

CLINICAL FEATURES AND EARLY DIAGNOSIS OF TYPHOID FEVER EMPHASIZING USEFULNESS OF DETECTING MESENTERIC LYMPHADENOPATHY WITH ULTRASOUND AS DIAGNOSTIC METHOD

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Abstract. Typhoid fever is endemic in Pakistan. Most patients are children. As the symptoms and signs are often unspecific, it is difficult to diagnose typhoid fever without blood culture. We retrospectively reviewed 51 cases of typhoid fever who were all admitted from 1 June through 31 August 2002. Sixteen cases were positive by blood culture and confirmed as typhoid fever. All cases had *Salmonella typhi*. Although 16 cases were culture-negative, they were clinically diagnosed as typhoid fever. The remaining 19 cases were clinically diagnosed without blood culture. The clinical features of the culture-confirmed cases were more severe than the culture-negative cases. Mesenteric lymphadenopathy was very frequently detected with ultrasonography, in both culture-confirmed and culture-negative cases. The rates of detecting mesenteric lymphadenopathy were 69% and 63%, respectively. Meanwhile, the rate in non-typhoid fever patients was 5.5%. It was considered that detecting mesenteric lymphadenopathy with ultrasonography was very useful in the diagnosis of typhoid fever in endemic areas.

INTRODUCTION

Our hospital is located in Peshawar City, Pakistan, near the border with Afghanistan. Although the number of Afghan refugees has been decreasing since they started returning to Afghanistan, the majority of patients visiting our hospital are still Afghans. We have four other clinics in remote rural villages in eastern Afghanistan and northern Pakistan.

Typhoid fever is endemic in this area (Mandal, 1992). Especially in summer, many patients with typhoid fever visit our hospital. In almost all cases, typhoid fever patients do not show specific symptoms or signs. For this reason, it is often difficult to clinically diagnose a case of typhoid fever. If diagnosis and treatment are delayed, severe consequences sometimes result, so early diagnosis and early treatment are essential.

In our hospital, we cannot perform blood culture for all patients. Fortunately, having ultrasonographs, we routinely examine all admitted patients with ultrasonography. Using ultrasonography, we have found, for the last three or four years, that patients clinically diagnosed with typhoid fever very frequently had mesenteric lymphadenopathies.

MATERIALS AND METHODS

We retrospectively reviewed typhoid fever patients

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who were clinically diagnosed with the disease from 1 June through 31 August 2002. Special emphasis was placed on the diagnostic value of mesenteric lymphadenopathy detected by ultrasonography.

We treated 51 cases of clinically-diagnosed typhoid fever during the period. All patients were admitted. Out of the 51 cases, 16 were positive by blood culture and definitely confirmed as typhoid fever (Group A). All cases had *Salmonella typhi*. Thirty-five cases were diagnosed clinically. Out of the 35 cases, 16 had negative blood cultures (Group B). In the remaining 19 cases, culture was not performed. The reason blood culture was performed was that typhoid fever was more strongly suspected. Therefore these cases, groups A and B, were reviewed for clinical features.

The criteria for clinical diagnosis of typhoid fever were as follows. Not all criteria need to be fulfilled to determine typhoid fever. 1) Persistent high-grade fever, 2) No specific symptoms or signs related to other diseases, 3) No clear examination results related to other diseases, and 4) Detection of mesenteric lymphadenopathy by ultrasonography.

RESULTS

The clinical features of culture-confirmed cases (A) and culture-negative cases (B) are shown in Table 1. The average ages were 7.6 and 9.4 years, respectively. The rates for patients less than 15 years old were 94% and 81%. The average numbers of days with fever higher than 38°C before admission were

8.2 and 13.3. The average number of days with fever higher than 38°C after admission were 6.9 and 2.8. Maximal fever higher than 40°C was seen in 81% and 31% cases respectively. The average numbers of days' hospitalization were 9.4 and 5.8.

Comparing the two groups of cases, culture-confirmed cases had more severe conditions than culture-negative cases. Culture-confirmed cases showed longer durations of fever after admission, higher rates of maximum fever higher than 40°C, and longer hospital stays. Meanwhile, in culture-negative cases, the duration of fever before admission was longer.

Symptoms and signs, were unspecific in almost all cases. Symptoms and signs related to the abdomen were observed more frequently in culture-confirmed cases. Rose spots were observed in only one case (Table 2).

As for the laboratory tests, the result of Widal test was 100% positive in culture-confirmed cases, while it was 50% in culture-negative cases. There were no differences in white blood cell count and hemoglobin, between the two groups. Mild anemia was seen in both groups. In most cases leukopenia was not seen

(Table 3).

The main ultrasonographic findings were mesenteric lymphadenopathy, splenomegaly and hepatomegaly (Table 4). Mesenteric lymphadenopathy was detected frequently in both groups of culture-confirmed cases and culture-negative cases (69% and 63%, respectively). There was no difference in the rate of detection of mesenteric lymphadenopathy between the two groups. These enlarged mesenteric lymph nodes were usually seen in the right lower quadrant of the abdomen and in multiple numbers. The average size of the lymph nodes was 1 to 2 cm. Compared with the other patients with fever more than 38°C and whose ages were less than 18 years, who were admitted during the same period but not diagnosed with typhoid fever, mesenteric lymphadenopathy was detected in 4 of the 73 patients (5.5%). These were two cases of abdominal tuberculosis, one of malaria and one of amebiasis.

Fig 1 is an ultrasonographic picture of the culture-confirmed 6-year-old female. Maximum fever exceeded 40°C. Fever subsided 10 days later. There were many enlarged lymph nodes in the right lower quadrant area. One of the largest measured 1.6 cm.

Table 1
Characteristics of the 32 patients.

Characteristics	Culture-confirmed cases (A) (N=16)	Culture-negative cases (B) (N=16)
Average age (yr)	7.6	9.4
<15 years old (%)	94	81
Sex (no.)		
Male	8	11
Female	8	5
Duration of fever >38°C before admission (day)	8.2	13.3
Duration of fever >38°C after admission (day)	6.9	2.8
Maximal fever >40°C (%)	81	31
Hospital stay (day)	9.4	5.8

Table 2
Symptoms and signs.

	Abdominal pain	Vomiting, nausea	Cough	Abdominal tenderness	Rose spots
A (N=16) no. (%)	4 (25)	7 (44)	1 (6.3)	4 (25)	1 (6.3)
B (N=16) no. (%)	2 (13)	5 (31)	1 (6.3)	2 (13)	0 (0.0)

A : culture-confirmed cases; B : culture-negative cases.

Fig 2 is an ultrasonographic picture of the culture-confirmed 8-year-old male. Fever reached 40°C, and took 5 days to subside. Multiple enlarged lymph nodes were detected. The largest was 1.8 cm in diameter.

Although this case (Fig 3) was culture-negative, the high grade fever (over 40°C) continued and there were no signs in relation to other diseases. Furthermore, typical mesenteric lymph node enlargements were detected. So we clinically diagnosed this case as typhoid fever.

Table 5, shows the result of the antibiotic sensitivity test. There was no resistant strain to fluoroquinolones. There were few strains that showed resistance to third generation cephalosporins. Although we did not use chloramphenicol as a first line drug in the sensitivity

test, it was considered that almost all cases were multi-drug resistant.

In most cases, fluoroquinolones were used as the first choice. In some cases, ceftriaxone was used (Table 6). All cases showed good response to medication and were cured.

DISCUSSION

The general clinical features of typhoid fever in this study are similar to those of other reports (Malik and Malik, 2001; Tohme *et al*, 2002). The majority of the cases had unspecific symptoms and signs. For this reason, the clinical diagnosis of typhoid is often difficult without blood culture. If diagnosis and

Table 3
Laboratory examination.

	Widal test	WBC/mm ³	Hemoglobin (g/dl)
A (N=16)	7/7 (100%)	6,306	10.3
B (N=16)	5/10 (50%)	6,325	10.4

A: culture-confirmed cases; B: culture-negative cases

Table 4
Ultrasonographic findings.

	Mesenteric lymphadenopathy	Hepatomegaly	Splenomegaly	Ascites
A (N=16)	11 (69%)	3 (19%)	6 (38%)	1 (6.3%)
B (N=16)	10 (63%)	1 (6.3%)	2 (13%)	0 (0.0%)

A: culture-confirmed cases; B: culture-negative cases

Table 5
Antibiotic sensitivity test.

Antibiotic	Rate of sensitivity
Ciprofloxacin	100%
Ofloxacin	100%
Cefotaxime	91%
Amoxicillin-clavulanate	79%
Cefoperazon	67%
Amoxicillin	9%
Cefuroxime	0%
Sulfamethoxazole-trimethoprim	0%

Table 6
Medication (51 cases).

Antibiotic	No.
Ciprofloxacin	39
Ceftriaxone	8
Ofloxacin	2
Amoxicillin	1
Cefixime	1

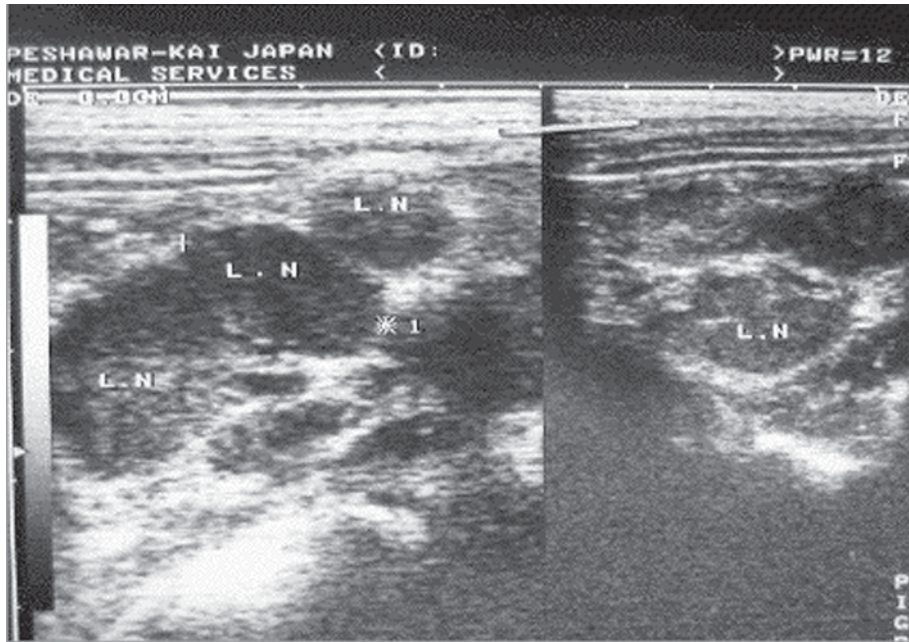


Fig 1- Ultrasonographic image of the culture-confirmed 6-year-old female case. Multiple enlarged lymph nodes were seen in the right lower quadrant area. One of the largest measured 1.6 cm.

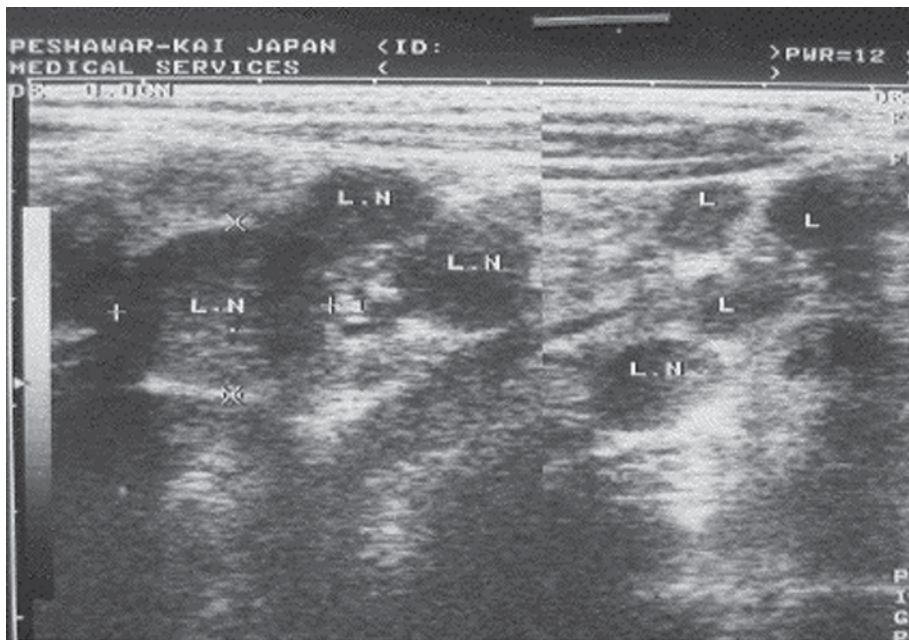


Fig 2- Ultrasonographic image of the culture-confirmed 8-year-old male case. Multiple enlarged lymph nodes were seen. The largest was 1.8 cm in diameter.

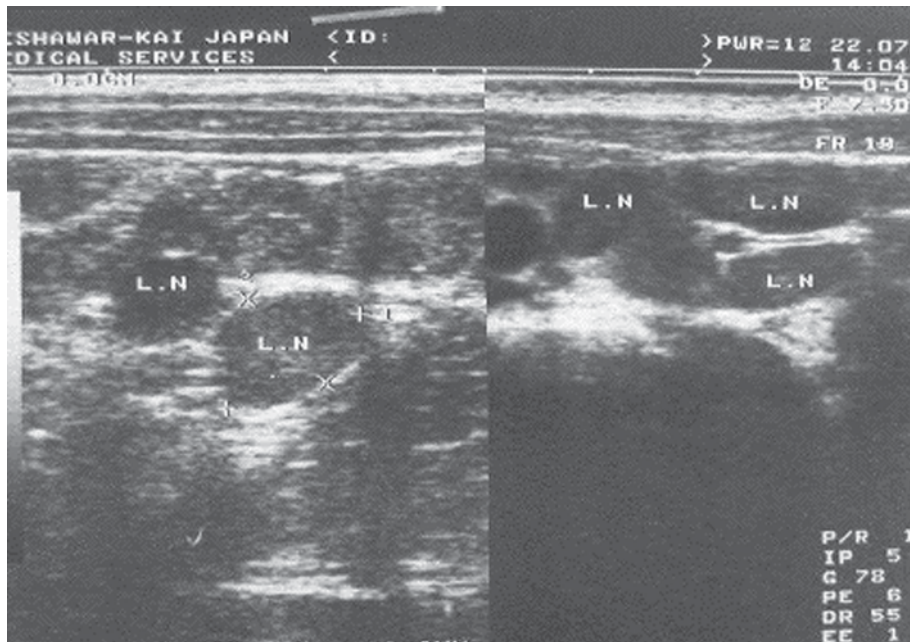


Fig 3- Ultrasonographic image of the culture-negative 10-year-old male case. Typical multiple mesenteric lymph node enlargements were seen. One of the largest measured 1.5 cm.

treatment of typhoid fever are delayed, it may lead to complications and severe consequences (Malik, 2002). Pakistan is an endemic area for typhoid fever (Mandal, 1992; Tohme *et al*, 2002). Examination of all patients admitted using ultrasonography revealed that typhoid fever patients often had mesenteric lymphadenopathy. There are many diseases which cause mesenteric lymphadenopathy, including appendicitis, tuberculosis, viral lymphadenitis and bacterial enteritis, including *Yersinia enterocolitica*, *Campylobacter jejuni*, and *Salmonella* or *Shigella* species (Lee *et al*, 1997). *Salmonella* reach the blood stream after proliferating in the mesenteric lymph nodes. For this reason it is considered that many typhoid fever patients may have mesenteric lymphadenopathy, and the most simple diagnostic method for detecting mesenteric lymphadenopathy is ultrasonography. Although there are case reports that show mesenteric lymphadenopathy in typhoid fever (Likitnukul *et al*, 2002), PubMed and the Cochrane Library, contained no report that reviewed the relation between typhoid fever and mesenteric lymphadenopathy with ultrasonography in numbers of typhoid fever cases. In this study, in the majority of cases of typhoid fever, mesenteric lymphadenopathy was detected by ultrasonography. Meanwhile, the rate of detection of mesenteric lymphadenopathy in other

febrile diseases was low. Therefore, ultrasonography may be considered very useful investigatory method for the early clinical diagnosis of typhoid fever especially in endemic areas, where most medical institutions are very poorly equipped.

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