

EDITORIAL

Dent. Med. Probl. 2011, 48, 2, 153–156
ISSN 1644-387X

© Copyright by Wrocław Medical University
and Polish Dental Society

ANUBHAV SHIVPURI¹, ABHAY SHIVPURI²

Dengue – an Overview

Denga – przegląd piśmiennictwa

¹ Senior Lecturer, Department of Oral and Maxillofacial Surgery, Mahatma Gandhi Dental College and Hospital, Jaipur, Rajasthan, India

² KMC Manipal, Karnataka, India

Abstract

Dengue, one of the most devastating mosquito-borne viral diseases in humans, is a significant life threatening problem in India and other developing countries. The disease, caused by dengue virus serotypes, ranges from asymptomatic infection to undifferentiated fever, dengue fever (DF), and severe dengue hemorrhagic fever (DHF). DHF is characterized by fever, bleeding diathesis and a tendency to develop a potentially fatal syndrome. Consistent hematological findings include vasculopathy, coagulopathy, and thrombocytopenia. Dengue is listed among the 40 emerging diseases of global importance affecting humans in terms of mortality and morbidity. It is important for dentists to have a basic knowledge about Dengue fever so that the early diagnosis is made and proper and quick treatment can be undertaken if such a patient is encountered in dental practice. Although dengue diagnosis and treatment is not the domain of dentists, the seriousness of the condition and its increased frequency throughout India some basic knowledge is necessary. This review outlines the clinical features, differential diagnosis, investigations, management, and prevention of dengue (**Dent. Med. Probl. 2011, 48, 2, 153–156**).

Key words: dengue, clinical features, management.

Streszczenie

Denga jest jedną z bardziej niebezpiecznych dla zdrowia człowieka chorób wirusowych przenoszonych przez komary. Jest poważnym zagrożeniem dla życia mieszkańców Indii i innych krajów rozwijających się. Chorobę wywołują serotypy wirusa dengi. Objawy są zróżnicowane, od infekcji bezobjawowej do niedającej się zróznicować gorączki, tzw. gorączki denga, aż po ciężką gorączkę krwotoczną. Ta ostatnia charakteryzuje się gorączką, skazą krwotoczną z tendencją do progresji zagrażającej życiu. Typowe objawy hematologiczne to skaza naczyńowa, koagulopatia i trombocytopenia. Denga jest na liście 40 nagłych chorób endemicznych o dużej chorobowości i śmiertelności. Jest to istotne dla lekarzy dentyków, którzy powinni mieć podstawową wiedzę o gorączce dengi, ponieważ wczesne rozpoznanie warunkuje właściwe i szybkie leczenie. Jest to szczególnie ważne w przypadku możliwości zetknięcia się z takim pacjentem w gabinecie. Chociaż rozpoznanie i leczenie dengi nie jest kompetencją lekarza dentyisty, to poważny przebieg tej choroby i wzrastająca częstość jej występowania wskazuje na konieczność zapoznania się z podstawową wiedzą na jej temat. Ten przegląd piśmiennictwa odnosi się do objawów klinicznych, diagnostyki różnicowej, leczenia i profilaktyki dengi (**Dent. Med. Probl. 2011, 48, 2, 153–156**).

Słowa kluczowe: denga, objawy kliniczne, postępowanie.

Dengue viruses (DV) belong to *Flaviviridae* family and have four serotypes (1 to 4). They are transmitted mainly by the *Aedes aegypti* mosquito and also by *Aedes albopictus* one.

Dengue viruses produce a subclinical infection that may progress to a mild self limiting disease, the dengue fever (DF) and a severe disease that may be fatal (the dengue haemorrhagic fever/ dengue shock syndrome). The mosquito vectors

are present in tropical and subtropical regions that determine the prevalence of DV in a region [1, 3].

Clinical Features

Infection with dengue virus may cause illness ranging from a mild undifferentiated fever to a se-

vere life-threatening presentation. The principal symptoms of dengue are [1–21].

1. Undifferentiated fever: This usually follows a primary infection but may also occur during the early phase of a secondary infection.

2. Dengue fever: Typically symptoms start with a sudden onset of high fever lasting 3 to 7 days. Other symptoms include intense headache, retro-orbital pain, fatigue, muscle and joint pain, unpleasant metallic taste in mouth, loss of appetite, vomiting, diarrhea, and abdominal pain. Dermatological manifestations include flushed skin (on face), a macular papular rash, or a fine skin rash on the arms and legs as the fever subsides are observed in many patients. Patients may present with diarrhea, seizure, vomiting, and abdominal pain. Minor bleeding (nose or gums), heavy menstrual periods, petechiae, and gastrointestinal bleeding may be present. A positive tourniquet test has been reported in many individuals with dengue fever.

3. Dengue hemorrhagic fever: Dengue hemorrhagic fever (DHF) usually follows a secondary dengue infection. It is characterized by a high fever, hemorrhagic phenomena, features of circulatory failure, and hepatomegaly.

DHF is divided into four grades according to severity:

- I No shock, only positive tourniquet test.
- II No shock, spontaneous bleeding other than a positive tourniquet test.
- III Shock.
- IV Profound shock with un-measurable blood pressure and/or pulse.

The clinical course of DHF is divided into three phases, namely, febrile, leakage, and convalescent phases. The febrile phase begins with sudden onset fever accompanied by generalized constitutional symptoms and facial flush. The fever is high grade (usually $> 39^{\circ}\text{C}$), intermittent, and associated with rigors. Clinical manifestations similar to DF are observed. A rash and bleeding manifestations appear in the early febrile phase. The fever lasts for 2–7 days and then falls to normal or subnormal levels when the patient either recovers or progresses to the plasma leakage phase.

Patients remain ill, despite normalization of temperature progress to DHF. Onset of plasma leakage is characterized by tachycardia and hypotension. The patient sweats, becomes restless, and has cold extremities. Most patients recover from this stage spontaneously or after a short period of fluid and electrolyte replacement. In severe cases with high plasma leakage, patients may develop full blown circulatory shock characterized by prolonged capillary refill time and narrow pulse pressures.



Fig. 1.
Mosquito
Aedes aegypti
Ryc. 1.
Komar
Aedes aegypti

During the phase of plasma leakage, pleural effusions (usually right side) and ascites are common. Pericardial effusions may also be observed. Myocarditis is associated with increased morbidity and mortality. Thrombocytopenia and hemoconcentration are usually detectable before the subsidence of fever and the onset of shock.

In DHF, bleeding may occur from any site and does not correlate with the platelet count. Hemorrhagic manifestations occur after fever has settled. The most common site of hemorrhage is the gastrointestinal tract (which manifests as hematemesis or melena), followed by epistaxis. Vaginal bleeding has been reported in females despite high platelet counts. Bradycardia and a confluent petechial rash with erythema and islands of pallor are seen during convalescence period.

WHO definition for dengue haemorrhagic fever:

- current or recent fever,
- platelet count $\leq 100\,000/\text{mm}^3$,
- haemorrhagic manifestations,
- objective evidence of plasma leakage caused

by increased vascular permeability manifested by at least one of the following: elevated haematocrit ($\geq 20\%$ over baseline or a similar drop after intravenous fluid replacement), pleural or other effusion (eg. ascites), low protein.

(World Health Organisation. Dengue, dengue haemorrhagic fever and dengue shock syndrome in the context of the integrated management of childhood illness. 2006).

4. Dengue shock syndrome: DSS is associated with very high mortality, tachycardia, hypotension, cold blotchy skin, congested peripheries, and circumoral cyanosis. Patients with DSS die due to the multiorgan dysfunctions and disseminated intravascular coagulation. The duration of shock is short and the patient rapidly recovers with appropriate supportive therapy.

Differential Diagnosis

Differential diagnosis of dengue fever and dengue hemorrhagic fever [21]:

- infectious mononucleosis,
- chikungunya viral infections,
- enteroviral infections,
- rickettsial infections,
- rubella influenza,
- leptospirosis.

Laboratory Investigations

Specific methods used for the diagnosis of dengue infections include virus isolation, serology, and molecular techniques [reverse transcriptase-polymerase chain reaction (RT-PCR)] [10, 15–21]. Laboratory diagnosis of dengue must consider the timing of clinical course and relevant parameters in their quantitative patterns.

Virus Isolation and Identification

Virus isolation is a gold standard for diagnosing DENV infections. Serotypes of DENV are determined using immunofluorescence (IF) staining in infected cells with serotype-specific monoclonal antibody. Viral isolation is useful when the samples are collected in early phase of disease (within 6 days). Dengue viruses can be isolated from serum, plasma, or leucocytes during the febrile phase and also from postmortem specimens such as liver, lung, spleen, lymph nodes, thymus, cerebrospinal fluid, or pleural/ascitic fluid. The most sensitive virus isolation method is *in vivo* amplification through mosquito inoculation.

Serological Diagnosis

Serological techniques include hemagglutination inhibition tests, enzyme-linked immunosorbent assay (ELISA), complement fixation test, and neutralization tests. Dengue IgM and IgG ELISA are sensitive (83.9–98.4%) and specific (100%), less expensive, quick, and simple tests to perform. Dengue IgM antibodies appear in serum by the fifth day of infection and become undetectable by 30–60 days of illness. The conventional or capture ELISAs have been used to identify different dengue viral serotypes.

Molecular Detection

RT-PCR is a valuable diagnostic tool with high sensitivity and specificity even before dengue-specific antibodies are produced.

RT-PCR is more sensitive when compared to virus isolation and also identifies the circulating serotype.

Management [3, 16–21]

Fever is treated with Paracetamol.

- 1–2 years: 60–125 mg/dose,
- 7–12 years: 250mg/dose,
- adult: 500 mg/dose.

Nonsteroidal anti-inflammatory drugs such as ibuprofen should be avoided. Sponging is helpful. In the early phase of illness, increased oral fluids are given; intravenous fluids should be used in the presence of severe vomiting or dehydration.

Monitoring platelet counts and packed cell volumes should be done daily from the third day of fever and continued until recovery.

Management of DHF

The mainstay of management is maintenance of fluid and electrolyte balance. A platelet count < 100,000 and a > 20% rise in packed cell volume reflect significant plasma loss, mandating prompt volume replacement. The rate of fluid administration is guided by changes in urine output and packed cell volume. Judicious fluid administration is necessary to avoid respiratory distress secondary to massive pleural effusions/ascites or pulmonary edema.

The WHO recommends using crystalloids for volume replacement in DHF. Initial resuscitation using colloids have been shown to restore the cardiac index and pulse pressure and normalize the packed cell volumes sooner than crystalloid solutions.

Significant hemorrhagic manifestations need platelet transfusions:

- In general there is no need to give prophylactic platelets even at < 20,000/cumm
- Prophylactic platelets may be given at level of < 10,000/cumm 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.

Management of Dengue Shock Syndrome

Dengue shock is a medical emergency. Prompt administration of intravenous fluid to expand plasma volume is essential. Close maintenance of vital parameters is needed. Oxygen saturations are monitored and investigations including grouping and cross-match, full blood count, renal, and liver function tests should be done. Electrolyte abnor-

malities, hypoglycemia, and metabolic acidosis should be corrected. Fresh frozen plasma, platelet concentrates, or cryoprecipitate are individualized depending upon clinical and laboratory parameters. Two to three intravenous fluid bolus with Ringer's acetate or normal saline may be needed.

Criteria of Discharge of Patients

- absence of fever for at least 24 hours without the use of medications,
- return of appetite,

- satisfactory urine output,
- no respiratory distress,
- platelet count > 50,000/cumm.

Prevention

Prevention of DHF depends on the control of the mosquito vector by limiting its breeding places and treatment of stored water. These measures against dengue are effective only with a high level of government commitment, education, and community participation.

References

- [1] CHATURVEDI U.C.: Dengue and dengue haemorrhagic fever: Indian perspective J. Biosci. 2008, 33, 429–441.
- [2] MARISSA M. ALEJANDRIA: Dengue haemorrhagic fever or dengue shock syndrome in children. Clin. Evid. (Online), 2009.
- [3] PADMALAL GURUGAMA: Dengue viral infections. Indian J. Dermatol. 2010, 55, 68–78.
- [4] NARAYANAN M. et al.: Dengue fever epidemic in Chennai – a study of clinical profile and outcome. Indian Pediatr. 2002, 39, 1027–1033.
- [5] PANCHAROEN C., RUNGSARANNONT A.: Hepatic dysfunction in dengue patients with various severity. J. Med. Assoc. Thai. 2002, 85 (Suppl. 1), 298–301.
- [6] KABRA S.K. et al.: Myocardial dysfunction in children with dengue haemorrhagic fever. Natl. Med. J. India 1998, 11, 59–61.
- [7] KALAYANAROOJ S. et al.: Can doctors make an accurate diagnosis of dengue infections at an early stage? Dengue Bulletin. 1999, 23, 1–9.
- [8] HALSTEAD S.B. et al.: Dengue hemorrhagic fever in infants: Research opportunities ignored. Emerg. Infect. Dis. 2002, 8, 1474–1479.
- [9] MENDEZ A., GONZALEZ G.: Dengue haemorrhagic fever in children: Ten years of clinical experience. Biomedica 2003, 23, 180–193.
- [10] HEMUNGKORN M.: Dengue infection: A growing global health threat. BioScience Trends 2007, 1, 90–96.
- [11] RICHARDS A.L. et al.: The first reported outbreak of dengue hemorrhagic fever in Irian Jaya, Indonesia. Am. J. Trop. Med. Hyg. 1997, 57, 49–55.
- [12] SRIKIATKHACHORN A. et al.: Natural history of plasma leakage in dengue hemorrhagic fever: A serial ultrasonographic study. Pediatr. Infect. Dis. J. 2007, 26, 283–290.
- [13] KALAYANAROOJ S. et al.: Dengue patients at the Children's Hospital, Bangkok: 1995–1999. Review, Dengue Bulletin 2002, 26, 33–43.
- [14] WALI J.P.: Dengue haemorrhagic fever in adults: A prospective study of 110 cases. Trop. Doct. 1999, 29, 27–30.
- [15] BRANCH S.L., LEVETT P.N.: Evaluation of four methods for detection of immunoglobulin M antibodies to dengue virus. Clin. Diagn. Lab. Immunol. 1999, 6, 555–557.
- [16] DE PAULA S.O. et al.: The use of reverse transcription-polymerase chain reaction (RT-PCR) for the rapid detection and identification of dengue virus in an endemic region: A validation study. Trans. R. Soc. Trop. Med. Hyg. 2002, 96, 266–269.
- [17] THISYAKORN U., NIMMANNITYA S.: Nutritional status of children with dengue hemorrhagic fever. Clin. Infect. Dis. 1993, 16, 295–297.
- [18] CHUANSMRIT A. et al.: Transfusion requirements in patients with dengue hemorrhagic fever. Southeast Asian J. Trop. Med. Public. Health. 2000, 31, 10–14.
- [19] LYE D.C.: Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adults with uncomplicated dengue infection. Clin. Infect. Dis. 2009, 48, 1262–1265.
- [20] DUNG N.M. et al.: Fluid replacement in dengue shock syndrome: a randomized, double-blind comparison of four intravenous-fluid regimens. Clin. Infect. Dis. 1999, 29, 787–794.
- [21] KALAYANAROOJ S.: Choice of colloidal solutions in dengue hemorrhagic fever. J. Med. Assoc. Thai. 2008, 91, suppl. 3, S97–103.

Address for correspondence:

Anubhav Shivpuri
Senior Lecturer
Department of Oral and Maxillofacial Surgery
Mahatma Gandhi Dental College and Hospital
Jaipur, Rajasthan, India
E-mail: dranubhavshivpuriomfs@gmail.com

Received: 12.04.2011
Revised: 18.05.2011
Accepted: 23.05.2011

Praca wpłynęła do Redakcji: 12.04.2011 r.
Po recenzji: 18.05.2011 r.
Zaakceptowano do druku: 23.05.2011 r.