JAMA Pediatrics Clinical Challenge

A Child With a Blistering Rash

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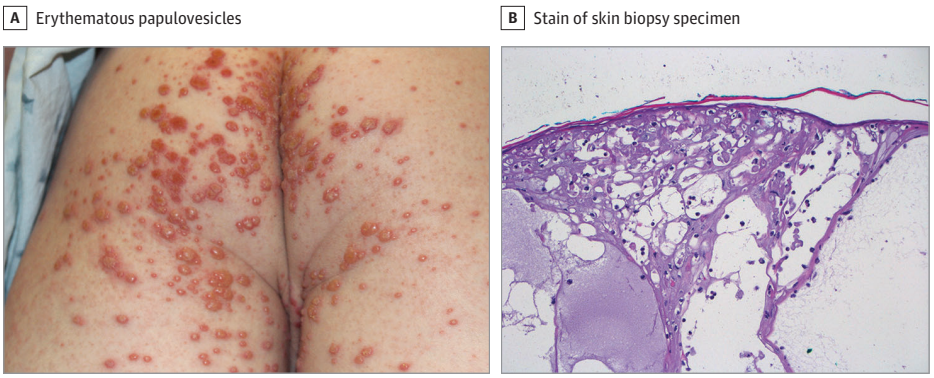

Figure. A, Bilateral buttocks and posterior thighs with erythematous papulovesicles. B, Skin biopsy specimen showing subepidermal vesicles with reticular degeneration (hematoxylin-eosin, original magnification ×20).

A 12-year-old boy presented with a 4-day history of rash that began on the trunk and spread to the face and extremities. He denied any skin pain or pruritus. There was no history of recent travel or illness, but he reported contact with a classmate who had painful oral sores. He denied malaise or decreased appetite. On physical examination, the patient was afebrile with normal vital signs. Examination of the skin revealed erythematous papulovesicles on the face, trunk, and extremities with prominent vesicles and bullae on his genitalia, buttocks, and posterior thighs (**Figure**, A). A skin biopsy specimen revealed subepidermal vesicles with focal reticular degeneration (Figure, B).

WHAT IS YOUR DIAGNOSIS?

A. Disseminated herpes simplex

B. Bullous impetigo

C. Atypical hand, foot, and mouth disease

D. Erythema multiforme

Diagnosis

C. Atypical hand, foot, and mouth disease

Discussion

Given the clinical distributions of lesions that involve the face, buttocks, and acral surfaces in the setting of known classroom exposure to a child with oral ulcers, the patient was diagnosed with atypical hand, foot, and mouth disease (HFMD). Enterovirus reverse transcriptase–polymerase chain reaction (RT-PCR) from an intact vesicle on the buttock at the time of presentation confirmed the diagnosis. Skin biopsy revealed subepidermal vesicles with focal reticular degeneration consistent with a diagnosis of coxsackie viral exanthem. However, these findings are not specific for coxsackievirus, and early lesions of erythema multiforme may have similar histologic features. Biopsy is rarely performed in HFMD but may be useful in suspected atypical cases or if PCR (sensitivity of 90% and specificity of 100% for enterovirus detection[1]) and culture results are unrevealing. In this case, a biopsy was performed before PCR results were obtained to exclude rare entities that require alternative treatment, such as immunobullous disease. Supportive care was continued, and the patient's skin lesions resolved during the subsequent week.

Hand, foot, and mouth disease is a common, highly contagious, viral syndrome that has received increased attention during the past 20 years because of its implication in epidemics worldwide.[2] Typically, HFMD is characterized by a prodrome of low-grade fever and malaise, painful oral ulcerations, and a vesicular exanthem classically distributed on the hands and feet. The fever, malaise, and pharyngitis are followed by the appearance of oral vesicular lesions that progress to painful superficial ulcers, which can result in decreased oral intake, leading to dehydration. Papulovesicles subsequently develop on the palms and soles.

Atypical HFMD is characterized by unusual cutaneous manifestations that deviate from the classic erythematous papules, vesicles, and erosions seen in classic HFMD. Atypical HFMD manifests as a more widespread eruption of papulovesicular lesions on the face, hands, feet, buttocks, and genitalia, followed by formation of gray vesicles with surrounding erythema.[2,3] The disease is typically mild and resolves spontaneously within 7 to 10 days without complications or residual scarring. Primarily, HFMD affects children younger than 10 years but has also been reported in adults.[2] Transmission occurs by the oral-oral or fecal-oral route.[4]

Multiple serotypes of *Enterovirus* are implicated in HFMD. The coxsackievirus A serotypes are the most common viruses to cause HFMD, with coxsackievirus A16 type being the most frequent serotype in the United States, followed by enterovirus 71 and coxsackieviruses A and B serotypes.[2,5] Enterovirus 71 has been associated with a more severe course of HFMD and with HFMD complications, including central nervous system disease and cardiopulmonary failure.[2] This severe course of HFMD is not deemed atypical because the term *atypical* is reserved for the presentation of unusual cutaneous manifestations, most commonly associated with the A6 viral strain. Presentations of HFMD that appear similar to eczema herpeticum have been described in children with underlying atopic dermatitis; this presentation is referred to as eczema coxsackium. The incidence of atypical HFMD has increased during the past 8 years.[6] Atypical HFMD caused by coxsackievirus A6 was first reported in Southeast Asia and Europe and is now endemic in North America.[5,6] A retrospective review[7] of outbreaks with the A6 viral strain have found variability in presentation and range of severity.

The differential diagnosis of HFMD includes herpangina, herpes simplex, eczema herpeticum, varicella zoster, erythema multiforme, and bullous impetigo. Hand, food, and mouth disease may present similarly to herpangina, with vesicular lesions and erosions of the oropharynx, but herpangina rarely presents with skin involvement, and lesions are classically localized to the tonsillar pillars, tonsils, soft palate, uvula, or tongue.[2] Atypical HFMD may be difficult to distinguish from eczema herpeticum. If present, the characteristic gray papulovesicles on the palms and soles are an important diagnostic clue. In addition, children with eczema coxsackium are often well-appearing, with normal appetite and behavior. In contrast, children with eczema herpeticum are typically febrile and ill-appearing. Although the diagnosis of HFMD is primarily clinical, serologic testing and RT-PCR or viral cultures of vesicular fluid can be performed to confirm the diagnosis. No antiviral agents have been proven to be effective for treatment of enteroviruses; therefore, supportive care is the mainstay of treatment.[2,8]

ARTICLE INFORMATION

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