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Oral Medicine

OROFACIAL MANIFESTATIONS OF DENGUE AND CHIKUNGUNYA: AN OVERVIEW

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ABSTRACT Dengue and Chikungunya are most common arboviral infections that represent major public health problem world wide in recent times. Both these infections are transmitted by common vector, namely aedes aegypti mosquito. The common clinical manifestations for both the diseases include fever, joint pains and maculopapular rash. Oral manifestations, although uncommon may represent a relevant contributive factor in early diagnosis of these vector borne diseases there by reducing the mortality and morbidity and improving patent outcome.

This review aims to portray the importance of oral lesions as early indicators in these mosquito borne diseases.

KEYWORDS : Dengue, Chikungunya, oral manifestations, Thrombocytopenia

INTRODUCTION:

Dengue and Chikungunya are two mosquito borne viral diseases of great public health concern in India. Dengue virus (DENV) and chikungunya virus (CHIKV) are transmitted by the same species of mosquito, Aedes aegypti and share spatiotemporal territories.[1]

Dengue: The name dengue originated from the Swahili word " bone breaking fever" [1] is seen mostly in the rainy season, affecting all the age groups.[2]

The first dengue-like illness to be documented in India was in madras and Calcutta was the first city to report virologica epidemic of DF.

Chikungunya: The name chikungunya is derived from kungunyala, the Swahili word for the contorted posture of patients because of their arthritic symptoms.[1]

VIROLOGY

Dengue:

Dengue virus (DENV) belongs to the family *Flaviviridae*, genus *Flavivirus*.[3]

Flaviviridae, is an arthropode-borne virus that includes four different serotypes (DEN-1, DEN-2, DEN-3, and DEN-4).[4]

Virus variation indicates the capacity of a virus to produce disease in a host. In the case of dengue, genetic differences among DENV isolates contribute to the severity of dengue disease.[5]

Chikungunya:

It is caused by chikungunya virus CHIKV, an RNA virus belonging to the genus *Alphavirus* of the family *Togaviridae*.[3]

ETIOPATHOGENESIS:

Dengue:

- **Cell and tissue tropism:** Langerhans cells (dermal dendritic cells) are generally proposed to be the initial target for DENV infection at the site of the mosquito bite, followed by the systemic infection of macrophages/monocytes and viral entry into the blood.
- **Antibody-dependent enhancement:** presence of pre-existing subneutralizing antibodies (Abs) is a major factor for developing dengue haemorrhagic fever (DHF)/ dengue shock syndrome (DSS) in both infants and adults. Enhancing Abs increase the efficiency of virus attachment and contribute to the binding of DENV to platelets.
- **Autoimmunity:** Autoantibodies represent another important factor involved in dengue disease pathogenesis. Several studies showed that the generation of autoantibodies against platelets, endothelial cells, and coagulatory molecules was associated with dengue disease.[5]

Chikungunya:

The exact pathogenesis of this virus is not known. Studies have suggested that the virus attacks fibroblasts explaining the involvement of muscle, joint and skin connective tissue. In addition epithelial, endothelial cells and macrophages were also found to be susceptible to the infection.[6]

CLINICAL FEATURES OF DENGUE:

Dengue virus infection may result in a broad spectrum of clinical presentations, ranging from asymptomatic or a mild, nonspecific fever, to classic dengue fever (DF), and severe presentations such as dengue hemorrhagic fever (DHF) or dengue shock syndrome.[7] (Table.1)

Table 1: Types of Dengue fever and Clinical features[2]

TYPE	CLINICAL FEATURES
Undifferentiated febrile illness or viral syndrome	**Follows a primary infection OR initial phase of a secondary infection**
Classic Dengue Fever	**Sudden onset of high fever lasting for 4-8 days. Intense headache, retro-orbital pain, fatigue, muscle and joint pain, unpleasant metallic taste in mouth, vomiting, diarrhea, and abdominal pain are the other symptoms.**
Dengue hemorrhagic fever	**Initial febrile stage- rapid onset intermittent high grade fever, lasting for 2-7 days, occasionally biphasic, hemorrhagic tendencies evidenced by at least one of the following:**

	A positive tourniquet test **Petechiae or purpura** **Mucosal bleeding** **Hematemesis, melena** **Platelet count ≤100 000/mm3.**
Dengue shock syndrome	**DHF associated with a weak rapid pulse, narrow pulse pressure, which is <20 mmHg, cold, clammy skin, restlessness, circumoral cyanosis .** **Death due to worsening shock and multi organ failure**

ORAL MANIFESTATIONS OF DENGUE:

Mucosal involvement is estimated to occur in 15% to 30% of patients with dengue viral infections and more commonly in patients with DHF than with DF.[8]

Erythema, crusting of lips, and tongue and soft palatal vesicles constitute the prominent oral features in dengue virus infection. Chadwick *et al*. reported higher cases involving the mucosa with scleral injection (90%), whereas Sanford noticed vesicular eruptions of the soft palate (>50%). Byatnal *et al*., reported numerous hemorrhagic bullae on the sublingual mucous membrane, lateral surface of the tongue, and floor of the mouth. Brown-colored plaque like lesions with a rough surface were seen on the buccal mucosa that showed bleeding on touch along with spontaneous bleeding from the gingiva and the tongue. Petechiae, purpura, ecchymoses, and nasal bleeding have also been reported. Mitra *et al*. reported bleeding gums, hemorrhagic plaques, and inflamed tonsils in a dengue-infected patient. Isolated hypoglossal nerve palsy following dengue infection is a rare occurrence.[4]

Oral candidiasis, osteonecrosis of dento-alveolar structure, and post-extraction bleeding,[9] Hyperplasia of fungiform papillae characterizing a transient lingual papillitis were also reported.[7]

CLINICAL FEATURES OF CHIKUNGUNYA:

After intra dermal inoculation of the virus by the mosquito, 72 to 97% of the patients develop the symptoms after an incubation period that can vary from 1 to 12 days (on average lasts from 2 to 4 days). Initially, the disease is characterized by a sudden onset of high fever with myalgia and severe arthralgia which may even interfere with sleep. Headache, photophobia, rash, weakness, fainting, confusion or deficit attention disorders can occur.

Joint affection is present in 70 to 100% of the patients , and it is characterized by severe arthralgia with sub acute to chronic arthritis, joint effusion, stiffness and, in some cases, tenosynovitis may appear. Since the onset of fever until 5 days later, 50% of the patients develop vesicular or bullous dermatosis with desquamation ,or maculopapular and petechial exanthema which is sometimes itchy and disappears with pressure (more often in adults) it affects the trunk, and can extend to palms, soles and face. It tends to be fleeting but it may persist over 2 days. Hyperemia of the outer ear, which reflects chondral inflammation possibly related to infection by CHIKV, is also observed.[10]

Some atypical manifestations of this disease include neurological, cardiovascular and ocular manifestations. Vertical transmission from infected mothers to their offspring has also been reported.[6]

ORO FACIAL MANIFESTATIONS OF CHIKUNGUNYA:

The most prominent complaint of patients with Chikungunya fever in relation to the oral cavity is the presence of distaste or dysgeusia. Another significant finding is the occurrence of minor apthous like oral ulcers. They are multiple and found to involve almost every part of the oral cavity, especially the tongue and the palate. Erosions, erythema and angular chelitis along with crustations at the angles of the mouth are also observed. Some rare findings are the presence of depigmented macules as well as oral mucosal pigmentations. Most of these oral lesions tend to last for 7-10 days and subside completely without any sequelae. Haemorrhagic manifestations are uncommon in Chikungunya. But when present they are mild and could be in the form of gingival bleeding. This was confirmed by Kannan who found that 1.4% of his patients complained of bleeding gums.

Kumar also reported of oral pseudomembranous candidiasis in several Chikungunya positive individuals. He postulated that the viral fever induced a transient immune depression which may lead to the development of this opportunistic infection.[6]

According to study conducted by Gowri Shankar, it was found that majority of the patients complained of burning mouth and erythema along with recurrent aphthous like ulcers. They also found that TMJ arthralgia was a significant finding. They recommended the introduction of the term "GUNYA STOMATITIS" to indicate TMJ arthralgia along with mucosal erythema and oral ulcers in a Chikungunya positive individual.[11]

Children may present with fever, facial rash, intra oral lesions described as "Koplik spots".[12]

Table 2: Summary of Oral lesions:[6]

Dysgeusia
Oral aphthous like ulcers
Gingivitis
Gingival bleeding
Crusted lesions on the lips and angles of mouth
Depigmented macules on the lips
Oral mucosal pigmentation
Oral candidiasis
Erosions
Erythema
Arthralgia of temporomandibular joint Koplik spots in children.12

DIFFERENTIAL DIAGNOSIS:

Dengue is the most alike and most often confused disease with chikungunya fever, partly because they share the same vector (A. aegypti) and, therefore, its same geographic space. The most important clinical data to differentiate it with dengue is the severe polyarthralgia, which is much more frequent in chikungunya fever; however, it should also be considered that it shows a more abrupt start, and a higher but of less duration fever than dengue. Rashes, conjunctival injections and arthralgias are more frequent in chikungunya fever than in dengue.10 (Table 3)

Table 3: Clinical comparison dengue and chikungunya:[10]

Clinical features	Chikungunya fever	Dengue
Fever	+++	++
Myalgia	+	++
Arthralgia	+++	+/-
Rashes	++	+
Blood dyscrasia	+/-	++
Shock	-	+/-
Leukopenia	++	+++
Lymphocytopenia	+++	++
Neutropenia	+	+++
Thrombocytopenia	+	+++

Other differential diagnosis includes viral exanthematous fevers measles, German measles, roseola infantum, acute retroviral syndrome, and others such as scarlet fever,[13] malaria, Rheumatic fever.[10]

Table 4: LABORATORY DIAGNOSIS OF DENGUE AND CHIKUNGUNYA:

Dengue	**Chikungunya**
Serologic Diagnosis: A decreased number of white blood cells (leukopenia), accompanied by a decreased number of platelet count (thrombocytopenia) and metabolic acidosis are the initial changes on laboratory examinations. Microbiological laboratory testing confirms the diagnosis of DF. Virus segregation in cell cultures, nucleic acid demonstration by polymerase chain reaction (PCR), and serological detection of viral antigens (such as NS1) or particular antibodies are the preferred microbiological assays.[4]	Serological diagnosis: The gold standard for confirmation of chikungunya fever is real time polymerase chain reaction (RT-PCR) directed toward the gene of the non-structural protein of CHIKV(NSP1) or the gene of the viral envelope of CHIKV(E) ,either in blood or synovial fluid. Other methods to confirm the diagnosis are the detection of response to antibodies with ELISA, indirect immunofluorescence, or reverse transcription loop-mediated isothermal amplification(RT-LAMP).[10]

Immunofluorescence De Andino *et al*. conducted a study on direct immunofluorescence involving the skin showed negative for the deposition of immunoglobulins and complement and for the presence of dengue viral antigen.[2]	

MANAGEMENT OF DENGUE:

Fluid replacement and antipyretic therapy with paracetamol is the preferred therapy following the febrile phase. Care should be taken not to use other non steroidal anti inflammatory drugs.

Judicious fluid administration forms the mainstay of treatment during the critical phase of the infection. Normal saline, Ringer's Lactate, and 5% glucose diluted 1:2 or 1:1 in normal saline, plasma, plasma substitutes, or 5% albumin are the routinely administered fluids.

WHO guidelines summarize the following principles of fluid therapy:

- Oral fluid supplementation must be as plentiful as possible. However, intravenous fluid administration is mandatory in cases of shock, severe vomiting, and prostration (cases where the patient is unable to take fluids orally)
- Crystalloids form the first-line choice of intravenous fluid (0.9% saline)
- Hypotensive states that are unresponsive to boluses of intravenous crystalloids, colloids (e.g., dextran) form the second-line measures
- If the patient remains in the critical phase with low platelet counts, there should be a serious concern for bleeding. Suspected cases of bleeding are best managed by transfusion of fresh whole blood.[4]

DENTAL CONSIDERATIONS IN DENGUE:

- Oral lesions are infrequently seen and are often misguided as platelet defects. Significant hemorrhagic manifestations need platelet transfusions. In general, there is no need to give prophylactic platelets even at <20,000/cu mm. Prophylactic platelets may be given at a level of <10,000/cu mm in absence of bleeding manifestations. In case of systemic massive bleeding, platelet transfusion may be needed along with red cell transfusion. Liver functions should be monitored.[4]

MANAGEMENT OF CHIKUNGUNYA:

There is no specific antiviral therapy available for chikungunya fever. The disease is generally self limitng and the goal of the therapy is symptomatic relief of complaints like fever and joint pain with paracetamol or NSAIDS.[14]

PREVENTION:

The measures recommended by the different international guidelines are aimed at preventing mosquitoes from biting and reproducing. They are listed below:

- Wear long-sleeved clothing.
- Use repellents with DEET (N,N-diethyl-meta-toluamide), IR3535 or icaridin. Avoid their use in infants under 2 months of age. These should be used in strict compliance with the instructions on the label.
- Avoid standing water and mosquito-breeding areas.
- Place mosquito nets over windows, doors and beds. Domestic insecticides in aerosol form, mosquito coils and other insecticides in vapourisers within the home can also be used.
- Treat clothing and equipment with permethrin.

Currently, the only vaccine that exists against these diseases, CYD-TDV, is for dengue and was approved for use in Mexico in December 2015. It is a recombinant, live attenuated tetra valent virus vaccine. It is recommended for people 9---45 years of age who live in endemic areas. The vaccine has higher efficacy for protecting against infections by serotypes 3 and 4 of DENV, has lower efficacy for protecting against DENV 1 and does not protect against DENV 2. It has also managed to decrease the risk of hospitalisation and severity of dengue in children between 9 and 16 years of age, but not younger children, who had a higher rate of hospitalisation due to dengue.[3]

CONCLUSION:

Dengue and chikunkunya viral infections present with a variety of systemic and oral manifestations. Though a rarity in chikungunya, Gingival bleeding in dengue may be an early marker of the disease which will aid in differential diagnosis of various febrile illnesses. Hence as dental professionals awareness of oral manifestations of these vector borne diseases is important for early diagnosis, prompt treatment thereby, evading significant complications.

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