

Case Report

The different symptoms determining management of hand foot and mouth disease and primary varicella zoster infection

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ABSTRACT

Background: Hand, foot and mouth disease (HFMD) is a medical condition endemic among children in South-East Asia, including Indonesia and, more specifically, Banjarmasin – the capital of South Sulawesi. The disease is mediated by Enterovirus 71 and Coxsackievirus 16 which attack the oral cavity, hands, feet, buttocks and genital areas. One differential diagnosis of this disease is Primary Varicella Zoster infection. Both diseases have similar clinical symptoms but different etiologies which can precipitate errors in the administration of therapy. **Purpose:** To elucidate the distinction between HFMD and Primary varicella zoster infection. **Case:** An 8 year-old male sought treatment complaining of ulcers on the upper maxillary gingiva followed by the appearance of itchy and painful lesions affecting the nose, upper lip, hands and feet. The patient's mother reported his history of 39°C fever followed by the development of red spots and ulcers on the face, hands and feet which caused itching. Clinically, it is similar to Primary varicella zoster infection which can affect any part of the body. The patient only used an immunomodulator once a day and was actively seeking available healthcare. **Case management:** Extraoral examination confirmed the presence of multiple erythematous vesicles and ulcers, 2 mm in diameter, which caused a sensation of itching around the nose and upper lip region. Multiple painful and itchy red macules and vesicles, 3-6 mm in diameter, appeared not only on the patient's palms, back of the hands and feet. Intraoral examination of the right maxillary gingiva revealed multiple painful ulcers, 1-2 mm in diameter and yellowish in appearance, surrounded by erythema. The results of history-taking implied that no lesions appeared on other parts of the body. **Conclusion:** While these conditions share similar clinical manifestations, their contrasting etiologies require different treatments. The ultimate diagnosis can be determined clinically by the dentist, thereby preventing errors in the administration of therapy.

Keywords: differential diagnosis; hand foot mouth disease; primary varicella zoster infection

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INTRODUCTION

HFMD or Singapore flu has frequently been endemic among children in the South East Asia region,¹ including Banjarmasin, Indonesia. A previous study estimated that in the city between 2014 and 2017 the prevalence of infectious diseases affecting the oral mucosal was 10.07%², one form of viral infection being HFMD.^{3,4}

HFMD is an infectious disease presenting in the oral cavity and integumentum areas particularly the hands, feet and buttocks⁴ which is mediated by Enterovirus 71 and Coxsackievirus 16 infection.^{5,6} Complications arising

from viral infection may cause severe CNS diseases such as meningitis and encephalitis, paralysis, pulmonary edema and death.⁴ Previous studies have shown that close monitoring and timely management may prevent the severity of such complications and prevent death.⁵

Clinical manifestations of HFMD include a fever followed by the development of red vesicles and ulcers in the oral cavity and integumentum system (on the hands, feet and genital area).^{7,8} Lesions on the skin appear as red macula which progress to vesicles and ulceration. Patients may also complain of a sore mouth and throat and ulcers may be present on all oral mucosal surfaces, the tongue,

gingiva, lips and cheeks. Oral mucosa lesions initially develop as red maculars which develop into vesicles and rupture into ulcers.^{4,8} The clinical oral manifestations of HFMD demonstrate certain similarities with other viral infections, resulting in differential diagnoses for this disease such as Primary Herpetic Gingivo Stomatitis (PHGS) and Primary varicella zoster infection.^{4,9,10}

HFMD is a fundamentally self-limiting disease which, consequently, requires supportive therapy to boost the immune system and prevent complications resulting from its treatment. Acyclovir is not indicated for HFMD. A vaccine against Coxsackie virus infection preventing the spread of HFMD is currently being developed for future research.⁸

This case report aims to elucidate the distinctions between HFMD and Primary varicella zoster infection. Clinically, both diseases exhibit similar manifestations, but further elaboration is essential to distinguish them from a variety of perspectives. They have similar clinical manifestations, but each disease has a different etiology, a fact which can cause errors in the administration of therapy. It would be advantageous for the dentist to both diagnose the disease and personally manage treatment of the patient.

CASE

An 8 year-old male sought treatment complaining of ulcers on the right maxillary gingiva accompanied by the

appearance of itchy and painful wounds around the nose, upper lips, hands and feet which he had suffered for the previous three days. This condition is clinically similar to Primary varicella zoster infection which can afflict any part of the body. The boy’s mother reported her son as having developed a 39°C fever accompanied by itchy red spots and ulcers on the face, hands and feet. The patient, who had no allergic history, was actively seeking available healthcare assistance and used an immunomodulator only once a day. His mother intimated that a neighbor of the family had previously been diagnosed with Singapore flu.

CASE MANAGEMENT

First visit (day 1): extraoral examination revealed the presence of multiple itchy erythematous vesicles and ulcers, 2 mm in diameter, surrounding the nose and upper lips (Figure 1). The palms, back of the hands and feet demonstrated the presence of multiple erythematous macules and vesicles, 3-6 mm in diameter, which caused itchiness and pain (Figure 2). Intraoral examination confirmed the presence of painful multiple ulcers, 1-2 mm in diameter and yellowish in appearance, surrounded by erythema on the right maxillary gingiva (Figure 3). Anamnesis conducted with the patient’s mother indicated that no lesions had appeared on other parts of his body, leading to a diagnosis of HFMD. The patient was prescribed a combination of bed rest and soft liquid food and beverages

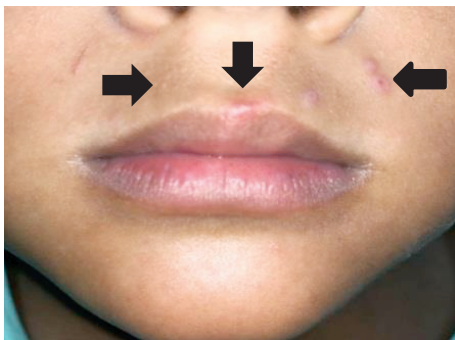


Figure 1. Upper lips and nose developed multiple itchy erythematous vesicles and ulcers, 2 mm in diameter.

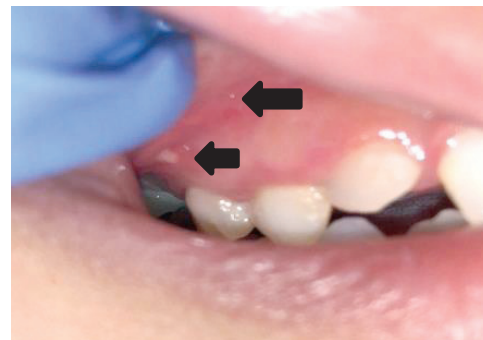


Figure 3. Upper right gingival developed multiple painful ulcers 1-2 mm in diameter with yellowish appearance surrounded by erythema.



Figure 2. Palm, back of the hands and feet presented multiple itchy and painful vesicles, erythematous maculas, 3-6 mm in diameter.

high in calories and protein. He was also instructed to use an aloe vera mouthwash three times a day, 250 mg of methisoprinol syrup three times a day, 250 mg of ibuprofen syrup three times a day and multivitamin B complex once a day for seven days. Patient follow-up was scheduled for seven days later.

Second visit (day 14): the patient arrived for follow-up treatment of ulcers on the right maxillary gingiva. The results of history-taking confirmed the existence of a painless ulcer from day 9. The painless wounds on the nose, upper lip, hands and feet which did not itch had been present since day 12. The patient's fever broke on day 5 and he consumed oral drugs and regularly applied mouthwash. Extraoral examination of the nose, upper lip, hands and feet confirmed a marked improvement in their condition. Intraoral examination indicated the presence of normal, lesion-free tissue and the patient was, therefore, declared healthy (Figure 4).

DISCUSSION

One differential diagnosis of HFMD is that of Primary varicella zoster infection.⁹ This case report discussed similarities and differences between both diseases from various perspectives. Although both diseases generally present similar clinical symptoms frequently found in children and the presence of lesion on oral mucosa and skin, they were mediated by different forms of viral infection. Both diseases have similar clinical manifestations, but contrasting etiology which necessitates different treatment.

In this case, patient experienced a cough and influenza accompanied by a high fever of 39°C. HFMD and Primary varicella zoster infection present similar symptoms such as fever and flu like syndrome prior to the appearance of lesions.¹⁰ As the fever resides, itchy erythematous macula, vesicles and ulceration appeared on the upper lip, nose, palms, backs of the hands and the feet. There was no lesion around buttocks and genital area. This differentiates HFMD from Primary varicella zoster infection as a result of which

similar lesions may appear on the entire body surface, including: the eyes, oral cavity and genital mucosa. It has been declared the first primary disease suffered during the patient's life.^{4,10}

The etiology of HFMD is Enterovirus 71 (EV 71) large outbreaks of which in the Asia Pacific region over the last decade have been associated with neurological disease and mortality. Enteroviruses constitute small, non-enveloped RNA viruses categorized as members of the picornaviridae family.⁹ Meanwhile, the Coxsackie virus is the RNA virus also belonging to the picornaviridae family. Group A coxsackie viruses associated with infections of the skin and mucous membrane, acute hemorrhagic conjunctivitis and HFMD.^{4,8}

Coxsackie virus replicates in the buccal and ileal mucosa. After initial infection, the virus can be detected in the respiratory tract for up to three weeks and in faeces for as long as eight weeks. The viruses replicate in the submucosal lymph nodes within 24 hours and disseminate through the reticuloendothelial system. Meanwhile, enteroviruses are transmitted primarily through the fecal-oral route or fomite before replicating in the mucosa of oropharynx, small intestine and lymphoid tissue of the intestinal mucosa.⁸

Varicella zoster virus is a pathogenic human alpha herpes virus causing Varicella zoster as a primary infection which occurs in unvaccinated children. Following the primary infection, this neurotropic virus becomes latent. Latency primarily exists in neurons of peripheral autonomic ganglia throughout the entire neuroaxis including the dorsal root ganglia, cranial nerve ganglia such as the trigeminal ganglia and autonomic ganglia, including those in the nervous system. After several years, the latent virus can reactivate as Herpes zoster, a complication of which may be Post Herpetic Neuralgia (PHN) which usually appears as a vesicle and painful mucocutaneous eruption demonstrating characteristic distribution. This viral reactivation increases in frequency with the increasing age of the patient. Immunosuppressive conditions, irritation, X ray irradiation, infection and malignancy may trigger virus reactivation.^{11,12}

Varicella zoster and HFMD infection can spread via the fecal-oral route, respiratory droplets or contact with



Figure 4. Upper lip, nose, hands and feet showed no sign of pain and itchiness.

vesicular liquid.^{5,11} No examination of this patient was conducted other than that of diagnosing the disease. This was conducted on the basis of particular clinical symptoms of HFMD such as lesions on the oral mucosa, lips, hands and feet without lesions affecting other parts of the body being considered. This caused difficulty in identifying the specific etiological virus. The diagnosis of HFMD and Varicella zoster are typically clinical because the association of the disease is highly predictive in endemic regions.^{8,11} The virus can be isolated via serology testing, cell culture and Polymerase Chain Reaction (PCR) testing.^{8,13}

Varicella zoster infection is mediated by the herpes virus, thus requiring prescription of Acyclovir or Methisoprinol. Acyclovir is an antiviral drug containing essential agents rendering the normal chain capable of blocking the virus's DNA. In cases where cyclic sugars are absent from acyclovir triphosphate termination of chain elongation occurs. Methisoprinol can be prescribed during the onset of the disease as a prophylaxis against reactivation of latent Varicella zoster infection.^{12,14}

The etiology of HFMD is Enterovirus 71 or Coxsackie virus, both of which constitute RNA viruses. The case reported here indicated that HFMD can be treated with methisoprinol which contains an antiviral and immunomodulator agent, as opposed to acyclovir, because HFMD is not a herpes virus.

An antiviral agent increases potency of depressed mRNA protein synthesis, disturbs translational ability process and inhibits polyadenylic acid attachment to viral messenger RNA. As an immunomodulator agent, methisoprinol can enhance dysfunctional cell-mediated immunity by stimulating a Th-1 response, triggering T-lymphocyte maturation and differentiation to induce lymphoproliferative responses in mitogen or antigen-activated cells. It can modulate T-lymphocyte and natural killer cell cytotoxicity, T4 helper and T8 suppressor cell functions.^{14,15}

Based on the foregoing discussion, it can be concluded that a dentist is responsible for detecting specific clinical symptoms of a disease to distinguish HFMD and Primary varicella zoster infection. Although these diseases share similar clinical symptoms, they have contrasting etiologies which require different treatment. Varicella zoster infection can be treated by acyclovir or methisoprinol. Since HFMD

is not caused by the Herpes virus methisoprinol, rather than Acyclovir, is used to treat it. The final diagnosis can be determined clinically by the dentist in order to avoid errors in the administration of therapy. Methisoprinol constitutes an antiviral which prevents viral replication by inhibiting viral DNA polymerase in Varicella zoster as a DNA virus infection. In HFMD, methisoprinol functions as an immunomodulatory.

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