Case Report

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Fatal disseminated strongyloidiasis after kidney transplantation

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ABSTRACT

Disseminated strongyloidiasis (DS) is a rare and severe parasitic disease that is difficult to recognize and affects immunocompromised individuals. We report the case of a kidney transplant recipient who presented with DS despite prophylaxis with albendazole. We have discussed the need for better prophylactic strategies and for a higher degree of suspicion in order to diagnose DS.

Keywords: Strongyloidiasis. *Strongyloides stercoralis.* Kidney transplantation.

INTRODUCTION

The first report of disseminated strongyloidiasis (DS) in the medical literature dates from 1974[1]. The disease is currently more common, with severe presentations in association with immunosuppression[2,3].

Strongyloides stercoralis is an intestinal nematode that is highly prevalent in tropical regions. It affects humans, in whom it typically presents as a long-term, unapparent infection. Levels of sanitation and personal hygiene are directly proportional to the prevalence of this infection[4].

The dissemination of strongyloidiasis occurs in immunocompromised patients. The larvae can reach the circulation and disseminate to multiple organs[5]. The occurrence of strongyloidiasis has been reported increasingly after organ transplantation, including heart, liver, pancreas, intestine, and kidney transplantation, even in non-endemic countries[6–9].

After receiving the patient's consent, we report the case of a kidney transplant recipient who presented with fatal DS.

CASE REPORT

A 50-year-old male received a kidney transplant from a deceased donor. In the immediate post-operative period, the patient presented with delayed graft function and required hemodialysis. A progressive increase in urinary output, accompanied by a slow decrease in creatinine levels, was subsequently observed. The immunosuppressive regimen consisted of tacrolimus, mycophenolate mofetil, and prednisone. The patient was treated prophylactically with a 3-day course of albendazole (400mg/day) for the prevention of strongyloidiasis. Although the patient was discharged from the hospital on postoperative day 9, he remained on hemodialysis until 20 days after discharge.

Four months after transplantation, the patient was hospitalized due to a 30-day history of asthenia, anorexia, weight loss (10kg), fever, hiccups, sleepiness, dyspnea, and productive cough with yellow expectoration, which progressed to frank hemoptysis within 3 days. Physical examination revealed fever (39°C), pallor, and abdominal distension.

The patient had poor personal hygiene. Pulmonary auscultation revealed rales throughout both lung fields. Laboratory tests revealed severe pancytopenia and 2% eosinophils (absolute white cells count, 2,300). Three blood cultures were obtained before beginning empiric antibiotic therapy; however, these yielded negative results. In addition, we detected hypoalbuminemia, together with elevated levels of urea and creatinine. Therefore, hemodialysis was again required. Serology for cytomegalovirus was negative. A chest X-ray revealed a diffuse alveolar interstitial infiltrate (**Figure 1**). Induced sputum samples were collected, and smear microscopy of the first sample revealed an abundance of *S. stercoralis* larvae (**Figure 2**).

The immunosuppressive therapy was discontinued, and ivermectin treatment was started, together with antibiotic therapy (imipenem and vancomycin) for febrile neutropenia. The overall health status of the patient rapidly improved, and his fever subsided. On the eighth day of antibiotic therapy, hemoptysis decreased and the radiological pattern showed improvement (**Figure 3**). On the tenth day, ivermectin was discontinued. Subsequently, there was a worsening of the clinical profile, characterized by obtundation associated with hallucinations and the appearance of purpura and bruises over the entire body. We established a working diagnosis of central nervous system impairment due to *S. stercoralis* infection and sepsis. Computerized tomography was performed but yielded unremarkable results. Analysis of cerebrospinal fluid did not show any parasite. Ivermectin was replaced with thiabendazole. However, the response was not favorable, and the patient developed hemodynamic instability, respiratory failure, and septic shock. He was then intubated, and mechanical ventilation was started. At 27 days after admission, he progressed to cardiopulmonary arrest, which did not respond to resuscitation.

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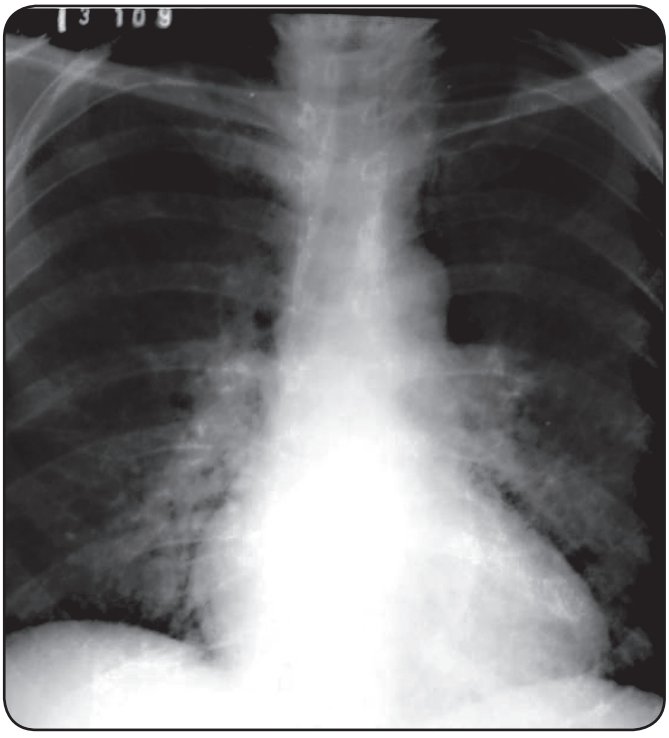

FIGURE 1 - Routine anteroposterior chest X-ray showing a diffuse interstitial infiltrate.

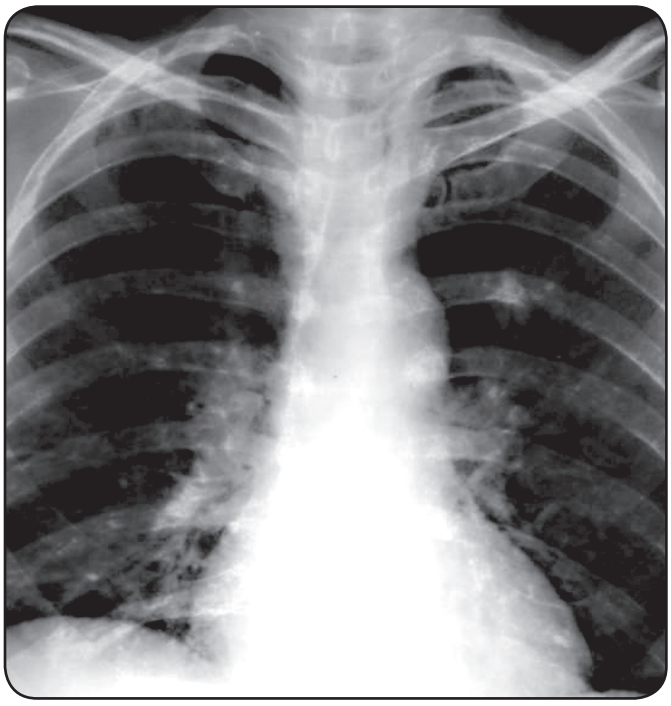

FIGURE 3 - Routine anteroposterior chest X-ray after 10 days of treatment with ivermectin.

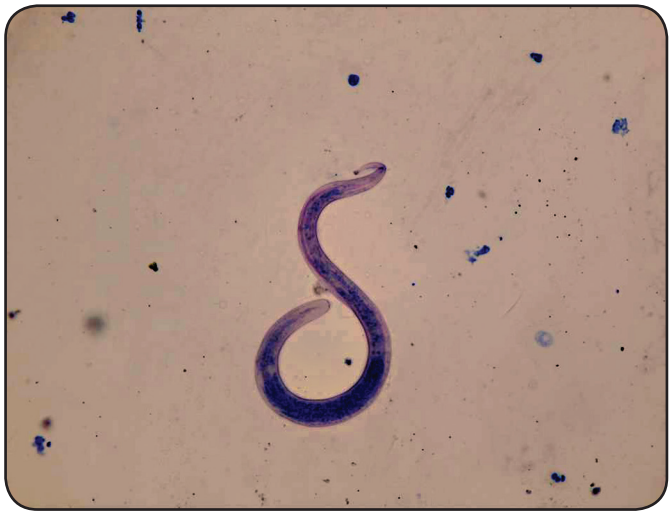

FIGURE 2 - *Strongyloides stercoralis* larvae in sputum (Ziehl-Neelsen staining/ hematoxylin and eosin staining; magnification ×400).

DISCUSSION

It has been more than 40 years since DS, a lethal form of strongyloidiasis seen in immunocompromised patients, was first described[2,3]. The disease involves multiple organs and systems other than the lungs and gastrointestinal tract. Mortality can be as high as 87%[10]. Other less common manifestations, including petechiae or purpura, headache, convulsions, and coma, have also been described[10].

In order to build an appropriate flowchart for the diagnosis of DS, it is necessary to understand the risk factors specific to the disease, as well as the most common presentations. The factors related to a higher probability of occurrence of DS are those that compromise cellular immunity, such as the use of aggressive immunosuppressive therapy (as used in the case reported here).

The clinical signs of DS are nonspecific. Unexplained gastrointestinal or pulmonary symptoms in susceptible patients should be warning signs, as in the present case. Abdominal pain and distension, acute respiratory distress, cough, hemoptysis, hypoxemia, and septic shock are common manifestations of the disseminated form of the disease[10]. Since *S. stercoralis* infection facilitates the translocation of enterobacteria across the intestinal mucosa, Gram-negative sepsis can occur[10]. In the case presented here, the patient improved rapidly after ivermectin administration; however, after drug withdrawal, he had a severe worsening and did not respond to the new treatment. He probably developed septic shock related to bacteria translocation with no response to the antibiotics and death, although blood cultures were negative.

Serological methods that determine the presence of antibodies in the serum of the host are more useful in asymptomatic patients with eosinophilia. In order to quantify the antibodies, the following methods can be used: enzyme-linked immunosorbent assay (ELISA), gelatin particle indirect agglutination, and western blotting[10]. Many studies have evaluated the accuracy of ELISA, demonstrating a sensitivity ranging from 80-97% and specificity ranging from 29-99%[11]. The indirect immunofluorescence antibody test (IFAT) is another serological test, but it is technically more complex than ELISA and requires specialized personnel for antigen preparation and reading the results; however, compared to ELISA, it gives quantitative results[12]. The sensitivity and specificity of IFAT is very high and cross-reactivity in subjects with other nematode infections is negligible[12].

The definitive diagnosis of DS is based on the finding of larvae in stool samples, tracheal secretions, bronchoalveolar lavage fluid, gastric aspirates, or in biopsy samples (from the stomach, jejunum,

skin, or lungs). In the case reported here, we identified *S. stercoralis* through the examination of induced sputum samples. Data regarding the diagnosis of DS are scarce and originate from small case series, which is due to the rarity of this condition.

Despite the severity of strongyloidiasis in patients with the disseminated form, diagnosis can usually be confirmed by minimally invasive methods. Therefore, in high-risk patients, a heightened clinical suspicion of DS should prompt the collection of biological material (e.g., gastric or duodenal aspirates and tracheal secretions) or the biopsy of suspicious lesions, thereby allowing the early initiation of an appropriate treatment.

The best strategy to prevent the severe forms of strongyloidiasis is to identify and treat infected patients and high-risk patients before the administration of immunosuppressants. Patients at a high risk of hyperinfection are those with pharmacologically induced immunosuppression for the treatment of autoimmune, allergic, and inflammatory diseases, during organ transplantation and post-cancer chemotherapy treatment. This is especially true with the use of corticosteroids, cyclosporine, vincristine, and others. The majority of cases reported have occurred after renal transplantation, when high doses of glucocorticoids were used to treat acute rejection[1,2]. Although considered an opportunistic infection in patients with acquired immunodeficiency syndrome (AIDS), *S. stercoralis* hyperinfection is unusual in the setting of solid organ transplantations[1].

The patients included in these groups should receive primary prevention of hyperinfection with ivermectin at a dose of 200 $\mu g \cdot kg^{-1} \cdot d^{-1}$ for 2 days and repeated after 2 weeks. In the treatment of *S. stercoralis* hyperinfection, no significant difference in efficacy was observed between ivermectin and thiabendazole, while side effects were far more frequent in thiabendazole-treated patients. Ivermectin is the drug of choice, but its efficacy at a single dose is suboptimal.

We believe that it is important to screen for chronic carriers of *S. stercoralis* infection among family members in order to avoid re-infection. It is necessary to provide comprehensive health education in areas where there is a lack of proper sanitation and hygiene.

ABSTRACT IN PORTUGUESE

Estrongiloidíase disseminada fatal após transplante renal

A estrongiloidíase disseminada (ED) é uma doença parasitária rara de difícil diagnóstico que acomete indivíduos imunocomprometidos. Relatamos um caso de um paciente transplantado renal que desenvolveu ED apesar do uso de profilaxia com albendazol. São discutidas estratégias profiláticas e de diagnóstico da estrongiloidíase disseminada.

Palavras-chaves: Estrongiloidíase. *Strongyloides stercoralis.* Transplante renal.

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