International Journal of Pharmaceutical Development & Technology

e ISSN - 2248 - 910X

www.ijpdt.com

Print ISSN - 2248 - 9096

ORAL MANIFESTATIONS OF DENGUE HAEMORRHAGIC FEVER: A REVIEW

Richa Wadhawan[1], Sumeet Sharma[1], Gaurav Solanki[1], Renu Solanki[2]

[1]Jodhpur Dental College General Hospital, Jhanwar Road, Boranada, Rajasthan 342012, India.
[2]Lachoo Memorial College of Science and Technology, Jodhpur, Rajasthan, India.

ABSTRACT

Dengue viral infection is a cause of considerable morbidity and mortality and may be associated with a variety of mucocutaneous manifestations that may provide important early clues to the diagnosis of this condition. Cutaneous and mucosal findings like confluent erythema, morbilliform eruptions, and hemorrhagic lesions may figure prominently in the clinical features of dengue. The differential diagnoses include a large number of bacterial and viral exanthems as well as drug rash.

Keywords: Dengue Fever, Rash, Oral Manifestations etc.

INTRODUCTION

Dengue fever is a severe flu-like illness that affects the infants, children, adolescents, and adults & it is one of the major health hazards which is prevalent and dangerous causing the death of many people [1]. The disease is transmitted among humans by the mosquito Aedes aegypti and is seen mostly in the rainy season.. This disease may be associated with a variety of mucocutaneous manifestations which may be of help in early diagnosis. Many biochemical assays and haematological investigations may aid in the further diagnosis and treatment of the fatal disease. Oral lesions are rare to occur and if present, are often mistaken for platelet abnormality [2].

Etiopathogenesis

There are four serotypes of the dengue virus (DEN 1-4). DHF is caused by one of four closely related, but antigenically distinct, virus serotypes (DEN 1-4) of the genus Flavivirus. Flavivirus is small and appears spherical with lipid envelope. Dengue virus is a single-stranded RNA virus transmitted mainly by the mosquito Aedes aegypti. Various hypotheses regarding the etiology are as follows:

1. Viral replication, which occurs primarily in macrophages, although dendritic cells (Langerhans cells) in skin may be the early targets of infection [3].
2. Direct infection of the skin by dengue virus [4].
3. Immunologic and chemically mediated mechanisms induced by interaction of the virus with the host [5].

Oral Manifestations: Oral involvement is seen in about 15-20% of patients with DHF. Most commonly affected sites are soft palate, lips and the tongue. More than 50% of cases have been reported in the soft palate by Stanford. In accordance with the current WHO and Pan American Health Organization, a case of DHF should meet the following clinical criteria: acute onset fever, hemorrhagic manifestations, thrombocytopenia, and hemoconcentration demonstrated by a rise in hematocrit value by 20% or more. The incubation period ranges about 4-7 days, after which the patient may experience acute onset of fever followed by non-specific signs and symptoms [6].

The febrile period may also be accompanied with rash which appears as maculopapular or macular that becomes diffusely erythematous later. The mucosal manifestations noted in dengue viral infections are conjunctival and scleral injection, where as oral manifestations appear assmall vesicles on the soft palate, erythema and crusting of lips and tongue. Chadwick *et al.* reported conjunctival involvement in 14% of patients; however, some reports have shown a higher percentage of mucosal involvement, e.g. scleral injection (90%) and vesicles on the soft palate (> 50%) [7].

Differential Diagnosis: When confronted with a febrile patient who has a rash similar to that seen with DF, the differential diagnosis is quite broad. The initial flushing erythema of the chest, head, and neck in association with fever can be seen in the early stages of many viral and bacterial infections. The generalized morbilliform eruption in association with fever can be seen in the later stages of various viral exanthems and bacterial infections. It is

Corresponding Author :- **Richa Wadhawan** Email:- richawadhawan@gmail.com

imperative to exclude Chikungunya fever as its clinical presentation is almost indistinguishable from DF and a similar epidemic is occurring in various parts of the world. Clinical features favoring Chikungunya fever over DF include a more rapid onset of symptoms, more severe rash, worse conjunctival injection, shorter febrile period, and fewer signs of easy bleeding. Although both conditions are associated with severe arthralgias, patients with Chikungunya fever are more likely to contort themselves into characteristic postures because of severe joint pain [8].

The rash in scarlet fever begins 12-48 hours after the onset of fever, starts as erythema of the neck, chest, and axillae and within 4-6 hours it becomes generalized. The rash consists of tiny papules on an erythematous background. Visually, it resembles 'sunburn with goose pimples' and feels like sand paper. Pastia's lines (linear petechial streaks) are seen in the axillary, antecubital, and inguinal areas. The cheeks are flushed with circumoral pallor. The tongue is initially white with bright red papillae, but later becomes beefy red (red strawberry tongue). After 7-10 days, desquamation occurs, most severely affecting the hands and feet, and lasts for 2-6 weeks [9].

Kawasaki Disease is an acute systemic vasculitis, predominately affecting children under 5 years of age. It is characterized by fever, bilateral non-exudative conjunctivitis, erythema of lip and oral mucosa, cervical lymphadenopathy, changes in the extremities and polymorphous exanthema. A skin eruption is seen in over 80% of patients with Kawasaki disease and is usually morbilliform or macular but may also be scarlatiniform, erythema multiforme-like, or pustular. A characteristic cutaneous feature is erythema of the perineum, which often desquamates within 48 hours. The conjunctival injection of Kawasaki disease is characterized by perilimbal sparing and lack of increased tearing or exudates [10].

The cutaneous manifestations are more extensive and predictable in staphylococcal toxic shock syndrome than in streptococcal toxic shock syndrome. Patients usually develop a diffuse scarlatiniform exanthem that starts on the trunk and spreads centripetally with erythema and edema of palms and soles. Erythema of the mucous membranes, a strawberry tongue, and hyperemia of the conjunctivae are also present. Desquamation of the hands and feet occurs 1-3 weeks after the onset of symptoms [11].

Erythema infectiosum, which is also known as fifth or slapped cheek disease, is another condition that has to be differentiated from DF, though it is most common in children between 4 and 10 years of age. The initial stage of the exanthem consists of bright red macular erythema of the cheeks, with sparing of the nasal bridge and circumoral regions. One to four days later, the second stage appears in the form of erythematous macules and papules, which progress to a lacy, reticulate pattern, occurring most often on the extremities and to a lesser extent on the trunk [12].

Measles classically presents with a prodrome and a pathognomonic exanthema Koplik's spots, appears during the prodrome, and is composed of gray-white papules on the buccal mucosa opposite the premolar teeth. The exanthem appears over 2-4 days and consists of erythematous macules and papules that begins on the forehead, hairline, and behind the ears and then spread in a cephalocaudal direction. On the fifth day, the exanthem starts to fade in the same order as it appeared [13].

Cutaneous manifestations of rubella typically presents 1-5 days following the prodrome as an eruption of erythematous macules and papules on the face and spreads in a cephalocaudal direction. In 2% of cases, petechiae on the soft palate occur late in the prodromal phase or early in the eruptive phase. The cutaneous eruption tends to fade in 2-3 days in the same order as it appeared [14].

Roseola infantum is a viral disease common in infants, characterized by high fever and skin rash. Cutaneous eruption in roseola is erythematous almond-shaped macules and papules on the trunk, neck, and proximal extremities. An exanthem of red papules on the soft palate and uvula (Nagayama's spots) may be seen; HHV-6 infection should be suspected in infants with febrile convulsions, even those without the examthem [15].

Cutaneous findings are observed in 5% of patients with infectious mononucleosis and include macular, papular, urticarial, petechial, scarlatiniform, or erythema multiforme like eruptions. Palatal petechiae may be present. Up to 90% of patients with infectious mononucleosis who receive ampicillin or amoxicillin develop a maculopapular eruption [16].

In secondary syphilis, the most commonly observed clinical presentation is a generalized nonpruritic papulosquamous eruption. Snail track ulcers in the oral cavity and Condyloma lata of the moist areas are other features [17].

Acute retroviral syndrome presents with generalized morbilliform exanthema that spares the palms and soles, lasts for 4-5 days, and is associated with fever, myalgia, and lymphadenopathy [18].

Rashes are among the most common adverse reactions to drugs. They occur in many forms and mimic many dermatoses. They occur in 2-3% of hospitalized patients. Exanthematous or maculopapular drug eruption are the commonest and they occur suddenly often with fever, 7-10 days after the drug is first taken. They are generalized, symmetric, and often pruritic. Maculopapular eruptions are often indistinguishable from viral exanthems and it is usually due to ampicillin or amoxicillin, but any drug can trigger it. Red macules and papules become confluent in a symmetric, generalized distribution that often spares the face [19].

Itching is common. Mucous membranes, vermilion border of lower lip, palms, and soles may be involved. Fever may be present from the onset. These eruptions are identical in appearance to a viral exanthem and routine laboratory tests usually fail to differentiate the two diseases. Lesions clear rapidly following withdrawal of the implicated agent and may progress to a generalized exfoliative dermatitis if use of the drug is not discontinued [20].

Management

Dengue fever is usually a self-limited illness with no specific currently available antiviral treatment. The World Health Organization (WHO) has provided guidelines for treatment of dengue fever/dengue hemorrhagic fever, which included supportive care with analgesics, fluid replacement and bed rest. Standard treatment is limited to electrolytic solutions, rest, measurements of body temperature, blood pressure, hematocrit, platelet count, and administration of antipyretics like paracetamol when fever is too high. Extracellular calcium plays a key role in platelet aggregation and for the regulation of the immune response in persons infected with Dengue Virus (DV), and dihydroxy-vitamin D has recently been found to alter IL-12 expression and dendritic cell maturation.

CONCLUSION

The prompt referral of the patient, made on the behest of observations of oral manifestations such as acute gingival bleeding, fever, ecchymosis on the arms and thrombocytopenia can save life of patient. This review emphasizes the value of taking correct and thorough history along with proper diagnosis as the dentist may become the first person who can actually diagnose and refer these patients for proper management.

REFERENCES

1. Bandyopadhyay S, Lum LC, Kroeger A. Classifying dengue, A review of the difficulties in using the WHO case classification for dengue hemorrhagic fever. *Trop Med Int Health*, 11, 2006, 1238-55.
2. Radakovic-Fijan S, Graninger W, Müller C, Hönigsmann H, Tanew A. Dengue hemorrhagic fever in a British travel guide. J *Am Acad Dermatol*, 46, 2002, 430-3.
3. Nagao Y, Koelle K. Decreases in dengue transmission may act to increase the incidence of dengue hemorrhagic fever. *Proc* Natl Acad Sci U S A. 2008 Feb 12, 105(6), 2238-43.
4. Loke H, Bethell D. Xuan C, Day C. et al. Susceptibility to dengue hemorrhagic fever in Vietnam, Evidence of an association with variation in the vitamin D receptor and FC_Receptor IIA Genes. *Am J Trop Med Hyg*, 67(1), 2002, 102–106.
5. Nimmannitya S, Halstead SB, Cohen SN, Margiotta MR. Dengue and Chikungunya virus infection in a man in Thailand, 1962-1964, Observations on hospitalized patients with hemorrhagic fever. *Am J Trop Med Hyg*, 18, 1969, 954-71.
6. Johnston L, Halliday H, King n. Langerhans Cells Migrate to Local Lymph Nodes Following Cutaneous Infection with an Arbovirus. *Journal of Investigative Dermatology*, 114, 2000, 560–568.
7. Chadwick D, Arch B, Wilder-Smith A, Paton N. Distinguishing dengue fever from other infections on the basis of simple clinical and laboratory features, Application of logistic regression analysis. *J Clin Virol*, 35, 2006, 147-53.
8. Rigau-Perez J, Vance Vorndam A, Clark G. The Dengue and Dengue Hemorrhagic Fever Epidemic in Puerto Rico, 1994–1995, *Am J Trop Med Hyg*, 64(1,2), 2001, 67–74.
9. Carlos C, Oishi K, Cinco M. Comparison of Clinical Features and Hematologic Abnormalities between Dengue Fever and Dengue Hemorrhagic Fever among Children in the Philippines. *Am J Trop Med Hyg*. 73(2), 2005, 435-40.
10. G.A. Scardina, F. Carini, V. Valenza , P. Messina and E. Maresi. Oral Manifestation of Kawasaki Disease. *Research Journal of Biological Science,* 2(4), 2007, 431-433.
11. Boon-Siang Khor, Jien-Wei Liu, Ing-Kit Lee, Dengue Hemorrhagic Fever Patients With Acute Abdomen, Clinical Experience Of Cases, *Am J Trop Med Hyg*. 74(5), 2006, 901–904.
12. Veraldi S, Rizzitelli G. Erythematous exanthem associated with primary infection by human parvovirus B19. Int J Dermatol, 34(2), 1995, 119.
13. Koplik H. The diagnosis of the invasion of measles from a study of the exanthema as it appears on the buccal mucous membranes. *Arch Pediatr*, 13, 1896, 918-22.
14. Ing-Kit Lee, Jien-Wei Liu, and Kuender D. Yang, Clinical Characteristics and Risk Factors for Concurrent Bacteremia in Adults with Dengue Hemorrhagic Fever, *Am J Trop Med Hyg*, 72(2), 2005, 221–226.
15. Ramos M, Mohammed H, Zielinski-Gutierrez E. et al. Epidemic Dengue and Dengue Hemorrhagic Fever at the Texas–Mexico Border, Results of a Household-based Seroepidemiologic Survey, December 2005. *Am J Trop Med Hyg*, 78(3), 2008, 364–369.
16. Akashi K, Eizuru Y, Sumiyoshi Y, et al. Brief report, severe infectious mononucleosis-like syndrome and primary human herpesvirus 6 infection in an adult. *N Engl J Med*. 329(3), 1993, 168-71.
17. Puneeta Vohra Singh, Ranjit Patil. Atypical oral manifestations in secondary syphilis. *Indian Journal of Dental Research*. 24(1), 2013, 142-14.
18. Tindall B, Barker S, Donovan B, Barnes T, Roberts J, Kronenberg C, et al. Characterization of the acute clinical illness associated with human immunodeficiency virus infection. *Arch Intern med*, 148, 1988, 945-9.
19. Loke H, Bethell D. Xuan C, Day C. et al. Susceptibility to dengue hemorrhagic fever in Vietnam, Evidence of an association with variation in the vitamin D receptor and FC_Receptor IIA Genes. *Am J Trop Med Hyg*, 67(1), 2002, 102–106.
20. Nagao Y, Koelle K, Decreases in dengue transmission may act to increase the incidence of dengue hemorrhagic fever. *Proc Natl Acad Sci USA*, 105(6), 2008, 2238-43.