Clinical Article

Clinical and Laboratory Presentation of Typhoid Fever

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Abstract

A total of 314 children with clinical and/or laboratory diagnosis of typhoid fever admitted to the Dicle University Hospital pediatric infectious diseases ward were reviewed for demographic data such as age, sex, clinical features, and results of laboratory tests. There were 187 male and 127 female patients, with a mean age of 9.6 years ranging from 6 months to 16 years. Eleven of all the children were less than one year of age, while 23 were under the age of five years. Predominant symptoms were fever, abdominal pain, vomiting, and headache. Hepatomegaly was almost twice as frequently observed as splenomegaly. Common clinical signs of typhoid fever in adults such as relative bradycardia and spots were seldom documented. A febrile convulsion was the presenting symptom in nine of the patients, all of whom were under the age of five years. Intestinal perforation was present in five of the patients. Antibiotic susceptibility tests in 67 cases revealed resistance rates of 17% for ampicillin, 5% for trimethoprim-sulfamethoxazole, 4% for ceftriaxone, and 6% for sulbactam-ampicillin. No resistance was detected against the quinolones and chloramphenicol. Elevated serum alanine and aspartate aminotransferase (50 > /U/L) levels were observed in 32% of our patients. At presentation, 38% of all patients were anemic (Hb <12 g/dl), 10% were thrombocytopenic (<105/mm3). Except the two bacteriologically confirmed typhoid fever patients died during the period of observation, all patients survived from their severe illness completely. Int Pediatr. 2001;16(4):227-231.

Key words: typhoid fever, S. typhi

Introduction

Salmonella typhi infection remains a serious problem in developing countries. It has been estimated that approximately 12.5 million cases of typhoid fever occur annually in the developing world (excluding China) with 7.7 million cases in Asia alone. The disease is predominantly a disease of school age children and young adults and is reported to be milder in infants and young children. Various organs have been involved in the course of enteric fever, resulting in a wide array of presentation. From the Department of Pediatrics (Dr Yaramis, Dr Katar, Dr Taş) and Infectious Diseases and Clinical Microbiology (Dr Hosoglu), Dicle University Hospital, Diyarbakir, Turkey; Department of Pediatrics Nizip State Hospital (Dr Yıldırım), Gaziantep, Turkey; Department of Pediatric Infectious Unit, University of Istanbul, Medical School of Istanbul (Dr Yalçın), Istanbul, Turkey.

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The presenting symptoms and sign of typhoid fever in children differ significantly from those in adults. Studies from endemic areas show that younger children are more likely to present with a non-specific febrile illness. The aim of our study was to determine the clinical and laboratory presentation of typhoid fever in hospitalized children in this endemic area between 1990 to 1999.

Material and Methods

We reviewed the medical records of all patients admitted to the Ward of Pediatric Infectious Diseases between January 1990 and May 1999. This is a pediatric referral hospital at the southeastern region of Turkey, where typhoid fever is endemic. In this study, the children were divided into two groups: those who had blood and/or stool culture positive for S. typhi, and who had clinical features strongly suggestive of enteric fever, and those who had culture-negative and serology positive and had clinical features strongly suggestive of enteric fever. There were 187 male and 127 female patients, with a mean age of 9.6 years ranging from 6 months to 16 years. Number of cases below 5 years of age was 34 (15 of them females). All of the cases were living in this endemic area, the southeastern region of Turkey, and none of the cases were vaccinated for typhoid fever that was not included in the routine immunization program.

Table 1 shows the clinical features of the children on admission. The predominant symptoms were fever (95%), abdominal pain (66%), vomiting (44%), and headache (38%). Fever, vomiting, abdominal pain, loss of appetite, diarrhea and cough were the predominant symptoms for those under 5 years of age. None of the patients presenting with a cough had radiological evidence of pneumonia. However, typical symptoms in adults such as cough, headache and constipation were uncommon, tending to occur in older children. Common clinical signs of typhoid fever in adults such as relative bradycardia and rose spots were seldom documented.

Hepatomegaly was detected in 132 (42%), splenomegaly in 63 (20%) patients. Intestinal perforation was present in five of the patients. Their mean age was 13.7 years. The predominant symptoms in those patients with intestinal perforation were fever and abdominal pain, with a mean duration of 12.3 days. The diagnosis of perfora-
Typhoid Fever

Laboratory Investigations

On admission blood was taken for hematocrit, platelet count, differential white cell count, liver function test, examination for malaria parasites and Widal test. A blood culture and fecal culture were performed before treatment. The antibiotic susceptibility tests to eight antibiotics (ampicillin, trimethoprim-sulfamethoxazole, ceftriaxone, sulbactam-ampicillin, ofloxacin, ciprofloxacin, and chloramphenicol) were determined by using the Kirby-Bauer disk diffusion technique or Scepter microdeletion method according to the recommendations of the National Committee for Clinical Laboratory Standards.12 Of the 314 patients with clinically suspected typhoid fever included in the study, 67 (21%) had blood cultures positive for S. typhi. Twenty-one and twenty-three patients with positive blood cultures also had positive stool cultures and positive Widal serology, respectively. Widal’s agglutination titers of at least 160 were positive in all children. The H agglutinin titer of ≥ 1:320 was found in 42 patients (20%). In the 67 blood culture isolates, the antimicrobial resistance rates were as follows: ampicillin (17%); trimethoprim-sulfamethoxazole (5%); ceftriaxone (4%); sulbactam-ampicillin (6%). There was no resistance to quinolones and chloramphenicol. Table 2 shows the hematological and biochemical profile of typhoid fever patients.

The mean total white blood cell count was 7.3 (2.4-18) 10^3/mm^3. The presence of a shift to left was found in a significantly larger proportion of patients (78%). A white blood cell count of < 4.5 x 10^9/L was found in 18% of all patients. Elevated serum alanine and aspartate aminotransferase (>50) levels were observed in 100 (32%) of our patients. At presentation, 38% of all patients were anemic (Hb <12 /dl), 10% were thrombocytopenic (< 10^5/ mm^3).

Discussion

Salmonella typhi infection remains a serious problem in developing countries. With an estimation of 12.5-16.6 million cases each year and 600 000 deaths, typhoid fever continues to be a major cause of morbidity and mortality in tropical countries, especially among children.1,13 However, in more affluent regions of the world, proper sanitation has successfully diminished the infections with S. typhi. In Turkey, the number of cases with S. typhi infections has shown an increase in recent years from 10 001/year in 1991 to 20 960/year in 1995.14

Typhoid fever in children in the first 2 years of life exhibits certain differences from the clinical course in adults.15 In our study, 17% of all patients with typhoid fever were under 5 years, which is close to the figure in some series.8,16 School-children were the most affected. Children in this series commonly presented with fever, headache, and gastrointestinal symptoms, and diarrhea was more common than constipation in this study, which is in accordance with the results from other studies.16-19

Typhoid fever may be particularly difficult to diagnose in infants, as M athieu et al. have reported, 10 patients in their series having mild illness characterized by non-specific symptoms such as fever and cough.20 In our series, 6 infant cases had fever and only one infant had cough. Fever and convulsion was the presenting symptom in 13 (20%) of the patients, all of whom were under the age of five years.

Hepatomegaly (42%) and splenomegaly (20%) were the major physical findings in our study. Seçmeer et al. reported that, in a large series in children with enteric fever, besides, 68.5% had elevated liver enzymes, while only 44.4% had hepatomegaly with or without splenomegaly.22 In a study, 31 children with typhoid fever with ages of 2 months to 12 years and blood culture positive for multidrug resistant S. typhi were prospectively studied for their hepatic functions at the time of hospitalization.22 Hepatic manifestations included hepatomegaly

<table>
<thead>
<tr>
<th>Feature</th>
<th>No (%) of Patients</th>
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<tr>
<td>Signs</td>
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<tr>
<td>Hepatomegaly</td>
<td>132 (42)</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>63 (20)</td>
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<tr>
<td>Abdominal tenderness</td>
<td>27 (8)</td>
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<tr>
<td>Rose spots</td>
<td>5 (1)</td>
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<tr>
<td>Relative bradycardia</td>
<td>6 (2)</td>
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<tr>
<td>Rales</td>
<td>6 (2)</td>
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<tr>
<td>Cervical lymphadenopathy</td>
<td>18 (6)</td>
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<td>Encephalopathy</td>
<td>16 (5)</td>
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Table 1 - Clinical Symptoms & Signs of Patients at Admission
Of the 314 patients with clinically suspected typhoid fever cases, and the H-agglutinin titer was reported that, in their large series, the O-agglutinin titer was of 1:50 or more as a criterion for diagnosis, a positive Widal test was found in 88% of typhoid fever cases on the first occasion when the test was done. Parry et al. also reported that in their studies, the usual symptoms were fever and abdominal pain, with a mean duration of 10.5 days and the mean age was 11.4 years.

The Widal test is a useful diagnostic test in children in endemic area. In a study in Hong Kong, the usefulness of the Widal test in diagnosing childhood typhoid fever in endemic areas was investigated. The test was done on 150 children with other febrile illnesses and 98 bacteriologically proven cases of typhoid fever. Of the 150 children with non-typhoidal fever, only one had an H-agglutinin titer of 1:50. By using an H or O-agglutinin titer of 1:50 or more as a criterion for diagnosis, a positive Widal test was found in 88% of typhoid fever cases on the first occasion when the test was done. Parry et al. also reported that, in their large series, the O-agglutinin titer was ≥ 100 in 83% of the blood culture-positive typhoid fever cases, and the H-agglutinin titer was ≥ 100 in 67%. Of the 314 patients with clinically suspected typhoid fever included into the present study, 67 (21%) had blood cultures positive for S. typhi. Twenty-three patients with positive blood cultures also had positive Widal serology. Widal’s agglutination titers of at least 160 were positive in all children. The H agglutinin titer of ≥ 1:320 was found in 42 patients (20%).

Typhoid hepatitis is associated with a significant morbidity, and in one series, the mortality rate reached to 20%. None of our patients had positive serology for acute viral hepatitis A. The Widal test is a useful diagnostic test in children in endemic areas. Oh et al. and Laditan reported that, in their series, hepatomegaly was almost twice as frequently observed as splenomegaly. Elevated serum aminotransferase levels were observed in 32% of our patients. Sixteen of our cases presented with encephalopathy and 32% had reactive splenomegaly.

In another study in Turkey, Kanra et al. found 17% encephalopathy, 73% reactive salmonella hepatitis, 4% pneumonia and 4% gastrointestinal bleeding. In our study, 3 patients had gastrointestinal bleeding and perforation.

Oh et al. and Thisyakorn et al. have reported increases in aminotransferase levels in 38% of the cases. The hepatic reticuloendothelial system plays a major role in engulfing the invading bacteria. The extent of liver involvement in typhoid fever varies from mild elevation of transaminases, almost all patients being in the second and third week of illness, to a more dramatic presentation with a picture indistinguishable from viral hepatitis in 1 to 26% of cases. Typhoid hepatitis is associated with a significant morbidity, and in one series, the mortality rate reached to 20%. N one of our patients had positive serology for acute viral hepatitis A.

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Table 2 - Hematological and Biochemical Profile of Typhoid Fever Patients

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<td>74</td>
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In another study of 65 patients with perforated typhoid enteritis, 45 were males and 20 females with ages ranging from 5 to 15 years, presenting symptoms were fever, abdominal pain, vomiting and either diarrhea or constipation. The overall mortality rate in this study was 20% and was adversely influenced by the longer duration of perforation, presence of shock and fecal peritonitis. In our study, intestinal perforation was present in five of the patients. The mean age was 13.7 years. The usual symptoms were fever and abdominal pain, with a mean duration of 12.3 days. The diagnosis of perforation was usually based on the history and physical examination alone. Among 5 children, 3 had a single perforation, and 2 had multiple perforations. None of these children with perforated typhoid enteritis died during and after operation in the pediatric surgery ward. In an endemic area of typhoid fever, 45 were males and 20 females with ages ranging younger than five years of age.

Leukopenia is thought to be a characteristic finding in patients with typhoid fever. Hemophagocytosis is an important mechanism in producing neutropenia, anemia and thrombocytopenia in several infectious and noninfectious disorders. In a study of 29 children with 8 month to 15 years of age, leukopenia was found in 6 (20%) patients. In the present study, the mean total white blood cell count was 7.3 (2.4-18) x 10^9/mm^3. A white blood cell count of < 4.5 x 10^9/liter was found in 18% of patients and the presence of a left shift was found in a significantly larger proportion of patients (78%). Complications noted in this series included thrombocytopenia (< 10^5/mm^3) in 10%, urine proteinuria in 36% and gastrointestinal perforation in 1.5% of patients. A stormy course with rhabdomyolysis, intestinal ulcers, intestinal perforation, and pancreatitis occurred rarely, as have been described by others.

References

Typhoid Fever


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