Typhoid Intestinal Perforations in Turkey

Kalemoglu E,[1] Kalemoglu M[2]

[1]Dokuz Eylul University,
Internal Medicine Department,
Izmir, Türkiye.

[2]Uskudar University,
Faculty of Medicine,
Istanbul, Türkiye.

Corresponding Author

Murat Kalemoglu
Vice Dean of Uskudar University Faculty of Medicine,
Chief of Surgical Sciences Departments,
Director of General Surgery,
Saray Mahallesi Siteyolu Cd. No: 27 Zip code: 34768 - Umraniye / Istanbul / Türkiye.
E-mail: mkalemoglu@yahoo.com, murat.kalemoglu@uskudar.edu.tr

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ABSTRACT

Typhoid fever is a systemic infection caused by Salmonella Typhi. One of the most serious complications is intestinal perforation due to inflammation of the terminal ileum. In this study, we aimed to examine three cases with intestinal perforation that developed during a typhoid epidemic in terms of clinical, laboratory findings and treatment follow-up. The patients were in the 20-22 age groups and are male patients. Fever, malaise, and loss of appetite were the complaints encountered in all cases. During admission, the clinical and laboratory findings were hepatomegaly in two cases, abdominal tenderness in three, leukocytosis, and elevated serum transaminases. Gruber-Widal agglutination positivity was detected in all cases. It was found that mortality and morbidity decreased with early diagnosis, appropriate medical and surgical intervention (primary repair or resection and anastomosis) combined with serious intensive care is lifesaving in the point of therapy, and be careful at reperforations could develop even during medical treatment.

KEY WORDS

Intestinal perforation, Ileal perforation, Salmonella Typhi, Typhoid fever

INTRODUCTION

Bowel perforation is one of the leading and oldest fatal complications of typhoid. It usually develops in the 3rd or 4th weeks of the disease.[1] Vomiting, severe abdominal pain, abdominal tenderness and distension are the main symptoms. Secondary bacteremia, peritonitis and hypovolemic shock often cause mortality. While its incidence in our country was approximately 14% in the 1990s, it decreased to 0.56 per hundred thousand in 2010.[2,3] However, we thought this health problem would increase in recent years due to immigration from neighboring countries. We believe that it should be kept in mind as a rare differential diagnosis element in cases of the acute abdomen. Therefore, we aimed to convey this case report to you. In this study, three cases with perforation that developed during the typhoid epidemic in the common living area were examined in terms of clinical, laboratory findings and treatment follow-up.

CASE SERIES

The patients of this study were admitted to our hospitals between 2000 and 2016. Identification of salmonella strains isolated from the blood cultures of our cases was performed in Sarıkamıs Military Hospital and a Hospitalium Umraniye Hospital using classical microbiological methods and serotype determination using polyvalent antisera. Antibiotic susceptibility was investigated by Kirby-Bauer Disk diffusion method using *Cefotaxime, Ceftriaxone, Imipenem, Ciprofloxacin, Chloramphenicol, Ampicillin,* and *Trimethoprim-Sulfamethoxazole (TMP-SMX)* discs. The morbidity rate was 0% and there were not any the most common postoperative complications, included burst abdomen, wound infection, residual intra-abdominal abscesses, wound dehiscence, and enterocutaneous fistula. Mortality was 0%. The mean duration of hospitalization days was 11.7 days with a range of 10-15 days.

Case 1: Case 1, 21 years old, male patient. The patient, who was hospitalized for three days in the first Health Centre he applied to and was treated with *Thiamphenicol* (3x500 mg/day), had decreased complaints in the first few days, but after the third day, his fever increased again and his complaints increased. Then the patient was admitted to Military Hospital Infectious Diseases Service with complaints of abdominal pain, nausea, fever, and vomiting. The vital

Table 1. **Laboratory findings**

Cases	BK	Hb	Htc	PLT	Leukocyte formula (%)			ESH	SUB	AST	Gruber-Widal agglutination test					
					PNL	Lymphocyte	Monocytes				TO	TS	PAO	PAH	PBO	PBH
Case 1	15.1	10.8	34.3	62	85	11	2	36	304	75	1/640	1/320	1/40	1/40	1/40	1/40
Case 2	13.4	12.2	37.2	153	86	10	2	42	273	392	1/320	1/60	1/20	1/20	1/40	1/20
Case 3	12.7	12.3	38.4	113	88	9	2	35	232	213	1/320	1/320	1/40	1/40	1/40	1/40

BK: Leukocyte (x 10^3 /mm^3); Hb: Hemoglobin, Htc: Hematocrit, PLT: Platelet Count (X 10^3), PNL: Polymorphonuclear Neutrophilic Leukocyte Count, ESR: Erythrocyte Sedimentation Rate (Mm/S), AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase

signs were as pulse 94/min (rhythmic), ABP 110/65 mmHg, Fever 39,2℃, tongue dry and rusty, abdomen free, liver and spleen non-palpable. There were 4-5 macular rashes on the abdominal skin in the physical examination of the patient when he came to our clinic. The reproduction was observed 24 hours after all three blood cultures taken on the first day of the patient. As a result of the bacteriological identification, it was determined that these were *Salmonella Typhi*. No lactose-negative bacteria were found in the stool culture taken simultaneously. Bacteria could not be isolated in the urine culture. Other laboratory findings of our case were summarized in "Table-1". The patient was started on *ciprofloxacin* treatment (500 mg 2x1/day, PO) on the first day of hospitalization, and an increase in abdominal pain was observed on the second day of the treatment. Physical examination revealed increased abdominal distension, rebound, and defense findings. The presence of free air in the right hypochondrium was observed in the standing plain abdominal X-ray. At the same time, the patient with a fever of 39,6℃. Case 1 had a pulse of 124/min and a leukocyte value of 15.200/mm^3, underwent surgery because intestinal perforation developed. During the operation, there was approximately one liter of small intestine content in the abdomen, the omentum showed adhesions in the intestinal area, and the cecum was approximately 20 cm. It was reported that a 1x1 cm perforation was seen in the anti-mesenteric border region of the terminal ileum. Primary repair was done. Following the operation, the patient was started on *Ciprofloxacin* (2 x 200 mg/day IV infusion for 10 days) + *Ornidazole* (2 x 500 mg/day IV infusion for 10 days). *Trimethoprim-Sulfamethoxazole* (TMP-SMX) was prescribed to be used for one month in order to prevent the carriage of the agent in the gallbladder. As a result of the medical and surgical treatment, the patient was completely cured.

Case 2: Case 2 is a 20-year-old male patient. The first complaints of the patient who applied to the Infectious Diseases Service of Military Hospital with the complaints of abdominal pain and fever. *Thiamphenicol* treatment (3x500 mg/day) was administered for seven days by the first Health Centre he applied for. The patient, who had increased abdominal pain and increased fever, was referred to our clinic. Cases 2 had a pulse of 114/min (rhythmic), ABP of 100/60 mmHg, and was conscious and cooperative. Abdominal examination revealed signs of distension and rebound. The tongue was dry and rusty, the skin was moist and cold. The liver was evaluated as palpable 2 cm below the midclavicular line, and the spleen was evaluated as non-palpable in a physical examination. The patient had a fever of 39,1℃. Free air was observed under the right diaphragm in Plain Abdominal Radiographs. Growth was detected after 24 hours in all three blood cultures taken on the first day. As a result of bacteriological identification, these bacteria were determined to be S. *Typhi*. Bacteria could not be isolated from the urine culture. No lactose-negative bacteria were found in the stool culture. Other laboratory findings of our case are summarized in Table1. Intestinal perforation due to typhoid fever was detected in the patient with acute abdominal findings, and he underwent surgery. In the operation performed, two terminal ileum perforations of 3 and 5 mm in length were observed on the anti-mesenteric edge, approximately 20 cm proximal to the ileocecal valve. The patient who underwent resection and anastomosis was treated with *Ciprofloxacin* (2x200 mg/day - IV infusion) + *Ornidazole* (2x500 mg/day - IV infusion) for 10 days as a medical treatment. Reperforation and anastomotic leakage were not observed in the patient, and completed healing was achieved after treatment. *TMP-SMX* was prescribed to be used for one month to prevent the carriage of the agent in the gallbladder.

Case 3: Case 3 is a 22-year-old male patient. *TMP-SMX* treatment was applied to the patient who applied to the other Health Centre with complaints of fever, weakness, loss of appetite and a headache. Despite the treatment, he was referred to a Private Hospital because his abdominal pains gradually increased, fever did not decrease, and his general condition worsened. Case three had a pulse of 120/min (rhythmic) and an ABP of 100/60 mmHg, and diffuse defense, rebound, and distension were detected in the abdomen. The tongue of our case was dry and rusty, and the skin was moist and cold. The liver was palpated 3 cm below the midclavicular line, with a painful, soft consistency. The spleen was evaluated as non-palpable. The presence of free air under the right diaphragm was detected in Plain Abdominal Radiographs. In the physical examination; the patient had a fever of 39,9℃. Growth was observed in 24 and 48 hours from all three blood cultures taken on the first day and S. *Typhi* was isolated. S. *Typhi* could not be isolated from simultaneous stool culture and urine culture. Other laboratory findings of our case are summarized in table-1. Intestinal perforation due to typhoid was detected in our patient who was operated on. In the operation, a perforation hole of approximately 6 mm in length was observed on the anti-mesenteric edge, at a

distance of 25 cm from the ileocecal valve, in which the abdomen was filled with the contents of the small intestine (Fig. 1). Roughly one liter of the contents of the small intestine was aspirated. In the operation, primary repair was done. After the operation, *Thiamphenicol* (2x750 mg/day IV-infusion) + *Ornidazole* (2x500 mg/day-IV infusion) treatment was administered for five days. *TMP-SMX* was prescribed to be used for one month to prevent the carriage of the agent in the gallbladder. Our case, whose general condition improved, was discharged on the 15th postoperative day with full recovery.

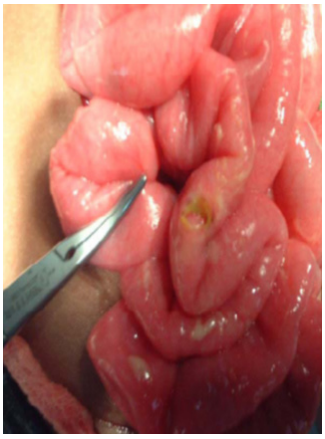

Figure 1. Photograph of the case with typhoid perforation

DISCUSSION

Complications in typhoid were seen at a rate of 5% in our country, and they were encountered more frequently in untreated or delayed treatment.[3-5] While mortality in typhoid was around 15% in the pre-antibiotic period, it has decreased to 0.1% today.[2] However, the morbidity rate was reported to be up to 16-100% especially in Africa and Southeast Asia in all over the world.[5-7] Conditions such as delay in treatment, underlying immunosuppressive or malignant diseases, inflammatory bowel disease, AIDS, malnutrition and organ transplantation increase the severity of complications and mortality-increasing factors.[7,8] Pneumonia, hepatitis, encephalopathy, hemolysis due to glucose 6 phosphate dehydrogenase enzyme deficiencies, myocarditis, and urinary infections are extra intestinal complications.[7]

Intestinal perforation is the deadliest. Serious intestinal complications of typhoid are hyperplasia, ulceration, necrosis and intestinal hemorrhage of lymphoid tissue in the ileocecal area. The incidence of complications had been reported to be about 14% in our country.[2] The incidence of intestinal hemorrhage is 6 and 9%, and the incidence of perforation was 12.9%.[3,6,10,11] In third-world countries, these rates varied between 1 and 39.3%.[6,11] It was around 3% in those who use antibiotics, but less frequently in children.[6] It revealed that the perforation rates reported from India and developing countries were around 10%.[6,12] The reason for the lower perforation rate among the cases we encountered may be due to early diagnosis, appropriate surgery and medical treatment. Intestinal perforation usually occurs in the third or fourth week of the disease, less frequently in the second week. Perforation occurred in the third week in two of our cases, and in the second week in one. The time of the occurrence of complications varied depending on the inoculation amount of the bacteria, immune structure, and efficacy of treatment.[7,8] Intestinal hemorrhage occurs as a result of necrosis and ulceration of Payer's plaques in the terminal ileum and destruction of capillaries. Lesions of typhoid in the small intestine were mostly limited to the mucosa and submucosa, but sometimes involve the muscular layer and serosa, causing penetration.[8] We thought that the common small intestine and bile contents encountered in the abdomen during the operation cause peritonitis due to shimic irritation and cause adhesions and fibrous structure formation in some areas. It was not uncommon for a second perforation to develop after starting treatment. It has been reported that this second perforation may be due to the inability of sufficient antibiotic concentration to reach the dense bacterial accumulation that involves the mucosa, submucosa, and Payer's plaques in the entire intestinal system, or to the inability to terminate the ongoing immunological events and inflammatory activity all at once. The adhesion, penetration, and proliferation of the bacteria into the epithelial tissue were due to the toxin structures that vary between serotypes.[13] The most responsible for this is Lipid A, which has a lipopolysaccharide structure.[14] The mediators released at the time of perforation cause the spread of inflammation, and with the increase in permeability in the endothelial bed, it also prepares the ground for the hypovolemic picture of septic shock. Apart from this, the extent of necrosis in the intestinal mucosa and lymphoid tissues of the submucosa is also extremely important.[13,15] Various risk factors have been investigated.[16] Another factor as important as the delay in surgical intervention in perforation is the lack of appropriate antibiotic therapy. Although *Chloramphenicol* was still the first choice in some classical books, resistant strains were reported in many studies. In their series of 204 cases, *chloramphenicol* resistance was found to be 94.7% in S. *Typhi*, 95.8% in S. Paratyphi strains, and 96.9% in S. Typhimurium.[15,17] *Thiamphenicol* resistance has been reported at lower rates than *chloramphenicol*.[3] In a study conducted by Singh et al. *Thiamphenicol* resistance was found to be 4%.[18] Untreated cases of typhoid are more likely to encounter complications. However, since there is such a possibility in the treated cases, it is important to monitor the fever, pulse, blood pressure and to perform regular abdominal examination in order to detect the complication early. In the operation, repair of the perforated area with primary suture, washing the abdomen with plenty of saline and then drains left in the abdomen are necessary applications for the control of the infection. While the probability of developing a new perforation is 40% with the repair of the perforated bowel with a single-layer

suture and then *Chloramphenicol* treatment alone, this rate has been reported to decrease to 19% with double-layered suture repair and subsequent *Chloramphenicol*, *Gentamicin* and *Metronidazole* treatment.[8,19] There were also those who recommend a 10 cm resection instead of the primary suture.[19-22] Complete evacuation of the swept fluid after the operation accelerates bacteriological eradication and tissue healing.[23] It should not be forgotten that complications such as intestinal perforation may develop despite the treatment with typhoid, and accordingly, the patient should be followed up regularly. The follow-up of reperforations and eradication of the gallbladder is also important. Thus, it will be possible to detect and correct many complications that may result in death early.

Nowadays, Typhoo disease is still important for morbidity and mortality, especially for third-world countries. We conclude that in typhoid intestinal perforations, early diagnosis, and medical and surgical approaches combined with serious intensive care is lifesaving at the point of therapy.

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