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Hand-foot-mouth disease in the elderly: A case report

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ABSTRACT

Hand-foot-mouth disease (HFMD), commonly caused by Coxsackievirus A16, is a contagious illness characterized by fever and vesicles on the hands, feet, and oral cavities. While well-documented in children, it is exceptionally rare in older adults. The case of a 65-year-old. illustrates this woman who presented at Dr. Sardjito General Hospital, Yogyakarta, with red spots on her hands and feet. Examination revealed multiple erythematous plaques on her palms, forearms, and lower legs, alongside target-like plaques with pseudo-vesiculation and a solitary oral ulcer. This case underscores the unusual presentation of HFMD in the elderly, highlighting that the disease, though predominantly pediatric, can occur in the elderly. The atypical clinical findings highlight the urgent need for accurate and timely recognition to ensure appropriate management. This report contributes to the growing evidence on HFMD's clinical spectrum in adults and signals the necessity for further research and case documentation to improve understanding and early diagnosis in the elderly population.

ABSTRAK

Penyakit kaki, tangan, dan mulut (PKTM) yang umumnya disebabkan oleh Coxsackievirus A16, adalah penyakit menular ditandai dengan demam dan vesikel pada tangan, kaki, serta rongga mulut. Meskipun banyak didokumentasikan pada anak, kasus pada lansia sangat jarang. Hal ini diilustrasikan oleh kasus seorang wanita berusia 65 tahun yang berobat ke RSUP Dr. Sardjito, Yogyakarta dengan keluhan bercak merah pada tangan dan kaki. Pemeriksaan menunjukkan plak eritematosa multipel pada telapak tangan, lengan bawah, dan tungkai bawah, disertai plak menyerupai target dengan pseudovesikulasi dan ulkus tunggal di mulut. Kasus ini menegaskan kejadian PKTM yang tidak biasa pada lansia, meskipun sebagian besar kaus terjadi pada anak. Temuan klinis atipikal tersebut menegaskan perlunya diagnosis yang akurat dan tepat waktu untuk memastikan tatalaksana yang tepat. Laporan ini berkontribusi pada bukti yang berkembang mengenai spektrum klinis PKTM pada dewasa dan menunjukkan perlunya penelitian lebih lanjut serta dokumentasi kasus untuk meningkatkan pemahaman dan diagnosis dini pada populasi lansia.

Keywords:
Hand-foot-mouth disease (HFMD);
elderly;
coxsackievirus infection;
Coxsackievirus A16;
Atypical presentation

INTRODUCTION

Hand-foot-mouth disease (HFMD) is a common viral infection, typically affecting young children and characterized by fever, oral ulcers, and a vesicular rash on the hands and feet. While adult cases are increasingly recognized, diagnosis remains primarily clinical, and management is focused on supportive care such as analgesia and hydration, as no specific antiviral therapy exists.[1] Hand-foot-mouth disease primarily affects infants and children, characterized by fever, sore throat, and painful lesions on the

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hands, feet, and mouth.[1] Coxsackievirus A16 is the most common cause, other enteroviruses can also be responsible.[2] Although traditionally considered a childhood disease, adult cases have been increasingly reported in recent years. The infection spreads easily through contact, particularly among children whose immune systems are still developing. Diagnosis is mainly clinical, based on the characteristic symmetric rash, with molecular diagnosis or skin biopsy available for confirmation. Treatment is supportive, focusing on pain relief, hydration, and blister care, as antibiotics are ineffective and no specific antiviral treatment or vaccine currently exists.[3]

Adult and geriatric patients frequently appear with a more severe and morphologically diverse clinical picture than the typical juvenile presentation. In adults, HFMD may present with a broader more widespread distribution of skin lesions involving atypical sites, such as the trunk, buttocks, perioral region, limbs, and even the scalp, rather than being restricted to the palms, soles, and oral mucosa typical of children.[4] Additionally, infections, especially those associated with Coxsackievirus A6, can produce atypical exanthems with targetoid or erythema multiforme (EM)-like appearances, vesiculobullous lesions, and purpuric eruptions, which may lead to misdiagnosis and diagnostic confusion with EM or other dermatoses.

Atypical HFMD presentations in adults are crucial for timely diagnosis and management. While typically a mild, self-limiting illness in children, HFMD in adults and particularly in elderly patients, in whom the disease remains rare, often presents with more severe symptoms that can mimic other skin conditions, leading to potential misdiagnosis and treatment delays. Improved awareness and understanding of HFMD in adults can lead to better results and prevent complications in this increasingly affected population. Given the rising incidence and atypical manifestations in adults, timely recognition is crucial to avoid misdiagnosis, unnecessary treatments, and potential complications. This case report aimed to highlight the atypical clinical features and diagnostic pitfalls of HFMD in an elderly patient, emphasizing the importance of considering this condition in the differential diagnosis of acute vesiculopapular and erythema multiforme-like eruptions beyond the pediatric population.

CASE

A 65 year-old woman presented to the outpatient clinic at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, with red patches on her hands and feet. She reported that the rash began approximately 2 weeks ago, first appearing on her forearms, palms, and feet, and gradually fading. This was followed by a fever above 38°C and an ulcer on her lower lip. After 6 days prior to her visit, the patient had been prescribed amoxicillin 500 mg 3 x/d, diclofenac sodium 50 mg 2 x/d, and methylprednisolone 4 mg 3 x/d by an internal medicine specialist for foot pain.

The skin lesions remained unchanged even though the pain improved. As a result, she was referred to dermatology, venereology, and an aesthetic specialist to rule out the possibility of a complicated SSTI or HFMD. None of her family members or close contacts has experienced similar symptoms, and she has no significant history of chronic medication use. She is a housewife.

The patient's vital signs showed normal symptoms: blood pressure 101/71 mmHg, pulse rate 81 bpm, respiratory rate 20 bpm, and body temperature 36.6°C. Physical examination showed numerous erythematous plaques of varying shapes and sizes on both palms, forearms, and feet. A poorly defined erythematous plaque with pseudo-vesiculation, resembling a targeted lesion, was noted on the right upper arm, along with a single aphthous ulcer on the lower lip as presented in FIGURE 1.

The differential diagnosis includes EM minor, Sweet Syndrome, secondary syphilis, Morbus Hansen (MH), primary cutaneous T-cell lymphoma, and primary cutaneous diffuse large B-cell lymphoma (leg type). Additional diagnostic tests ruled out syphilis, as the VDRL and TPHA results were non-reactive. The minor criteria for Sweet syndrome were not met due to a leukocyte count of less than 8,000/μL and neutrophils below 70%. Furthermore, the absence of numbness or reduced sensitivity in the lesions helped exclude the diagnosis of Hansen's disease.

A skin biopsy revealed interface dermatitis with notable vacuolar changes and eosinophilic infiltration, ruling out erythema multiforme and Sweet Syndrome. Immunohistochemical analysis did not indicate primary cutaneous T-cell lymphoma or primary cutaneous diffuse large B-cell lymphoma (leg type). Based on the biopsy and clinical findings, a clinicopathologic conference diagnosed the patient with HFMD. Symptomatic treatment included analgesics/antipyretics, vitamin supplements, and wound care.

The diagnosis was confirmed following a skin punch biopsy (4 mm) taken from a representative lesion on the right forearm. Histopathological examination of hematoxylin and eosin (H&E) stained sections under magnification (40x to 400x) revealed features characteristic of a viral exanthem. Key findings included interface dermatitis with prominent basal vacuolar change, epidermal spongiosis, scattered dyskeratotic keratinocytes, intraepidermal vesicles containing neutrophils and eosinophils, and a mild to moderate perivascular lymphocytic infiltrate, consistent with a viral exanthem such as HFMD. To definitively exclude primary cutaneous lymphoma, an immunohistochemical (IHC) panel was performed on the biopsy specimen. Immunohistochemical analysis revealed CD3 positivity in the majority of infiltrating lymphoid cells, CD20 negativity in all infiltrating cells, and a predominance of CD4-positive T cells over CD8-positive cells. While this immunoprofile can be seen in patch-stage cutaneous T-cell lymphoma, the absence of cytologic atypia, lack of epidermotropism and absence of Pautrier microabscesses, along with the overall clinicopathologic correlation, favoured a reactive inflammatory process rather than a lymphoproliferative disorder, thereby excluding cutaneous lymphoma in this case. These findings are consistent with previously reported histopathological features of adult HFMD presenting with interface dermatitis and neutrophil-rich epidermal changes. Enterovirus PCR/typing was not performed in this case due to limited availability, the diagnosis was made based on clinicopathologic correlation.

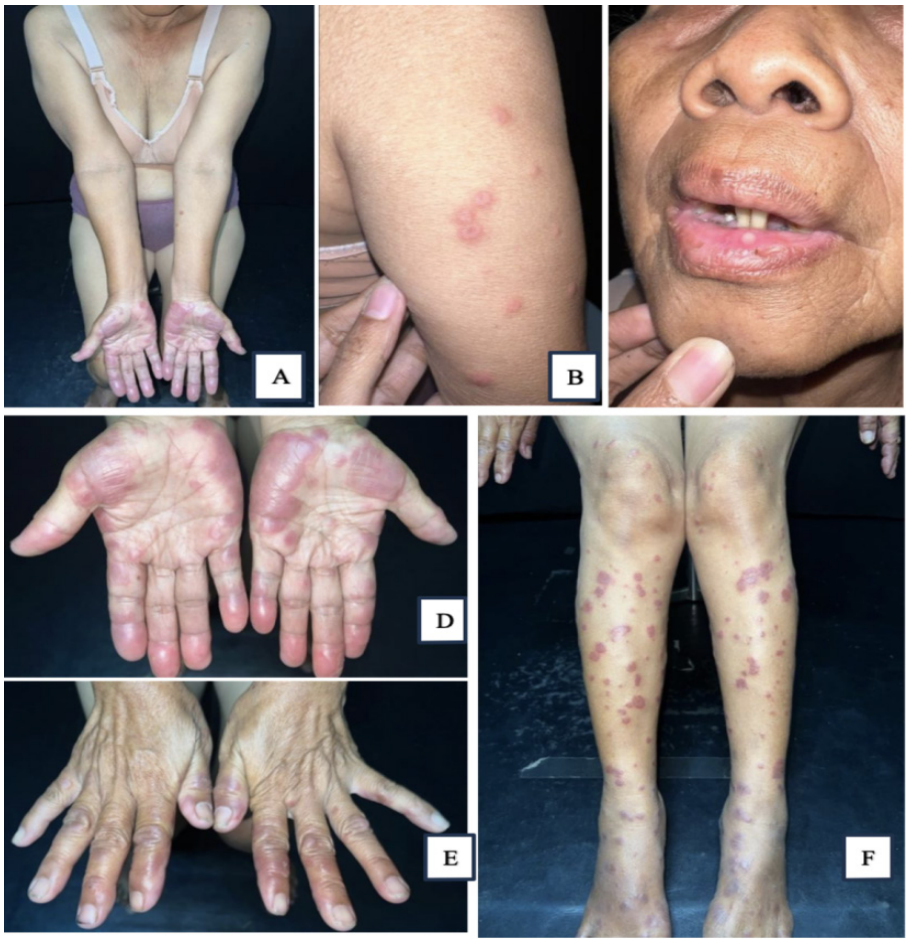

FIGURE 1. (A-F) Skin lesions at the initial clinic visit. (A): Erythematous plaque with pseudo-vesiculation on the right upper arm. (B): Aphthous ulcer on the lower lip. (C-F): Multiple erythematous plaques with varying shapes and sizes on the arms, palms, and feet.

DISCUSSION

In this case, the patient's persistent target-like lesions prompted consideration of erythema multiforme, sweet's syndrome, syphilis, and cutaneous lymphomas, all of which were systematically excluded: syphilis through negative serology, sweet's syndrome via unmet clinical and hematologic criteria, Hansen's disease due to absent neurological findings, and lymphomas based on histopathological absence of atypical cells. As investigated by Weiss *et al.*,[5] the diagnostic challenge of differentiating HFMD from erythema multiforme was resolved through histopathology, which revealed interface dermatitis with a characteristic neutrophil-rich infiltrate and minimal necrosis. As investigated by previous studies, this pattern contrasts sharply with EM's presentation of significant necrosis but few neutrophils,[6] confirming the HFMD diagnosis and highlighting histopathology's critical role in distinguishing these entities in atypical adult cases.[7]

It can be challenging to differentiate between HFMD and EM lesions in adults,

particularly in the later stages of lesion development, when it can be impossible to do so. Histopathological findings show both similarities and differences. Both conditions exhibit lymphocyte-dominated dermal infiltrates, but HFMD lesions typically have fewer intradermal lymphocytes than EM lesions. Farah *et al.*,[8] also reported that Neutrophils are more commonly found in HFMD dermal infiltrates and are more likely to be present in the epidermis, a feature less common in EM. Accurate differentiation depends on evaluating the localization of necrosis and comparing neutrophil levels within the lesions. As investigated by Hoang *et al.*,[9] epidermal necrosis tends to attract neutrophils, and studies on adult HFMD cases have shown an increase in neutrophil count despite minimal necrosis. In contrast, neutrophils are rare in EM lesions, even with significant necrosis, suggesting that neutrophils play a role in HFMD rash formation. Histopathological analysis in this case also revealed interface dermatitis, a characteristic feature of HFMD (FIGURE 2). Immunohistochemistry confirmed the absence of atypical cells, ruling out primary cutaneous T-cell lymphoma and primary cutaneous diffuse large B-cell lymphoma (leg type).[10]

The patient's recent exposure to amoxicillin and a non-steroidal anti-inflammatory drug (diclofenac sodium) appropriately raised the differential diagnosis of drug-related EM, as medications are well-recognised triggers of EM and may be clinicopathologically similar to infection-associated forms.[11] However, several clinicopathological considerations argued against a primary drug-induced etiology in this case. First, the temporal relationship was not supportive, as the cutaneous eruption had already developed prior to the initiation of the suspected medications, making a causal drug reaction unlikely.[12]

Second, although both drug-related and infection-related EM can demonstrate interface dermatitis, the histopathological findings in this case were more consistent with a viral process. The biopsy showed intra-epidermal vesiculation with a neutrophil-rich inflammatory infiltrate and a relative absence of extensive epidermal necrosis or numerous necrotic keratinocytes.[13] In contrast, drug-related EM typically exhibits more prominent keratinocyte necrosis with a predominantly lymphocytic, neutrophil-poor infiltrate at the dermoepidermal junction. Taken together, the atypical temporal sequence, the neutrophil-predominant vesicular histology, and the compatible clinical distribution favored a viral etiology and supported the diagnosis of HFMD presenting with EM-like lesions rather than a drug-induced EM.[14]

Indonesian case series have reported that HFMD in adults is frequently underdiagnosed due to its atypical morphology and low clinical suspicion outside pediatric settings. In elderly patients, overlapping drug exposure and age-related immune dysregulation further obscure the diagnosis, often delaying appropriate recognition.[15] Local dermatology publications emphasize that histopathology plays a pivotal role in differentiating HFMD from erythema multiforme and drug eruptions in atypical adult presentations.[16]

The discussion can be significantly strengthened by structuring it to explicitly link the diagnostic challenges directly back to the unique aspect of this case: the patient's advanced age. Adult-onset HFMD is rare and can present with atypical, severe, or prolonged eruptions, as seen here with persistent target-like lesions, which naturally prompts a broad differential, including drug reactions and autoimmune conditions more common in older adults.[17] The systematic exclusion of these mimics, particularly drug-induced erythema multiforme,

given her recent NSAID and antibiotic exposure underscores the diagnostic pitfall. In elderly patients, in whom immunosenescence, polypharmacy, and multiple comorbidities are common, HFMD may present with atypical, erythema multiforme–like lesions, substantially increasing the risk of misdiagnosis.[18] In this case, the neutrophil-rich infiltrate and the specific pattern of epidermal necrosis were pivotal in distinguishing viral HFMD from drug-related erythema multiforme, underscoring the importance of clinicopathologic correlation to avoid unnecessary investigations and interventions in older adults.

The administration of methylprednisolone shortly after symptom onset is a highly relevant clinical detail, as systemic corticosteroids can potentially modify the presentation and course of viral exanthems. In this case, the steroid may have attenuated the inflammatory response, which could account for the partial fading of the initial rash and the absence of systemic fever at presentation. However, this immunosuppressive effect might also have contributed to the persistence and atypical morphology of the cutaneous lesions by interfering with the normal immune-mediated clearance of the virus, thereby prolonging the clinical course. This possibility underscores the diagnostic challenge in this presentation, as the steroid therapy likely blurred the classic temporal and morphological progression of HFMD, leading to a more indolent and ambiguous clinical picture that mimicked other entities like erythema multiforme.[19]

The limitations of this study include the single-case nature of the report and the absence of enterovirus PCR or viral typing, limit definitive etiologic confirmation and generalizability.

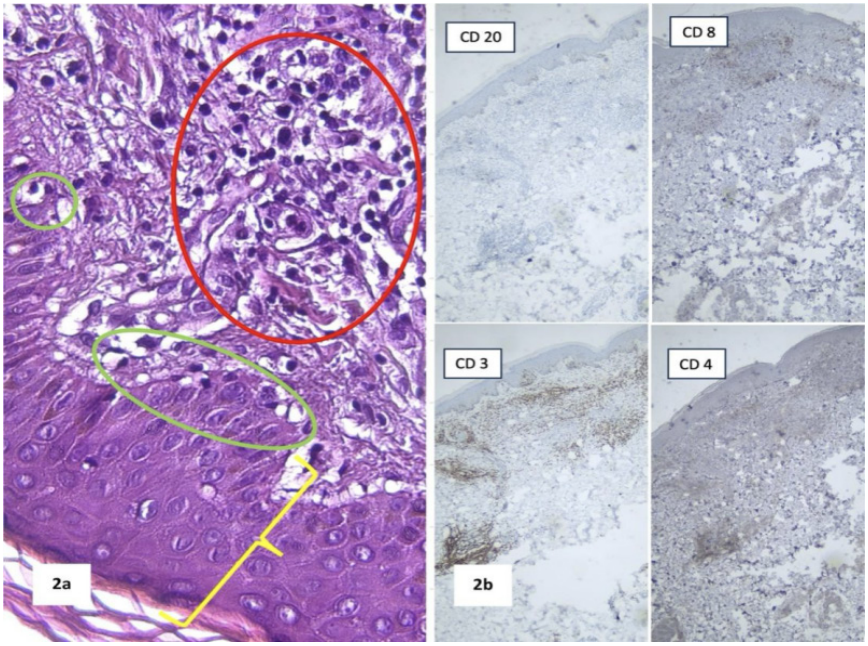

FIGURE 2. (A–B) Histopathological findings (A): HE staining showing dermal spongiosis (yellow mark), basal cell vacuolization (green circle), and inflammatory cell infiltration (red circle). No Pautrier microabscesses, epidermotropism, or atypical lymphocytes were observed (400x magnification)

HFMD spreads primarily through oral-faecal transmission, direct contact, and respiratory droplets, with children aged 1-3 years being most susceptible due to their developing immune systems and exposure in crowded environments. While incidence in adults remains low (0.38 per 100,000), age-related physiological changes, including elevated cortisol levels and immunosenescence, may contribute to susceptibility in the elderly.[19] The patient in this case responded well to symptomatic treatment comprising ibuprofen for pain relief, Becom-zet supplements, and topical desoximetasone with coconut oil, showing significant improvement within 2 wk, demonstrating the effectiveness of supportive care even in atypical adult presentations.[20] This study is limited by being a single case report despite its definitive clinicopathologic correlation, which inherently restricts the generalizability of its findings. Furthermore, the absence of viral PCR or serological confirmation, while not uncommon in clinical practice, means the specific enterovirus serotype responsible could not be identified.

CONCLUSION

This case underscores that HFMD in elderly patients can clinically mimic erythema multiforme and other inflammatory dermatoses, thereby posing a diagnostic challenge. In such atypical presentations, histopathological evaluation is decisive for accurate diagnosis, while supportive care remains an effective management strategy.

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