous, 0.5 to 1 cm papulovesicular lesions on bilateral palms and dorsum of hands (Fig1&2). The oral cavity was spared. No biopsy or cultures were taken and a diagnosis of HFMD was made based on the characteristic history, exposure and clinical manifestations. She was treated symptomatically and no complications were observed during follow-up. Her lesions resolved in two weeks with no scarring.



**Fig 1:** Erythematous papulovesicular lesion on the left palm.



**Fig 2:** Erythematous papulovesicular lesion on dorsum of both hands.

**Case 2:** 18-year-old male student (neighbour of case 1) reported with papulovesicular eruptions on hands and feet, 2 weeks after case 1 reported. He had history of fever and sore throat 1 day before the onset of lesions, which was managed with Paracetamol 500 mg and Azithromycin in ENT OPD. Subsequently, tender erythematous papules appeared on the heel of left foot and sole of right foot. Examination revealed multiple painful erythematous papulovesicular lesions on the sole and medial surface of right foot and the heel of left foot and measured about  $4 \times 5$  mm (Fig 3). By the third day, similar lesions appeared on the palms of both hands (Fig 4). Routine blood examinations were normal. Since the lesions were similar to those of case 1, diagnosis of HFMD was made. The student was then treated symptomatically. Lesions resolved completely in 2 weeks without scarring.

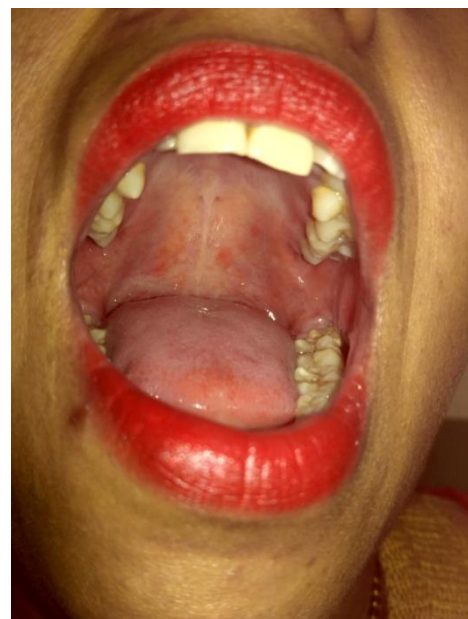


**Fig 3:** Erythematous papulovesicular lesion on the sole and medial surface of right foot.



**Fig 4:** Erythematous papulovesicular lesion on both the palms.

**Case 3:** A 29-year-old female, with no significant medical history, presented in November 2017 with a 2-days history of papulovesicular skin rash and oral ulcers following a 3-days history of high fever, chills and malaise. There was history of similar cutaneous lesions in her two sons who were 3 years and 6 years old. Physical examination showed numerous erythematous papular lesions on her palms bilaterally. On oral examination, diffuse erythematous areas were observed on the soft palate (Fig 5). Multiple erythematous papulovesicular and vesicular lesions were seen on the palms, soles, dorsum of hands and feet of both the children. The lesions were more prominent in the younger child (Fig 6). Routine blood examinations were normal. No biopsy or cultures were taken and a diagnosis of HFMD was made based on the characteristic history, exposure and clinical manifestations. All were treated symptomatically and no complications were observed during follow-up. Lesions resolved in two weeks with no scarring.



**Fig 5:** Diffuse erythematous areas on the soft palate





**Fig 6:** Erythematous papular lesion on the both the palms of the mother and erythematous papulovesicular lesion on both the palms of her sons.

### Discussion

The term HFMD is derived from typical maculopapular or vesicular lesions involving the skin of the hands, feet and oral mucosa. Children and immunocompromised adults are most susceptible to HFMD. Other at-risk categories include elderly people and pregnant women. To our knowledge, only a few HFMD cases have been described in the literature in immunocompetent adults. Disease transmission among family members occurs commonly and involves fecal-oral and/or respiratory routes. Children are usually infected by asymptomatic or mildly symptomatic adults. However, in our cases, close contact with mildly symptomatic children suffering from HFMD initiated a strong, symptomatic infection in the immunocompetent adults. The literature shows many cases of child-to-child or/and adult-to-child HFMD household transmission. The prodromal phase including low-grade fever, malaise and sore throat is commonly observed. In adults, the clinical picture of the

mucocutaneous lesions can mimic erythema multiforme or other infectious diseases, such as syphilis. Enanthem usually precedes the onset of the skin rash. Additionally, oral lesions may appear in the absence of cutaneous symptoms. Two of our cases had no apparent mucosal lesions at the time of the physical examination (case 1 & 2). Similar cases of HFMD without oral involvement have rarely been reported in the literature. During recent outbreaks of HFMD in Spain and Taiwan, caused by Coxsackievirus A6, the disease had a broader spectrum of manifestations. In addition to the typical rash on the palms, soles and oral cavity, lesions were also present on the buttocks, trunk and perioral zone. Some lesions were vesiculobullous, bigger and present on different sites of the body. The exact pathogenesis of atypical clinical manifestation has not been revealed so far.<sup>1</sup> It is not known whether Coxsackievirus A6 might have transformed into a more virulent strain. However, these uncommon manifestations may be helpful for early diagnosis of Coxsackievirus A6 infection and can sometimes spare unnecessary and expensive molecular analysis. High infectivity of HFMD has contributed to several large outbreaks of this disease which occurred in the last 2 decades in East and Southeast Asia, United States and Finland. During these outbreaks, most of the cases of HFMD followed a benign and self-limiting course. However, HFMD cases with severe or lethal complications such as encephalitis, meningitis, pulmonary edema and myocarditis have been reported, mostly in children, but also in adults. Genetic typing to distinguish the exact virus strain, is usually not necessary to confirm the HFMD diagnosis. Nonetheless, in some cases of HFMD information on the exact type of the virus is crucial for appropriate disease management and for reliable assessment of the risk of potential complications. Significant differences are reported in the literature about the course of HFMD depending on the pathogen with greater frequency of fatalities and serious complications (especially pulmonary and

neurological) was observed with Enterovirus 71 when compared to Coxsackievirus A16. Hence, it is of great importance to develop rapid and reliable diagnostic methods in order to differentiate the exact type of HFMD virus<sup>5</sup>. As treatment is mainly supportive, recognition and prevention play a vital role in limiting spread of HFMD and decreasing outbreaks. Physicians can help is to identify affected patients and educate them on preventive measures. Enteroviruses are shed in the stool for many weeks after initial infection, so good hand hygiene should be made a mandatory practice, especially in health care settings, daycare centers and other places where outbreak is common<sup>1</sup>.

The Centers for Disease Control and Prevention recommends that all affected patients and their close contacts should practice the following practices to prevent further spread of infection: frequent hand washing, especially after changing diapers and using the restroom; frequent disinfection of commonly used surfaces and objects and avoiding close contact with infected individuals<sup>6</sup>.

### Conclusion

Even though HFMD is a self-limiting contagious viral disease usually occurring in small children and immunocompromised adults, the current scenario points out that coxsackie and human enteroviruses can affect healthy individuals too. It is important for physicians to be aware of this fact and try to confine and avoid the infection spreading to more vulnerable persons. The diagnosis is based on clinical grounds and treatment is mainly supportive. Adults caring for children with HFMD should be educated that they are not immune to the disease and should be instructed to take appropriate preventive measures by maintaining proper hygiene and hand washing.

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