REVIEW ARTICLE
Volume-7 | Issue-9 | September-2018 | PRINT ISSN No 2277 - 8179
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

HAND, FOOT AND MOUTH DISEASE: ETIOPATHOGENESIS, PRECAUTIONS AND TREATMENT

Oral Pathology

Dr. Supriya Sharma* — Senior Resident, Dept of Oral Pathology and Microbiology, Faculty of Dental Sciences, King George's Medical University, UP, Lucknow *Corresponding Author

Dr. Shaleen Chandra — Professor and Head, Dept of Oral Pathology and Microbiology, Faculty of Dental Sciences, King George's Medical University (KGMU), UP, Lucknow

Dr. Shalini Gupta — Professor, Dept of Oral Pathology and Microbiology, Faculty of Dental Sciences, King George's Medical University (KGMU), UP, Lucknow

Dr. Surya Kant — Professor and Head Dept of Respiratory Medicine, King George's Medical University (KGMU), UP, Lucknow

ABSTRACT

Hand, foot, and mouth disease (HFMD) is a syndrome, caused by Coxsackie virus, characterized by fever with vesicular eruptions principally on the skin of the hands and feet and the oral cavity. HFMD primarily affects infants and young children. Although infection is usually self-limited, severe neurological complications in the central nervous system can present in some cases, which can lead to death. Most Coxsackie virus infections are mild and self-limiting. The patient may be manifested with the common cold, sore throat and distinctive rashes on the palms, soles, inside the oral cavity, tongue, gums and cheek, known as a hand-foot-mouth disease (HFMD), more frequent in children under 5-10 years. The diagnosis of Coxsackie virus infection is typically clinical. Usually, no treatment is required for mild infection because of the ability of the body immune system to destroy the viruses. Patient with severe signs and symptoms treatment is supportive. Hand hygiene, Environmental hygiene and creating public awareness are the key steps for the prevention and control of this viral infection.

KEYWORDS

Hand, Foot and Mouth Disease; Etiolopathogenesis; Precautions; Treatment

INTRODUCTION

Hand, foot and mouth disease which was first reported in 1958 is a potentially life-threatening illness that is usually seen in young children mostly younger than five years of age. It is caused by enterovirus Coxsackie A16 and has been reported to be caused less commonly by types A5 and A6, and occasionally even by B2, B5 or enterovirus 71. Despite the similarity in names, it bears no relationship to foot and mouth (hand and mouth) disease, another viral disease with an animal vector.[1,2]

EPIDEMIOLOGIC CHARACTERISTICS AND SPREAD

Coxsackievirus infections have extensive dissemination and seasonality in place of higher latitude. Immune-compromised individuals and neonates are at higher risk. An affected individual may spread the viruses through close personal contact, by sneezing or coughing sneezing, contact with contaminated objects and surfaces or contact with faeces. [3]

ETIOLOGY

EV71 and CVA16 are the principal causative agents, while few different serotypes, involving CVA4-10, CVA24, Coxsackievirus B2-5 (CVB2-5), and Echovirus 18 (ECHO18), can also lead to this disease. One of the subdivisions of the family of viruses known as picornavirus (precisely, small pico RNA virus) is the Coxsackie group named after the New York town where the virus was first identified. Certain Coxsackie subtypes cause oral vesicular eruptions: hand-foot-and-mouth (HFM) disease and herpangina. In the recent years, other enteroviruses such as CV-A6 and CV-A10 have been widely associated with both sporadic cases and outbreaks of HFMD worldwide. [4]

PATHOGENESIS OF ENTEROVIRUS

In most of case epidemic hand-foot-and-mouth disease (HFMD) viral infections are caused by coxsackievirus A16, A6, or enterovirus 71. Besides this, sporadic cases with coxsackievirus infections are associated with types A4-A7, A9, A10, B1-B3, and B5. Coxsackie viruses infections are transmitted primarily via the faecal-oral route, respiratory droplets, and fomites. Initially, the viruses replicate in the buccal and ileal mucosa. After the initial infection, the virus can be detected in the respiratory tract for up to 3 weeks and in faeces for up to 8 weeks. The viruses replicate in the submucosal lymph nodes within 24 hours and disseminate to the reticuloendothelial system. In severe cases dissemination occurs to target organs following a secondary viremia. (Figure 1) Enteroviruses are transmitted primarily through the faecal-oral route or fomite. Then the viruses replicate in the mucosa of the oropharynx, small intestine and the lymphoid tissue (tonsils, Peyer's patches of the intestinal mucosa followed by shed into the faeces. This time may be taken months after the primary infection. Within 7 days the level of the neutralizing antibody increase and the virus is eliminated. However, one study showed that the neutralizing antibody may not correlate with disease severity.[4,5,6]

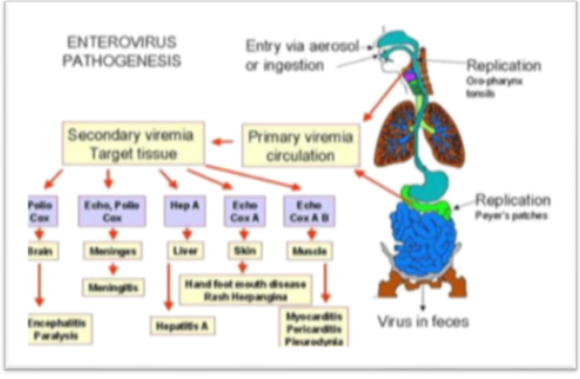

FIGURE 1: Pathogenesis of Enterovirus

CLINICAL FEATURES

This viral infection typically occurs in endemic or epidemic proportions and predominantly affects children younger than 5 years of age. After a short incubation period, the condition resolves spontaneously in 1 to 2 weeks. Signs and symptoms are usually mild to moderate in intensity and include low-grade fever, malaise, lymphadenopathy, and sore mouth. Pain from oral lesions is often a patient's chief complaint. It is common for the Coxsackie virus to cause a febrile upper respiratory tract infection with a sore throat with or without a runny nose. Skin rashes are other clinical findings which may not appear until the infection has started to get better. The rash itself is not contagious, resemble a light sunburn appearance. Sometimes the rashes appeared like small, tender blisters on the palms, soles of the feet, and inside the mouth including the tongue, gums, and the cheek. This condition is known as a hand-foot-mouth disease (HFMD) (Figure 2A) and is caused by group A coxsackievirus.[7] Vesiculobullous

lesions are generally localized in the perioral and perinasal areas of the face, but also on the scalp. Palmar purpuric macula is a typical feature in adult patients and it is the clinical expression of vesicles more deeply located in the epidermis, probably due to the greater thickness of the palmoplantar epidermis. Children younger than 5 years are often affected because they do not yet have immunity (protection) to those viruses. In children, the disease usually presents with vesicles or ulcers in the oral cavity occurring chiefly on the buccal mucosa and tongue with few sores around the soft palate, tonsils (Figure 2B) and also blisters in the hands, feet, and buttocks. This illness is commonly mild, and approximately all people improve in 7–10 days without medical treatment. Complications are uncommon.[3]

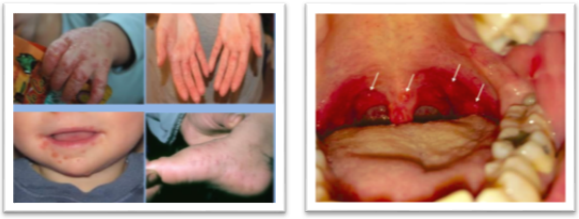

Figure 2: A. Showing the clinical and biologic signs of Coxsackievirus virus infection. B. Showing inflammatory signs on the soft palate and pharynx with multiple vesicles and ulcers (white arrows).

HISTOPATHOLOGY

Hand and Mouth Disease is rarely biopsied. On Histopathological examination, section shows acral skin with a lymphocytic infiltrates which infiltrates the epidermis. In early lesions, the infiltrate is related with keratinocytes apoptosis. On higher magnification papillary dermal oedema is observed in lower half of the area associated with epidermal necrosis, Dyskeratosis and vesiculation within epidermis as a consequence of epidermal oedema. Eosinophilic inclusions may be are seen within some of the infected epithelial cells.[8,9]

DIAGNOSIS

The diagnosis of coxsackievirus infection is customarily clinical because the association of acute fever and rash is highly predictive in areas where the disease is endemic. Isolation of the virus in cell culture the specific diagnosis. Samples from stool or rectal swabs, oropharynx are generally collected. To exclude aseptic meningitis and encephalitis cerebrospinal fluid (CSF) evaluation are needed. The virus can be isolated via cell culture (sensitivity, 30-35%) or Polymerase Chain Reaction (PCR) (sensitivity, 66-90%).[3]

ROLE OF INTERLEUKIN -8 IN PROGRESSION OF DISEASE

IL-8 is strongly associated with the disease severity of HFMD and may be used as a predictive marker for disease progression. IL-6 and IL-10, although elevated in patients with HFMD, are not related to disease severity.[10]

DIFFERENTIAL DIAGNOSIS

Because this disease may manifest itself primarily within the oral cavity, a differential diagnosis should include Herpangina, Varicella, Erythema Multiforme, Primary Herpes Gingivostomatitis.[2]

CONVENTIONAL PRECAUTIONS

These preventive measures are planned against transmission of the infectious agents. These precautions are focused on all blood, body fluids including saliva and coughed up material, excretions such as wound drainage, urine and stool but not sweat, secretions, non-intact skin and mucous membrane have the possibility of spreading the infection. Instructions for Standard Precautions have been taken from various guidelines published by HICPAC/CDC, the IDSA, and the World Health Organization (WHO).

Few preventive measures under Conventional Precautions are:

a. Hand hygiene: Hand washing can be done with plain soap and water or soap containing an antiseptic agent or waterless alcohol-based hand rub containing at least 60% alcohol.

b. Use of Gloves: Gloves are not alternatives to hand hygiene. It is a supplemental requirement to prevent contact with blood, body fluids, secretions, excretions, non-intact skin and mucous membrane. Instantly after removal of gloves, we should wash our hand properly.

c. Respiratory hygiene: All respiratory secretions are considered potentially infectious. The following precautions are required to take into action:

- To cover the mouth and nose with tissues during sneezing and coughing.
- Vulnerable groups such as Immunocompromised children and the elderly are required to keep at least 3- 6 feet (1-2 meters) away from the infected person.
- Immediately disposal of the tissues succeeded by hand hygiene.
- In a public or crowded place, people with Immunocompromised status are required to wear masks.

d. Blood and body fluid precautions: The following measures are required to take:

- A family member is required to avoid sharing personal items such as razors, toothpaste and clothes etc.
- To prevent the entrance of an individual with open skin lesions.
- Isolation of the infected patient.

e. Practice for safe infection: The caregivers should follow the following precautions:

- Needles are required to be disposed of separately in a puncture-resistant container.
- The housekeeping staff should practice caution during cleaning the linens and clearing the rooms.
- For medication, single-dose vials are always favoured than multi-dose.
- A single person is needed for monitoring the medication vials, insulin pens and fingerstick device

f. Environmental Hygiene: Viruses and Bacteria can survive for long times on the environmental surface. So it is needed to clean by removal of dirt and contaminated surface scrubbing with a detergent succeeded by rinsing with water.

g. Precautions for Highly Immune-compromised Patients: To decrease the airborne transmission at home subsequent measures can be undertaken :

- To avoid carpeting which is a major source retained mole spores.
- If carpeting essential it is required to use a high-efficiency particulate air (HEPA)-filtered vacuum for clean the area regularly in the absence of the patient.
- To reduce dust overload it is needed to maintain the heating, ventilation, and air conditioning (HVAC) device accurately.
- To avoid exposure to construction sites or the outdoors on windy days.
- To wear a special type of mask such as N95 respirator during travelling to and from the hospital. [11,12,13,14,15]

TREATMENT

Bland mouth rinses such as sodium bicarbonate in warm water may be used to help alleviate oral discomfort. Supportive medical care can be offered on an outpatient basis. Any complications may require inpatient management. For aseptic meningitis, medicine such as Pleconaril, shown to decrease the symptoms. Antibiotics may be effective until bacterial meningitis is excluded. In case of myopericarditis medication with carvedilol, a non-selective beta-blocker has shown to decrease the replication of the virus in a murine model but this has not been evaluated in humans. Patient suffering from epidemic pleurodynia has been shown to recover completely within 1 week after taking analgesics, narcotics and heating pads for their medical therapy.[3]

CONCLUSION

Generally, the prognosis is very good for Coxsackie virus infection. Although key advances have been made in understanding the biologic aspects and pathogenesis of Coxsackie virus infections still there are few questions crucial to the advancement of targeted and preventive strategies. Patients should be reassured that it is a self-limiting illness that commonly does not require any antibiotics for the treatment. Creating awareness between the patient as well as the general people for good hygiene practices to avoid transmission is compulsory.

REFERENCES

1. R. Rajendran.Textbook of oral pathology. 5th edition, Elsevier New Delhi, (2006).
2. Pintor E, Herreros B, Gargantilla P, Gutiérrez MJ. Hand, foot and mouth disease in an adult Infection. https://doi.org/10.1007/s15010-018-1118-4
3. Afrose T. Coxsackie Virus: The Hand, Foot, Mouth Disease (HFMD). JOJ Pub Health .,2017;1(4): JOJPH.MS.ID.555566.

4. Lei X, Cui S, Zhao Z, Wang J. Etiology, pathogenesis, antivirals and vaccines of hand, foot, and mouth disease. Natl Sci Rev.,2015;2(3):268-284.
5. Muehlenbachs A, Bhatnagar J, Zaki SR .Tissue tropism, patholo¬gy and pathogenesis of enterovirus infection. J Pathol.,2014;235(2): 217-228.
6. Kadambari S, Bukasa A, Okike IO, Pebody R, Brown D et al. Enterovirus infections in England and Wales, 2000-2011: the impact of increased molecular diagnostics. Clin Microbiol Infect.,2014; 20(12): 1289- 1296.
7. Stewart CL, Chu EY, Introcaso CE, Schaffer A, James WD et al. Cox¬sackievirus A6-induced hand-foot-mouth disease. JAMA Dermatol.,2014;149(12): 1419-1421.
8. Weedon's Skin Pathology (Third edition, 2010). David Weedon.
9. Pathology of the Skin (Fourth edition, 2012). McKee PH, J. Calonje JE, Granter SR.
10. Wang W, Li W, Yang X, Zhang T, Wang Y, Zhong R, Jiao Y, Li T , Jiang T, Tian Y, Wu H et al . Interleukin-8 is elevated in severe hand, foot, and mouth disease. J Infect Dev Ctries., 2014; 8(1):094-100.
11. WHO (2009) WHO guidelines on hand hygiene in health care. Geneva, Switzerland.
12. Sandora TJ, Taveras EM, Shih MC, Resnick EA, Lee GM et al. A randomized, controlled trial of a multifaceted intervention including alcohol-based hand sanitizer and hand-hygiene education to reduce illness transmission in the home. Paediatrics.,2015; 116(3): 587-594.
13. Mott PJ, Sisk BW, Arbogast JW, Ferrazzano Yaussy C, Bondi CA, et al. Alcohol-based instant hand sanitizer use in military settings: a prospective cohort study of army basic trainees. Mil Med.,2007; 172(11): 1170-1176.
14. CDC (2003) Guidelines for environmental infection control in health-care facilities: recommendations of the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee (HICPAC). US Department of Health and Human Services, CDC, USA.
15. American Academy of Pediatrics Enterovirus (nonpoliovirus) infections. In: Pickering L, Baker C, Kimberlin D, Long S, (eds), Red Book: 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics.,2012: 315-318.