Journal of Transplantation Technologies & Research

Patel et al., J Transplant Technol Res 2015, 5:2
DOI: 10.4172/2161-0991.1000150

Case Report Open Access

Incidental Schistosomiasis in Transplant Liver: A Case Report and Review of the Literature

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Abstract

Background: We report a rare case of incidental allograft liver schistosomiasis within the United States.

Methods: A 52-year-old Filipino female received a liver transplant for decompensated cirrhosis and hepatocellular carcinoma secondary to hepatitis B viral infection and alcoholic liver disease.

Results: Her posttransplant course was unremarkable. However, a protocol liver allograft biopsy revealed multiple dead and calcified *Schistosoma* eggs. The patient's explant liver showed cirrhosis but no signs of *Schistosoma*. This finding of incidental hepatic schistosomiasis prompted a retrospective review of the donor's profile. The donor had no history of liver disease, schistosomiasis, or any signs to suggest an active parasitic infection. It was elected to follow this patient without any empirical treatment. The patient was discharged on standard posttransplant immunosuppression. Currently after four months of followup she remains disease free.

Conclusions: With many immigrants migrating into the United States, plausible guidelines are necessary at large liver transplant centers in regard as screening donor livers and management for *Schistosoma*.

Keywords: Schistosomiasis; Liver transplantation; Allograft

Introduction

Schistosoma is the second most prevalent tropical disease in the world and is commonly found in Africa, Middle East, Southeast Asia, and parts of South America. Nearly 200 million people are affected worldwide with approximately 20 million people with a severe form of schistosomiasis [1]. The primary method of transmission is via direct contact through the skin, usually through the feet or hands, while traversing fresh waters, or having contact with vegetation or water infected with *Schistosoma cercaria*. Gastrointestinal and hepatic schistosomiasis is caused by *S. mansoni* and *S. japonicum* species. Hepatic schistosomiasis is a well-known cause of chronic liver disease in many parts of the world, although it is uncommon in the United States and exclusively seen in the immigrant population. Herein, we reported a rare case of incidental *Schistosoma* in an allograft liver within the United States.

Case report

A 52-year-old Filipino female received a liver transplant for decompensated cirrhosis and hepatocellular carcinoma secondary to hepatitis B viral infection and alcoholic liver disease. Preoperatively, she presented multiple times for clinical complications including bleeding from esophageal varices, erosive gastropathy, ascites, and encephalopathy. Her magnetic resonance imaging (MRI) showed an unresectable posterior dome liver lesion that was highly suspicious for hepatocellular carcinoma. Her alpha-fetoprotein (AFP) was elevated at 34 U/L. She then received Y90 radio-embolization of the tumor. However, she still complained of fatigue, some confusion, shortness of breath with activity, constant abdominal pain, nausea, insomnia, and nocturia. The positron emission tomography-computed tomography (PET/CT) scan showed no evidence of metastatic disease. Her hepatitis B virus infection was well controlled on tenofovir and her hepatic encephalopathy was controlled with lactulose and rifaximin. Ascites was tolerated with diuretics. She had a history of alcohol abuse with six drinks per day for approximately twenty years. The patient moved to the United States from Thailand in 1980s. Other past medical history consisted of dyslipidemia, gall stones, and gastric ulcer. Her case was discussed and the decision was made to proceed with a liver transplantation when the appropriate donor was found. During the liver transplant surgery, a biopsy was taken of the newly transplanted donor liver. It, along with the explanted native liver, was sent to pathology for examination.

The patient's posttransplant course was unremarkable. A fascial closure of the allograft liver revealed multiple dead and calcified *Schistosoma* eggs in the venules without inflammation, granulomas, or fibrosis (Figure 1). The patient's explant liver showed cirrhosis and few hyalinized nodules with central necrosis but no viable malignant cells or signs of *Schistosoma*. This finding of incidental hepatic schistosomiasis in the liver allograft prompted a retrospective review of the donor's profile. The donor was a 51-year-old Pacific Islander female who died from diffuse subarachnoid hemorrhage. She lived in the Philippines until 1983 and then moved to the United States. On physical exam, there was no evidence of jaundice, swollen glands, or enlarged lymph nodes. Her liver enzymes were as follows: aspartate aminotransferase (AST) 23 U/L, alanine aminotransferase (ALT) 40 U/L, alkaline phosphatase 104 U/L, and total bilirubin 0.5 mg/dL. CT imaging showed no mass or adenopathy in thorax, abdomen, and pelvis. She had no history of liver disease, schistosomiasis, or any signs to suggest an active parasitic infection, although no autopsy was performed.

Conclusions

Several questions stem from this particular case on the subject of *Schistosoma* and liver transplantation. What is the appropriate standard

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Received: August 03, 2015; **Accepted:** September 26, 2015; **Published** October 10, 2015

Citation: Patel RA, Cummings OW, Mangus RS, Patel PM, Nagaraju S, et al. (2015) Incidental Schistosomiasis in Transplant Liver: A Case Report and Review of the Literature. J Transplant Technol Res 5: 150. doi:10.4172/2161-0991.1000150

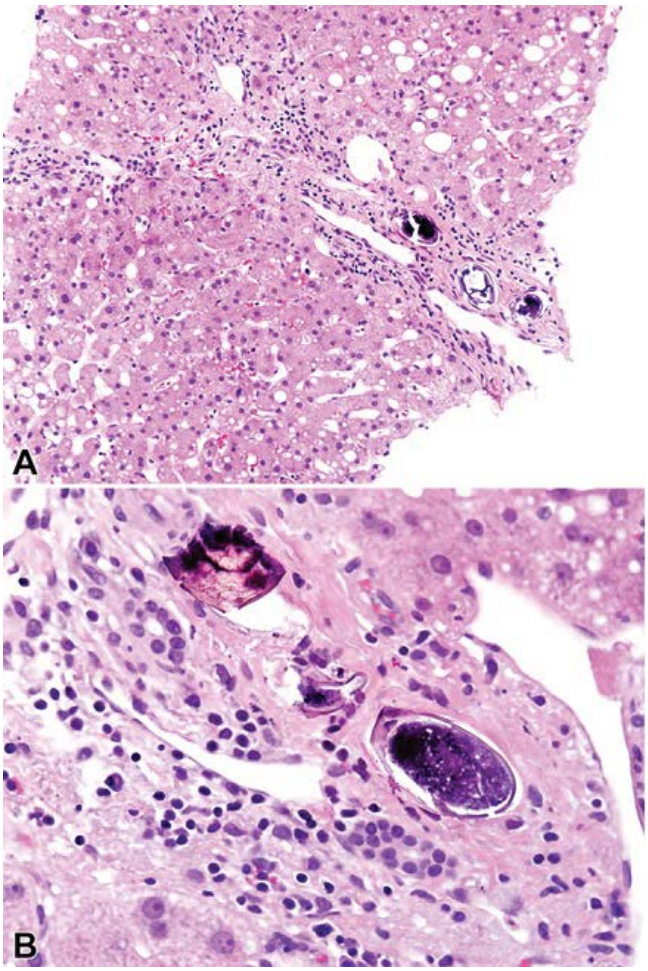

Figure 1: Incidental hepatic schistosomiasis in allograft liver. A, Basophilic and refractile oval structures within venules in an otherwise relatively normal-appearing portal triad (x100). B, Multiple dead and calcified Schistosoma eggs in the venules without associated inflammation, granulomas or fibrosis (x400).

to screen donor livers for *Schistosoma* and is this really necessary? Should treatment be offered empirically to all transplant patients with evidence of *Schistosoma*? Although there is paucity of schistosomiasis in the United States and other Western countries, with the large diversity of immigrants migrating worldwide, plausible guidelines to this issue are pertinent at large liver transplant centers. Herein, we reviewed the literature as regards the current concepts of schistosomiasis and liver transplantation.

The presentation of acute schistosomiasis varies greatly from no symptoms to hypersensitive reactions such as Katayama fever or cercarial dermatitis [2]. It is thought that a dramatic presentation as Katayama fever is uncommon in liver transplants; however, the answer is largely unknown because it may be masked by immunosuppression or misinterpreted as acute rejection [3]. Often, there is a vague flu-like prodromal illness including fever, muscle aches, and headaches. Early phase involves the intestinal tract with symptoms of abdominal pain and diarrhea, whereas later phase affects the liver indicating transition to a chronic stage. Eggs of *S. mansoni* and *S. japonicum* are laid in intestinal veins by inhabiting adult worms. The eggs then migrate to the liver where they become lodged in the small veins and venules. The chronic phase is quite common and may affect up to 50% of affected individuals. However, the damage is generally mild; only about 5% of liver shows pathologic evidence of granulomatous inflammation, perivenular fibrosis, or total vascular obstruction leading to a noncirrhotic portal hypertension resulting in end stage liver disease [2]. Cirrhosis is rare in *Schistosoma* infection alone, but when the patient is coinfected with hepatitis B or C virus, progression to cirrhosis is brisk––this is common in endemic regions such as Egypt and the Middle East [4-7].

The gold standard to diagnose hepatic schistosomiasis is microscopic examination of eggs in the tissue. However, practically speaking, liver biopsy is not the first choice due to the invasive nature of the procedure. Alternatively, the diagnosis of schistosomiasis can be accomplished by serologies and direct visual microscopy of eggs in stool or urine. Mild infections with lower levels of ova in stool can cause false negative result. Although serologic testing is highly sensitive, false positivity does exist. Another drawback of serology is the limitation to discriminate between old and new infection [3,5].

Schistosomiasis in liver transplants can occur in three ways. First, latent infection that the recipient had before is reactivated as a result of posttransplant immunosuppression. Second, the infection is passed from the allograft liver to the recipient. Third, a new infection occurs during travel to an endemic location.

A few cases of *Schistosoma* in the allograft liver passed from transplantation have been reported, as shown in Table 1. The first case was reported in 2003; the donor liver was from a 20-year-old brain-dead individual with previously known hepatic schistosomiasis [8]. After 7 months followup, the recipient was doing well without any anti-*Schistosoma* treatment. In 2005, Pannegeon reported a 23-year-old male who had liver transplantation due to hepatitis B virus infection-induced cirrhosis [9]. The transplant liver on subsequent biopsy was incidentally found to have *S. mansoni* eggs. The patient was treated with a 2-day praziquantel regimen twice perioperatively. At 2 weeks and 6 months followup, the liver biopsies showed no evidence of eggs or fibrosis. Pungpapong et al. demonstrated three cases of *Schistosoma* in allograft liver in Puerto Rico treated with praziquantel on three separate days posttransplant, which showed no evidence of active hepatic schistosomiasis on followup [10]. Given the relatively high incidence of schistosomiasis in Brazil, Vincenzi et al. screened pediatric liver transplant cases between 1991 and 2010, and discovered six donors with hepatic schistosomiasis which were incidentally transplanted to the recipients [11]. The methods for donor screening included liver enzymes, abdominal sonogram, and fecal parasite test, all of which were within normal limits. Treatment specifically targeting schistosomiasis was not given to the recipients, since the organism's presence was unknown. Of the six patients, two died from other complications including lymphoma and Kaposi sarcoma. One patient had primary graft failure requiring a second transplant and did fine afterwards. The remaining three patients were alive and well. None of the living patients showed any adverse effect from *Schistosoma* after 3 years of followup and the two patients who died of other complications did not show any signs of *Schistosoma* infection [11]. In 2012, Andraus et al. reported two cases with known *Schistosoma* eggs in the donor liver which were used in liver transplant [12]. One recipient died at day 14 owing to sepsis. The other recipient remained alive and healthy after 2 years of followup. Taken together, it appears that donors who had schistosomiasis can be acceptable. At least so far there is no apparently worse consequence using *Schistosoma*-infected livers for transplantation as such cases have been explored by a few institutions and demonstrated favorable outcome. However, the experience of using *Schistosoma*-infected liver remains limited and requires more evidence to support the conclusion.

In the United States, a nonendemic region, it might not be mandatory to screen for *Schistosoma* in donors. Such donor livers with

Table 1: Case reports over past 15 years highlighting treatment and outcomes of schistosomiasis in transplanted livers

Study	1 (Kayler [8])	2 (Pannegeon [9])	3 (Pungpapong [10])	4 (Vincenzi [11])	5 (Andraus [12])		6 (this study)
Patients (N)	1	1	3	6	2		1
Recipient Age; Gender	51 M	23 M	40 M, 48 M, 49 M	All children (10 months to 28 months; 2 M and 4 F)	27 M	57 M	52 F
Donor History	20 M with history of treated intestinal schistosomiasis 2x; Travel history to Zimbabwe, England, and Mexico	59 M; Travel history N/A	All lived in Puerto Rico (endemic); Travel history N/A	Lived in an endemic area; Travel history N/A	36 M with history of schistosomiasis; Travel history N/A	31 M w/ travel history N/A	51 F from Philippines; Travel history N/A
Donor Screening	AST 101, ALT 56; Normal liver U/S	Normal LFTs; Normal liver U/S	All stored donor sera retrospectively showed *Schistosoma* antibody positivity	All with normal LFTs, negative fecal test and normal abdominal U/S	Known to have *Schistosoma* eggs	*Schistosoma* eggs on fecal parasite test	Normal LFTs; Normal CT
Transplant Liver Histology	No evidence of schistosomiasis	Granulomas and *Schistosoma* eggs	All with granulomas and *Schistosoma* eggs	All with granulomas and *Schistosoma* eggs	Granulomas and *Schistosoma* eggs	N/A	Calcified *Schistosoma* eggs in venules; No granulomas
Treatment	No treatment	Two 2 day treatment with Praziquantel (imm. postop)	All took Praziquantel on days 2, 18 and 42, bid (imm. postop)	No treatment for all	No treatment	Pretransplant donor treated with Praziquantel	No treatment
Followup	7 m	6 m	35, 100, 20 weeks	From 3 days to 56 m	14 days	2 years	4 m
Outcome	Alive; No active schistosomiasis	Alive; No active schistosomiasis	All alive with no active schistosomiasis	All with no active schistosomiasis; 4 alive; 2 Dead (Kaposi sarcoma at 14 mos. and lymphoma at 31 mos.)	Dead (Postoperative Sepsis); No active schistosomiasis	Alive; No active schistosomiasis	Alive; No active schistosomiasis

Schistosoma may be still suitable especially considering the limited supply. Rejecting majority of *Schistosoma*-infected livers would not be cost, time, or resource efficient in the face of a lack of readily available livers. If a transplant patient does show *Schistosoma* recurrence or activation, treatment should be considered on a per case basis. An institution, alternatively, may adopt a conservative approach to screen donors from *Schistosoma* prevalent regions, especially if the recipients have hepatitis B or C virus infection. An algorithm suggested by Mossad includes screening with serology and stool egg test [13]. If the stool shows *Schistosoma* eggs, a liver biopsy should be pursued. If the stool is negative but the serology is positive, a rectal biopsy should be done. If the rectal biopsy is positive it should followup with a liver biopsy; whereas if rectal biopsy is negative, the liver is accepted for donation [13].

To our knowledge, this is the second case report and the fourth patient with an incidental schistosomiasis in transplant liver within the United States. After consulting with Departments of Pathology and Infectious Disease, no treatment was recommended as the current regimen affects the flukes but not the eggs. The patient, anyway, would not have the fluke derived from the dead and calcified eggs. Furthermore, based on published reports, the long term outcome, even without treatment, appears favorable [11]. The consensus is that the patient will be followed and if she does have eosinophilia in the future, further workup would be considered. The patient was discharged on posttransplant day 10 after an otherwise uneventful postoperative course with full diet and standard posttransplant immunosuppression. Currently, after 4 months of followup, the patient is doing well without any evidence of active schistosomiasis.

References

1. Papamatheakis DG, Mocumbi AO, Kim NH, Mandel J (2014) Schistosomiasis-associated pulmonary hypertension. Pulm Circ 4: 596-611.
2. Burke ML, Jones MK, Gobert GN, Li YS, Ellis MK, et al. (2009) Immunopathogenesis of human schistosomiasis. Parasite Immunol 31: 163-176.
3. Schwartz BS, Mawhorter SD; AST Infectious Diseases Community of Practice (2013) Parasitic infections in solid organ transplantation. Am J Transplant 13 Suppl 4: 280-303.
4. Ahmed K, Safdar K, Kemmer N, Atiq M, Wang J, et al. (2007) Intestinal schistosomiasis following orthotopic liver transplantation: a case report. Transplant Proc 39: 3502-3504.
5. Hoare M, Gelson WT, Davies SE, Curran M, Alexander GJ (2005) Hepatic and intestinal schistosomiasis after orthotopic liver transplant. Liver Transpl 11: 1603-1607.
6. Kamal SM, El Sayed Khalifa K (2006) Immune modulation by helminthic infections: worms and viral infections. Parasite Immunol 28: 483-496.
7. Ross AG, Bartley PB, Sleigh AC, Olds GR, Li Y, et al. (2002) Schistosomiasis. N Engl J Med 346: 1212-1220.
8. Kayler LK, Rudich SM, Merion RM (2003) Orthotopic liver transplantation from a donor with a history of schistosomiasis. Transplant Proc 35: 2974-2976.
9. Pannegeon V, Masini JP, Paye F, Chazouillères O, Girard PM (2005) Schistosoma mansoni infection and liver graft. Transplantation 80: 287.
10. Pungpapong S, Krishna M, Abraham SC, Keaveny AP, Dickson RC, et al. (2006) Clinicopathologic findings and outcomes of liver transplantation using grafts from donors with unrecognized and unusual diseases. Liver Transpl 12: 310-315.
11. Vincenzi R, Neto JS, Fonseca EA, Pugliese V, Leite KR, et al. (2011) Schistosoma mansoni infection in the liver graft: The impact on donor and recipient outcomes after transplantation. Liver Transpl 17: 1299-1303.
12. Andraus W, Pugliese V, Pecora R, D'Albuquerque LA (2012) Intentional use of Schistosoma mansoni-infected grafts in living donor liver transplantation. Liver Transpl 18: 867-868.
13. Mossad SB (2011) Region-specific challenges for minimizing endemic donor-transmitted infections. Liver Transpl 17: 1241-1243.