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Case report

Strongyloides stercoralis infection in an intestinal transplant recipient

C.N. Hsu, S.H. Tseng, S.W. Chang, Y. Chen. *Strongyloides stercoralis* infection in an intestinal transplant recipient.
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Abstract: *Strongyloides stercoralis* is a helminth in tropical and subtropical areas. It may cause latent infection and progress to *Strongyloides* hyperinfection syndrome, which is associated with a high mortality rate. Transplant recipients under the treatment of immunosuppressant agents are at risk of severe *S. stercoralis* infection. According to related literature, most cases of *S. stercoralis* infection after solid organ transplantation are caused by reactivation of latent infections in the recipients, whereas only a few are acquired from the donors. We report on an intestinal transplant recipient who had *S. stercoralis* infection diagnosed by a larva of this parasite found in the stool from the ileostomy stoma 1 month after transplantation. Tl e donor was considered the source of the infection because the donor was from an endemic area and had marked eosinophilia, and the recipient had no contact history or clinical manifestations related to the *S. stercoralis* infection before transplantation. The patient was treated with ivermectin and exhibited no evidence of infection after 7 months.

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Strongyloides stercoralis is an intestinal helminth that is distributed worldwide; however, it is mainly found in tropical and subtropical areas with warm and humid climates (1–3). It is seldom encountered in Taiwan (4). The infection can persist for decades without considerable symptoms in immunocompetent hosts; however, it may progress to *Strongyloides* hyperinfection syndrome in immunocompromised hosts because of defects in cell-mediated immunity and accelerated autoinfection (5). Transplant recipients under the treatment of immunosuppressants are at risk of severe *Strongyloides* infection (1). Most cases of *Strongyloides* infection after organ transplant are caused by reactivation of latent infection in the recipients, whereas only a few *Strongyloides* infections are acquired from the donors (1). We describe an intestinal transplant recipient who had a larva of *S. stercoralis* in the stool from the ileostomy stoma 1 month after transplantation. The donor was considered the source of the infection because the donor was from an endemic area and had marked eosinophilia, and the recipient had no contact history or clinical manifestations related to *S. stercoralis* infection before transplantation.

Case report

The 17-year-old Taiwanese female patient had short bowel syndrome after a large intestinal resection (from 10 cm distal to the ligament of Treitz to 6 cm proximal

to the ileocecal valve), performed because of paraduodenal hernia with extensive bowel necrosis at another hospital at the age of 10 years. Approximately 16 cm of small intestine remained after resection. Subsequently, total parenteral nutrition was provided for nutritional support. When the patient was 12 years old, multiple joint swelling over hands and knees, hematuria, proteinuria, and positive serum rheumatoid factor were found, and juvenile rheumatoid arthritis was diagnosed. She was treated with corticosteroids and etanercept (Pfizer, New York, New York, USA). Because of repeated catheter-related sepsis and loss of venous access, she was considered as a candidate for intestinal transplantation. On admission, she was thin and had clear consciousness. Her body temperature was 36°C. A complete blood count revealed hemoglobin of 10.4 g/dL, hematocrit of 31.9%, platelet count of $106 \times 10^3/\mu L$, and white cell count of $4270/\mu L$, with eosinophils of 0.4%. The serum biochemistry was within normal limits. A stool examination did not reveal any ova, parasites, or ameba. An abdominal sonogram showed increased hepatic echogenicity, and upper gastrointestinal (GI) and small bowel series revealed that the small bowel length was approximately 16 cm, with smooth passage of the contrast medium. The gastric emptying time was normal.

Immunosuppressant agents, including peri-transplantation induction therapy with 5 mg/kg of anti-thymocyte globulin (Thymoglobulin; Genzyme/Sanofi, Cambridge, Massachusetts, USA), were administered before surgery. Subsequently, she underwent intestinal transplantation using allograft from a deceased donor from the Philippines. The patient tolerated the operation well. After transplantation, maintenance therapy with tacrolimus (to maintain a trough level of approximately 15–20 ng/mL for the first month) and low-dose methylprednisolone (1 mg/kg for 1 month, followed by gradual dose reduction) was administered. The patient recovered smoothly. Endoscopy examinations with graft biopsy and microscopic examinations of the stool from the ileostomy stoma were performed twice a week during the first month after the operation, then once a week during the second month. At day 21 after transplantation, a small bowel biopsy showed no acute rejection, and the patient started oral intake and gastrostomy feeding.

However, at day 30 after transplantation, a rhabditiform larva of *S. stercoralis* was revealed in the stool from her ileostomy stoma (Fig. 1), although there were no acute rejection, abnormal erythematous spots, erosions, or ulcerations detected from the endoscopy examination and graft biopsy. At that time, the patient was treated with tacrolimus to maintain a trough level of approximately 15–20 ng/mL and methylprednisolone (1 mg/kg). She had no symptoms related to *S. stercoralis* infection, such as change in stool consistency or frequency, abdominal pain or tenderness, or other symptoms. However, the eosinophils were 6.0% of the white cell count. The patient was subsequently treated with oral ivermectin (200 μg/kg daily) for 2 days, and an additional 2 days of ivermectin treatment was administered 2 weeks later. Serial examinations of the stool from the ileostomy stoma revealed no larva of *S. stercoralis* after starting the ivermectin treatment. The eosinophils decreased to 0.4% of the white cell count at 4.5 months after transplantation, and at that time, the patient was treated with tacrolimus to maintain a trough level of approximately 10–15 ng/mL, but without using corticosteroids.

After 7 months, she had smooth oral intake without the requirement of an intravenous fluid supply. Tacrolimus was used to maintain a trough level of approximately 7–10 ng/mL, and no corticosteroids were used. Regular endoscopy examinations and biopsies revealed no rejection or *S. stercoralis* larvae.

Retrospectively, the recipient had no history of traveling to endemic areas of *S. stercoralis* or walking outside with bare feet. She had no known close contacts with anyone who may have been infected with *Strongyloides* before transplantation. Conversely, the donor was a Filipino; his country is an endemic area of strongyloidiasis (1–3). The white cell count of the donor before transplantation was $13.81 \times 10^3/\mu L$, with eosinophils of 18.3%. The recipients of heart, liver, kidney, and pancreas transplants from the same donor showed no evidence of *Strongyloides* infection. Neither

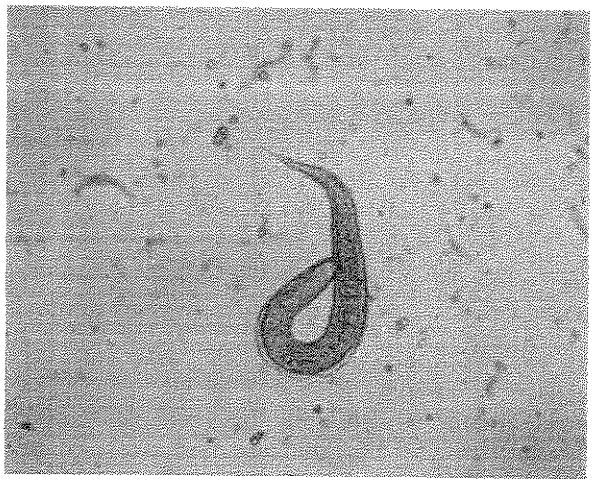

Fig. 1. Microscopic stool examination revealed a rhabditiform larva of *Strongyloides stercoralis*.

the recipient nor the donor received serological testing for *S. stercoralis*. No family members had been tested for *Strongyloides* infection or had history of travel to endemic areas.

Discussion

S. stercoralis infection may be symptomatic or asymptomatic (2–4). In symptomatic infections, it may present with various clinical manifestations, including constitutional, cutaneous, GI, and pulmonary symptoms; the most common findings are abdominal pain, diarrhea, and eosinophilia (2, 4). In addition, the infection may progress to *Strongyloides* hyperinfection syndrome, which often develops when immunosuppression reduces the immune surveillance, triggering reactivation of latent infection of the parasite, and causing substantial increases in the reproductive cycle of larvae (3, 6). Conversely, approximately half of all patients with chronic strongyloidiasis are asymptomatic, and the other half is associated with minimal or intermittent GI symptoms (3). The mortality of *Strongyloides* hyperinfection syndrome is approximately 50%, with a higher mortality in extraintestinal strongyloidiasis (3). Our patient had *S. stercoralis* infection based on having a rhabditiform larva of the parasite found in stool from the ileostomy stoma; however, she was asymptomatic. Therefore, the infection in our patient might be categorized as a chronic strongyloidiasis without increased parasitic burden that is usually seen in chronic *Strongyloides* infection. Furthermore, the donor was a Filipino; therefore, this larva should be differentiated from that of *Capilaria philippinensis*, which may also cause autoinfection (7). The larva in our patient had a club-shaped anterior end, short buccal cavity, and sharp pointed tail, and there were no stichocytes surrounding the esophagus, which suggested that this was not a larva of *C. philippinensis* (7).

Hematologic malignancy, stem cell or solid organ transplantation, hypogammaglobulinemia, human immunodeficiency virus, human T-cell lymphotropic virus-1, and the use of immunosuppressive agents are common risk factors for severe *S. stercoralis* infection (1, 6, 8). Our patient was an intestinal transplant recipient and had received immunosuppressant treatment; thus, she had an increased risk for such infection. Various immunosuppressants used for organ transplantation may have different effects on the parasites. Corticosteroids, which were used in our patient, are considered a major risk factor for severe *Strongyloides* infection (3). Tacrolimus, the primary immunosuppressant used in intestinal transplantation and also used in our patient, does not have anthelmintic effects and may have enhanced the risk of parasite infection in our patient (6, 9). By contrast, although cyclosporine is an immunosuppressant, it exerts direct antiparasitic activity in mice (6, 10) and may protect against *Strongyloides* infection; however, it is not used routinely in intestinal transplantation (3).

S. stercoralis infections have been reported in heart, liver, kidney, intestine, lung, pancreas, bone marrow, and combined heart and kidney transplant patients (1, 2, 11–16). Most cases of strongyloidiasis in transplant recipients are caused by reactivation of latent infection in recipients (3, 6, 17), whereas only a few cases of strongyloidiasis are acquired from the donor (1, 2, 6, 12, 18). Donor derivation is difficult to prove, especially when the recipient is from an endemic region and may have been infected before or after transplantation (1). Two recipients of renal allografts from a single donor developed *Strongyloides* hyperinfection syndrome, and such infection was thought to be acquired from the donor; however, this could not be proved by examinations of the autopsy material or serological studies of the donor (18). Another report mentioned 2 renal allograft recipients who developed *Strongyloides* hyperinfection syndrome after receiving organs from a common donor who was found to have positive serum *Strongyloides* antibody using enzyme-linked immunosorbent assay (ELISA) (1). In addition, the donor was considered the source of strongyloidiasis in a pancreas allograft recipient, because the recipient was not exposed to an endemic area; the donor was retrospectively confirmed to have an infection using ELISA. However, other organ recipients from the same donor are reported to be asymptomatic (12). Furthermore, a common donor was considered the source of *Strongyloides* infection in liver and kidney–pancreas transplant recipients; the donor retrospectively tested positive for *S. stercoralis* immunoglobulin G (IgG) antibody (2).

Regarding intestinal transplantation, the risk of developing donor-acquired strongyloidiasis may be greater in intestinal transplant recipients because the intestinal tract is the site of latent infection (6). Related literature reported 1 intestinal transplant recipient who had *Strongyloides* infection, which was hypothesized to be acquired from the donor (6). That patient developed *Strongyloides* hyperinfection syndrome 7 months after transplantation, and the donor was considered the source of such infection because the recipient had no history of eosinophilia, GI symptoms, sick contact, or travel to endemic area; previous biopsies of the graft did not demonstrate *S. stercoralis*; and the donor was a Honduran man living in Florida (6). However, previous

medical records of the donor were not described in that report, and the history of the donor regarding GI symptoms, parasite infection, or eosinophilia was unclear.

The *S. stercoralis* infection in our patient may have originated from several sources, including a new infection during her hospitalization after transplantation, reactivation from a latent infection, or transmission from the donor. New infection was considered unlikely, because she did not leave the hospital after transplantation and had no known close contact with anyone who may have been infected with *Strongyloides* after transplantation. In addition, our hospital had no patients with such infection in the past 3 years. Another possibility is reactivation from a latent *S. stercoralis* infection. However, our patient lived in Taiwan, which is not an endemic area of *S. stercoralis* (4). Although a recent report found that the number of *Strongyloides* infections was increased in Taiwan, the increase was mainly in the indigenous people in the eastern part of Taiwan, not in Han Chinese or people living in the western part of Taiwan (19). Furthermore, leptospirosis was considered an important underlying factor for strongyloidiasis, and alcoholism was one of the reasons why indigenous males had a higher infection rate than Han Chinese males (19). Our patient is a Taiwanese (also a Han Chinese) girl who lived in the western part of Taiwan, and did not drink alcohol or have leptospirosis. Thus, she did not have the risk factors to have increased chance of *Strongyloides* infection in Taiwan. She had no history of traveling to endemic areas of *S. stercoralis* or walking outside with bare feet. In addition, she had no eosinophilia, skin rash, and no ova or parasites on stool examination before transplantation.

Furthermore, although she had been treated with immunosuppressant for juvenile rheumatoid arthritis since she was 12 years old, there was no evidence of parasite infection during that period. In addition, both corticosteroids and etanercept (an anti-tumor necrosis factor-α agent) block the immune system, which may make the pre-existing *Strongyloides* infection worse. It is unlikely that this girl had a chronic *Strongyloides* infection pre-transplant, as steroids and etanercept would have predisposed her to more severe infection, which likely would have manifested before the transplant. However, only a single stool study would have been insufficient to diagnose this infection pre-transplant. In addition, no antibody testing was done pre-transplant, so the possibility that this could be recipient-derived cannot be completely excluded. As a whole, reactivation of latent infection was less likely; however, this possibility cannot be excluded completely.

By contrast, the most probable source of the infection was the donor. The donor is from the Philippines, which is an endemic area of *S. stercoralis* (1–3). In addition, the donor had marked eosinophilia of up to 18.3%, although we did not know whether he had GI symptoms previously. However, the intestinal graft in our patient had no mucosal change, which is inconsistent with the literature that intestinal mucosal changes are often present even in patients with mild symptoms (20). We did not know why there were no mucosal lesions detected from the endoscopy examination in our patient. We speculate that this might be related to the low parasite burden in the intestine and the biopsied specimen not representing the whole intestine.

The diagnosis of *S. stercoralis* infection in our patient was straightforward because the larva was noted in the stool from the ileostomy stoma. However, such infection may be overlooked. The absence of eosinophilia cannot exclude *Strongyloides* infection, because only 50–80% patients manifest eosinophilia (13). In addition, examination of ova and parasites in stool has relatively inferior sensitivity because larvae are excreted in small quantities and intermittently; a single specimen has a sensitivity of only 15–30% (3). More frequent stool examinations, as performed for our patient, may increase the sensitivity. In recent years, more specific tests, including *Strongyloides* IgG ELISA antibody testing, luciferase immunoprecipitation system to detect *S. stercoralis*-specific antibodies, and real-time polymerase chain reaction method, have been developed to improve diagnoses (3, 8). These methods may be used to screen patients from an endemic area, or patients with GI symptoms or eosinophilia before transplantation (3, 8). Although *Strongyloides* screening is not routinely recommended for donors, it may be considered in high-risk donors, even if eosinophilia is not present (2). However, pre-transplant screening of donors may be difficult, because the time interval between the appearance of a potential donor and organ procurement is often short.

In conclusion, we present the case of a recipient of an intestinal transplant who developed *S. stercoralis* infection, which was considered to be transmitted from the donor. The patient was free of infection 7 months after ivermectin treatment. Because this infection may progress to *Strongyloides* hyperinfection syndrome, which is associated with high mortality rate in immunocompromised transplant patient, early diagnosis and treatment are crucial (2, 3). The serendipitously early detection of such infection in our patient before development of symptoms, and proper treatment, might have averted a catastrophic event. This case

indicates the importance of considering the possibility of *S. stercoralis* infection in intestinal transplant recipients, and the possibility that this infection might be transmitted from the donor.

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