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Hand, foot, and mouth disease progressing into sialadenitis in an adult patient: a rare complication

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Dear Editor,

In April 2024, a 24-year-old non-smoker female patient with controlled asthma presented with a sore throat, left-sided cervical lymphadenopathy, and a painful, red maculopapular rash on the hands and feet (Figure 1 A,B). Intraorally, multiple ulcers were observed on the soft palate (Figure 1C). She reported that her niece had experienced similar lesions over the past 2 weeks. Subsequently, the patient developed severe pain, dysphagia, difficulty in mouth opening, and fever, prompting her to attend the emergency room. She was managed supportively with analgesics and intravenous (IV) fluids before discharge. The following day, she experienced severe pain on the left side of the face and neck and developed trismus. She presented to the emergency department with nausea, vomiting, hypotension (blood pressure 88/57), and hoarseness in voice, with a swelling that rapidly developed on the left submandibular area (Figure 1D). Intraorally, there was no pus discharge detected from the orifice of Wharton's duct, indicating a non-bacterial infection.

Neck computerized tomography without IV contrast showed moderate swelling of the left submandibular salivary gland with associated mild fat stranding and a reactive lymph node, consistent with sialadenitis, without evidence of stones or ductal dilatation. Panoramic radiograph showed no dental or jaw lesions. All relevant blood tests were normal except for increased C-reactive protein, neutrophils, and monocytes, while lymphocytes, serum sodium, and serum urea were reduced. Virology was positive for Coxsackievirus B (CVB; 1-6) IgG and IgM.

She was prescribed paracetamol 1.0 g IV, methylprednisolone 40 mg IV, and ondansetron 8 mg IV to reduce nausea, as well as a magic mouthwash consisting of a 1:1:1:1 mixture of sodium bicarbonate, nystatin, dexamethasone, and xylocaine.

After 2 days of hospitalization, the swelling in the left submandibular region had completely resolved. Given her stable clinical condition, the patient was discharged. She remains well, with no recurrence, 12 months after the infectious episode.

Hand, foot, and mouth disease (HFMD) has lately shown new trends in manifestations and severity of symptoms, with a spectrum of signs and symptoms that require close monitoring and appropriate management to prevent possible complications. Classically, HFMD is caused by Coxsackievirus A16 (CVA16); however, CVA6 has become a major cause of HFMD outbreaks worldwide in recent years.[1] This strain has also been associated with adult HFMD, and since 2008, a more severe CVA6 variant has emerged as a global cause of this disease, leading to an increase in adult cases.[1] CVA6 has also been linked to a more severe, "atypical" presentation that may include a higher fever, longer duration of symptoms (often 2 weeks), a wider distribution of skin findings, delayed desquamation at the palms and soles, and onychomadesis.[1]

In the current case, CVB was identified as the cause, which highlights the role of this strain in causing adult HFMD, besides the already confirmed strain of CVA.

Sun *et al.* (2018) reported that severe infection of HFMD is characterized by a history of contact with infected children, fever for >3 days, vomiting, limb trembling, lethargy, convulsions, and pathologic reflexes.[2] Group B CVs are known to cause spastic paralysis attributed to degeneration of neuronal tissue and focal muscle injury. They also cause infection of the heart, pleura, pancreas, and liver, causing pleurodynia, myocarditis, pericarditis, hepatitis,[3] and systemic neonatal disease.[4]

Less than 1% of adults affected by HFMD develop symptoms.[1] These patients should be closely monitored to control severe symptoms, particularly orofacial manifestations of oral ulcers and sialadenitis. Adult cases of HFMD are often clinically atypical, frequently presenting with extensive skin lesions, including blisters and purpuric rashes.[5] Other reported complications include onychomadesis,[6] nephrotic syndrome,[7] and exacerbation of bullous pemphigoid.[8] Salivary complications, such as excessive salivation associated with sore throat, have been rarely reported;[9] however, no cases of viral sialadenitis caused by CVs have been documented. Despite the identification of CVs among the viruses causing sialadenitis, no cases have been reported in the literature yet. Further, no cases have been reported for HFMD progressing into sialadenitis. In this patient, the causative virus was CVB. This virus exerts its pathogenic influence by binding to CV and adenovirus receptor (CAR), as well as decay-accelerating factor (CD55).[10] Both of these receptors are expressed in various epithelial tissues, including salivary glands, where they facilitate cellular adhesion and viral entry (CAR), particularly for Coxsackie B viruses. Our

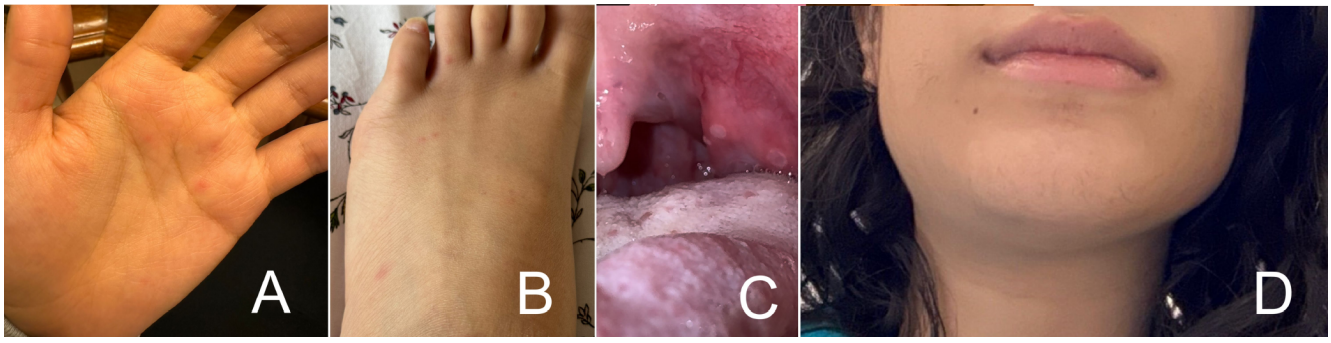


Figure 1. Mucocutaneous lesions and submandibular sialadenitis developing in an adult female with hand, foot, and mouth disease. **A, B**) Maculopapular rash affecting the hands and feet; **C**) oral ulcers affecting the soft palate; and **D**) left submandibular sialadenitis.

patient had a compromised airway due to swelling in the submandibular area. Fever and associated oral ulcers predisposed the patient to difficulty in eating and swallowing, which necessitated emergency treatment to control infection and supplement hydration and nutrition. The anticipated adverse outcomes of HFMD in adult patients necessitate timely diagnosis, immediate management, and close monitoring to prevent complicated outcomes that may develop into potentially life-threatening complications.

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Availability of data and materials: all data underlying the findings are fully available.

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