Published in final edited form as:

Pediatr Dermatol. 2016 ; 33(2): e140–e142. doi:10.1111/pde.12769.

Recurrent Coxsackievirus Infection in a Patient with Lamellar Ichthyosis

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Abstract

We describe a case of coxsackievirus (CV) A6 infection in a patient with lamellar ichthyosis followed by subsequent CV A8 infection within the same year. Atypical cutaneous features characterized the infection. This observation, combined with the rapidity with which reinfection occurred, suggests that the natural history of CV infection may be altered in patients with underlying ichthyoses.

A 6-year-old boy with a history of lamellar ichthyosis (LI) and recurrent methicillin-resistant *Staphylococcus aureus* skin infections presented with fever and rash for 1 day. The patient has known compound heterozygous mutations in transglutaminase 1 (c.232 C>T leading to R78X and c.1264 A>T leading to K422X).

Physical examination revealed a febrile patient (40°C). Skin examination demonstrated diffuse, platelike scale that was accentuated on the lower extremities, consistent with the known diagnosis of LI. Approximately one hundred 0.2- to 0.7-cm pink macules intermixed with approximately twenty 0.5- to 1.2-cm deep-seated, oval-shaped vesiculopustules were distributed on the trunk, arms, hands, legs, and feet (Fig. 1). There were no perioral or mucosal lesions.

Analysis of the vesiculopustules revealed clear fluid with 1+ white blood cells; no organisms were noted on Gram stain and bacterial cultures were ultimately negative. The vesicular fluid was negative for herpes simplex virus (HSV) and varicella zoster virus, but polymerase chain reaction (PCR) was positive for coxsackievirus (CV) A6.

On day 2, hundreds of additional coalescing pink-red macules and approximately 100 additional vesicles developed (Fig. 2). Despite initial progression, the patient subsequently improved with supportive care. Widespread dry desquamation and late onychomadesis were observed.

Seven months later, the patient presented with low-grade fever and approximately 20 scattered, similar-appearing 0.3- to 0.8-cm deep-seated inflammatory vesicles (Fig. 1). The hands, feet, face, and oral mucosa were unaffected. PCR of the vesicle fluid showed CV A8 infection.

DISCUSSION

CV A16 causes classic hand-foot-and-mouth disease (HFMD). Infection with CV A6 has been reported to result in a more widespread distribution, with a predilection of lesions to form in areas of prior skin injury or inflammation (1,2). CV A8 infection has been reported to be more commonly associated with herpangina than HFMD (3) and may frequently go unrecognized because of the lack of cutaneous manifestations. CV infection with individual strains is not generally thought to be fully cross-protective against other strains (4).

This patient had atypical features during CV A6 and A8 infection. Most vesicles were deep seated (macular) and appeared pustular clinically, likely resulting from the hyperkeratosis of LI overlying the intraepidermal vesicles characteristic of cutaneous CV infection (5). It is likely that impaired sweating exacerbated his fevers.

In general, histopathologic analysis of the skin in patients with LI shows superficial perivascular lymphocytic inflammation (5). This is notable given the widespread distribution of lesions in this case, particularly with CV A6. We hypothesize that a scenario analogous to that seen in patients with atopic dermatitis, in which cutaneous lesions favor sites of inflammation (1,2), combined with an epidermal barrier defect, may have facilitated widespread lesion distribution.

The rapid reinfection with CV A8 in this patient is notable. Underlying LI might predispose to CV infection or might escalate otherwise subclinical disease to clinically evident cutaneous disease. LI has not been reported to be associated with a greater propensity for cutaneous viral infection, but other individual genodermatoses have. For example, Darier's and Hailey–Hailey diseases are thought to increase susceptibility to HSV infection.

Evaluation for CV in vesiculopustular lesions (especially when oval-shaped as in classic HFMD) in patients with ichthyoses may be informative moving forward.

ACKNOWLEDGMENTS

The authors would like to thank the Yale New Haven Hospital virology laboratory and the Centers for Disease Control and Prevention, Division of Viral Diseases for performing the Enterovirus and strain-specific CV PCRs, respectively.

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Figure 1. Cocksackievirus (CV) A6 infection on day 1 (left panel) and CV A8 infection (right panel) in lamellar ichthyosis. Discrete pink macules (arrowheads) with scattered deep-seated vesiculopustules (arrows) were present. An erosion can also be seen in the right panel.

Figure 2. Cocksackievirus A6 infection in lamellar ichthyosis, day 2. Pink-red macules coalesced into patches that became confluent in many areas. Vesiculopustules were more numerous (arrows).