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บทคัดย่อ

โรคมือ เท้า ปากเป็นกลุ่มอาการที่พบได้จากการติดเชื้อคอกซาก็ไวรัส โดยเฉพาะคอกซาก็ไวรัส เอ16 และ เอนเตอโรไวรัส 71 โดยโรคนี้มักพบในเด็กเล็กและทารกแต่ก็สามารถพบในผู้ใหญ่ได้เช่นกัน ผู้ป่วยด้วยโรค มือ เท้า ปาก จะมีอาการไข้และพบรอยโรคแผลเล็กๆ หรือปั้นแดง โดยมีลักษณะเฉพาะคือพบทั้งในบริเวณช่องปาก มือและเท้า อย่างไรก็ตามลักษณะรอยโรคที่พบนั้นอาจทำให้วินิจฉัยไปเป็นโรคอื่นๆได้ บทความนี้ได้กล่าวถึงโรค มือ เท้า ปากและการวินิจฉัยแยกโรค รวมไปถึงรายงานกรณีศึกษาผู้ป่วยหญิงไทยซึ่งพบรอยโรคที่ผิวหนังรวมทั้ง รอยโรคในช่องปากโดยที่ไม่มีอาการไข้ก่อนที่จะมารับการรักษาทางทันตกรรมประจำปี โดยก่อนหน้านี้ผู้ป่วยได้รับ การวินิจฉัยว่าเป็นเพียงอาการผื่นผิวหนังอักเสบ แต่ภายหลังได้รับการวินิจฉัยโรคเป็นมือ เท้า ปาก โดยใช้ลักษณะ ทางคลินิกที่ปรากฏ ผู้ป่วยได้รับยาชาทาเฉพาะที่เพื่อลดอาการเจ็บปวดในช่องปาก จากการติดตามผลการรักษา พบว่ารอยโรคหายไปได้เองภายใน 10 วันโดยไม่มีอาการแทรกซ้อนใดๆ การวินิจฉัยโรคได้อย่างถูกต้องมีความสำคัญ ต่อผู้ปฏิบัติงานทางด้านสาธารณสุขรวมทั้งทันตแพทย์ เนื่องจากรอยโรคในช่องปากอาจเป็นอาการแสดงแรก รวมทั้งลักษณะทางคลินิกที่พบอาจทำให้เกิดความสับสนในการวินิจฉัยแยกรอยโรคอื่นๆ ซึ่งอาจนำไปสู่การวินิจฉัย โรคที่คลาดเคลื่อนและอาจส่งผลต่อการให้การรักษาที่เหมาะสมต่อไป

คำสำคัญ : คอกซากีไวรัส เอนเตอโรไวรัส โรคมือ เท้า ปาก แผลในช่องปาก

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Hand-foot-and-mouth disease

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Abstract

Hand-foot-and-mouth disease (HFMD) is a condition of viral origin caused by coxsackieviruses especially coxsackievirus A16 and enterovirus 71. It generally affects infants and small children but can also cause disease in adults. Patients with HFMD have a fever with characteristic lesions in the mouth, hands and feet that may be mistaken with other diseases. This article describes HFMD and its differential diagnosis. We report a case of HFMD in a young woman in whom skin and oral lesions developed without a fever before coming for a routine dental check up. She had been diagnosed with eczema by a dermatologist before final diagnosis was established later based on clinical features. The topical anesthetic ointment was prescribed for her painful oral lesions. The whole condition cleared out by 10 days without any complications. Differential diagnosis is very important to dental and medical professionals since oral lesions may be the first signs, and associated symptoms can be confused with other ulcerative conditions, which may lead to mismanagement.

Key words: Coxsackievirus, Enterovirus, hand-foot-and-mouth disease, oral ulcer Abbreviations: HFMD: hand-foot-and-mouth disease; PCR: polymerase chain reaction

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Introduction

Hand-foot-and-mouth disease (HFMD) is a highly contagious disease caused by intestinal viruses of the Picornaviridae family, most commonly by coxsackie A16 and enterovirus 71 [1, 2]. HFMD affects primarily infants and children younger than 5 years old [1, 3]. However, cases have been reported among adolescents and adults [4]. Starting in the late 1990s, HFMD epidemics associated with enterovirus 71 have become more frequent in the Asia-Pacific region including Taiwan, Singapore and Thailand [5-7]. Here we give a concise review on HFMD, and report a case of a young Thai woman who was initially diagnosed as having an eczema on the skin but later proved to be a HFMD infection.

Hand-foot-and-mouth disease (HFMD)

HFMD is a mild infectious disease, which spreads from person to person through unwashed, virus-contaminated hands, surfaces and/or by direct contact with mucosa, saliva or feces of an infected person. The disease is commonly found in children attending crowded nurseries or daycare centers. It occurs most often in children younger than 5 years old. However, HFMD has been reported in adult community as well [1]. Individual cases and outbreaks of HFMD occur around the world. In country with temperate climates, cases occur more often. HFMD is an arising public health problem in Asia. In China, an incidence rate of 2,468,174 cases was reported in 2016 [8]. In Thailand, average incidence during January to October 2017 was a total of 60,483 cases from 77 provinces [9].

Symptoms and signs of HFMD include sore throat with or without a low-grade fever, a body rash on hands and feet usually following

the oral ulcerative lesions. Incubation period is 3-7 days. Fever is often the first sign and is usually followed by sore throat with or without poor appetite and malaise. These prodromal signs and symptoms may be mild or absent. Normally they occur 1-2 days before the onset of oral and skin lesions. The oral mucosa is usually the first site to be involved, primarily on the buccal mucosa and on the tongue [10]. By nature, the disease tends to subside within 7-10 days. Therefore, treatment is often unnecessary. However, due to its highly contagious nature, the disease can spread widely and readily among small children attending nurseries, and/or care centers, leading to burden in care and school absence. More severe clinical presentation with neurological symptoms such as meningitis, encephalitis and polio-like paralysis may occur. The risk for developing complications depends on the age and the pathogen. This disease can pose severe danger even death to immunocompromised individuals [11] or in case of neurological involvement [12].

Diagnosis of HFMD is based on clinical manifestations. Though available, laboratory identification of virus such as polymerase chain reaction (PCR) or viral isolation by culture is barely carried out. The test can be useful in specific circumstances such as outbreaks. Swabs can be taken from throat, vesicle or stool [13, 14]. Differential diagnoses to be considered include herpangina, herpes simplex infection, varicella zoster infection, aphthous stomatitis and erythema multiforme (Table 1). These viral diseases including HFMD, herpangina, herpetic gingivostomatitis and chickenpox are presented with vesicles and later ulcerations in the oral cavity [15, 16]. The cutaneous lesions of HFMD can resemble chickenpox. Though, the vesicles found in chickenpox usually start on the face and trunk and then spread to extremities. Involvement of the palms and soles and the presence of oral lesions are rare in chickenpox. In herpangina, no associated exanthema is usually seen. The distribution of the lesions of herpangina also differentiates it from primary herpetic gingivostomatitis, which affects the gingiva, whereas herpangina is mainly an oropharyngitis [15, 16]. Early lesions of HFMD may resemble that of erythema multiforme. However, the characteristic distribution of HFMD lesions on the hands and feet may help to eliminate other diseases in the differential diagnosis. Erythema multiforme also has a characteristic feature of hemorrhagic crusts at lips. Intact vesicles in the oral cavity are rarely seen and there are typically more ulcerations. Early skin lesions of erythema multiforme are usually round, erythematous, edematous papules that may look like papular urticaria. However, these lesions may enlarge and develop concentric alterations in morphologic features and color, resulting in the target-like cutaneous lesions [17]. In recurrent aphthous stomatitis, the ulcers can be seen on nonkeratinized oral mucosa. The lack of systemic symptoms may help to differentiate between the viral diseases and recurrent aphthous stomatitis [18].

Treatment of HFMD is supportive. The disease usually subsides within 7-10 days. There is no specific treatment for HFMD. Nonetheless, painful oral lesions may lead to eating difficulties. Therefore, adequate fluid intake should be guaranteed, antipyretics may be prescribed in case of high fever, and pain could be treated with analgesic drugs such as acetaminophen or ibuprofen. In the oral cavity, topical analgesia such as Kamistad(R) gel containing lidocaine may be used to relieve the pain. There have been rare reports of complications of HFMD such as aseptic meningitis, encephalitis and paroxysmal supraventricular tachycardia [19-21]. In those cases, hospitalization is required.

Diseases	Etiology	Skin lesions	Oral lesions	Other features	
HFMD	Coxsackie virus	Erythematous	Erythematous macules	A low-grade fever, malaise,	
	A16 and	macules or	and papules then	a body rash on hands and	
	Enterovirus 71	papules with	later turn into	feet. May be on the	
	(most common)	a central gray	vesicles and ulcers	proximal extremities and	
		vesicle		buttocks.	
Herpangina	Coxsackie virus	Not typically	Gray-white	Fever, malaise, sore throat	
	group A1 to	seen	papulovesicular		
	6, 8, 10 and 22		lesions that progress		
			to ulcers at posterior		
			oral cavity		

Table	1.	Differential	diagnoses	of	HFMD
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Diseases	Etiology	Skin lesions	Oral lesions	Other features
Primary	HSV-1	No	Vesicles and ulcers	Lymphadenopathy,
herpes			on the oral mucosa	malaise
simplex			and acute marginal	
virus (HSV)			gingivitis	
infection				
Chickenpox	Varicella zoster	Maculopapular	Resemble vesicles/	Lymphadenopathy,
	virus	lesions and	ulcers seen in primary	fever, headache, nausea,
		rapidly develop	HSV	vomiting, malaise
		into fluid-filled		
		vesicles on an		
		erythematous		
		base		
Aphthous	Unknown, cell	No	Non-keratinized oral	May be recurrent
stomatitis	mediated immune		mucosa	
	response			
Erythema	Immunologic	Round,	Hardly seen intact	Prodromal symptoms are
multiforme		erythematous,	vesicles, more	usually absent
		edematous	ulcerations,	
		papules,	hemorrhagic	
		targetoid lesions	crusts at lips	

A Case Report

A 22-year-old Thai woman came for a routine dental check-up at the Faculty of Dentistry, Srinakharinwirot University. She was referred to the Oral Medicine and Oral Diagnostic Clinic to evaluate several oral ulcerations after the dentist had performed a routine prophylactic treatment comprised of ultrasonic, superficial tartar cleaning, and tooth polishing of the whole mouth.

On her visit to the Oral Medicine clinic, through a complete history taking, oral examination and physical examination, we noticed multiple reddish, and slightly elevated red lesions/papules on her palms and feet (Figure 1). On intraoral examination, we observed several ulcers of 2-3 mm in diameter with an erythematous halo on labial mucosa, buccal gingiva, soft palate and ventral surface of tongue (Figure 2). These lesions were slightly painful. Three days earlier, patient had seen a doctor regarding the skin rash on her palms and a sore throat. She was diagnosed with eczema and given systemic prednisolone, and cetirizine to relieve the symptoms, along with a topical steroid to apply on the skin lesions. She declined any history of having a fever prior to the onset of the skin rash and oral ulcerations, as well as any previous symptoms in the past similar to this episode. She had a history of having small, shallow ulcers in the mouth before, but only 1-2 ulcers at a time and lasted about 7-10 days. The differential diagnosis included, HFMD, recurrent aphthous ulcerations, and Behcet's disease. The clinical impression of HFMD was made based on clinical findings including locations and distribution of skin lesions.

Management plan included, 1) discussion with the patient about the likely viral infection nature of her oral/skin conditions and its contagious nature, 2) prescription of a 5% benzocaine ointment for her painful oral lesions, 3) discontinuation of oral prednisolone, ceterizine, and topical steroid on the skin lesions, and 4) advice on self-care such as avoidance of hot and spicy foods to reduce the pain and sensitivity, regular tooth brushing without any use of alcoholcontaining mouthwash, soft diets, and care should be taken on direct/close contacts with other people especially young children. On her follow-up visit at 48 hours later, lesions on her hands and feet slightly faded away and by 10 days, the whole condition cleared out without any complications.



Fig. 1 Cutaneous lesions on hands (a) and feet (b)



Fig. 2 Multiple Aphthous-like lesions on labial mucosa (a) buccal-vestibular gingiva (b) soft palate (c) and ventral surface of tongue (d)

Discussion

As mentioned earlier, though this disease primarily affects children, however, outbreaks can be found in adults and adolescents. In this case, the patient was unable to recall how she might be exposed to the affected person. She denied having been in contact with small children and/or any community with affected individuals. Nevertheless, risk factors for HFMD exposure include attendance to nurseries, schools and/ or crowded places [22]. HFMD is usually mild and self-limiting but highly contagious. In our case, the skin lesions were developed in an adult who is otherwise healthy, presented with a mild symptom of sore throat. Altogether led her doctor to treat her as having an eczema only. Oral lesions usually appear at the same time with or precede cutaneous lesions [10, 15, 23]. In this case, oral lesions could have been overlooked at the first time of diagnosis. Occasionally, HFMD can follow a severe course. In our case, patient's signs and symptoms were absent within 10 days without any complications. The treatment is symptomatic. Most patients were managed conservatively with topical antibiotics, oral antihistamines, antipyretics and non-specific rinses with anesthetic substances [24, 25].

Recent epidemics of HFMD in Asia have reported severe cases with complications in children. Enterovirus 71 has been recognized as the causative agent of HFMD with high neurological, and cardiopulmonary involvement [10, 26]. There has been other cases of HFMD in adults with predominant skin component which resembles other conditions such as herpes zoster infection, and autoimmune bullous diseases [27]. Because of the clinical manifestations of HFMD, which mimics other skin and oral conditions, the clinician could easily miss the diagnosis if presented early in the course of its infection, leading to an inappropriate management and a wider spread of the disease. In our case, the general dentist unsuspectingly performed an ultrasonic tooth cleaning despite the presence of multiple oral ulcers. There was no report of any new cases in our dental clinic within a month after her visit to our clinic. A thorough history taking, oral and physical examination can help identifying the cause of oral ulcers. However, HFMD rarely affect an immunosufficient adult, and in our case, she denied any contacts with small children in the previous week.

Conclusions

It is important for the general dentists to be familiar with the course and clinical presentation of HFMD since the oral lesions are usually the first clinical signs. The epidemic nature of the disease makes it likely that the dentist will contract the disease himself or perhaps become a carrier of the virus [28]. A quick identification will prevent the infection from spreading to both children and adults. Therefore a thorough differential diagnosis is important especially in children who present to the clinic with aphthouslike lesions, as a wrong diagnosis may result in mismanagement, and further exposure.

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