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CASE STUDY

Papulo-vesicular eruption and profound unilateral hearing loss in a 20-year-old man

Henning Klapproth[1] | **Jonas Rauterberg**[1] | **Sami Shabli**[2] | **Steffi Silling**[3] | **Sindy Böttcher**[4] | **Esther von Stebut**[1] | **Mario Fabri**[1,5]

[1]Department of Dermatology and Venereology, Faculty of Medicine, University of Cologne, and University Hospital of Cologne, Cologne, Germany

[2]Department of Otorhinolaryngology, Head and Neck Surgery, Faculty of Medicine, University of Cologne, and University Hospital of Cologne, Cologne, Germany

[3]Institute of Virology, Faculty of Medicine, University of Cologne, and University Hospital of Cologne, Cologne, Germany

[4]National Reference Centre for Poliomyelitis and Enteroviruses, Robert Koch Institute, Berlin, Germany

[5]Center for Molecular Medicine Cologne (CMMC), Faculty of Medicine, University of Cologne, Cologne, Germany

Correspondence
Henning Klapproth, MD, Department of Dermatology and Venereology, University Hospital Cologne, Kerpener Strasse 62, 50937 Köln, Germany.
Email: henning.klapproth@uk-koeln.de

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coxsackie A6, enterovirus, Papulovesicular exanthema, sudden sensorineural hearing loss

HISTORY AND CLINICAL FINDINGS

A 20-year-old man presented to our clinic with a non-pruritic exanthema that had developed over the previous 2 days favoring the palms and spreading to the trunk. On the palms, irregularly formed, sharply demarcated, bright-erythematous macules and papules in conjunction with translucent, polygonal, targetoid vesicular to bullous lesions were present (Figure 1a). Additionally, partially erupted or crusted, round papulovesicles measuring 1–2 mm in diameter with erythematous halo were grouped on flexural surfaces and showed disseminated distribution on the trunk (Figure 1b–d). There were no mucosal findings; genitals, perineal surfaces were spared; no signs of scabies were seen. Lymphadenopathy was not present. In the course of disease, acral desquamation was noted.

One day before presenting to our clinic, the patient noticed impaired hearing of his right ear. A unilateral profound, sudden sensorineural hearing loss (SSHL) was diagnosed and confirmed by our clinic's otorhinolaryngology specialists (Figure 2). The right tympanic membrane was occupied by two vesicles. The auditory canal was spared. Tinnitus, vertigo, and acoustic trauma were denied.

The patient lived in a monogamous, homosexual relationship. Two weeks prior, his partner had developed similar cutaneous symptoms that were treated with an unknown oral antibiotic plus cortisone and had disappeared within 10 days. He reported that a previously performed screen for sexually transmitted infections was negative.

His past medical history was positive for atopic dermatitis. Otherwise, he had no chronic disease and denied regular drug intake or allergies. Laboratory findings revealed increased ALAT (96 U/l; normal range < 50 U/l), increased γ-GT (314 U/l; normal range < 60 U/l), increased CRP (18.2 mg/l; Normal range < 5.0 mg/l). The lymphocyte count was decreased (970/µl; normal range 1,260–3,300/µl).

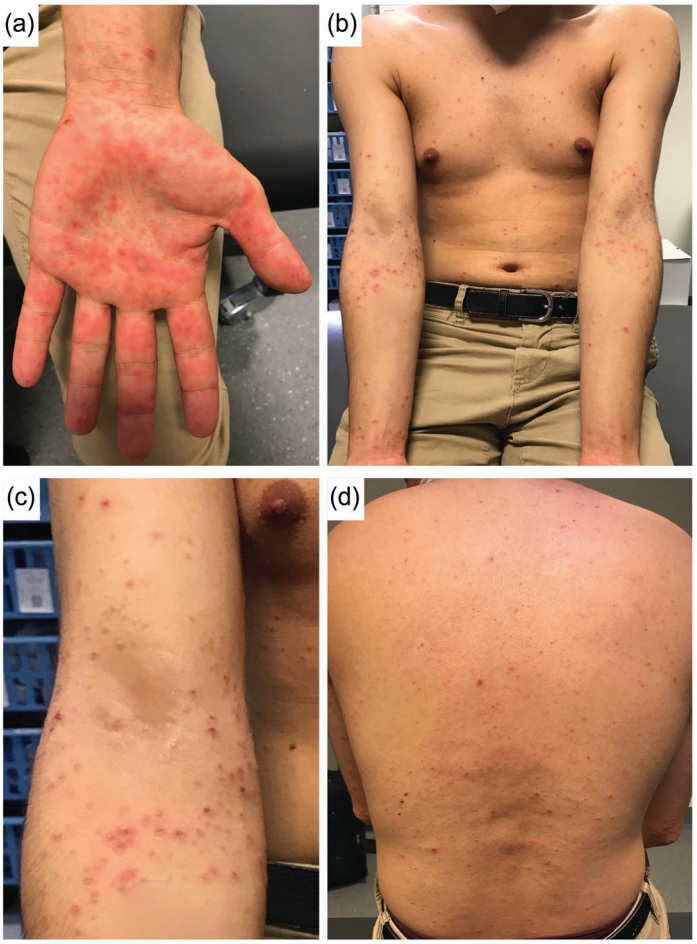

FIGURE 1 (a) Papulo-vesicular exanthema of the palms, (b, c) of the flexural upper extremity, (b) ventral trunk and (d) dorsum at admission. Note: Tattoos on both forearms were turned unrecognizable.

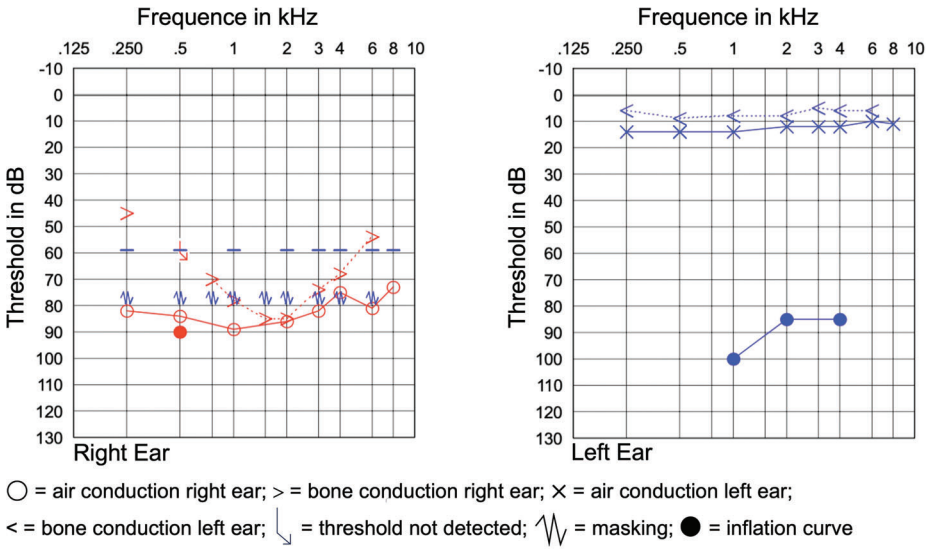

FIGURE 2 Pure-tone threshold audiometry of the right and left ear showing profound, pantonal sensorineural hearing loss of the right ear at admission.

Your diagnosis? …

Diagnosis:
Atypical hand, foot, and mouth disease (HFMD)

DIAGNOSTIC WORKUP

Due to sudden onset and previously diseased partner, we suspected a primarily infectious cause. The *Treponema pallidum* particle agglutination assay (TPPA) remained negative. Vesicular fluid from skin lesions tested negative for herpes simplex virus (HSV), varicella-zoster virus (VZV), and monkeypox (MPX) virus by polymerase chain reaction (PCR). The immediate cerebrospinal fluid puncture ruled out meningitis and acute syphilitic central nervous impairment. Cerebrospinal fluid remained negative for Lues IgG/IgM, as well as Epstein-Barr virus (EBV)-, cytomegalovirus (CMV)-, HSV1/2-, and VZV-DNA. However, PCR of serum and stool samples were positive for enterovirus-RNA. Further analysis of the serum identified Coxsackievirus A6-RNA. Cerebrospinal fluid analysis for enterovirus RNA was negative.

CLINICAL COURSE

After admission, the patient was initially treated with acyclovir in suspicion of disseminated varicella infection affecting the CNS. With regard to the SSHL, cortisone pulse therapy starting at 250 mg prednisolone was initiated. After virology results showed enteroviral infection, acyclovir was terminated. Local therapy with corticosteroid-free macrogol- and zinc oxide-containing drying lotion was continued until dismissal.

DISCUSSION

Typical hand-foot-and-mouth disease (HFMD) caused by enterovirus infection presents as a vesicular eruption of palms and soles.[1] Typically, these changes go along with oral vesicular or erosive lesions and can be accompanied by fever and malaise,[1] all of which were not present in this case.

Enteroviruses are highly contagious and spread from human-to-human by fecal-oral or respiratory transmission.[1]

Atypical HFMD caused by Coxsackievirus A6 often presents with extensive, disseminated papulo-vesicular exanthema of the trunk (Figure 1b–d) and typically spares the oral mucosa.[2,3] Hand-foot-and-mouth disease caused by Coxsackievirus A6 is characterized by a higher incidence in adults and winter onset compared to HFMD induced by other viruses.[4] Dorsal aspects of hands and feet were not involved in our patient, but are often found in atypical HFMD.[2] Whereas in typical HFMD, bullae and crusts usually do not develop, these features are frequently found in atypical HFMD.[2] Additionally, Koebner phenomenon of underlying skin diseases, such as psoriasis, following HFMD is possible.[5] Remarkably, inspection of cubital and carpal flexural surfaces of both arms showed accentuated eruption in areas of pre-existing atopic dermatitis (Figure 1b),[3] thereby resembling aspects of eczema coxsackium.[6]

Causative relation of enterovirus infection and SSHL has continuously caused reason for debate.[7] However, availability of PCR has improved screening for viral infectious causes of SSHL, among which enteroviruses have been identified.[8,9]

Neurocutaneous disorders with papulo-vesicular manifestations and SSHL are challenging to diagnose clinically. In primary VZV infection, CNS involvement and acral manifestation of vesicles are uncommon; yet, it is frequently observed in immunocompromised patients.[10] Depending on the affected dermatome(s) and the patient's immune status, neurological involvement can occur in (disseminated) herpes zoster.[10] In secondary syphilis, SSHL, vertigo, or tinnitus are suggestive of otosyphilis and should be regarded as part of an acute meningitic syndrome.[11,12] Rapid spread of monomorphic, crusted erosions and vesicles along flexural sites can represent eczema herpeticum as a complication of atopic dermatitis.[13] Targetoid vesicular to bullous skin changes can also mimic erythema multiforme.[14] Albeit HFMD commonly manifests as a mild disease, cardiopulmonary and neurologic complications, such as SSHL, can occur.[4] Therefore, auditory symptoms should be inquired. Due to its infectiousness, it is important to recognize and correctly diagnose typical as well as atypical HFMD. Meanwhile, considering different diagnoses causing papulo-vesicular exanthema, especially in the context of CNS involvement, can be pivotal.

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CONFLICT OF INTEREST STATEMENT

M.F.: Lecture fees: AbbVie, medupdate, Consilium (InfectoPharm), Forum für Medizinische Fortbildung; Consulting fees: Novartis, LEO Pharma; Member of professional societies/committees: Arbeitsgemeinschaft Dermatologische Forschung (Working Group for Dermatological Research), Deutsche Dermatologische Gesellschaft (German Dermatological Society), European Society for Dermatological Research, Arbeitsgemeinschaft für Dermatologische Infektiologie und Tropendermatologie (Working Group for Dermatological Infectiology and Tropical Dermatology), Deutsche STI Gesellschaft (German STI Society), Kommission Antiinfektiva, Resistenz und Therapie am Robert Koch Institut (Committee for Anti-Infective Agents, Resistance, and Treatment at the Robert Koch Institute, Berlin). All other authors declare no conflicts of interest.

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