ORIGINAL ARTICLE

Is It Safe to Use a Liver Graft From a Chagas Disease–Seropositive Donor in a Human Immunodeficiency Virus–Positive Recipient? A Case Report Addressing a Novel Challenge in Liver Transplantation

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This is the first report presenting a human immunodeficiency virus (HIV)–positive patient with fulminant hepatic failure receiving a liver graft from a Chagas disease–seropositive deceased donor. We describe the history of a 38-year-old HIV-positive female patient who developed fulminant hepatic failure of an autoimmune etiology with rapid deterioration of her clinical status and secondary multiorgan failure and, therefore, needed emergency liver transplantation (LT) as a lifesaving procedure. Because of the scarcity of organs and the high mortality rate for emergency status patients on the LT waiting list, we decided to accept a Chagas disease–seropositive deceased donor liver graft for this immunocompromised Chagas disease–seronegative patient. The recipient had a rapid postoperative recovery and was discharged on postoperative day 9 without prophylactic treatment for Chagas disease. Fifteen months after LT, she was still alive and had never experienced seroconversion on periodic screening tests for Chagas detection. Although there is an inherent risk of acute Chagas disease developing in seronegative recipients, our report suggests that these infected organs can be safely used as a lifesaving strategy for HIV patients with a high need for LT. ***Liver Transpl 18:979–983, 2012.*** © **2012 AASLD.**

Received December 10, 2011; accepted April 3, 2012.

The organ shortage is a well-established problem, and it is the most important factor leading to the deaths of patients on liver transplantation (LT) waiting lists worldwide.[1-3] The constant struggle between supply and demand has led LT centers to seek different strategies for increasing the liver pool (eg, the use of extended criteria donors). Our group recently reported the experience of using "livers that nobody wants" to palliate the scarcity of livers in Argentina.[4] Forced by continuous increases in mortality on the LT waiting list in Argentina, we recently decided to expand the pool of acceptable donors to include donors who could potentially transmit infectious diseases to their recipients.[4,5] Here we report a case of successful LT using an infected organ in an emergency status patient on the LT waiting list who was positive for human immunodeficiency virus (HIV).

CASE REPORT

On November 2010, we received a 38-year-old female patient with an HIV infection diagnosed 9 months before her admission during her first pregnancy. She was transferred to our center with a diagnosis of fulminant hepatic failure of an autoimmune etiology. Symptoms became evident 5 days before her hospital admission, and they progressed rapidly. She developed refractory hypotension, acute renal failure, and

Abbreviations: EIA, enzyme immunoassay; HIV, human immunodeficiency virus; IFA, immunofluorescence assay; LT, liver transplantation; PCR, polymerase chain reaction; TESA, trypomastigote excreted-secreted antigens.

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DOI 10.1002/lt.23452
View this article online at wileyonlinelibrary.com.
LIVER TRANSPLANTATION.DOI 10.1002/lt. *Published on behalf of the American Association for the Study of Liver Diseases*

progressive encephalopathy, which led to the need for inotropic drug use, sedation, and mechanical ventilation plus the placement of an intracranial catheter for monitoring brain pressure. Both her liver function tests and her coagulation markers were impaired. Because of these findings and the clinical context of progressive secondary multiorgan failure, she was immediately placed on the waiting list for LT with an emergency status. She was receiving antiretroviral therapy with a CD4 cell count of 470 cells/μL and with an undetectable viral load. A week after the onset of her liver injury and 48 hours after her hospital admission, a Chagas disease–seropositive deceased donor liver became available. Because of the clinical context of a critically ill HIV-positive patient and despite her serological negativity for a Chagas infection, the organ was accepted for this patient with her family's consent and with the approval of our institutional ethics committee.

At the time of transplantation, her clinical status was stable. LT was performed according to the standard technique with preservation of the native vena cava (the piggyback technique) without the need for intraoperative red blood cell transfusions and without intraoperative or postoperative complications. She recovered satisfactorily with good liver graft function; the mechanical ventilation was stopped and the intracranial catheter was removed on postoperative day 2. The patient improved significantly after LT and was discharged on postoperative day 9.

Her immunosuppressive regimen included tacrolimus (given twice a day at an initial dose of 0.025 mg/kg/day with target plasma levels of 10-12 ng/mL), mycophenolate mofetil, and steroids. Steroids were tapered progressively and were discontinued after 90 days. Confirmatory testing for the donor's Chagas infection was performed at our center with 2 different methods (indirect hemagglutination and indirect immunofluorescence). She did not receive prophylactic treatment for Chagas disease, but she was screened with 2 direct parasitic detection techniques [polymerase chain reaction (PCR) and Strout test (parasitic element detection by centrifugation techniques)] weekly for the first 2 months, every 2 weeks during the third month, and monthly thereafter for the next 10 months, as recently recommended by the Chagas in Transplant Working Group.[6] The results of screening tests for Chagas infections and HIV viral loads remained negative after LT. For the prevention of drug toxicity to the transplanted liver and because of the good clinical status of the recipient, antiretroviral therapy was restarted 4 months after LT. At the time of this writing (15 months after LT), her liver graft function was normal, she had no episodes of acute rejection, and she never experienced seroconversion for Chagas disease.

DISCUSSION

The shortage of liver grafts has stimulated the use of organs from donors with transmissible infectious diseases.[5] Thus, liver grafts from deceased donors with a positive Chagas disease serology could be accepted when the mortality risk of recipients during the waiting period is high.[7] To the best of our knowledge, this is the first reported case of successful LT in an HIV-positive patient receiving a Chagas disease–seropositive liver graft. Although data about the use of infected organs in such immunocompromised recipients are scarce in today's literature, we decided to accept this infected organ for our HIV-positive patient because of her emergency status on the LT waiting list and progressive multiorgan failure.

The prerequisites for LT in HIV-positive patients include a $CD4^+$ cell count > 200 cells/μL and an HIV viral load < 50 copies/mL.[8] These conditions are not considered in an acute liver failure scenario, in which HIV-positive patients should undergo an assessment similar to the one used for HIV-negative patients.[8] Our patient not only had an adequate $CD4^+$ cell count and an undetectable viral load but also was experiencing fulminant liver failure; she thus fulfilled both criteria for the inclusion of an HIV patient on the LT waiting list.

However, this case raises some questions. Should we have used an organ from an infected donor for this young HIV-positive recipient? In other words, can we accept a Chagas disease–seropositive liver graft for a Chagas disease–seronegative recipient? Mortality on the waiting list and organ allocation would be less problematic if the shortage of liver grafts did not exist.[1,9] In the last decade in Argentina, despite the increasing number of LT procedures and the implementation of the Model for End-Stage Liver Disease allocation system, the mortality rate on the liver waiting list for emergency status patients has been stable (approximately 25%).[2] In this scenario, any effort to optimize organ allocation should be accompanied by similar efforts to increase the number of organ donors. One strategy is the use of so-called extended criteria donors even though their use implies a higher risk of poor allograft function, allograft failure, or the transmission of a donor-derived disease in comparison with the use of ideal grafts.[4,9,10] In our case, the first available organ was a liver graft from a deceased donor who was serologically positive for Chagas disease. It should be noted that every potential deceased donor in Argentina is routinely screened for Chagas disease with 2 indirect methods, and at our center, we have a policy of retesting donor's blood once the organ is accepted. Given the patient's severe condition, we decided to accept this organ because we believed that the benefits of a new liver outweighed the risk of acquiring Chagas disease.[5,11] We hope that the excellent outcome observed in our case will encourage other centers to push the limits in accepting these marginal liver grafts to expand the liver pool and reduce mortality on their waiting lists.

It remains unclear whether we should use prophylactic treatment when a Chagas disease–infected organ is transplanted into an HIV-positive recipient. Previous reports have already stated the acceptability

TABLE 1. Characteristics of Chagas Disease–Seronegative Patients Receiving Chagas Disease–Seropositive Liver Grafts

Study	LT Center	Case Number	Etiology of Underlying Liver Disease	Waiting-List Status	Prophylactic Treatment	Screening Test	Seroconversion After LT	Chagas Disease After LT	Follow-Up/ Status
Barcán et al.[11] (2005)	Hospital Italiano, Buenos Aires, Argentina	1	Autoimmune	Elective	No	IFA, EIA, and Strout test	Yes	No	18 months/ dead (sepsis)
D'Albuquerque et al.[13] (2007)	Beneficiencia Hospital, San Pablo, Brazil	2	Hepatitis C virus	Elective	Yes	EIA and serum hemagglutination	No	No	17 months/alive
		3	Hepatitis C virus	Elective	Yes	TESA blot assay*	No	No	59 months/alive
		4	Primary sclerosing cholangitis	Elective	Yes	TESA blot assay*	No	No	23 months/alive
		5	Primary sclerosing cholangitis	Elective	Yes	TESA blot assay*	No	No	79 months/alive
		6	Alcohol	Elective	Yes	Not tested	No	No	3 months/dead (sepsis)
		7	Alpha-1-antitrypsin deficiency	Elective	Yes	Not tested	No	No	4 months/dead (tuberculosis)
Salvador et al.[14] (2011)	Vall d'Hebron Hospital, Barcelona, Spain	8	Hepatitis C virus, Alcohol, and hepatocellular carcinoma	Elective	Yes	EIA and PCR	No	No	8 months/dead (hepatocellular carcinoma recurrence)
		9	Alcohol and hepatocellular carcinoma	Elective	Yes	EIA and PCR	Yes	No	14 months/alive
This Case	Hospital Alemán, Buenos Aires, Argentina	10	Autoimmune	Emergency	No	PCR and Strout test	No	No	15 months/alive

*Confirmatory immunoblotting test for Chagas disease.

of Chagas disease–seropositive donors for kidney transplantation[12] and, more recently, LT.[13,14] Interestingly, none of the reported seronegative patients who received infected liver organs developed Chagas disease when prophylactic treatment was administered after LT (Table 1). Chagas disease is a parasitic infection caused by *Trypanosoma cruzi*; vectorial transmission by a Triatominae insect during biting after either damaged skin or mucus membranes are exposed to insect excrement is the most frequent mode of transmission. However, infections after blood transfusions[15] and organ transplantation have also been described.[11,16] Although Chagas disease is neither more frequent nor more severe in HIV-positive patients versus the general population in endemic areas, reactivation of this disease is far more frequent in HIV patients (just like *Toxoplasma gondii* infection).[17] Chagas disease is endemic in Argentina, in which 10% of the population is estimated to be infected[18]; the incidence of infection is higher in children, and there is a case fatality rate of approximately 5% in its acute phase. It mainly affects the heart, digestive system, and central nervous system in immunosuppressed patients. Acute Chagas disease in recipients receiving a solid organ from a deceased donor seropositive for Chagas disease has been described in kidney transplantation[16] and LT.[11] As a result, some groups have decided to use prophylaxis with benznidazole after LT when these infected grafts are used; the estimated incidence of seroconversion is 20% (see Table 1).[13,14] Unfortunately, the 2 drugs used for the treatment of Chagas disease (nifurtimox and benznidazole) have severe and frequent side effects such as bone marrow suppression and liver toxicity. In the literature, strong evidence favoring prophylactic treatment is lacking, so the Chagas in Transplant Working Group, whose members are North American, has recommended not using a prophylactic antitrypanosomal treatment after LT.[6] In contrast to the situation in the United States, the availability of the drugs used for the prophylactic treatment of Chagas disease is probably better in Argentina. However, aiming to avoid the toxicity to the liver and bone marrow caused by these drugs in a patient receiving immunosuppression and antiretroviral therapy, we decided to use this infected liver graft without prophylactic treatment and to initiate treatment only if evidence of seroconversion or clinical signs of disease appeared.[6,11,19] During 1 year of follow-up, the patient never developed seroconversion. Although our strategy was successful, we must highlight the importance of adequate informed consent. This should be a meticulous process in which information is exchanged between the patient, his or her family, and the entire transplant team. In this open discussion, each important issue related to the patient's mortality risk on the waiting list and the probability of Chagas disease transmission from an infected organ must be extensively clarified and explained. Moreover, information about the pros and cons of prophylactic treatment with such organs must be shared with patients and their families. Because the reported data are very limited, we urgently need larger series to provide further knowledge in this field.

We conclude that Chagas disease–infected liver grafts from deceased donors can be safely used in patients listed for LT. However, we recommend that this strategy be used only in an emergency situation or for elective patients with a high need for LT. The need for prophylactic treatment for Chagas disease after transplantation is challenged by our case, and proper recommendations might arise only from larger series undergoing prospective validation in a randomized study.

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