Hand, Foot, and Mouth Disease

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Hand, foot, and mouth disease (HFMD) is a contagious disease, which affects young children predominantly aged under 5 years old, but can also occur in adults. The disease is characterized by maculopapule and erythema on hands, feet, mouth, and buttocks. The neurological disorders and cardiovascular disease were reported in severe cases (Robinson et al., 1958; Huang et al., 1999; Yan et al., 2000; Legay et al., 2007; Chen et al., 2008; Hong et al., 2012).

HFMD is caused by enteroviruses which belong to the genus Enterovirus in the family Picornaviridae. The enteroviruses are small, non-enveloped, single-stranded, positive-sense RNA viruses. The viruses are classified into four individual species, based on their molecular and biological properties, including Poliovirus serotypes 1 to 3 (PV); Coxsackievirus groups A and B (CAV, serotypes 1 to 22 and 24 and CBV, serotypes 1 to 6); Enterovirus (EV) serotypes 68 to 71, 73 to 107 and finally the Echovirus (ECHO) serotypes 1 to 7, 9, 11 to 21, 24 to 27 and 29 to 33 (Hyypia et al., 1997; Muir et al., 1998; Pallansch and Roos, 2007; Yamashita et al., 2010).

Coxsackie virus A 16 (CAV 16) and enterovirus 71 (EV 71) are the most common serotypes, which cause HFMD. However, more severe forms of the disease are always associated with EV 71. HFMD was initially reported in New Zealand in 1957 (Kamahora et al., 1985). CAV 16 was first isolated in Canada in 1958, while EV 71 was first recognized in the United States between 1969 and 1972 (Robinson et al., 1958; Schmidt et al., 1974). Since the 1970s, HFMD has widely spread to other continents, especially in the Asia-Pacific region including Thailand (Mcminn, 2003). Based on the surveillance data, CAV 16 was the most frequently isolated strain during the 1970s and 1980s; however, EV 71 has replaced it since the 1990s (Chan et al., 2011).

HFMD has become a serious disease causing death in young children in Sarawak, Malaysia since 1997 (Chan et al., 2011), in Taiwan since 1998 (Wu et al., 1999), in Singapore since 2000 (Chan et al., 2003), in India since 2003 (Sasidharan et al., 2005), in China since 2008 (Yang et al., 2009) and in Vietnam since 2011 (WHO, 2012). In April 2012, 78 Cambodian children suffered from a severe form of HFMD and 54 deaths were reported (Joint press release between the Ministry of Health Kingdom of Cambodia and the World Health Organization, 2012).

The disease is spread through direct contact with infectious viruses via respiratory secretions, blister fluids and stool of infected patients. The virus can be detected in the stool and pharynx of infected persons several days before onset of clinical signs and can be shed via the stool for several weeks (Wang et al., 2011). HFMD has a short incubation period of 3 to 6 days. Most clinical signs are asymptomatic or mild. Early symptoms begin with low-grade fever, cough, and a sore mouth and throat leading to malaise and loss of appetite. After the first symptoms, the exanthema begins as small red spots or papules with blisters that commonly become ulcer. The lesions usually develop inside the mouth including buccal mucosa, hard palate, surfaces of the cheeks, gums and tongue, on palms of hands and soles of the feet. The lesions may also appear on the buttocks and genitalia (Batirbaygil and Altay, 1988; Jennifer and Antoinette; 1999; Russo et al., 2006; Choi et al., 2011). The pattern of HFMD rashes caused by CAV 16 differs from that caused by EV 71. The vesicles seen in infections caused by CAV 16 are usually larger than those observed in EV 71 infections. However, the rashes originated from EV 71, which are frequently found on the trunk and limbs, are more common and more petechial (Chen et al., 2008).

In some cases, HFMD may cause severe complications including myoclonic seizure, motor weakness, tremor, nystagmus, brainstem encephalitis, aseptic meningitis, poliomyelitis-like paralytic disease, opsoclonus-myoclonus syndrome and benign intracranial hypertension. Some cases show paroxysmal supraventricular tachycardia, pulmonary edema and pulmonary hemorrhage following sudden death due to cardiopulmonary failure (Fu et al., 2004; Chen et al., 2008; Cho et al., 2010; Choi et al., 2011; Hu et al., 2012).

Aside from the clinical manifestation, HFMD can be diagnosed by isolating the viruses from patients. Cell lines such as human rhabdosarcoma cells (RD Cells) and African green monkey kidney cells (Vero cells) have been wildly used for CAV 16 and EV 71 isolation. For virus identification and serological analysis, neutralization test, reverse transcription-polymerase chain reaction (RT-PCR), sequencing, and immunofluorescence assay can be used to identify the viruses and antibodies against the viruses in clinical specimens (WHO, 2011).

There is no specific treatment for the disease. The general supportive and symptomatic therapy is necessary to control viral spread and prevent the disease complication. Topical analgesics such as benzydamine mouthwash or spray, choline salicylate gel or lidocaine gel can be used to relief pain (MHRA, 2009; Muppa et al., 2011). Recently, low-level laser therapy has been applied for treating painful oral ulcers (Toida et al., 2003). Fever can be treated with antipyretics. Additionally, the usefulness of intravenous immunoglobulin has shown some potency in HFMD cases (Chan et al., 2003). However, in case of no common complications most patients recover without medical treatment in 7 to 10 days (Thomas, 2009).

There is currently no vaccine available for HFMD. Good personal and environmental hygiene and the avoidance of contact with infected individuals are necessary to protect from the disease (McMINN, 2003).

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