Comparison of the clinical manifestations exhibited by dengue and nondengue patients among children in a medical center in southern Taiwan

Shih-Tien Pan, Po-An Su, Kuo-Tai Chen, Hung-Jung Lin, Wen-Pin Lai

* Corresponding author. Emergency Department, Chi-Mei Medical Center, 901 Chung-Hwa Road, Yung Kang, Tainan 710, Taiwan.
E-mail address: shumiin@seed.net.tw (W.-P. Lai).

Abstract

Background: Dengue is one of the most important mosquito-borne diseases. Taiwan is located in an epidemic area for dengue, and several dengue outbreaks have been reported in southern Taiwan. Therefore, we conducted this study to determine the incidence and clinical manifestations of symptomatic dengue infection.

Methods: We reviewed the medical records of 177 pediatric patients (age < 16 years) who underwent serum tests for dengue (polymerase chain reaction or capture enzyme-linked immunosorbent assay for dengue immunoglobulin M and immunoglobulin G antibodies) in the pediatric outpatient clinic, the pediatric ward, or the emergency department of the Chi-Mei Medical Center from January 1, 2007 to December 31, 2007. We evaluated the differences in the clinical characteristics and laboratory data between the dengue and nondengue patients.

Results: Most of the dengue cases appeared starting in July and peaked during November. In the dengue group, there were more school-age patients (age > 7 years) and a more frequent history of mosquito contact. There was no difference in the sex distribution. Most of the dengue patients had obvious symptoms including skin rash (79.0%), nausea/vomiting (47.4%), high fever (> 39°C; 44.7%), diarrhea (26.3%), abdominal pain (23.7%), and petechiae (15.8%). Leukopenia, thrombocytopenia, elevated aspartate aminotransferase levels, and elevated alanine aminotransferase levels were found in 78.4%, 79.3%, 34.5%, and 29.0% of the patients, respectively. Nondengue patients showed elevated C-reactive protein levels (57.5%).

Conclusion: Dengue is commonly found in older pediatric patients and is rare in infants. High fever and skin and gastrointestinal manifestations were usually found in dengue patients. The laboratory findings of leukopenia, thrombocytopenia, elevated levels of liver enzymes, and low C-reactive protein levels were common in dengue patients, and these markers could help confirm the suspicion of pediatric dengue infection.

Keywords: Clinical manifestations; Dengue fever; Pediatrics

1. Introduction

Dengue virus is endemic in tropical and subtropical areas and is the most common cause of arboviral disease in the world. In adults, the classical presentation of dengue includes fever, headache, myalgia, and skin rash. However, the clinical features of dengue vary with age, and secondary infections are more likely to result in severe symptoms. In addition, the limitations of verbal expression in the pediatric population might influence the presentation of dengue and make the diagnosis of dengue more difficult in children.

Taiwan is located in an epidemic area of dengue, and several dengue outbreaks have been reported in southern Taiwan. The accurate diagnosis and reporting of dengue infection is crucial for public health and disease control.
Pediatricians and emergency physicians need clear descriptions of the clinical features and laboratory findings for pediatric dengue patients. Therefore, we conducted a retrospective study to identify the common clinical and laboratory findings for pediatric dengue patients.

2. Materials and methods

This study was approved by the Institutional Review Board for Human Research of the Chi-Mei Medical Center, Tainan, Taiwan. We reviewed the charts of all pediatric patients (age < 16 years) who underwent serum tests for dengue [polymerase chain reaction or capture enzyme-linked immunosorbent assay for dengue immunoglobulin (Ig)M and IgG antibodies] in the pediatric outpatient clinic, the pediatric ward or the emergency department of the Chi-Mei Medical Center from January 1, 2007 to December 31, 2007. These patients were considered clinically suspected dengue cases.

All suspected cases were reported to the Centers for Disease Control (CDC), Taiwan, R.O.C. and blood samples from these patients were sent to the CDC. The diagnosis of dengue was established by the official report from the CDC. The diagnostic criteria for dengue included typical manifestations and positive results for virus isolation, dengue polymerase chain reaction, the presence of dengue nonstructural protein 1 antibody or the presence of paired dengue IgM and IgG antibodies with seroconversion or a 4-fold increase. The patients whose first serum test for dengue IgM and IgG antibodies was positive but who did not meet the other diagnostic criteria were classified as probable cases.

We reviewed the cases of 177 patients during the study period and excluded 18 patients because they were probable cases. Among the included patients, 38 patients had dengue, and the other 121 patients had a different disease. We used the Chi-square test to evaluate the differences in the clinical characteristics and laboratory data between the dengue and nondengue patients.

3. Results

3.1. General characteristics and clinical features

The monthly distribution of dengue patients is shown in Fig. 1. The dengue cases appeared starting in July and peaked in November, which is in line with the temporal distribution of dengue infections in Taiwan. The numbers of dengue and nondengue patients increased simultaneously. A comparison of the general characteristics of the dengue and nondengue patients revealed that both groups showed a slight male predominance (60.5% vs. 55.4%, p = 0.58). The age of the dengue patients varied from 1 year to 16 years. None of the dengue patients and 11 of the nondengue patients were younger than 1 year. There were more school-age patients (> 7 years) in the dengue group than in the nondengue group (73.7% vs. 43.8%, p < 0.05). There was a trend of more mosquito contact for the dengue patients (39.5% vs. 24.0%, p = 0.06; Fig. 2).

We selected 10 common clinical features that were present in > 15% of the dengue patients: skin rash, nausea/vomiting, fever > 39°C, cough, anorexia, diarrhea, myalgia/arthritis, abdominal pain, malaise, and petechiae. A comparison of the frequencies of these clinical features between the dengue and nondengue groups revealed that there were statistically significant differences in the occurrence of skin rash, nausea/vomiting, fever > 39°C, diarrhea, abdominal pain, and petechiae between the groups (Table 1).

3.2. Laboratory findings

Serum tests to determine the complete blood cell count and levels of C-reactive protein (CRP), alanine aminotransferase (AST), and aspartate aminotransferase (ALT) were performed in 154/159 (96.9%), 126/159 (79.2%), and 65/159 (40.9%), respectively, of the reviewed patients. In the dengue group, we found that 27/37 (73.0%) were leukopenic (white cell count < 3.5 × 10^9/L), 32/37 (84.5%) were thrombocytopenic (platelets < 150 × 10^9/L), 23/29 (79.3%) had elevated AST levels, 10/29 (34.5%) had elevated ALT levels and only 9/31 (29.0%) had elevated CRP levels (> 6 mg/L). By contrast, the nondengue group contained fewer patients with leucopenia (22/
Data are presented as %.

**Table 2**

<table>
<thead>
<tr>
<th>Laboratory data</th>
<th>Dengue</th>
<th>Nondengue</th>
<th>( p^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC ( \times 10^9/\text{L} )</td>
<td>3.11 ± 1.68</td>
<td>7.43 ± 3.72</td>
<td>—</td>
</tr>
<tr>
<td>WBC &lt; 3.5 ( \times 10^9/\text{L} )</td>
<td>27/37 (73.0)</td>
<td>22/17 (18.8)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Platelets ( \times 10^9/\text{L} )</td>
<td>123 ± 30</td>
<td>236 ± 92</td>
<td>—</td>
</tr>
<tr>
<td>Platelets &lt; 150 ( \times 10^9/\text{L} )</td>
<td>32/77 (48.4)</td>
<td>28/117 (23.1)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>127 ± 95</td>
<td>48 ± 86</td>
<td>—</td>
</tr>
<tr>
<td>AST &gt; 50 U/L</td>
<td>23/29 (79.3)</td>
<td>5/36 (14.0)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>57 ± 55</td>
<td>31 ± 59</td>
<td>—</td>
</tr>
<tr>
<td>ALT &gt; 50 U/L</td>
<td>10/29 (34.5)</td>
<td>2/36 (5.6)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>5 ± 5</td>
<td>21 ± 32</td>
<td>—</td>
</tr>
<tr>
<td>CRP &gt; 6 mg/L</td>
<td>9/31 (29.0)</td>
<td>43/95 (57.5)</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Data are presented as \( n/\text{sample size} \) or mean ± SD.

ALT = aspartate aminotransferase; CRP = C-reactive protein.

**4. Discussion**

The rainy season in southern Taiwan, the area in which the Chi-Mei Medical Center is located, starts in May and ends in September.1 Hot and wet environmental conditions increase the number of *Aedes aegypti* mosquitoes, the dengue vector.8 A study by Wu et al9 revealed that high temperature and high humidity have the most prominent effect on the occurrence of dengue at a time lag of 2 months. Accordingly, the numbers of dengue patients increased in July and peaked in November. The presence of dengue patients indicates that physicians should consider dengue infection in the differential diagnosis of febrile patients. However, in most months with a high incidence of dengue, the percentage of negative serum tests for dengue was > 50%. This result implies that it is still difficult for pediatricians and emergency physicians to differentiate dengue infection from other febrile diseases in pediatric patients.

The average age of dengue patients was higher than that of nondengue patients. Almost three-quarters of the dengue patients were older than 7 years, and no dengue patient was younger than 1 year. This finding is similar to the results of a survey in Thailand that found that most pediatric dengue patients are in the age group of 5–14 years.10 School-age children are more likely to spend time outdoors and thus are at a higher risk of being bitten by mosquitoes. Additionally, compared with infants and toddlers, children have better verbal skills and can better describe their symptoms. These factors might contribute to the higher incidence of dengue in school-age children.

The classical features of dengue infection in adults include high fever, headache, myalgia/arthralgia, nausea/vomiting, and skin rash.3 In our study, we found that skin rash, nausea/vomiting, fever > 39°C, cough, anorexia, diarrhea, myalgia/arthralgia, abdominal pain, malaise, and petechiae were the most common symptoms. Nevertheless, these symptoms are also present in patients with various other pediatric infectious diseases, and the presence of these symptoms does not confirm dengue infection. Accordingly, we compared the frequencies of these clinical features in dengue and nondengue patients to identify the predominant symptoms of dengue infection. We found that skin rash, nausea/vomiting, fever > 39°C, diarrhea, abdominal pain, and petechiae were commonly observed in dengue patients and that cough, anorexia, myalgia/arthralgia, and malaise were nonspecific presentations in both dengue and nondengue patients. We found the expression of the nonspecific symptoms, including anorexia, myalgia/arthralgia, and malaise, requires a higher verbal ability and that the ability of a patient to report these symptoms cannot be adequately replaced by the observations of the patient’s family. The different levels of verbal ability might partially explain the differences in the clinical features in adult and pediatric dengue patients.

There were obvious differences in the results of the serum tests between the dengue and nondengue groups. Leukopenia and thrombocytopenia are commonly present in patients with dengue, which may contribute to early bone-marrow suppression combined with increased peripheral destruction of cells during the febrile and early convalescent phases of dengue.1 These unique findings are seldom found in children who do not have dengue.

The liver is an organ that can be infected by the dengue virus. The histological hepatic changes reported for dengue include microvesicular steatosis, hepatocellular necrosis, Kupffer cell hyperplasia and destruction, Councilman bodies, and cellular infiltrates in the portal tract.11 Clinically, hepatomegaly and increased serum liver enzyme levels occur frequently in dengue patients.11–13 The elevation of the serum AST level appears to be greater than the elevation of the ALT level, which differs from the characteristics of viral hepatitis (ALT levels are usually higher than AST levels).14 We found similar findings in our pediatric dengue patients, and elevated AST and ALT levels...
could serve as guides to distinguish pediatric dengue patients from children with other febrile diseases.

Determining the CRP level is a useful serum test to identify severe bacterial infection in febrile children.\textsuperscript{15} We found that elevated CRP levels are seldom present in dengue patients and that the elevation in the CRP levels is small when present (the highest CRP level in the dengue group was 12.7 mg/L). Markedly increased CRP levels are less likely to occur in dengue patients, and therefore, pediatricians and emergency physicians should consider other febrile diseases in the differential diagnosis when increased CRP levels are found.

In conclusion, dengue is commonly found in older pediatric patients and is rare in infants. High fever and skin and gastrointestinal presentations were usually found in dengue patients. Laboratory findings including leukopenia, thrombocytopenia, elevated liver enzyme levels, and low CRP levels are commonly present in dengue patients, and these markers could help confirm the suspicion of pediatric dengue infection.

Conflicts of interest

All contributing authors declare no conflicts of interest.

References