Clinical presentations and laboratory findings in suspected cases of dengue virus

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ABSTRACT

Objectives: To study the clinical presentations and laboratory findings of patients presented with fever in a Hospital in Portsudan, Sudan and to detect dengue virus antibodies in their blood.

Methods: This study was carried in Almwani Hospital during the period from April to July 2005. Eighty-four patients were included in this hospital-based study. All of them had fever. Their blood films, Widal tests for typhoid, stools and urine investigations were normal. The clinical data were collected using questionnaires. Two samples of blood were taken. One was for general hematological investigation (white blood cell and platelets count), while serum was taken from the other sample for serological detection of the dengue virus antibodies using the enzyme-linked immunosorbent assay (ELISA) technique.

Results: The fever was associated with vomiting (22 patients) and abdominal pain (44 patients). In 93% of the cases bleeding (epistaxes, purpura, malena, hematemesis, and others) occurred. Routine laboratory findings were leucopenia (90% of the cases) and thrombocytopenia (88% of the cases). The diagnosis was confirmed by ELISA detection of dengue virus immunoglobulin M antibodies (in 88% of the patient’s sera).

Conclusion: In endemic areas with mosquitoes such as Aedes aegypti, infection with dengue virus should highly be suspected in patients presented with fever. The ELISA or rapid tests for detection of the viral antibodies should be added to the routine investigations to any patient with complain of fever with no obvious cause. Surveillance program and mosquito control measures should be activated in Portsudan.

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Dengue and dengue hemorrhagic fever (DHF) are caused by one of 4 closely related, but antigenically distinct, virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4), of the genus Flavivirus. Dengue is primarily a disease of the tropics, and the viruses that cause it are maintained in a cycle that involves humans and Aedes aegypti, a domestic, day-biting mosquito that prefers to feed on humans. Infection with dengue viruses produces a spectrum of clinical illness ranging from asymptomatic or mild self-limiting infection to severe and fatal hemorrhagic disease.¹ According to the World Health Organization reports on the world distribution of dengue virus and its vector (Aedes mosquito), the studied area is one of the endemic zones with this mosquito.² Infection with dengue virus manifests a wide spectrum of clinical presentations. In most of the cases, especially in children younger than 15 years, the patient is asymptomatic or has a mild undifferentiated febrile illness. Typically, dengue fever is a self-limiting, acute, febrile illness, which occurs after an incubation period of 4-7 days. In younger children, it may be
accompanied by maculopapular rash. In older patients, the disease also may be very mild, or it may be more incapacitating, with complaints of rapid onset of high fever, headache, retroorbital pain, diffuse body pain, weakness, vomiting, sore throat, altered taste sensation, and a maculopapular rash, among others. This painful (break bone) and febrile phase lasts 2-7 days and, afterward, most patients improve slowly. Dengue virus disappears from bloodstream at approximately the same time that the fever dissipates. Leucopenia and thrombocytopenia are common finding in Dengue fever and are believed to be caused by direct destructive action of the virus on the bone marrow precursor cells. The resulting active viral replication and cellular destruction in the bone marrow are believed to cause the bone pain. Approximately one third of the patients with Dengue fever may have mild hemorrhagic symptoms, including petechiae, gingival bleeding, and a positive tourniquet test. Dengue fever is rarely fatal.

**Results.** In this study 38% of the patients were between 10-15 years old, 31% of them were between 5-10 years and 31% were less than 5 years. All of them were under 15 years. All of the studied cases had fever. Out of the total patients, 22 presented with vomiting and 44 with abdominal pain. They also presented with bleeding (93% of the cases) from different sites of the body. Fourteen patient complained of epistaxes, 28 had hematemesis and 8 had bleeding per gum. Twelve patients presented with purpura, 24 with malena and 24 with bleeding from venipuncture sites (Table 1). Two blood tests were carried out, the first was for the platelets in which 22% of the patients had platelets count less than 50000/mm, 55% were between 50000-100000/mm, 11%were between 100000-150000/mm, and 12% were more than 150000/mm. The second blood test was for the WBCs in which 8 of the patients had WBCs count less than 2000/mm, 42 were between 2000-3000/mm and 22 between 3000-4000/mm (normal range 4000 - 10000 /mm).

The results of the ELISA test showed that, the IgM antibodies against the dengue virus were detected in 88% of the patients’ sera. When we looked at the platelets count in patients reactive to the dengue virus antibodies, we found that 14 patients had less than 50000/mm count, 42 patients

<table>
<thead>
<tr>
<th>Clinical presentation*</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>84</td>
</tr>
<tr>
<td>Vomiting</td>
<td>22</td>
</tr>
<tr>
<td>Epistaxes</td>
<td>28</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>44</td>
</tr>
<tr>
<td>Hematemesis</td>
<td>28</td>
</tr>
<tr>
<td>Malena</td>
<td>24</td>
</tr>
<tr>
<td>Gum bleeding</td>
<td>8</td>
</tr>
<tr>
<td>Skin rash</td>
<td>12</td>
</tr>
<tr>
<td>Bleeding at venipuncture sites</td>
<td>24</td>
</tr>
<tr>
<td>Other sites</td>
<td>4</td>
</tr>
</tbody>
</table>

*Most of the patients had more than one symptom

**Methods.** This was a hospital-based study carried out in Almwani hospital, Portsudan, Sudan in the period from April to July 2005. Eighty-four patients (in the pediatric age) were included in this study. All of them had fever. Their blood films, Widal tests for typhoid, stools and urine investigations were normal. The other presenting symptoms (vomiting, abdominal pain, epistaxes, purpura, and others) were recorded using questionnaires. Two blood samples were taken. One in EDTA container for hematological investigations and the other in plain container for enzyme-linked immunosorbent assay (ELISA) immunoglobulin M (IgM) detection of the dengue virus. The white blood cells count (WBC) and the platelets count were carried out using the routine counting chamber. The sera in the plain containers were used for the detection of the antibodies of the virus by using the ELISA technique (Nova Tec company, Germany). The qualitative immuno-enzyme determination of IgM class antibodies against dengue virus was based on the ELISA technique.

Microtiter strip wells were pre coated with dengue virus antigen type 2 to bind to the corresponding antibodies of the specimen. After washing the wells to remove all the unbound sample material horseradish peroxidase (HRP) labeled anti-human IgM conjugate was added. The conjugate bound to the captured dengue virus-specific antibodies. The immune complex formed by the bound conjugate was visualized by adding Tetramethylbenzidine (TMB) substrate, which gives a blue reaction product. The intensity of this product was proportional to the amount of dengue virus-specific IgM antibodies in the specimen. Sulfuric acid was added to stop the reaction. This produced a yellow endpoint color. Absorbance at 450 nm was red using an ELISA microwell plate reader.
were between 50000-100000/mm, 10 patients were between 100000-150000/mm, and 8 had more than 150000/mm.

**Discussion.** Although the number of cases was small, this study highly reflects the importance of putting dengue fever on the top of the diseases that cause febrile illness in Portsudan. Despite poor surveillance for dengue in Africa, epidemic dengue fever has increased dramatically since 1980. Most activity has occurred in East Africa, and major epidemics were reported for the first time in Seychelles (1977), Kenya (1982), Mozambique (1985), Djibouti (1991-92) and Somalia (1982-1993). Now, cases of dengue fever also appear in Portsudan (2005). In 1997, dengue is the most important mosquito-borne viral disease affecting humans; it’s global distribution is comparable to that of malaria, and an estimated 2.5 billion people live in areas at risk for epidemic transmission. Each year, tens of millions of cases of dengue fever occur, and depending on the year, up to hundred of thousands of DHF. The case-fatality rate of DHF in most countries is approximately 5%. Fortunately, there were no deaths in our studied population, but severe forms of the disease with fatal cases will be expected to occur if no control measures to the disease take place.

In Portsudan, as well as in many regions in Africa and South-East Asia, the reasons for the emergence of dengue fever as a major health problem are complex and not well understood. However, several important factors can be identified. First, effective mosquito control is virtually nonexistent in most dengue-endemic areas. Second, major demographic changes have occurred, the most important for which have been uncontrolled urbanization and concurrent population growth. Third, increased travel by airplane and ship provides the ideal mechanism for transporting dengue virus between population centers. Lastly, in most countries the public health infrastructure has deteriorated.

The scenario of dengue in Portsudan indicates that many of the dengue cases may pass unnoticed or even misdiagnosed as other endemic febrile illness like malaria. We must, therefore, develop improved, laboratory-based surveillance systems that can provide early warning of an impending dengue epidemic. At least, this can alert the public to take action and the physicians to diagnose and properly treat dengue/DHF cases.

The mosquito-control program should be activated, since the only way to control the disease is by getting rid of the vector. Neither specific treatment nor vaccine is available for dengue virus.8

**References**