

Atypical hand, foot, and mouth disease in adults



To the Editor: We read with interest the paper by Second et al¹ on atypical hand, foot, and mouth disease (HFMD) in adult patients mainly caused by coxsackievirus (CV) A6 and would like to share our experience with this disease.

In the last 2 years, we observed 34 adults 19-42 years old with HFMD mostly during the spring and autumn, when picornaviruses usually circulate in our climate zone.² All patients had nonspecific symptoms, mainly gastrointestinal symptoms but also low-grade fever, asthenia, and sore throat. Erythematous-vesicular oral lesions were infrequently found (3/20 patients, 15%), and 7/20 patients (35%) did not show any mucosal lesions. As reported for picornavirus infections,² most patients (11/20, 53%) showed oral petechiae, and frequently patients had a strawberry tongue (5/20 patients, 25%). All patients showed erythematous-vesicular lesions on the hands. In 8 patients (40%), these lesions were localized only to the extensor and lateral surfaces of the fingers. Similar lesions occurred on the feet in 12/20 patients (60%), and in 11 patients (58%), they involved only the extensor surface and the borders of the toes. The lesions were described as painful, burning, or itchy. In most patients (19/20 patients, 95%), vesicular lesions were present on the trunk, raising reasonable doubt that lesions were due to chickenpox. However, the lesions were never pustular and rarely umbilicated (only 4/20 cases). The buttocks and genitalia were rarely involved. The lesions healed within 10-20 days (average of 14 days) with slight scaling.

In 20 patients, the virologic features were also studied (Table 1) by means of virus neutralization tests and complement fixation against CV. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) to amplify enterovirus sequences in the serum were performed as previously described.³ An IgM antibody response or a ≥ 4 -fold increase of IgG antibody titers in paired (acute and convalescent) serum specimens were considered a reliable indicator for active infection. In some patients, both serology and real-time RT-PCR were performed. A CV infection was demonstrated in all patients with HFMD. The most frequent type was CV-A6 (8/20 patients, 40%), followed by CV-A16 (4/20 patients, 20%), CV-A9 (4/20 patients, 20%), CV-A7 (2/20 patients, 10%), CV-A21 (1/20 patients, 5%), and CV-A24 (1/20 patients, 5%).

The claimed rarity of HFMD in adults is in contrast with our experience (34 cases in 2 years). Possibly, most of the adult cases are clinically atypical² and erroneously diagnosed as atypical exanthems or drug reactions. In fact, vesicular oral lesions were rare in our patients and often petechiae or strawberry tongue were detected instead. The lesions involved more frequently the hands than the feet and were often limited to the extensor and lateral surfaces of the fingers, hands, toes, and feet. Notably, vesicular lesions were frequently spread on the trunk mimicking chickenpox. However, chickenpox gives more severe prodromal symptoms and a centripetal distribution of the lesions that usually appear as hundreds and in crops. Furthermore, chickenpox lesions quickly progress from papules to vesicles and then to pustules, with the different forms appearing at different stages. They are intensely itchy and resolve with crusts.⁴ Last, we would like to stress that several types of CVs can cause atypical HFMD and that, as found by Second et al,¹ CV-A6 definitely prevails. There is a marked variation in the clinical expression of a viral infection; the same virus might cause a different pattern of exanthem during the same epidemic or even in the same patient.⁵

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REFERENCES

1. Second J, Velter C, Calès S, Truchetet F, Lipsker D, Cribier B. Clinicopathologic analysis of atypical hand, foot, and mouth disease in adult patients. *J Am Acad Dermatol.* 2017;76(4):722-729.

Table I. Clinical and virologic features of 20 adult patients with hand, foot, and mouth disease

Patient no.	Sex	Age, y	Month	Oral mucosa involvement	Skin involvement	Lesions umbilication	Skin symptoms	Scab formation	Symptoms	Virus detection	Virus detection method	Clinical resolution time, d
1	F	42	May	Oropharyngeal petechiae, strawberry tongue	Erythematous vesicles on palms and soles; papulovesicles on trunk (>10 elements) and limbs	No	Burning, pruritus	None, only palmoplantar desquamation	Fever, cough, conjunctivitis, asthenia, headache, abdominal pain	CV-A24	Serology	20
2	F	40	June	Oropharyngeal petechiae	Erythematous-macular vesicles on palms and soles; vesicles on trunk (>10 elements) and face	No	Pruritus	None, only palmoplantar desquamation	Asthenia, inappetence	CV-A7	Serology	15
3	M	24	June	Oropharyngeal petechiae, vesicles on lips	Erythematous vesicles on trunk (>10 elements), scalp, buttocks, extensor surfaces, and hands (borders of fingers) and feet	No	Pain, pruritus	None, only desquamation	Fever, soar throat, asthenia	CV-A9	Serology	14
4	M	28	Sept	None	Erythematous vesicles on palms, soles, and genitalia	No	Burning, pain, pruritus	None, only desquamation	Asthenia, abdominal pain	CV-A6	Serology and real-time RT-PCR	10
5	F	24	June	Petechiae, strawberry tongue	Erythematous vesicles on trunk (<10 elements), feet (dorsum and borders), and hands (borders of fingers)	No	Pruritus	None	Fever, diarrhea	CV-A9	Serology	14

Continued

Table I. Cont'd

Patient no.	Sex	Age, y	Month	Oral mucosa involvement	Skin involvement	Lesions umbilication	Skin symptoms	Scab formation	Symptoms	Virus detection	Virus detection method	Clinical resolution time, d
6	M	21	May	None	Erythematous vesicles on trunk (<10 elements); vesicles on hands (dorsum and border of fingers)	No	Burning, pain	None	Fever, sore throat, abdominal pain, diarrhea	CV-A6	Real-time RT-PCR	18
7	M	30	Sept	Petechiae, strawberry tongue	Erythematous vesicles on trunk (>10 elements) and limbs; vesicles on hands (palms and borders of fingers) and feet (soles)	No	None	None	Fever, soar throat, asthenia	CV-A6	Serology and real-time RT-PCR	14
8	F	20	July	Palatal petechiae	Erythematous vesicles on trunk (>10 elements) and buttocks; vesicles on hands (dorsum and borders of fingers)	No	Burning	None	Asthenia, headache	CV-A16	Serology and real-time RT-PCR	15
9	F	23	May	Vesicles	Erythematous vesicles on trunk (>10 elements), hands (palms and borders of fingers), and feet (dorsum)	No	Burning, pain	None, only desquamation	Fever, arthralgias, abdominal pain	CV-A6	Real-time RT-PCR	14
10	F	31	June	Petechiae, strawberry tongue	Erythematous vesicles on trunk (<10 elements) and hands (dorsum and borders of the fingers)	Yes	Burning, pain	None	Asthenia, nausea, abdominal pain	CV-A6	Real-time RT-PCR	10

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Table I. Cont'd

Patient no.	Sex	Age, y	Month	Oral mucosa involvement	Skin involvement	Lesions umbilication	Skin symptoms	Scab formation	Symptoms	Virus detection	Virus detection method	Clinical resolution time, d
11	M	26	April	None	Erythematous vesicles on trunk (<10 elements) and hands (palms and borders of fingers)	No	Burning	None	Sore throat	CV-A7	Serology	12
12	F	20	Oct	Oropharyngeal petechiae	Erythematous vesicles on trunk (<10 elements), hands (palms and borders of fingers), and feet (soles)	Yes	Burning	None, only desquamation	Fever, asthenia, nausea, headache	CV-A6	Real-time RT-PCR	14
13	M	19	June	None	Erythematous vesicles on trunk (<10 elements), hands (dorsum and borders of fingers), and feet (dorsum)	No	Burning, pain	None, only desquamation	Fever, asthenia, sore throat, nausea, inappetence	CV-A16	Serology and real-time RT-PCR	12
14	F	19	May	Oropharyngeal petechiae	Vesicles on trunk (<10 elements), buttocks, hands (palms and borders of fingers), and feet (borders of toes)	No	Burning	None, only desquamation	Asthenia, abdominal pain	CV-A16	Serology and real-time RT-PCR	15
15	M	28	April	Palatal petechiae, strawberry tongue	Vesicles on trunk (<10 elements) and hands (palms and borders of fingers)	No	Burning, pain	None	Asthenia, sore throat	CV-A6	Real-time RT-PCR	12

Continued

Table I. Cont'd

Patient no.	Sex	Age, y	Month	Oral mucosa involvement	Skin involvement	Lesions umbilication	Skin symptoms	Scab formation	Symptoms	Virus detection	Virus detection method	Clinical resolution time, d
16	M	23	July	None	Erythematous vesicles on trunk (<10 elements); vesicles on hands (palms, dorsum, and borders of fingers)	No	Burning, pruritus	None	Asthenia, arthralgias, sore throat	CV-A9	Serology	15
17	M	25	June	None	Erythematous vesicles on trunk (<10 elements), limbs, and hands (palms and borders of fingers)	No	Burning	None, desquamation	Asthenia, arthralgias, sore throat, abdominal pain	CV-A16	Serology and real-time RT-PCR	15
18	F	20	July	None	Erythematous vesicles on trunk (<10 elements), buttocks, and hands (dorsum and borders of fingers)	No	Pruritus	None, only desquamation	Sore throat, asthenia, headache	CV-A9	Serology	12
19	M	21	May	Vesicles on the tongue borders and gums	Erythematous vesicles on trunk (>10 elements) and buttocks; vesicles on hands (dorsum and borders of fingers) and feet (borders of toes)	No	Burning, pain	None, only desquamation	Fever, sore throat	CV-A6	Serology and real-time RT-PCR	15
20	F	36	Oct	Oropharyngeal petechiae	Erythematous vesicles on trunk (>10 elements), face, and limbs; vesicles on hands (palms and borders of fingers) and feet (dorsum)	No	Burning, pain	None, only hand desquamation	Fever, sore throat, asthenia, abdominal pain	CV-A21	Serology	20

CV, Coxsackievirus; F, female; M, male; Oct, October; RT-PCR, reverse transcriptase polymerase chain reaction; Sept, September.

2. Drago F, Paolino S, Rebora A, et al. The challenge of diagnosing atypical exanthems: a clinico-laboratory study. *J Am Acad Dermatol*. 2012 Dec;67(6):1282-1288.
3. Drago F, Ciccarese G, Broccolo F, Toniolo A, Javor S, Parodi A. Localized exanthem due to echovirus 9. *J Med Virol*. 2015;87:1447-1448.
4. Drago F, Ciccarese G, Gasparini G, et al. Contemporary infectious exanthems: an update. *Future Microbiol*. 2017;12:171-193.
5. Drago F, Rebora A. Viral reactivation and skin eruptions. *Dermatology*. 2003;207:1-2.

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