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Case Report

Donor-derived *Strongyloides stercoralis* hyperinfection syndrome after simultaneous kidney/pancreas transplantation

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SUMMARY

Most cases of strongyloidiasis associated with solid organ transplantation have been due to the reactivation of a latent infection in the recipient as a result of the immunosuppressive therapy; however, donor-derived infections are becoming increasingly frequent. The case of a patient who nearly died of a *Strongyloides stercoralis* hyperinfection after receiving simultaneous kidney/pancreas transplants is described herein. No specific parasitological tests were performed pre-transplantation, despite the fact that both the recipient and the donor originated from endemic areas. Serological analysis of the donor's serum performed retrospectively revealed the origin of the infection, which if it had been done beforehand would have prevented the serious complications. Current practice guidelines need to be updated to incorporate immunological and molecular techniques for the rapid screening of *Strongyloides* prior to transplantation, and empirical treatment with ivermectin should be applied systematically when there is the slightest risk of infection in the donor or recipient.

1. Introduction

Strongyloides stercoralis is an intestinal nematode parasite that affects about 30–100 million people around the world, but is mainly found in tropical and subtropical areas where hygiene standards and sanitary conditions are deficient. However, there are small endemic foci of the disease in countries with a temperate climate.[1] In immunocompetent individuals, this infection is often asymptomatic or has a mild symptomatology, characterized by high eosinophilia, pulmonary symptoms, dermatological manifestations, and intestinal symptoms. However, there are some risk factors, such as co-infection with HIV or human T-cell lymphotropic virus (HTLV1), corticosteroid treatment, and induced immunosuppression, which can lead to a hyperinfection syndrome (HS) or disseminated strongyloidiasis (DS), the latter having a fatal course in most cases.[2]

The case of an intestinal hyperinfection of *S. stercoralis* associated with simultaneous kidney/pancreas transplantation is described herein. The recipient presented acute duodenitis and a profound nutritional decline after the solid organ transplantation. This represents a case of donor-derived strongyloidiasis. The donor originated from an endemic area, Bolivia, and was diagnosed with two important parasitic diseases – trypanosomiasis and toxoplasmosis – before donation. However, in the case of *Strongyloides*, no parasitological tests or empirical treatment, as recommended in the national guidelines, were performed.

2. Case report

The case patient was a 37-year-old male from Segorbe, Valencia (Spain), whose medical history included type 1 diabetes mellitus for 32 years. The patient was the recipient of a kidney and pancreas from a single donor (who had also donated his other kidney and his liver), without rejection and with a favourable course. Post-transplantation, the following drug scheme was followed: (1) trimethoprim/sulfamethoxazole (400 mg/80 mg/day for 6 months), ganciclovir (900 mg/day for 90 days), and fluconazole (200 mg/day for 60 days), to prevent opportunistic parasitic infections, cytomegalovirus (CMV), and fungi, respectively; (2) basiliximab

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for the induction of immunosuppressive therapy; and (3) prednisone, tacrolimus, and mycophenolate mofetil as immunosuppressive maintenance.

Two months after surgery, he attended the hospital accident and emergency unit complaining of profuse diarrhoea, weakness, and abdominal pain. At the time of admission, he presented no fever, mucocutaneous dryness, hypotension, or malnutrition. A complete blood test confirmed anaemia (haemoglobin of 10.6 g/dl), with a white cell count of 9.26×10^9/l and eosinophil count of 0.12×10^9/l. His abdomen was soft and depressible; the kidney graft on the left iliac fossa was palpable, without pain or signs of peritoneal irritation.

Laboratory tests were performed for the diagnosis of possible infectious agents responsible for the diarrhoea. The patient was positive for *Clostridium difficile* toxin, which masked the parasitosis, and was thus started on metronidazole treatment (500 mg/8 h for 7 days). Further testing for *Clostridium* 1 week later was negative, but the episodes of diarrhoea continued. Oesophago-gastroduodenoscopy revealed an oedematous and ulcerated mucosa of the duodenal bulb, as well as necrotic tissue. The mucosal condition extended to the second duodenal portion. A biopsy of the first duodenal portion revealed an intense immune response caused by the presence of the parasite *S. stercoralis* (Figure 1). Stool samples were sent to the laboratory for microscopic observation and culture, resulting in the finding of rhabditiform larvae. The patient was started on treatment with ivermectin (200 g/kg/day for 7 days), which was repeated 15 days thereafter and prolonged for another 5 days to ensure eradication of the parasite. New stool samples were analyzed and were eventually negative.

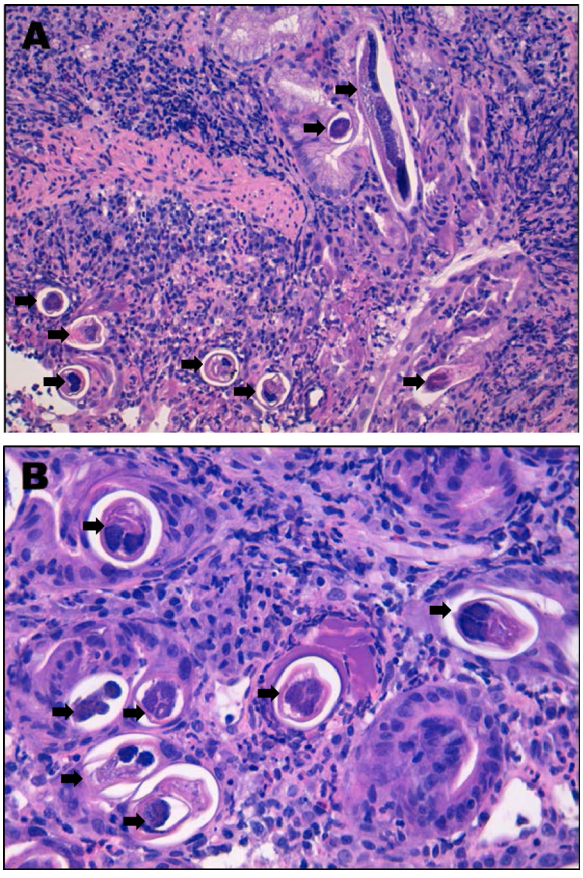

Figure 1. Histology of the duodenal biopsy taken during the first oesophago-gastroduodenoscopy (haematoxylin and eosin): (A) multiple *Strongyloides stercoralis* larvae in the duodenum mucosa (arrows); (B) magnified image showing transverse sections of the larvae.

Due to the severity of this patient's protein–energy malnutrition, parenteral nutrition was necessary. His general condition improved progressively, and he recovered normal intestinal function.

The recipient was born in the region of La Safor (Spain). He reported having travelled to the Dominican Republic, an area considered endemic for *Strongyloides*, 10 years ago. Nonetheless, he had not presented eosinophilia either before or immediately after the intervention, and had also never presented symptoms consistent with parasitism.

The donor was a 34-year-old man from Bolivia. In the pre-transplant blood tests he showed slight eosinophilia (2.5%), so there were no clear signs of helminthiasis. Furthermore, the recommended tests for *Strongyloides* (stool examination and culture of larvae) were not performed before donation. However, his test results were positive for *Trypanosoma cruzi* and *Toxoplasma gondii*. His liver and the other kidney were transplanted into two other recipients, who did not develop strongyloidiasis. Following the diagnosis of HS in the recipient, the donor's serum was obtained from the biobank and analyzed by ELISA; the sample showed a positive titre for anti-*Strongyloides* (IgG) antibodies, thereby demonstrating the origin of the infection.

3. Discussion

The region of La Safor (Valencia) on the Spanish Mediterranean Coast was once considered an endemic focus of strongyloidiasis. Most documented cases involved people with jobs related to manual rice cultivation, irrigation ditches or their maintenance. Today, due to improvements in health infrastructure and the mechanization of farming, it is considered that there is no transmission of the disease in this region.[3]

In the case presented here, the patient originated from this part of Spain, but neither he himself nor any other member of his family had performed activities posing a risk. He reported having travelled to the tropics, but had been careful to avoid possible infection with parasites, including walking barefoot, and had not presented any symptoms during or after this trip. Also, it should be noted that this patient, because of his chronic illness, was subject to strict medical control.

Donor-derived *Strongyloides* infections have been considered rare, but an increasing number of cases have been reported recently.[4] In all of these, the donor was native to an endemic area, as in the case presented here, in which the donor was from Bolivia. Surprisingly, both the liver and the other kidney were also donated to two different patients, and neither of them developed the disease. However, a patch of duodenum tissue was transplanted with the pancreas in the case presented here, thus it may be that the parasites reached the recipient's intestine through this tissue.

This case highlights the importance of updating the Spanish Organización Nacional de Trasplantes (ONT) consensus document[5] to include new more sensitive and rapid diagnostic tools for strongyloidiasis and also emphasizes the need to assess the potential risks not only in the donor but also in the recipient. Screening serum by ELISA or faeces by real-time PCR may be very useful for more rigorous control pre-transplantation, although positive tests should not automatically lead to the exclusion of potential donors or recipients. In certain situations, depending on the risk factors present, empirical treatment with ivermectin is recommended; thus, had the guidelines been followed, perhaps the HS would have been avoided in this case.

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