CLINICAL FEATURES AND DIAGNOSIS IN PATIENTS WITH DENGUE INFECTION

Dr. ALI JAWA  MD (USA), MPH (USA), FACE (USA)
Diplomate American Board of Endocrinology & Diabetes
Diplomate American Board of Internal Medicine
Diplomate American Board of Physician Nutrition Specialists
Assistant Professor of Endocrinology/Diabetes
Allama Iqbal Medical College, Lahore
DENGUE VIRUS SEROTYPES

DENV 1

DENV 2

DENV 3

DENV 4
Dengue virus

Life long immunity

Short term cross-protection

DENV 1  DENV 2

DENV 3  DENV 4

Short term cross-protection
Clinical Course of Dengue Infection

<table>
<thead>
<tr>
<th>Course of dengue illness</th>
<th>FEBRILE</th>
<th>CRITICAL</th>
<th>RECOVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of illness</td>
<td>1 2 3</td>
<td>4 5</td>
<td>6 7 8 9 10</td>
</tr>
<tr>
<td>Temperature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential clinical issues</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dehydration</td>
<td></td>
<td>Shock / Bleeding</td>
<td></td>
</tr>
<tr>
<td>Reabsorption / Fluid overload</td>
<td></td>
<td></td>
<td>Organ Impairment</td>
</tr>
<tr>
<td>Laboratory changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td></td>
<td></td>
<td>Platelet</td>
</tr>
<tr>
<td>Serology and virology</td>
<td></td>
<td></td>
<td>IgM/IgG</td>
</tr>
<tr>
<td>Viraemia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dengue Virus Infections WHO 2011 Classification System

- Dengue Virus Infection
  - Asymptomatic
    - Undifferentiated Fever
  - Symptomatic
    - Dengue Fever Syndrome
      - Without Hemorrhage
      - With Unusual Hemorrhage
    - Dengue Hemorrhagic Fever
      - No Shock
    - Dengue Shock Syndrome
    - Expanded Dengue Syndrome/ Isolated organopathy/ Unusual manifestation
Case Definition for Dengue Fever

* Probable
* Confirmed
* Reportable
Suspected

**Clinical Criteria:**

- Fever of 2 to 10 days duration (essential criterion) and two of the followings:
  - Headache
  - Retro orbital pain
  - Myalgia
  - Arthralgia/ severe backache/ bone pains
  - Rash
  - Bleeding manifestations (epistaxis, hematemesis, bloody stools, menorrhagia, hemoptyisis)
  - Abdominal pain
  - Decreased urinary output despite adequate fluid intake
  - Irritability in infants
2. Probable Case – (Suspected Case with both Supportive Lab Evidence)

**Supportive Lab Evidence:**

- Thrombocytopenia
- Leukopenia
3. **Confirmed Case** – (Probable case with any one of the three Confirmatory Evidence)

Confirmatory evidence of viral infection would therefore, be based on:

- Detection of IgM

  OR

- Detection of viral antigen (NS1 antigen in blood)

  OR

- Detection of virus by PCR

  OR

- Demonstration of ≥ 4 fold rise in IgG antibody titre in paired acute and convalescent serum
Out-patient department

Febrile patient (2-10 days)

Emergency department

Suspected Case

NS - 1 antigen

Probable case

CBC

Admit

Day 2-5 NS-1 antigen

Confirmed case

Day 6-10 IgM

REPORT
An acute febrile illness with **two** or more of the following manifestations:

* Headache
* Retro-orbital pain
* Myalgia
* Arthralgia
* Rash
* Hemorrhagic manifestations
* Leukopenia
* **Thrombocytopenia (less than 150,000)**
* **Rising Hct (5-10%)**

And

* **Supportive Serology** (a reciprocal Hemagglutination-inhibition antibody titer $\geq 1280$, a comparable IgG ELISA titer or a positive IgM antibody test on a late acute or convalescent-phase serum specimen)

Or

* **Occurrence at same location and time as other confirmed cases of dengue**
## Differential Diagnosis

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arboviruses</td>
<td>Chikungunya</td>
</tr>
<tr>
<td>Other viral Diseases</td>
<td>Measles; rubella and other viral exanthems; Epstein-Barr Virus, Enteroviruses, Influenza; hepatitis A, Hantavirus</td>
</tr>
<tr>
<td>Bacterial diseases</td>
<td>Meningococcemia, leptospirosis, <em>typhoid</em>, melioidosis, rickettsial diseases, Scarlet fever</td>
</tr>
<tr>
<td>Parasitic diseases</td>
<td>Malaria</td>
</tr>
</tbody>
</table>
CONFIRMED DENGUE FEVER

* A case confirmed by laboratory criteria

- Isolation of Dengue Virus from serum or Autopsy Sample
- ≥4 fold rise in IgG or IgM antibody titres in paired serum samples
- Demonstration of Dengue Antigen in autopsy specimen, serum or CSF
- Detection of Dengue Virus Genomic Sequence by PCR
Any probable or confirmed case of dengue should be reported to Health Department and requires admission to the hospital.
The following must **ALL** be present:

**Fever**, or h/o acute fever, lasting 2-7 days, occasionally biphasic

**Hemorrhagic tendencies**, evidenced by at least one of the following
- A positive tourniquet test
- Petechiae, ecchymoses or purpura
- Bleeding from mucosa, gastrointestinal tract, injection sites, or other locations
- Haematemesis or malena

**Thrombocytopenia** (≤100,000 per mm³)

**Evidence of Plasma Leakage** manifested by at least one of the following
- A rise in Hct ≥20% above average for age, sex and population
- A drop in Hct ≥20% after volume-replacement treatment
- Signs of plasma leakage such as pleural effusion, ascites and hypoproteinemia
CASE DEFINITION FOR DENGUE SHOCK SYNDROME

All of the **four** criteria of DHF  

**plus**

**evidence of circulatory failure** manifested by:

- Rapid and weak pulse, and
- Narrow Pulse Pressure ($\leq 20$ mmHg)
  Or manifested by
- Hypotension for age, and
- Cold, clammy skin and restlessness
Liver failure
- central nervous system (CNS) dysfunction
- myocardial dysfunction
- encephalopathy and seizures
- acute pure motor weakness

Mononeuropathies
- Polyneuropathies
- Guillain-Barré syndrome
- transverse myelitis
- myocarditis

EXPANDED DENGUE SYNDROME

Organopathy in the setting of acute dengue virus infection
CASE REPORT

Expanded dengue syndrome: subacute thyroiditis and intracerebral hemorrhage

Muhammad Zaman Khan Assir¹, Ali Jawa² and Hafiz Ijaz Ahmed³

Abstract

Background: Although most symptomatic dengue infections follow an uncomplicated course, complications and unusual manifestations are increasingly being reported due to rising disease burden. Expanded dengue syndrome is a new entity added into World Health Organization (WHO) classification system to incorporate this wide spectrum of unusual manifestations. We report a case of expanded dengue syndrome with subacute thyroiditis and intracerebral hemorrhage. This is the first case report of thyroiditis in dengue infection.

Case presentation: A 20 years old man presented with fever, myalgias, arthralgias, retro-orbital pain, vomiting and gum bleeding during a large dengue outbreak in Lahore, Pakistan. On 7th day of illness patient became afebrile, but he developed severe headaches, unconsciousness followed by altered behavior. On 9th day of illness patient developed painful neck swelling accompanied by fever, tremors, palpitations, hoarseness of voice and odynophagia. Examination revealed acutely swollen, tender thyroid gland along with features of hyperthyroidism. Laboratory evaluation revealed stable hematocrit, thrombocytopenia and leukopenia. Patient had seroconverted for anti-dengue IgM antibodies on the 10th day of illness. A non-contrast Computed Tomogram (CT) of the brain showed right frontal lobe hematoma. Thyroid profile showed increased free T3 and T4 and low TSH. Technetium thyroid scan showed reduced tracer uptake. He was diagnosed as having subacute thyroiditis and treated with oral prednisolone and propranolol. Follow up CT brain showed resolving hematoma. Patient's recovery was uneventful.

Conclusion: Subacute thyroiditis may develop during the course of dengue fever and should be included as a manifestation of expanded dengue syndrome. It should be suspected in patients with dengue fever who develop painful thyroid swelling and clinical features of hyperthyroidism.

Keywords: Dengue fever, Expanded dengue syndrome, Thyroiditis, Intracerebral Hemorrhage
EXAMINATION

- Tourniquet test
- **Pulse** (Bradycardia, Tachycardia in an afebrile patient)
- Blood Pressure
- **Pulse Pressure**
- Temperature
- Capillary refill time
INJECTED PHARYNX
PETECHIAL RASH
SUBMUCOSAL HEMORRHAGE
BRUISING
CAPILLARY REFILL TIME
TOURNIQUET TEST
TOURNIQUET TEST
Positive TT serves as the **only** indicator of hemorrhagic tendency in grade 1 DHF.

The sensitivity of the test varies widely from as low as 0% to 57%, depending on the phase of illness the test was done and how often the test was repeated, if negative.

In addition 5-21% of patients with dengue like illness had positive tourniquet test but subsequently have negative dengue serology

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Reference</th>
</tr>
</thead>
</table>
A recent study demonstrated that there was 95.3% positive predictive value if fever, positive tourniquet test, leucopenia/ thrombocytopenia/ hemoconcentration were used as screening criteria.

Presence of $\geq 10$ petechiae per square inch should be considered positive.

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Reference</th>
</tr>
</thead>
</table>
Dengue Fever and DHF could be indistinguishable at the time of presentation

All probable and confirmed dengue fever cases need to be admitted and reported to health department

Careful attention physical signs and symptoms as well as appropriate and timely laboratory tests are key to diagnosis
Thank You