

## A case of coxsackievirus A16-induced hand-foot-mouth disease mimicking erythema multiforme

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Dear Editor,

A 19-year-old woman was referred to the otolaryngology department for hearing loss in the right ear. She was diagnosed with secretory otitis media and started on oral administration of ofloxacin and carbocysteine. Nine days later, she developed a fever and edema of the lips and stopped taking these medications. However, her condition worsened, and she visited our hospital. She had no relevant medical past or medication history. Her temperature was 38.7°C; erythematous papules partially mimicking small vesicles were clustered on the face, trunk, and extremities, predominantly on soles and palms (Figure 1a-b). The bilateral ocular conjunctiva was hyperemic, and the lips were swollen and fissured (Figure 1c-d). The mucous membranes extending from the oral cavity to the pharynx were erythematous, and the labia showed erosions. The skin biopsy of the trunk showed a bullous and necrotic epidermis infiltrated with lymphocytes and neutrophils (Figure 1e). We initially suspected erythema multiforme

due to drug eruptions and started steroid pulse therapy, followed by oral prednisolone administration. The skin rashes and clinical symptoms improved, and prednisolone was tapered off.

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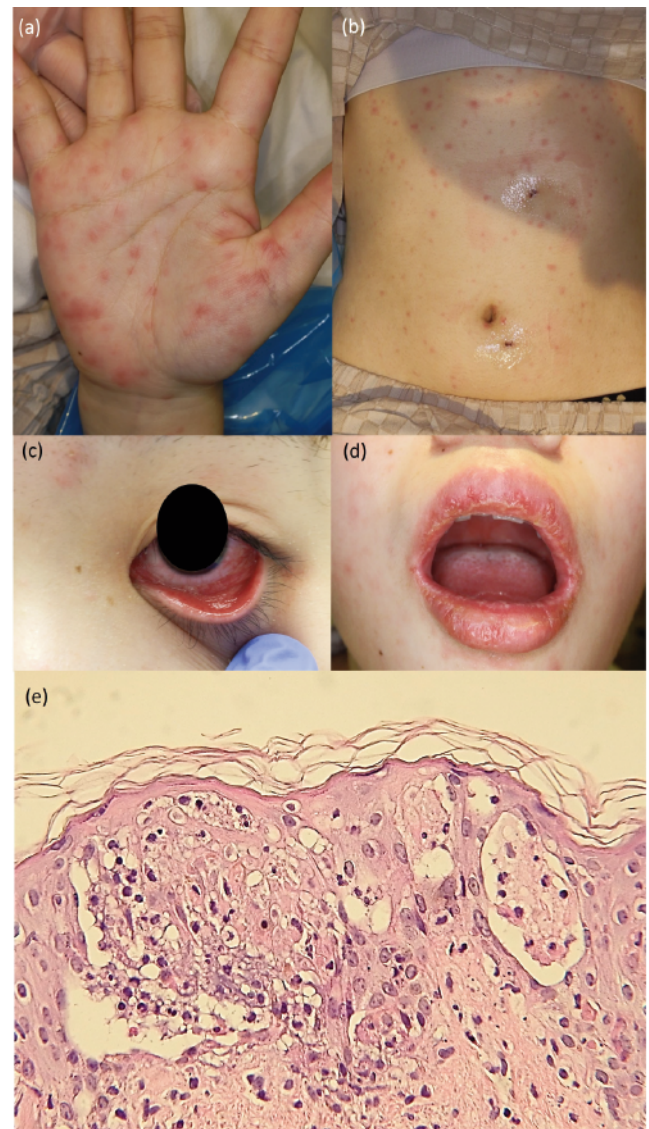
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**Figure 1.** a, b) Erythematous papules are scattered on the palm and trunk; c) the ocular conjunctiva is hyperemic; d) lips are swollen and fissured with some erythematous papules on the face; e) a skin biopsy of the trunk showing epidermal necrosis in intra-epidermal vesicle containing lymphocytes and neutrophils.

The oral challenge test for both drugs, which was performed later, was negative. Virological examination revealed that the neutralizing antibody for coxsackievirus (CV)A16 increased significantly in the paired sera; CVA6 and enterovirus (EV) 71 were negative. Since skin rashes were mainly on the soles and palms, we diagnosed the patient with hand-foot-mouth disease (HFMD). Histopathologically, necrosis of the epidermis with neutrophil infiltration was atypical of a drug eruption, consistent with the HFMD.<sup>1</sup>

HFMD is a common viral infection among children and is caused by CVA6, CVA16, and EV71. The disease is characterized by fever, malaise, and skin rashes. HFMD disease induced by CVA6 is known to cause atypical or severe skin rashes and systemic symptoms in adults.<sup>2</sup> However, HFMD caused by CVA16 has never been reported to show severe skin and mucocutaneous rashes, as in our case.

In general, the treatment of HFMD is preservative. However, owing to the history of the causative drugs, we initially suspected erythema multiforme as drug eruption, and high doses of steroids were administered. A case of HFMD caused by CVA6, clinically suspected as Stevens-Johnson syndrome, and systemically treated with steroids has been reported.<sup>2</sup> Although extremely rare, a healthy person may have HFMD caused by CVA16 presenting

with severe clinical symptoms, mimicking erythema multiforme. HFMD should be diagnosed serologically. A definitive diagnosis at the first visit is difficult. If a patient has a severe drug eruption, a delay in the systemic administration of steroids may cause sequelae. When a patient presents with systemic skin rashes, predominantly on the soles and palms, and mucocutaneous rash, considering the patient's history and general condition, systemic steroids should be administered, in accordance with the treatment of severe drug eruption. A detailed physical examination of the entire body and a virological examination could be necessary to diagnose HFMD. We recognize the limitations of our small sample size and the need to study more patients.

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## References

1. Böer-Auer A, Metze D. Histopathology of hand-foot-mouth disease in adults and criteria for differentiation from erythema multiforme. *Am J Dermatopathol* 2019;41:273-80.
2. No TH, Jo KM, Jung SY, et al. Coxsackievirus A6-induced hand-foot-and-mouth disease mimicking Stevens-Johnson syndrome in an immunocompetent adult. *Infect Chemother* 2020;52:634-40.