Double Infection with *Giardia lamblia* and *Salmonella paratyphi A* Associated with Acute Renal Failure

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While traveling in India, a previously healthy twenty-year-old man had febrile diarrhea. The patient was prescribed medical therapy, and all symptoms were resolved. Fourteen days later, however, similar symptoms recurred. The patient was admitted to a local hospital, but was transferred to our department because of oliguria. *Salmonella paratyphi A* was isolated from blood and stool specimens, and *Giardia lamblia* was identified in his stool. The patient’s condition was complicated by acute renal failure. The patient received tosufloxacin and metronidazole. Renal function recovered completely without hemodialysis. Paratyphoid fever and giardiasis were resolved. It is suggested that giardiasis exacerbated the paratyphoid fever.

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**Key words:** giardiasis, paratyphoid fever

**Introduction**

With the advent of rapid, convenient means of transportation, millions of persons travel each year from industrialized countries to developing countries in the tropics and subtropics. These travelers are at increased risk for a variety of infectious diseases that are endemic to these regions. The most frequent condition experienced by travelers is diarrhea. Acute traveler’s diarrhea may be caused by viral, bacterial, or protozoal enteropathogens (1).

*Giardia lamblia* is an intestinal parasite (2) that is found throughout the world, but is most prevalent in tropical and subtropical countries. This organism is rare in Japan. Recently, *G. lamblia* has been implicated in sexually transmitted diseases in homosexual men (3) and opportunistic infectious disease in immunocompromised hosts (4) in addition to its more traditional role as a pathogen in travelers returning from developing countries. Giardiasis is most commonly associated with watery diarrhea, abdominal pain, and dysentery. Symptoms often resolve spontaneously, but some asymptomatic hosts persistently excrete cysts for many years (5).

Paratyphoid fever caused by *Salmonella paratyphi A*, which is legally designated as a communicable disease in Japan, is less serious than typhoid fever. Usually, its clinical course is shorter and milder than that of typhoid fever (6); consequently, severe complications, such as acute renal failure, are uncommon.

Here, we report a patient infected with *S. paratyphi A* and *G. lamblia* in whom acute renal failure developed.

**Case Report**

While traveling in India, a twenty-year-old Japanese man had severe watery diarrhea, a high grade fever with shaking chills, and colic on August 2, 1997. He returned to Japan to receive medical treatment. He initially consulted a local hospital and was given antibiotics (oral fosfomycin, 1,500 mg daily) on August 7, 1997. All symptoms resolved completely. Two weeks later, however, he was admitted to the same hospital with a seven-day history of similar symptoms. He was treated with 2,000 ml of intravenous fluid replacement and intravenous fosfomycin (2 g twice daily). Two days after admission, the patient was transferred to our hospital because of oliguria and renal dysfunction.

There was no personal or family history of renal disease. Physical examination showed peripheral edema, pyrexia of 38.8°C, tenderness of the entire abdomen, a normal pulse of 86/ min, and blood pressure of 122/72 mmHg. There was no rash, hepatosplenomegaly, or lymphadenopathy.

On initial admission, the hemoglobin concentration was 12.7 g/dl, white cell count 5,100 cells/µl with a normal differential count, platelet count 10.9 x10^4/µl, and erythrocyte sedimentation rate 5 mm in the first hour. Aspartate amino trans-
A rapid rise in international travel to developing countries has increased the prevalence of infectious diseases caused by pathogens normally not found in Japan among Japanese travelers. Acute infectious diarrhea, in particular, can be caused by many bacterial, viral, and parasitic organisms (1).

The present patient had fever and diarrhea complicated by acute renal failure. Bacteriological evidence of \textit{S. paratyphi} \textit{A} in his blood and stool strongly suggest that this organism was the main pathogen. Although the Widal reaction was negative, the diagnostic insignificance of Widal titer has been emphasized (7). Clinical signs and symptoms of remission may have reflected the natural history of the underlying disease and its response to antibiotic treatment. The clinical manifestations of paratyphoid fever are similar to those of typhoid fever, but paratyphoid fever usually runs a shorter and milder course (6). Because paratyphoid fever is usually associated with minimal toxicity, few complications, and lower mortality, it is often covered only briefly in textbooks of medicine. The present patient, however, was severely ill owing to the presence of bacteremia and acute renal failure in addition to paratyphoid fever.

\textit{G. lamblia} was identified by direct microscopy of a wet mount of a stool specimen. Giardiasis can produce non-life-threatening gastrointestinal distress and diarrhea (2, 5). It is very unusual for \textit{Giardia} infection alone to cause severe abdominal pain, fever, or dysentery (2). Because symptoms often resolve spontaneously, giardiasis is considered a benign disease, similar to paratyphoid fever. The present patient, however, was severely ill and presented with acute renal failure while infected with these benign diseases.

Hypochlorhydria and achlorhydria increase the risk of intestinal bacterial and parasitic infections (8). Bacteria increase in the stomach in patients with gastric carcinoma, those who receive H2-receptor antagonists and after gastrectomy. Hypochlorhydria is also sometimes present in \textit{S. typhi} infections (9), but it is unknown whether or not this condition can lead to a life-threatening situation. Many persons infected with \textit{G. lamblia} have either achlorhydria or hypochlorhydria (5, 8). Patients with abnormally low immunoglobulin levels or those who undergo gastric surgery often present with severe \textit{G. lamblia} infections (5), but a cause-effect relationship has not been established definitively. Because the present patient was previously healthy and had never received H2-receptor antagonists nor undergone gastric surgery, it is unlikely that his severe illness was caused by hypochlorhydria alone.

Renal complications (acute renal failure) have been reported in 2.5% of patients with typhoid fever (7). Acute renal failure may have exacerbated a preexisting glomerular lesion as a result of toxic damage by \textit{Salmonella} septicemia and renal hypoperfusion due to vomiting and severe diarrhea. Circulatory failure due to septicemia or toxemia is the main cause of death in typhoid fever (6), but is less common in paratyphoid fever. Although paratyphoid fever is usually associated with minimal toxicity, the clinical symptoms of the present patient suggested considerable toxic damage, equivalent to that seen in typhoid fever.

Not only \textit{S. typhi} but also \textit{S. paratyphi} \textit{A} invade the intestinal tract and produce symptoms similar to those seen in typhoid fever. However, paratyphoid fever usually runs a shorter and milder course (6). The present patient had fever and diarrhea complicated by acute renal failure. Bacteriological evidence of \textit{S. paratyphi} \textit{A} in his blood and stool strongly suggest that this organism was the main pathogen. Although the Widal reaction was negative, the diagnostic insignificance of Widal titer has been emphasized (7). Clinical signs and symptoms of remission may have reflected the natural history of the underlying disease and its response to antibiotic treatment. The clinical manifestations of paratyphoid fever are similar to those of typhoid fever, but paratyphoid fever usually runs a shorter and milder course (6). Because paratyphoid fever is usually associated with minimal toxicity, few complications, and lower mortality, it is often covered only briefly in textbooks of medicine. The present patient, however, was severely ill owing to the presence of bacteremia and acute renal failure in addition to paratyphoid fever.

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Giardiasis and Paratyphoid Fever

TFLX | Metronidazole
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Culture of blood urine stool bile-j. +* NG NG NG NG NG NG NG NG NG NG NG NG
Culture of stool urine bile-j. +* NG NG NG NG NG NG NG NG NG NG NG NG
Microscopic exam. of stool +* +* +* +* +* +* +* +* +* +* +* +* +* +* +* +* +* +* +*

Figure 1. Clinical course after admission.


mucosa and enter the bloodstream and cause systemic febrile disease. Perhaps, the concurrent presence of Giardia infection promoted invasion of the intestinal tissue by S. paratyphi A. Once Giardia's cysts are ingested, trophozoites emerge in the small intestine (2, 5). These trophozoites do not directly invade tissue, but have sucker plates by means of which they attach themselves to the intestinal villi (2, 5). Trophozoites adhering to the mucosal epithelium cause irritation and disturb nutrient absorption. Severe damage and atrophy of the intestinal villi occur in severe infections. The microbiological findings in our patient suggest the presence of severe G. lamblia infection, because G. lamblia was reidentified in the feces even after standard treatment with metronidazole. In the present case, therefore, severe mixed infection involving G. lamblia appar-
ently promoted invasion of the intestinal tissue by *S. paratyphi* A. Endotoxins produced by the high numbers of organisms affected the release of various inflammatory mediators into the bloodstream, resulting in circulatory failure.

Thus, mixed infection with intestinal parasites and bacteria occurs in infectious diarrhea (10–12). In Japan, a mixed infected case similar to ours has been previously reported (10). Shukry et al reported that *G. lamblia* was identified in 35% of fatal and potentially fatal cases of diarrhea in Egypt (11). Unfortunately, however, that report did not emphasize that mixed *Giardia* infection may trigger fatal bacterial diarrhea.

The main objective of this report is to increase awareness among physicians that fecal microscopic examination for parasites as well as stool culture for bacteria should be performed in patients presenting with traveler’s diarrhea. Patients in whom *G. lamblia* is identified are at increased risk for worsening of combined bacterial intestinal infection.

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**References**

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