Microbes and Infectious Diseases 2023; Article-In-Press, **DOI:** 10.21608/mid.2023.201784.1491

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Review article

Review of hand foot mouth disease

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ARTICLE INFO

Article history:
Received23 March2023
Received in revised form 4 April 2023
Accepted7April2023

Keywords:
Picoranaviridae family
Enterovirus genus
Real time PCR
NSAID
Pleconaril

ABSTRACT

Background: Hand foot mouth disease (HFMD), a disease of childhood is also reported in adults caused by Coxsackie virus A type 16. Clinical condition is characterized by vesicular eruptive lesion in mouth, hand, foot, buttock, or genitalia. Coxsackie virus is a member of picoranaviridae family that includes non-enveloped SSRNA viruses. Spread in humans in the case of HFMD is through oral route, by the shed virus from intestine of infected person or through upper respiratory tract by the secretions or vesicle fluid of the diseased individual. Incubation period is 3 to 6 days. Diagnosis of HFMD most of the time is based clinically depending on the patient's age, symptoms and clinical presentation of rash. Samples include stool, oral samples, biopsy & vesicular scrapings. Viral culture is the gold standard. Treatment is mainly supportive, to maintain hydration, acetaminophen and NSAIDS to reduce temperature. Novel agents like pleconaril play a vital role in the management of viral infection cases. Hand hygiene is the main stay of prevention.

Introduction

Children are infected with several microbial infections including virus. One of the recent epidemic reported from different parts of India, is hand foot mouth disease (HFMD) [1]. The clinical condition is characterized by acute illness associated by vesicular eruptive lesion in mouth, hand , foot , buttock &/or genitalia [2].

A childhood disease below 5 years, is commonly caused by Coxsackie virus A type 16 (CVA 16) [3], but the illness is also associated with A5, A7, A9,A10,B2,B5 strains. One characteristic feature of A6 is that it's associated with seasonal outbreaks as noted in France & Finland [4].

Coxsackie virus is a member of picoranaviridae family, that includes non enveloped single stranded RNA viruses, [2] causing outbreaks in daycare center, summer camps, within family [5]. Usually occurring during late spring, it is associated with increased infection rate with rise in environmental temperature & it has a fatality rate of 0.03% [6].

DOI:10.21608/MID.2023.201784.1491
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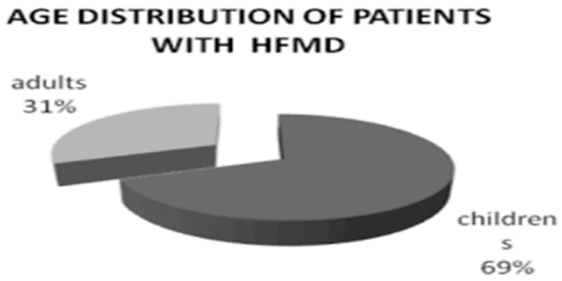
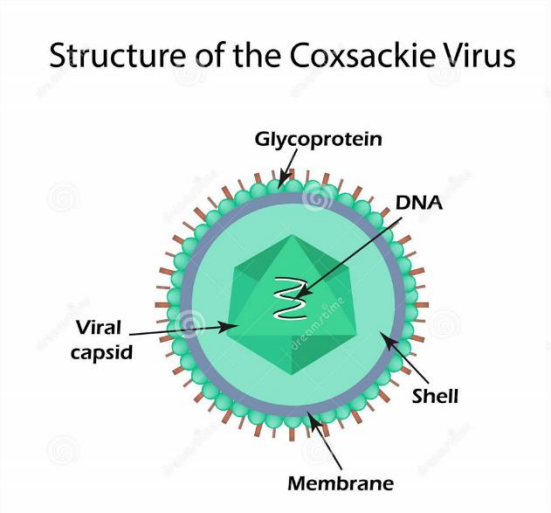
Figure 1: Age distribution of Patients with HFMD



Morphology of the HFMD virus

This virus belong to Enterovirus genus , first isolated in 1948, in New York state by D**alldorf et al**., who were investigating an outbreak of paralytic poliomyelitis in Coxsackie village [7].The virus is single stranded RNA, surrounded by icosahedral capsid made up of proteins , size is 22 to 30nm, divided into 2 subgroups A& B. Coxsackie A contains 24 serotypes, while Coxsackie B 6 serotypes [8].

Figure 2. Structure of the Coxsackie virus



Pathophysiology

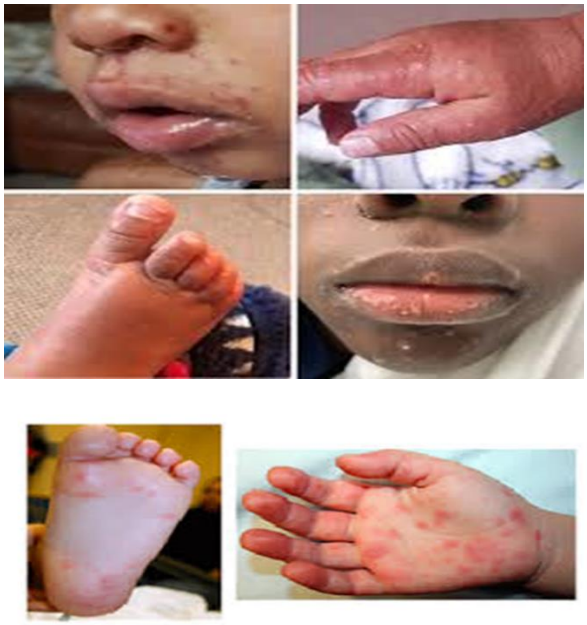
Spread in human in the case of HFMD is through close personal contact like coughing, sneezing fomites etc by the shed virus from intestine of infected person or through upper respiratory tract by the secretions or vesicle fluid of the diseased individual.Patients tend to be most infectious in the first week of the clinical condition, It is a benign illness resolving in 1- 2 weeks. After ingestion, the virus replicates in lymphoid tissue of the intestine & pharynx, spread to regional lymph nodes, then to multiple organs including CNS, heart, liver & skin.

Clinical features

Initially begins with low grade fever, reduced appetite , general malaise, not eating & drinking, more drooling than usual, only drinking cold fluids .

Most common presenting symptom is pain in throat &mouth. Presence of vesicles,which is surrounded by thin halo of erythema,eventually rupturing & forming superficial ulcers with grey yellow base & erythematous rim, heals without scar, rarely can be associated with aseptic meningitis [9].

Figure 3 . Clinical presentation of hand foot mouth disease



Lab diagnosis

Diagnosis is mostly clinical. Diagnosis of HFMD most of the time is based clinically depending on the patient's age, symptoms and clinical presentation of rash.

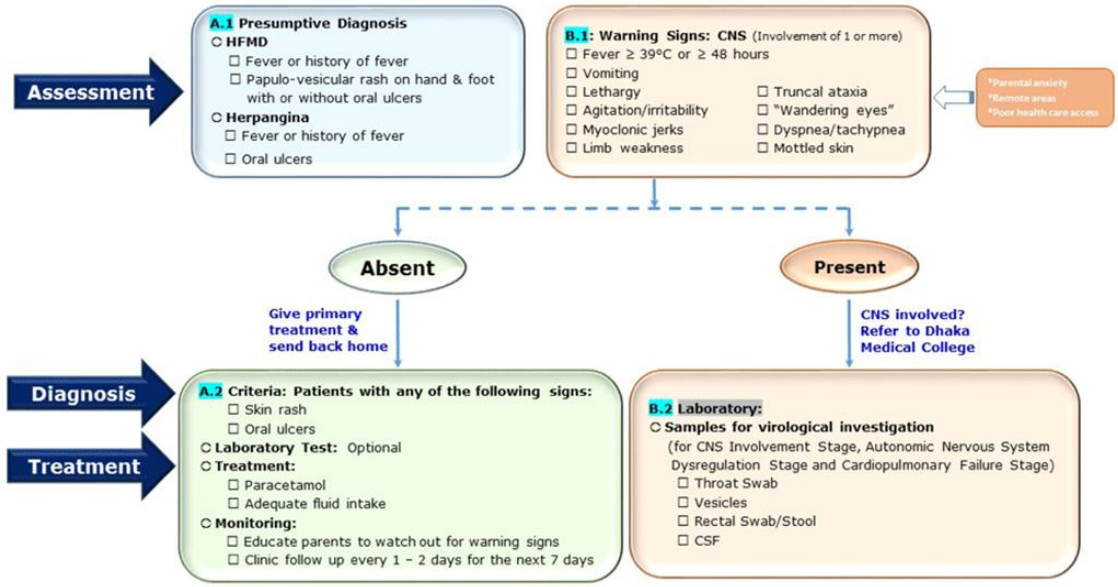
Laboratory diagnosis involves collection of samples from various sites. Throat/ nasopharyngeal samples, faecal samples should be collected within 48 hours of illness. The virus is seen in stool sample upto 6 weeks whereas it is less than 4 weeks for oropharynx samples. Although samples from multiple sites can be taken, the most useful sample is tested first followed by rest of the other samples [10]. Other samples includes biopsy of skin lesions and skin scrapings (preferably from palm of hands/ soles of feet). Blood is collected for serological tests.

The samples have to be transported in viral transport media and transported immediately to the laboratory, in case of delay the samples can be

stored at -200C for 2-3 days. Lab diagnosis is for supportive evidence. Samples include stool , oral samples , biopsy & vesicular scrapings Absence of giant cells from scrapings of vesicles in light microscope differentiate HFMD from Varicella and Herpes [11].Viral culture is the gold standard [12]. Characteristic cytopathic effects are rounding ,shrinking, nuclear pyknosis, refractivity and monolayer degeneration.

Although, serology is not sensitive, levels of IgG can be used to monitor recovery. Stool can be used for detecting the pathogen, up to 6 weeks after the onset of infection, oral samples are useful for less than 4 weeks.Real time PCR is used for molecular confirmation [13].

Figure 4: Clinical Management guide to HFMD



Adopted from WHO: A guide to Clinical management and public health response for Hand, Foot & Mouth Disease.[1](WHO, 2011)

Treatment

Main stay of treatment is supportive therapy, to control the temperature & hydration of the patient NSAIDs &acetaminophen for controlling the fever, fluid replacement to keep the patient well hydrated.Liquid ibuprofen will be used as gargle to ease the pain in the throat.Novel agents –molecular decoys, translational inhibitors , receptor antagonists, replication inhibitors play a vital role in the management of the viral infection case. Pleconaril –anti picornoviral agent [14] plays an important role .

Anecdotal reports of acyclovir clinical response need to be remembered at this juncture [15] . Hand hygiene is the main stay of prevention [16], isolation of immunocompromised individuals to be done due to the potential risk getting infected.

Vaccines

Strain specific inactivated whole virus aluminium adjuvant vaccine is available in China [16] approved for widespread use –EV71C4a vaccine showed overall 94.7% efficacy with protection for 2 years .

VLPs vaccine,DNA vaccine, peptide vaccine, subunit vaccines are in various stage of clinical trials

Conclusion

Hand foot mouth disease is a self limiting viral infection, prevented by proper hygienic precaution, for which each one of us are responsible.

Conflicts of interest : None.

Financial disclosure: None

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