Woman, 18, With Sore Throat, Fever, and Painful Rash

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An 18-year-old woman presents to urgent care with a one-day history of sudden-onset sore throat, chills, malaise, and fever (102.5°F). On physical examination, the tonsils and pharynx are erythematous, and anterior cervical lymph nodes are tender on palpation. A rapid strep test is negative. The patient is instructed to use throat lozenges and take ibuprofen (400 mg every 8 h) as needed for pain.

On day 2, the patient’s fever resolves, but a painful rash develops on her palms and soles. Clinical examination reveals multiple erythematous plaques on the hands and feet (see Figure 1). The patient is diagnosed with hand-foot-and-mouth disease (HFMD).

DISCUSSION
HFMD is caused by enteroviruses, most commonly coxsackievirus A16 (CV-A16) or enterovirus 71 (EV71). However, a newly recognized strain, CV-A6, has caused worldwide outbreaks of HFMD in both children and adults. Although less common than CV-A16 or EV71, CV-A6 is associated with a more severe disease course. The CV-A6 strain was first identified in Finland in 2008 during a major outbreak of HFMD; it reached the United States in 2011. Accurate statistics on the prevalence of CV-A6 in the US are difficult to obtain because HFMD is not a reportable condition.

Clinical presentation
HFMD typically manifests with painful oral lesions, with or without a macular, maculopapular, or vesicular exanthema. If a fever is present, it is usually below 101°F. The oral lesions are typically benign and manifest as erythematous macules that progress to vesicles with an erythematous halo. These lesions tend to be painful and may interfere with eating or drinking. Signs and symptoms associated with the more virulent form, CV-A6, may include
- Higher fever
- Wider distribution of lesions
- More extensive skin involvement
- Longer duration
- Palmar and plantar desquamation
- Nail dystrophy

Laboratory diagnosis
Most symptomatic enterovirus infections are diagnosed based on clinical findings alone, reducing the need for laboratory testing. Laboratory confirmation may be warranted for more severe infections and

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during outbreaks. Molecular methods, such as reverse transcriptase polymerase chain reaction, are typically used for identifying enteroviruses, as they are rapid, sensitive, and widely available in hospital and commercial laboratories. Viral culture methods are labor-intensive, expensive, and reserved for typing the isolate. Serology is not useful in the diagnosis of acute infection.

**Differential diagnosis**

The differential diagnosis of HFMD includes conditions with oral lesions and maculopapular, vesicular lesions involving the palms and/or soles, as well as erythroderma.

**Oral lesions.** Aphthous ulcers are shallow, painful oral lesions not accompanied by skin rashes. Herpes gingivostomatitis, caused by herpes simplex virus (HSV), is often preceded by a prodrome of fever. The associated lesions manifest as vesicular clusters on a red base that evolve into large, painful ulcers. HSV mouth lesions can populate the gingivae, pharynx, hard palate, lips, and perioral skin. Skin lesions may occur unilaterally.

**Rashes involving palms and soles.** A number of conditions manifest with skin lesions similar to those of HFMD. An au-toeczematization reaction consisting of a pruritic, papulovesicular eruption secondary to dermatophyte infection (eg, tinea pedis, tinea manuum, tinea cruris, tinea corporis, tinea capitis) should be ruled out. This type of reaction is thought to be a delayed hypersensitivity response to fungal antigens. Pruritus and the absence of mouth sores distinguishes this reaction from HFMD.

Secondary syphilis can manifest with a short-lived macular rash involving the palm and soles, as well as oral mucous patches and generalized lymphadenopathy. Syphilis testing, including rapid plasma reagin or Venereal Disease Research Laboratory test with fluorescent treponemal antibody absorption, can rule out this diagnosis.

Erythema multiforme, which is more common in young adults, is characterized by target lesions on the palms and soles and erosions and/or bullae in the mouth and mucous membranes. It is usually preceded by a trigger, such as HSV infection.

**Erythroderma.** In addition to a rash, erythema multiforme can cause desquamation later in the disease course. Toxic shock syndrome (TSS), a life-threatening condition caused by Streptococcus or Staphylococcus, has an abrupt onset that is associated with high fever and hypotension. TSS causes a sunburn-like rash on the palms and soles that desquamates weeks after onset. Scarlet fever, caused by group A Streptococcus, can cause an erythematous rash with desquamation in children and adolescents. Scalded skin syndrome is a desquamative condition caused by Staphylococcus that occurs primarily in infants and young children.

**Management**

There is no specific antiviral treatment for HFMD, and thus management is mainly supportive. Fever and pain can be managed with ibuprofen or acetaminophen. Children who are unable to maintain oral hydration...
may require hospitalization for IV fluids.

Prevention of HFMD requires strict hand hygiene—washing with soap and water—as well as thoroughly cleaning and disinfecting surfaces that come in contact with infected oral secretions or feces.8

**OUTCOME FOR THE CASE PATIENT**
The patient was discharged and instructed to take ibuprofen as needed.

About three weeks later, the patient’s palms and soles began to peel. Clinical examination at follow-up revealed painful, diffuse, scaly desquamation of the hands and feet (see Figure 2, page e12). The patient also experienced loosening and shedding of the proximal nails (see Figure 3). She was diagnosed with postviral shedding.

About eight weeks after the desquamatory rash manifested, complete resolution was seen. The patient experienced continued onychomadesis three months after the initial presentation.

**CONCLUSION**
Clinicians should be mindful of the increasing incidence of HFMD in the adult population, since it may mimic other disease states. The extent and chronicity of this patient’s clinical manifestations were unusual and may have been caused by CV-A6.

**REFERENCES**