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Case Report

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Multiorgan failure due to strongyloides infection in liver transplant recipient: A case report and literature review

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Abstract

Strongyloidasis is caused by an intestinal nematode *Strongyloides stercoralis* which is widely distributed in tropical and subtropical countries. In immunocompetent individuals, *Strongloides stercoralis* infection usually does not produce any symptoms or causes gastrointestinal, cardiopulmonary, or skin symptoms. However, in some patients especially immunsupressive (e.g post-transplant, taking exogenous corticosteroids), its infection associated with severe and life-threatening disease like hyperinfection syndrome and disseminated tissue infestation. The limitation of diagnostic test make it challenging to diagnose strongyloidasis. Therefore, it is important to suspect infection of *Strongyloides stercoralis*. We describe a case of Strongiloides infection with a fatal outcome in liver transplant recipient.

Keywords: *Strongyloides stercoralis*, liver, liver transplatation, acute respiratory distress syndrome

1. Introduction

One of the most common problems caused by immunosuppressive treatments used after solid organ transplantation is infections (1). Strongyloidasis is a known complication of solid organ transplantation and it may cause severe parasitic infection which is lead to septisemia, multorgan failure and death (2). Strongyloidiasis is caused by infection with *Strongyloides stercoralis* which is an intestinal nematode and is widely found in tropical and subtropical countries (2, 3). Humans are the final hosts in the parasite cycle which has autoinfection which is rare and charecterstic feature in its life cycle (2, 4).

Human infection occurs by intact skin contact with filariform larvae and infection has also been induced by drinking water contaminated with the filariform larvae (2, 3). After contact with the skin, the larvae enter the venous system and can be found in the skin, gastrointestinal tract and lungs due their life cycle. However, in some patient, the larvae are found various tissue such as heart, brain, muscle, etc. The larval proliferation in tissue may leads to systemic sepsis, multi-organ failure and death (5).

Its infestation in human is usually asymptomatic or causes gastrointestinal, cardiopulmonary or skin symptoms in immunocompetent individuals. Immunosuppressed patients (e.g. taking exogenous corticosteroids or immunsuppressive drugs, solid organ tansplantation) are at risk for life-threating complication like hyperinfection syndrome and disseminated tissue infestation (2, 4). Mortality rate can be approaches upto 50% in hyperinfection syndrome and upto 70% in disseminated disease (6, 7).

In this article, we present a case of severe strongyloidiasis occurring in patient five years after liver tranplantation and that cause death due to Acute Respiratory Distress Syndrome (ARDS) and Multiple Organ Dysfunction Syndrome (MODS).

2. Case Report

A 45-year-old male patient having a history of liver transplantation due to chronic hepatitis B, was followed up tacrolimus monotherapy on the 4th year after transplantation without any problem. Acute hepatitis type transaminases (AST: 600 IU/L, ALT: 1300 IU/L, ALP:450 IU/L, GGT: 48 IU/L, bilirubin: 1.97 mg/dl) were found to be high in blood test performed during the control examinations of the patient; he was hospitalized considering the pre-diagnoses of recurrent hepatittis B, toxic hepatitis, de-novo autoimmune hepatitis. He did not use any new medication. HBV-DNA and HCV-RNA results were negative. On the laboratory tests after detection positive antinuclear antibody (ANA, 1/100) which is an autoimmune marker, liver biopsy was performed. The result of liver biopsy was reported as de-novo autoimmune hepatitis. Prednisolon 60 mg/day, mycophenolate mofetil 2x1000 mg, tacrolimus 2x1.5 mg treatments were started after the result of the liver biopsy.

Approximately 6 months after the new immunosuppresive

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therapy, he was hospitalized due to nausea, vomiting, diarrhea, loss of appetite, bloody sputum and detoriation in the general condition. On initial physical examination, he was conscious, co-operative and orientated. Mucous membranes were dry and pale. In respiratory examination, respiratory sounds were bilaterally coarse and there were rales in places. Blood pressure was 90/60 mmHg, heart rate was 110 bpm, respiratory rate was 22/minute. PA chest radiography showed an increase in the cardiothoracic index, centrally located infiltration in both lungs, increased opacity and occasional reticular densities (Fig. 1). In blood test hemoglobin was 7.9 gr/dl, leukocyte 650 /mm^3 and platelet 50.000 /mm^3. Owing to the findings on chest computer tomography examination including atelectasis area in the lower lobes of both lung, pleural irregularity and thickening, levofloxacin treatment was given.

The upper gastrointestinal endoscopy was performed due to anemia and vomiting, observing the fragile, spontaneous bledding areas and granular mucosal appearance in duodenum; biopsies were taken from these areas. Strongyloides were detected in duodenal biopsy (Fig. 2) and oral ivermectin treatment was initiated. Direct microscopic stool examination for diarrhea and their culture was unremarkable. No growth was detected in the tracheal aspirate culture taken due to ongoing bloody sputum. On the second day of ivermectin treatment, the patient's clinical condition gradually deteriorated, respiratory distress increased and ARDS developed. The patient, not responded despite all supportive treatment, died due to multiorgan's failure.

3. Discussion

Strongyloidiasis is usually an asymptomatic or mildly symptomatic disease in immunocompetent individuals (8). Chronic infection lasts for many years, and is usually asymptomatic. Sometimes causes gastrointestinal, cardiopulmonary or skin symptoms (9). Rapid replication and spread of filiform larvae are observed in some patients whose immune system is compromised due to exogenous steroid use and organ transplant. Strongyloides hyperinfection syndrome and disseminated disease may develop in these patients and cause acute severe illness and high mortality (10). *Strongyloides stercoralis* hyperinfection syndrome can develop many months or years after transplantation. However severe disseminated disease tends to occur within the first three month (11).

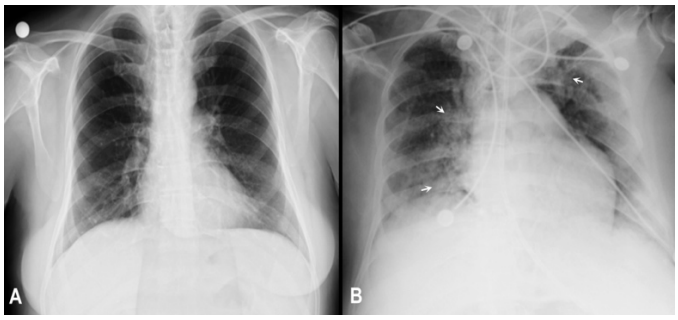

Fig. 1. PA chest radiography: (A) normal findings, (B) an increase in the cardiothoracic index, centrally located infiltration in both lungs, increased opacity and occasional reticular densities (arrows)

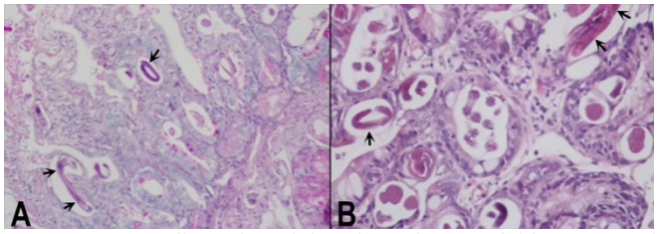

Fig. 2. Hematoxylin eosin staining showed strongyloides (arrows) in duodenal biopsy (A, B)

Table 1. Previously reported cases of strongyloidiosis in liver transplantation recipients

Age/ gender	Cause of transplantation	Time from transplantation (months)	Immunsuppresive treatment	Demograpic risk factor	Initial symptoms/ findings	Treatment for strongyloidiasis	Complications Of sepsis and/or Bacteremia	Outcome	Cause of death	Reference
59 / Female	Non-alcoholic steatohepatitis with cirrhosis	4	Induction:Alemtuzumab, methylprednisolone Maintenance: tacrolimus and prednisone	First donor from Puerto Rico Second donor's serologic test was negative	Nausea, poor appetite, weight loss, and constipation	Ivermectin and albendazole	Bacteremia / Coma	Alive	-	(1)
43 / Male	Hepatitis C infections and hepatocellular carcinoma	12	Tacrolimus and high dose corticosteroids	-	Elevation of liver enzymes	Thiabendazole and ivermectin	Septisemia	Death	ARDS	(2)
61 / Male	Alcoholic cirrhosis	7	Prednisone, Mycophenolate and tacrolimus	-	Progressive early satiety, bloating, weight loss, and fatigue	Ivermectin and albendazole	Bacteremia	Alive	-	(3)
67 / Male	Cholangiocarcinoma	2,5	Tacrolimus, micofenolic acid and prednisone	Donor from Ecuador	Fever, asthenia anorexia, diarrhea, dyspnea, cough, eosinophilia	Ivermectin and albendazole	Bacteremia	Alive	-	(15)
58 / Male	Hepatitis C / history of alcohol abuse	-	Induction: Basiliximab Maintenance: Mycophenolate,	Donor from Dominican Republic	Asymptomatic	Ivermectin and albendazole	None	Alive	-	(16)

			tacrolimus, and prednisone							
- / -	-	4	-	Donor from Suriname	Eosinophilia	Ivermectin	None	Alive	-	(17)
72 / Female	Hepatitis C infections and hepatocellular carcinoma	3	Tacrolimus, prednisone and mycophenolate mofetil	Donor from Guyana	Diffuse abdominal pain, nausea and nonbloody emesis	Ivermectin and albendazole	Bacteremia	Alive	-	(18)
60 / Male	Hepatitis B-related end-stage liver disease	2	Induction: methylprednisolone Maintenance: prednisone, mycophenolate and tacrolimus	Donor from Indian GCC-born recipients with a history of travel	Fever, anorexia, headache, and change in mental status	Ivermectin and albendazole	Bacteremia	Alive / GCS:6 connecting to MV	-	(19)
53 / Female	Liver cirrhosis due to Autoimmune liver disease	4	Mycophenolate Mofetil Tacrolimus, and Prednisolone	Donor from Bangladesh	Abdominal pain, nausea, vomiting, and diarrhea	Ivermectin and albendazole	None	Alive	-	(20)
58 / Male	Laennec's cirrhosis	104 days	Induction: antithymocyte globülin, rituximab and methylprednisolone Maintenance: tacrolimus	Donor and the recipient had positive *Strongyloides* serology	Abdominal rash, hyponatremia, ileus, and respirator failure	Ivermectin and albendazole	Bacteremia	Death	Multi-organ failure	(21)
66 / Female	End-stage hepatic cirrhosis by hepatitis C infection	9 days	Basiliximab, methylprednisolone, and mycophenolate mofetil.	Donor from Paraguay and has positive serology	Asymptomatic (On 9 day posttransplant, donor's serologic test was found positive)	Ivermectin	Abdominal septic shock, bacteremia and bilateral pneumonia	Death (Post-Tx 34th day)	Multi-organ failure	(22)
59 / Female	Non-alcoholic steatohepatitis with cirrhosis	4	Induction: Alemtuzumab, methylprednisolone Maintenance: tacrolimus and prednisone	First donor from Puerto Rico Second donor's serologic test was negative	Nausea, poor appetite, weight loss, and constipation	Ivermectin and albendazole	Bacteremia / Coma	Alive	-	(1)

Our PubMed literature review identified 11 cases of *Strongyloides stercoralis* infections in liver transplant recipients. Characteristics of 11 cases, such as: recipients's demographics including age and gender, cause of transplantation, time of onset *Strongyloides stercoralis* infection from the transplantation, epidemiology of donors (demographics risk factors), immunosuppressive therapy, initial clinical symptoms and complications including presence of bacteremia and sepsis, management and outcomes including death are shown in the Table 1.

The clinical symptoms of the disease are variable. Gastrointestinal symptoms are the most common and usually non-specific symptoms (such as abdominal pain, nausea, vomiting, diarrhea and bleeding) (12). Lung findings include cough, haemoptysis, wheezing and sometimes very severe lung collapse (13). In the present case, while the patient firstly admitted with gastrointestinal symptoms and bloody sputum, and then progressed to multi-organ failure and ARDS.

Filiform larvae can be detected in many secretions of the body in hyperinfection syndrome and disseminated disease. It may be found in stool, sputum, surgical drainage, and in bronchoalveolar lavage, pleural, and peritoneal fluid (14). In addition, as in our patient, larvae can be detected in biopsies taken from lesions detected in endoscopic findings (gastritis, duodenitis, aphthous ulcer, etc.). The limitation of diagnostic test makes it challenging to diagnose strongyloidasis and a delayed diagnosis may lead to severe illness especially in immumsupressed individuals. Therefore, it is important to suspect infection of *Strongyloides stercoralis.*

Epidemiological risk stratification should be determined for Strongyloides hyperinfection syndrome and disseminated infection in patients undergoing solid organ transplantation. If there is a history of living or visiting places where the parasite is endemic in immunosuppressive patients, it should be kept in mind that there is a risk of Strongyloidiasis infection. When a prompt diagnosis is not possible, Strongyloides hyperinfection syndrome and disseminated syndrome should be considered and due to its risk of fatal outcome, an urgent empirical preventive treatment planning should be done.

Opportunistic infections in transplant recipients have high mortality and it requires a multidisplinary approach. Here, we present a rare case of strongyloides infection with a fatal outcome. Therefore, it is important to suspect strongyloides infections due to severe disease and high mortality risk in immunosuppressed patients.

Informed consent: None.

Conflict of interest: The authors declare no conflict of interest.

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