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# *Schistosoma mansoni* Infection Following Allogeneic Bone Marrow Transplantation

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## ABSTRACT

A case of *Schistosoma mansoni* infection in a 28 year old male after allogeneic bone marrow transplantation presenting with portal hypertension and gross hematuria is described. Schistosomiasis was confirmed by the discovery of parasites in the feces, together with the failure the patient to respond to multiple antimicrobial and antifungal treatment. After praziquantel administration, toxic or septic shock syndrome evolved and the patients died of acute renal failure on day 39 post-transplant. In this report, we would like to emphasize the importance of pre-transplant stool and urine cultures, and appropriate serologic tests in patients coming from endemic areas. Patients diagnosed with schistosomiasis must be treated at least 3 to 7 weeks before transplantation.

Key Words: *Schistosoma mansoni*, Bone marrow transplantation.

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## INTRODUCTION

Schistosomiasis is an endemic disease affecting humans and animals. The disease is endemic in South East Asia, South America and in a wide area of Africa and the Middle East<sup>[1]</sup>. *Schistosoma(S) haematobium* infection has been reported in Turkey very rarely<sup>[2]</sup>. However, to date we are not aware of any reported cases of *S. mansoni* infection in Turkey. The larval cercariae are carried

by a specific fresh water snail and are transmitted to humans through the skin through contact with infested water. The cercariae become schistosomes as they reach general circulation via lymphatic and peripheral veins, about five to seven days after skin penetration. *S. mansoni* eggs are primarily deposited in the small veins around the large intestine; some of the eggs may be trapped in the gut wall or enter the small intrahepatic venules via portal circulation and bring about fib-

roobstructive lesions and obstruction of portal blood flow through the liver<sup>[1]</sup>.

Schistosomiasis was seen very rarely in immunocompromised patients<sup>[3]</sup>. This is the first described case in the literature of *S. mansoni* infection after allogeneic bone marrow transplantation (BMT).

### CASE REPORT

We describe a case of a 28 year-old male diagnosed as AML FAB M2, of *S. mansoni* infection after allogeneic BMT. In second complete remission, allogeneic BMT was performed from his one locus mismatch brother. The preparative regimen for BMT was fractionated total body irradiation with 12 Gy and high dose cyclophosphamide (2.5 g/m<sup>2</sup>/day on day-2 and-3), followed by marrow infusion (0.87x10<sup>8</sup> cells/kg). Because of failure to achieve a sufficient number of nucleated cells, donor leukocytes were collected from his brother after recombinant human G-CSF 16 g/kg s.c. and recombinant human GM-CSF 3.75 g/kg IV on day +1 to 7. Leukapheresis was started on day +7 for 2 consecutive days using a Cobe Spectra continuous flow blood cell separator with a blood volume of 7500 ml per procedure. Peripheral venous access was used. No side-effects related to G-CSF and GM-CSF or leukapheretic procedures were seen. A total of 4.76 x 10<sup>8</sup>/kg CD34+ cells, 3.53x10<sup>8</sup>/kg mononuclear and 3.35x10<sup>8</sup>/kg polymorphonuclear was infused. The graft versus host disease prophylaxis was methotrexate 15 mg/m<sup>2</sup> on day +1, +3, +6, +11, and then once a week, and cyclosporin (CsA) at an initial maximum dosage of 5 mg/kg, followed by 3 mg/kg daily. Hemopoietic reconstitution was rapid with an absolute neutrophil count of > 0.5x10<sup>9</sup>/L on day +18.

HBs antigenemia was observed both in the patient and the donor. Other hematological and laboratory findings immediately prior to BMT were within normal limits. An episode of fever of unknown origin following BMT was treated with ceftazidime, amikacin, vancomycin, and liposomal amphotericin-B.

On day +10, abdominal distention and ascites developed and these symptoms increased gradually and portal hypertension was determined. On

day +27, gross hematuria appeared. *S. mansoni* eggs were demonstrated both in the feces and the urine at three consecutive days of examination (Figure 1). On day +29, the patient was treated with a single dose praziquantel (40 mg/kg). After two days from therapy, shock syndrome evolved. Hypothermia and hypotension developed, and absolute neutrophil count decreased to < 0.5x10<sup>9</sup>/L. Starting on day +27 post-transplant the urea concentration increased from 21 mg/dL to 360 mg/dL gradually. Peritoneal dialysis was performed because of acute renal failure on day +38. He died of shock and acute renal failure 18 hours after dialysis. An autopsy could not be performed because of the religious considerations of his family.

### DISCUSSION

A significant number of parasitic infections are caused by a variety of opportunistic organisms in the immunocompromised patient. These infections significantly increase the morbidity and mortality in these patients<sup>[3]</sup>. To our knowledge, the present case is one of the few reports of schistosomiasis as an unusual clinical picture after allogeneic BMT.

Schistosomiasis is a major health problem in endemic areas and is known to cause urinary and hepatic dysfunction and portal and pulmonary hypertension. Schistosomiasis has an effect on the immune response by cell mediated or humoral mediated immunity<sup>[4]</sup> and causes kidney lesions directly through glomerular immune complex deposition<sup>[5]</sup>. The patient received antischistosomiasis

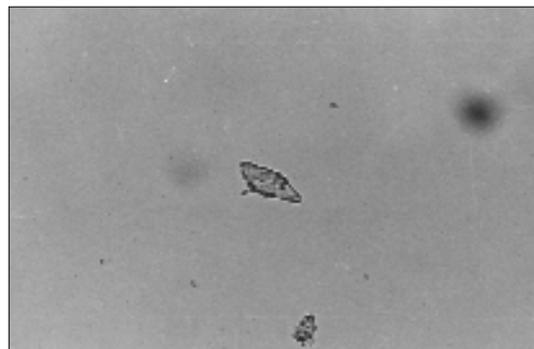


Figure 1. Photomicrography from a urine specimen showing the characteristic appearance of a *S. mansoni* egg (Original magnification x 100).

mal treatment. Two days after antischistosomal treatment, there had been a significant increase in the serum urea, creatinine, and the 24-h urinary protein excretion. A sudden onset of nephropathy in this case cannot be attributed to the antischistosomal drug. Sobh et. al<sup>[6]</sup> reported the effect of antischistosomal treatment using praziquantel in patients with Schistosoma-specific nephropathy in which there was no significant, immediate, or short term changes in the serum creatinine or the proteinuria in any of their patients examined. However, Falcao and Grould<sup>[7]</sup> described a patient with nephropathy in schistosomiasis. In their report, there was an increase in the serum creatinine and the urinary protein excretion following the antischistosomal treatment, and this was attributed to a sudden increase in serum schistosomal antigens due to the adult worms being killed by the antischistosomal drug. This caused an increase in circulating immune complexes which were trapped in the glomeruli, causing nephropathy. Based on this literature we concluded that the same phenomenon most likely occurred in our case.

In the current report, portal hypertension following BMT may be due to hepatosplenic schistosomiasis. Byres et. al<sup>[8]</sup> reported a case of *S. mansoni* complicated by portal hypertension. Moreover, embolization by ova and dead adult worms, especially after antischistosomal treatment, may occur in the portal tract with consequent portal tract fibrosis.

HBs antigenemia is observed more frequently in schistosomal patients. Interestingly, HBs antigenemia was observed in our patient, too. It has been reported that the survival of the patient with schistosomiasis is significantly decreased in HBV carriers<sup>[9]</sup>. Probably this is due to the increased incidence of liver cell failure and hepatocellular carcinoma.

Schistosomiasis leads to the impairment of the absorption of CsA. This can be due to the effect of schistosomiasis on the intestinal mucosa. Sobh et al<sup>[10]</sup> reported that patients with schistosomiasis needed significantly greater oral doses (65-75% higher) of CsA to achieve the target blood levels than that of control patients.

After the allogeneic BMT, hematopoietic reconstitution was achieved, but leukocyte count rapidly decreased after antischistosomal therapy. This may be related to the effect of schistosomiasis on the host immune response to the graft. Ottesen et. al<sup>[11]</sup> stated that, despite the progressive loss of the host cellular response to *S. mansoni* when the infection become chronic, this loss is not a manifestation of a state of generalized cellular immune depression; it is rather limited to a response to schistosoma antigen. This was documented by a normal response to a nonschistosomal antigen (phytohemagglutinin). They also reported intact humoral responses in their patients. However, Borojevic et al<sup>[12]</sup> reported an inhibitory effect of sera from schistosomiasis patients on the bone marrow neutrophilic maturation in cultures.

From this case report, we have concluded that schistosomiasis may have a detrimental effect on patients undergoing an allogeneic BMT by causing a complicated clinical picture involving portal hypertension, septic or toxic shock, and renal failure. Moreover, schistosomiasis may interfere with oral doses of CsA economic to achieve the target blood levels with its consequences. Schistosomiasis is also significantly associated with an increased incidence of HBs antigenemia with a possible long term negative effect on patient survival. Routine stool and urine examinations and serological tests of schistosomiasis should be performed for recipients coming from endemic areas and proper treatment of schistosomiasis at least 3-8 weeks before BMT is recommended.

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