



Letter to the Editor

Strongyloides stercoralis after renal transplantation—A global threat

Strongyloides stercoralis después del trasplante renal: una amenaza mundial

Dear Editor,

As we know, despite of the several efforts made in the last decades to minimize the infectious risk in kidney transplantation, including pre-transplant screening, vaccination, and antimicrobial prophylaxis, post-transplant infections remain a major cause of morbidity and mortality.¹

Strongyloides stercoralis (Ss) is a parasite frequently forgotten, that affects about 613.9 million people,² and it is associated with a high mortality rate in kidney transplant recipients. We present a case that illustrates the importance of pre-transplant screening and prompt recognition of this parasite in this population.

A 53-year-old portuguese Caucasian female, resident in Lisbon, with end-stage renal disease of unknown cause, underwent deceased donor renal transplantation after four years on hemodialysis. Past medical and travel history unremarkable.

The pre-transplant workup showed normal blood eosinophil count and immunization against hepatitis B virus and Cytomegalovirus. *Strongyloides stercoralis* IgG by the enzyme-linked immunosorbent assay was negative.

She started induction immunosuppression protocol with basiliximab, and immunosuppression maintenance therapy with tacrolimus, mycophenolate mofetil and prednisolone. Donor-specific antibodies were negative. The post-transplant period was uneventful, and she was discharged with a serum creatinine (SCr) of 1.4 mg/dL.

After three months, she started complains of anorexia, fatigue, weight loss and presented periumbilical and dorsal region petechiae. The laboratory results revealed peripheral eosinophilia and worsening of graft function (SCr of 2.4 mg/dL). The coprological examination confirmed the presence of *S. stercoralis* larvae. Pulmonary involvement was excluded by chest computerized tomography.

Treatment with ivermectin (15 mg/day) in association with albendazole (400 mg 2 id) was started as well as prophylactic

cotrimoxazole (480 mg/day). Tacrolimus levels were reduced to less than 8 mg/dl.

The patient evolved favorable with rapid graft function recovery and resolution of the symptoms. A negative stool testing was obtained after 6 days. Peripheral eosinophilia resolved after one month. Albendazole was suspended after the first negative stool. Ivermectin was maintained in a daily dose until day 21 and in a monthly administration (200 mg) until complete 6 months of therapy. After the discontinuation, stool cultures remained negative.

The other receptors (kidney, heart, and liver) from the same donor were evaluated. No clinical symptoms of strongyloidiasis, blood eosinophilia or Ss IgG were identified. Despite of that, a prophylactic regimen of ivermectin (15 mg/month) was performed.

Presently, the patient remains without symptoms, with normal peripheral eosinophil count and renal function preserved with SCr of 1.5 mg/dl.

Strongyloides stercoralis is an intestinal nematode able to remain in the same host indefinitely, due to a process known as autoinfection. It can be asymptomatic or cause nonspecific symptoms like abdominal pain, diarrhea and urticaria.³

The latency and missed diagnosis of Ss infection, as we know, can be a problem if we prescribe high doses of immunosuppressive agents, as the regimes used nowadays in kidney transplantation.

With the cell-mediated immunity impaired, after immunosuppression initiation, Ss larvae can freely disseminate in the gut and lungs, causing gastrointestinal hemorrhage and dyspnea, a clinical illness named as Strongyloides Hyperinfection Syndrome. If not promptly controlled, the larvae proliferation will cause multiple organ failure, known as Disseminated Strongyloidiasis.²

The incidence of hyperinfection and dissemination in kidney recipients remains unidentified but it is well-known the higher risk associated with latent Ss reactivation, primary infection, and less frequent, donor-derived infection.⁴

Donor strongyloidiasis does not contraindicate transplantation or delay kidney implantation. The purpose of pre-transplant screening is to identify donor/receptor pairs at higher risk of Ss reactivation that will benefit of prophylactic treatment and closer surveillance, especially in the early post-transplant period.

Some medical societies have recommended Ss pretransplant screening in recipients and donors from endemic areas^{5,6} but, what about the non-endemic areas and the impact of globalization and population migration flows in Ss global spread? In fact, recent data have confirmed a prevalence of Ss infection or seropositivity of 3% in Central Europe, among renal transplant recipients.²

One of the concerns with Ss screening and prophylactic eradication are the costs. However, if we consider the improvement in overall patient and graft survival,⁶ it seems reasonable to justify the implantation of the Ss screening in the pre-transplant protocol, as we did it in our center.⁷

One important aspect to retain is that only a high level of suspicion by the clinicians will allow an early diagnosis and prompt treatment and Ss should not be forgotten.

Regarding the therapeutic options available, monotherapy may not be enough to control the dissemination in immunocompromised patients.⁸

We proposed albendazole and ivermectin association, given the different mechanisms of action and absence of known interactions, followed by a maintenance course with ivermectin for 6 months, given the higher risk of relapse and great tolerance.^{3-5,9}

The purpose of this letter is to remind the high level of suspicion needed to a prompt diagnosis and treatment of Ss infection in kidney recipients and reinforce that pre-transplantation protocols should include Ss screening, even in non-endemic areas.

Acknowledgements

Ana Messias, Miguel Bigotte Vieira, Rita Magriço, Cecília Silva, Inês Aires, Francisco Remédio.

REFERENCES

1. Khoury JA, Brennan DC. Infectious complications in kidney transplant recipients: review of the literature. *Saudi J Kidney Dis Transplant*. 2005;16. <http://www.sjkdt.org>

2. Winnicki W, Eder M, Mazal P, Mayer FJ, Sengölge G, Wagner L. Prevalence of *Strongyloides stercoralis* infection and hyperinfection syndrome among renal allograft recipients in Central Europe. *Sci Rep*. 2018;8. <http://dx.doi.org/10.1038/s41598-018-33775-3>.
3. Roxby AC, Gottlieb GS, Limaye AP. Strongyloidiasis in transplant patients. *Clin Infect Dis*. 2009;49:1411–23. <http://dx.doi.org/10.1086/630201>.
4. Catalán SB, Albiach JF, Garcia AI, Martínez EG, Teruel JL, Mateu ML. *Strongyloides stercoralis* infection in kidney transplant patients. 2009. <http://www.senefro.org>
5. Mazhar M, Ali IA, Agudelo Higueta NI. Strongyloides hyperinfection in a renal transplant patient: always be on the lookout. *Case Rep Infect Dis*. 2017;2017:1–4. <http://dx.doi.org/10.1155/2017/2953805>.
6. Arkell P, Pan D, Riley P, Cooper P, MacPhee, Cosgrove C, et al. Should prospective renal transplant recipients be screened for *Strongyloides stercoralis*? *Clin Kidney J*. Published online 2020:1–3. doi:10.1093/ckj/sfaa047.
7. Camargo JF, Simkins J, Anjan S, Guerra G, Rodrigo V, Salama S, et al. Implementation of a *Strongyloides* screening strategy in solid organ transplant donors and recipients. *Clin Transplant*. 2019;33. <http://dx.doi.org/10.1111/ctr.13497>.
8. Abdalhamid BA, al Abadi AN, aser M, al Saghier MI, Joudeh AA, Shorman MA, Amr SS. Strongyloides stercoralis infection in kidney transplant recipients. *Saudi J Kidney Dis Transplant*. 2015;26:98–102. <http://dx.doi.org/10.4103/1319-2442.148752>.
9. Pornsuriyasak P, Niticharoenpong K, Sakapibunnann A. Disseminated strongyloidiasis successfully treated with extended duration ivermectin combined with albendazole: a case report of intractable strongyloidiasis. *Case Rep*. 2004;35.

Rita Abrantes^{a,*}, Rui Barata^b, Fernando Caeiro^b, Aníbal Ferreira^b, Fernando Nolasco^b

^a Nephrology and Dialysis Department – Centro Hospitalar do Médio Tejo, EPE, Portugal

^b Transplantation Department – Hospital Curry Cabral, Centro Hospitalar Lisboa Central, EPE, Portugal

* Corresponding author.

E-mail address: anaritamabrantes@gmail.com (R. Abrantes).

0211-6995/© 2021 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). <https://doi.org/10.1016/j.nefro.2021.09.012>