Role of Abdominal Ultrasound in the Diagnosis of Typhoid Fever in Pediatric Patients

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Received 18 July 2016; accepted 5 September 2016
Available online 19 November 2016

Abstract  An early diagnosis of typhoid fever caused by Salmonella typhi is difficult because of several spectra of clinical findings, identical to those of several other types of infections. A definitive diagnosis of typhoid fever is made by hemoculture as well as the Widal test. With pediatric patients, this life-threatening infection remains inherently long enough, demanding urgent attention. In typhoid fever, splenomegaly, enlarged mesenteric lymph nodes (MLNs), bowel wall thickening, acalculus cholecystitis, and hepatomegaly occur, which are diagnosed by the ultrasonography (USG) test. USG is a noninvasive, easily available, economical, fairly acceptable, and fairly sensitive test. The high-resolution real-time gray-scale USG method has simplified the evaluation of pathologic conditions, with remarkable clarity; consequently, an accurate assessment of the associated lesions can be done. In typhoid-endemic areas, USG findings as cited above could be used for diagnosis of typhoid fever, particularly when serology is equivocal and hemocultures are negative or not available. It was evident from USG studies that 12 of 52 patients had calculus cholecystitis; these individuals as well as eight patients without cholecystitis having hemocultures negative for S. typhi were excluded from the study. The rest of the cases (n = 32) were included in this USG-based study for evaluation of features specific for typhoid fever. The following observations were recorded: splenomegaly in 32 patients, enlarged MLNs in 30 patients, bowel wall thickening in 25 patients, acalculus cholecystitis in 20 patients, and hepatomegaly in 10 patients. It can be concluded that these USG features—spleenomegaly, enlarged MLNs, bowel wall thickening, and acalculus cholecystitis—should strongly favor the diagnosis of typhoid.

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Conflicts of interest: The authors declare that they have no conflicts of interest.
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Introduction

Typhoid fever caused by Salmonella typhi is endemic in Third World countries, with a remarkable predominance in India. Indeed, an early diagnosis is difficult because of several spectra of clinical features of the disease. The serological Widal test and hemoculture are the confirmatory tests, which require some 7 days and 4 days, respectively [1]. However, in most situations, an improper/inadequate use of antibiotics by the patient prior to any medical consultation leads to the failure of proper diagnosis. Systemic manifestations such as enlarged mesenteric lymph nodes (MLNs) and mural thickening of the terminal ileum are seen in typhoid patients [2]—along with other findings such as splenomegaly, acute acalculus cholecystitis, and hepatomegaly, which are confirmed using the ultrasonography (USG) test. USG was recognized as the most accepted imaging modality for the evaluation of typhoid fever, being quick, noninvasive, and nonionizing; eventually, it was considered safe for children. Emphasis on the usefulness of detecting MLNs with ultrasound as a diagnostic method during the early stage of typhoid was given [3]. MLNs are vital barriers against the systemic dissemination of S. typhi in a mouse model [2]. Obviously, typhoid cases are difficult to diagnose early, which remains an important goal in this field. USG examination of the abdomen is helpful in the diagnosis of typhoid during the 1st week of onset of fever. The bowel wall thickening of the ileocecal region with MLNs is not specific for any one causative organism for bacterial enteritis, but a proper diagnosis of typhoid fever could be possible along with the typical USG features described above.

The present study was aimed at elucidating the usefulness of USG over the routine Widal test and hemoculture, in the diagnosis of typhoid fever. The high-resolution real-time gray-scale USG method has simplified the evaluation of pathologic conditions, with remarkable clarity; consequently, an accurate assessment of the associated abdominal lesions in suspected cases of typhoid fever can be done. In this study, hemoculture results confirmed typhoid fever cases; additionally, the relationship between USG findings and manifestation of typhoid pathogenesis is explained. Thus, USG findings might be helpful toward the early diagnosis of typhoid fever.

Methods

This 1-year study (which lasted up to February 2016) was conducted with 52 pediatric patients aged 4 years to 14 years, who were clinically suspected of having enteric fever in the past 2–5 days with consistent abdominal pain, and who presented to the pediatric outpatient department of the hospital. On the same day, along with USG procedures, blood samples of patients were used for culture in xylose deoxycholate agar. Subsequently, these patients underwent routine Widal test after 7 days of fever. A convex transducer with a frequency of 4 MHz and a linear transducer with a frequency of 12 MHz on the ultrasound machine (Voluson S6, GE Healthcare, New York) were used for a thorough evaluation of the abdomen with emphasis on liver, spleen, and gall bladder (GB), as well as the small and large intestines. USG Murphy’s sign along with peri-cholecystic edema and fluid collection were evaluated according to the graded compression method [2] in suspected cases of acalculus cholecystitis. A GB wall thickness of 3 mm was considered normal. After the initial USG procedure on Day 1, repeated scans were done with selected patients on 5-day intervals up to 15 days of presentation. The average duration of the USG examination was 20 minutes, and no patient required analgesia to achieve the adequate bowel compression.

Microbial analysis

To determine the presence of the causative bacterium, a 1-mL blood sample taken from each patient was serially diluted to 1:10 in 0.1% peptone water, and an aliquot of 0.5 mL was plated on xylose deoxycholate agar; one or two drop(s) of Tween 80 was/were added to the first of each dilution with each blood sample. Plates were incubated at 37°C for 24 hours. In each trial, a few presumptive colonies were picked and were confirmed as S. typhi [4]. At the end of 4 days, the growth of S. typhi was confirmed (Figure 1).

Results

It was evident from USG studies that 12 of 52 patients had calculus cholecystitis; these patients as well as eight patients without cholecystitis and whose hemocultures tested negative for S. typhi were excluded from the study. The rest of the cases (n = 32) were included in the USG-based study for the evaluation of specific features of typhoid such as splenomegaly, enlarged MLNs, bowel wall thickening, acalculus cholecystitis, and hepatomegaly. Splenomegaly was found in 32 patients; 30 patients had enlarged MLNs; 25 patients had bowel wall thickening; 20 patients had acalculus cholecystitis; and 10 patients had hepatomegaly (Table 1).

Figure 1 Salmonella typhi in xylose lysine deoxycholate (XLD) agar.
Among the 32 splenomegaly cases, six patients had abscess formation in the spleen. Splenomegaly persisted in 19 (60%) patients with 40% resolution on the 15 days of USG examination; nevertheless, there was a significant decrease in spleen size (Figure 2). We also noted that in 30 of 32 cases, enlarged MLNs ranged from 12 mm to 32 mm (mean, 16 mm) in long axis diameter. Lymph nodes were oval or rounded hypoechoic structures with well-defined margins seen in the 8–14 years age group. However, MLNs continued to be observed in 12 (40%) cases in 15 days, which showed significant diminution in size. Bowel wall thickening due to edema of mucosa and submucosa with preserved layered structure of the intestinal wall was noted in 25 cases, and it persisted in eight (30%) cases at 10 days, whereas it was resolved in all cases at 15 days. Furthermore, 11 cases had increased wall thickness of the terminal ileum and cecum; 14 cases had only ileal thickening (Figure 2), where the maximum thickness was 9 mm. Acalculus cholecystitis presented as distended and thick-walled GB in 20 cases (Figure 2); positive U/S Murphy’s sign, dense biliary sludge, and pericholecystic edema were also noted. Moreover, the color Doppler study revealed an increase in vascularity in thickened wall regions, and pericholecystic fluid collection and dense biliary sludge persisted in 5 cases at 15 days. The liver was enlarged with no change in parenchymal echotexture in eight cases. Overall, liver sizes returned to normal in all cases at 10 days, except one (Figure 2).

**Discussion**

Enteric fever is an acute systemic disease consisting of malaise, fever, abdominal discomfort, transient rash, hepatosplenomegaly, and leukopenia. Most commonly, enteric fever is caused by *S. typhi* and is referred to as typhoid fever. Less commonly, enteric fever can be caused by other *Salmonella* serotypes and is referred to as paratyphoid fever.

Basically, biliary infections are asymptomatic, but GB and bile ducts are commonly infected during typhoid fever. Initially, infecting bacilli multiply in the small intestine and further invade the intestinal lymphatic system and MLNs, causing enlargements. Consequently, bacilli occupying the liver and biliary ducts cause bacteremia and get excreted.

<table>
<thead>
<tr>
<th>Follow-up scan</th>
<th>Splenomegaly (32 cases)</th>
<th>MLNs (30 cases)</th>
<th>Bowel thickening (25 cases)</th>
<th>Acalculus cholecystitis (20 cases)</th>
<th>Hepatomegaly (10 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>32 (100)</td>
<td>30 (100)</td>
<td>25 (100)</td>
<td>20 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Day 10</td>
<td>29 (90.6)</td>
<td>21 (70)</td>
<td>8 (30)</td>
<td>14 (70)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Day 15</td>
<td>19 (59.3)*</td>
<td>12 (40)*</td>
<td>0</td>
<td>5 (25)</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as *n* (%).

MLNs = mesenteric lymph nodes; USG = ultrasonography.

* Significant diminution in sizes.

**Figure 2** Abdominal ultrasonography (USG) findings for typhoid fever in children. (A) Enlarged mesenteric lymph nodes (MLN). (B) Splenomegaly (SPLN). (C) Thickened gall bladder (GB) with biliary sludge. (D) Edematous mural thickening of terminal ileum.
into the bile, and remain concentrated in the GB in high titers during the progress of the infection. Thus, enlarged MLNs, bowel wall thickening, acalculus cholecystitis, and hepatosplenomegaly are the typical pathophysiological changes seen with the infection during USG procedures. Owing to S. typhi infections, two case reports have recorded dilated or hydropic GB from USG studies [5,6].

Furthermore, Vi capsular polysaccharide was first identified as a virulence antigen in S. typhi, and it regulates the early inflammatory response from intestinal epithelial cells during S. typhi infection [6]. This is in marked contrast to the findings in other forms of salmonellosis involving severe intestinal inflammation. Thus, an early diagnosis of typhoid fever in endemic areas by USG-based detection of enlarged MLNs may be useful.

Mural thickening of the bowel may be an inflammatory response triggered by systemic infection from bacilli, which was observed after the onset of typhoid fever. Enlarged MLNs should have given rise to the described systemic manifestations in patients with typhoid fever. Although an early diagnosis of typhoid fever is crucial for improving prognosis and suitable treatment, the nonspecific nature of its clinical features makes diagnosis difficult. As other febrile infections—such as malaria, extrapulmonary tuberculosis, and viral enteritis—are often found in developing countries [1,7], specific findings typical for these diseases can be taken as exclusion criteria. For example, enlarged MLNs in tubercular enteritis can be differentiated as being more hypoechoic because of the loss of fatty hilum and the presence of central necrotic changes.

Splenomegaly and a moderately large liver are the main USG features for the diagnosis of malaria. Specifically, patients infected with the malarial parasite must have a positive result in a blood test that is 85–95% sensitive and 95–100% specific, depending on the microscopic test or with fluorescent microscopy and several advanced tests involving the antigen diagnostic test. In cases of typhoid fever with delayed diagnosis and lack of proper clinical management, the patient may experience complications, bleeding gut, and peritonitis, and in severe cases, renal impairment, retinopathy, and encephalitis with convulsions may occur.

In this study, in typhoid fever cases enlarged MLNs appeared shortly after fever onset. The use of USG to assess typhoid fever pathogenesis would help febrile children with some long-standing morbidity; emergent attentions are needed in comparison to adults for diagnosis of this life-threatening infection.

**Conclusion**

Sonographic features specific for typhoid fever, splenomegaly, enlarged MLNs, bowel wall thickening, acalculus cholecystitis, and hepatomegaly were evaluated. Thus, sonography is an additional diagnostic tool for typhoid fever with the above positive findings.

**Acknowledgments**

This work, as well as SN Rath as a Junior Research Fellow, is supported by a major research project (BT/PR8214/PBD/17/863/2013), from the Department of Biotechnology, Government of India, New Delhi.

**References**


