Case Report/Case Series

Coxsackievirus A6–Induced Hand-Foot-Mouth Disease

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IMPORTANCE Hand-foot-mouth disease (HFMD) is an acute, self-limited, highly contagious viral illness that commonly affects children younger than 5 years. It is most typically caused by enterovirus 71 or coxsackievirus A16 and results in asymptomatic infection or mild disease. Immunocompetent adults are rarely affected. Recently, there have been increasing reports of a more severe form of HFMD associated with fevers, joint pains, and widespread painful eruptions. Some of these patients required hospitalization for supportive care. These severe cases were most commonly caused by coxsackievirus A6.

OBSERVATIONS We describe a 37-year-old white man with widespread, crusted, pruritic papules on the scalp, ears, and face and a purpuric and targetoid painful vesicular eruption on his hands and feet, with associated fevers, neurologic symptoms, and arthritis, who required hospitalization for supportive care. His infection with coxsackievirus A6 was confirmed based on polymerase chain reaction from his oral mucosa and cutaneous vesicle fluid.

CONCLUSIONS AND RELEVANCE Dermatologists should be familiar with the severe variant of HFMD caused by coxsackievirus A6, include it in their differential diagnosis of acute febrile blistering diseases, and be aware that certain patients may require hospitalization.

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Hand-foot-mouth disease (HFMD) is an acute, self-limited, highly contagious viral illness that commonly affects children younger than 5 years. It is most typically caused by enterovirus 71 or coxsackievirus A16 and results in asymptomatic infection or mild disease. Immunocompetent adults are rarely affected. Recently, there have been increasing reports of a more severe form of HFMD associated with fevers, joint pains, and widespread painful eruptions. Some of these patients required hospitalization for supportive care. These severe cases were most commonly caused by coxsackievirus A6 (CVA6).

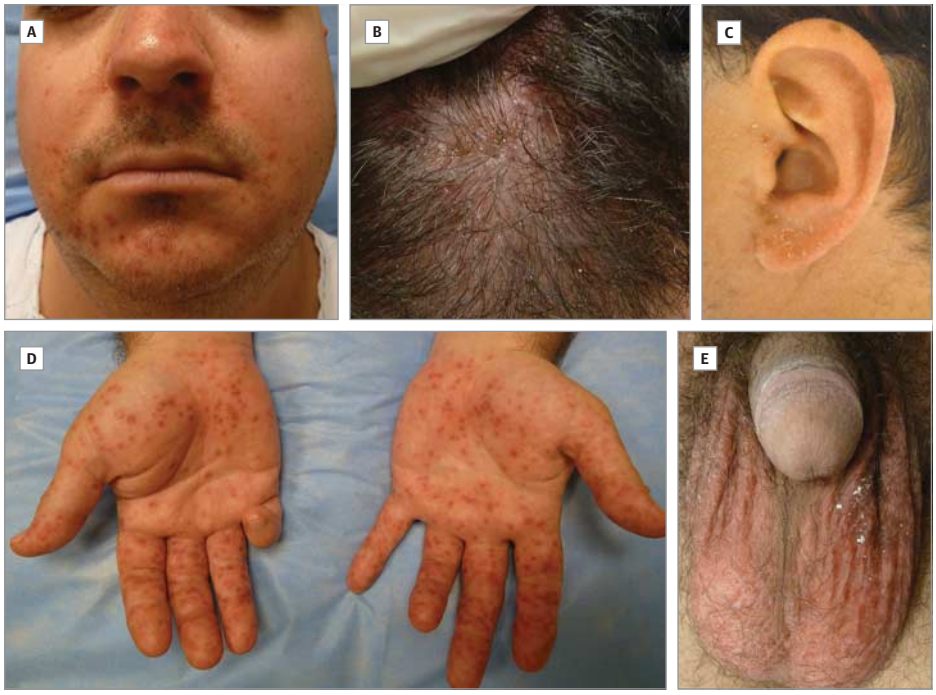
Report of a Case

A 37-year-old man developed a pruritic, crusting papular eruption on his posterior scalp. Three days after the eruption appeared, he developed fevers; fatigue; sweats; headaches with photophobia; joint pains of the hands, neck, and back; nausea; diarrhea; and a burning pain on his palms and soles, limiting ambulation and daily activities. His eruption progressed on the palms and soles into targetoid purpuric macules and several targetoid papulovesicles with clear fluid. On the scalp, ears, and cheeks and concentrated around his mouth and cutaneous lip, there were numerous red-pink papules with overlying yellow-brown crust. His scrotum was deep red and fissured with a fine white scale (**Figure 1**). His family history was significant for a 10-month-old infant at home with HFMD clinically diagnosed 1 week before the onset of the patient's symptoms.

The patient was admitted to the hospital based on his systemic symptoms. He was covered empirically with oral doxycycline for possible rickettsial disease and intravenous acyclovir for possible herpesvirus infection while laboratory study results were pending.

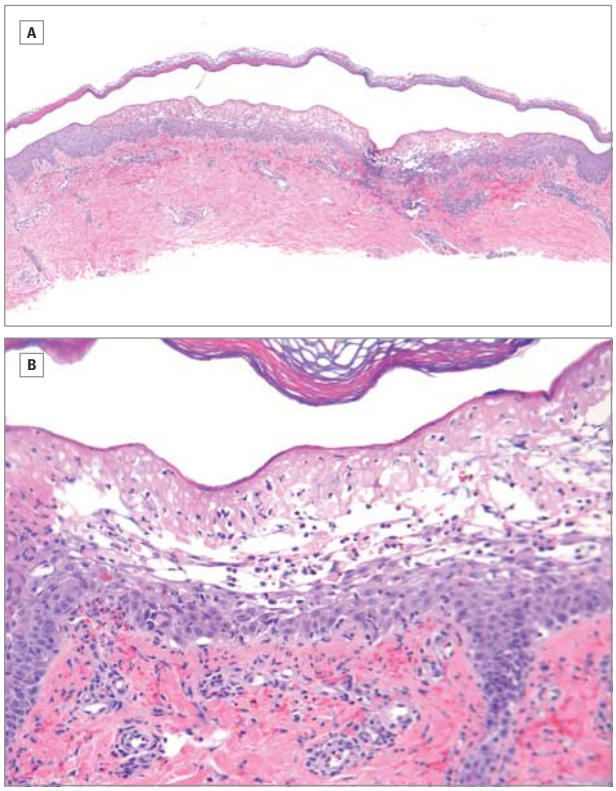
Biopsy specimens obtained from his right cheek and the left palm revealed inflammatory scale crust, parakeratosis, interface dermatitis, papillary dermal hemorrhage, and a mixed perivascular infiltrate. A biopsy specimen of a right dorsal wrist vesicle revealed an intraepidermal bulla with focal reticular degeneration and confluent necrosis of the blister roof (**Figure 2**). Viral inclusion bodies or multinucleated keratinocytes were not seen. Periodic acid-Schiff stain result was negative for fungal elements. The results of blood tests, including complete blood cell count with differential, complete metabolic panel, rapid plasma reagin, rickettsial antibodies, and coxsackievirus B1 through B6 antibodies, were unremarkable. The vesicle fluid tested negative for herpes simplex virus and varicella-zoster virus by polymerase chain reaction (PCR) and direct fluorescence antibody testing, respectively. Routine bacterial culture of vesicle fluid was negative. The PCR result was positive for enterovirus from the oral cavity and right dorsal wrist vesicle, and the viral strain was identified as CVA6, confirming the diagnosis of HFMD.

Figure 1. Severe Adult Hand-Foot-Mouth Disease in Caused by Coxsackievirus A6



A 37-year-old man developed grouped papules with yellow crust located on the periorificial face (A), occipital scalp (B), and external ear (C). The patient also had purpuric targetoid macules and vesicles on the palms (D) and a fissured scrotum with a fine white scale (E).

Figure 2. Biopsy Specimen of the Patient's Wrist



Biopsy specimen of the patient's right dorsal wrist vesicle showed an intraepidermal bulla with focal reticular degeneration and confluent necrosis of the blister roof (A, hematoxylin-eosin, original magnification ×4; B, hematoxylin-eosin, original magnification ×20).

The patient's systemic symptoms resolved within 2 days, and he was discharged from the hospital. Within 7 days his cutaneous lesions had mostly healed, with minimal postinflammatory erythema.

Discussion

Hand-foot-mouth disease is an acute, highly contagious viral illness that commonly affects children younger than 5 years, normally in the summer and fall. It is generally mild and self-limited; however, certain uncommon viral strains cause severe illness in children and adults. The infection is often asymptomatic, but the clinical manifestations include mild fever with a characteristic vesicular eruption on the hands, feet, and oral cavity.[1] These symptoms resolve in 7 to 10 days; however, onychomadesis can occur 1 to 2 months after infection.[2,3] Most commonly, HFMD is caused by coxsackievirus A16 and enterovirus 71, but it can be caused by coxsackievirus A5, A6, A7, A9, A10, B2, and B5.[4]

Between 2004 and 2011, several outbreaks have occurred of a more severe variant of HFMD associated with CVA6 in Singapore, Taiwan, Finland, Spain, and Japan.[1,5] More recently, between November 2011 and February 2012, 63 cases of severe HFMD have been reported to the Centers for Disease Control and Prevention by Alabama, Connecticut, California, and Nevada. Seventy-four percent of the tested cases were PCR positive for CVA6. Approximately 25% of these reported cases were in adults, most of whom had contact with children. The presentations of these cases were generally more severe than typical HFMD, with higher temperatures and extensive cutaneous eruptions, and many patients were hospitalized for de-

hydration and severe pain.[1] Since the initial Centers for Disease Control and Prevention report, several cases of severe atypical HFMD in children have been reported to be caused by CVA6.[6]

In this report, we demonstrate the clinical and histopathologic features of this severe variant of HFMD in an adult with PCR-confirmed CVA6 infection. The pathologic findings were consistent with HFMD, with areas of reticular ballooning degeneration of the epidermis, perivascular inflammation, and interface dermatitis.[4,7] Our case illustrates the unusual aspects of this variant of HFMD: an adult with severe disease and systemic symptoms who presented in the springtime. Generally, HFMD is rare in immunocompetent adults.[7] The patient had debilitating systemic and neurologic symptoms, arthritis, and pain of his hands and feet that required hospitalization, whereas most cases of classic HFMD are managed at home.[5-7] His eruption differed from classic HFMD because his scalp, ears, and scrotal skin were profoundly affected.

Given that most of the US population has not yet been exposed to CVA6, it is likely that more of these cases will appear in clinics and hospitals in the coming years. It is important for dermatologists to recognize this atypical presentation of HFMD, include it in their differential for acute febrile blistering diseases in both children and adults, and ensure that the patients are hospitalized for appropriate supportive care when needed.[6]

ARTICLE INFORMATION

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Acquisition of data: Stewart, Chu, Schaffer, James.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: Stewart, Schaffer.
Critical revision of the manuscript for important intellectual content: All authors.
Administrative, technical, and material support: Stewart, Introcaso, James.
Study supervision: Schaffer, James.

Conflict of Interest Disclosures: None reported.

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