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First Liver Transplant in an HIV Patient in Colombia: Case Report and Literature Review

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Abstract

Appropriate antiretroviral treatment and management has transformed HIV into a chronic disease with good long-term survival rates. Currently more than half of the deaths of these patients are due to non-HIV-related causes among which terminal liver disease resulting from various etiologies is the second most frequent cause of death. Consequently, liver transplantation has become a treatment option for selected patients whose HIV infections have been controlled. Post-transplant survival rates are similar to those of other liver transplant patients. This report presents the first liver transplant in Colombia of an HIV infected patient. This patient had a coinfection with Hepatitis B virus as well as cirrhosis of the liver and hepatocellular carcinoma. The procedure was performed in the Hospital Pablo Tobón Uribe in 2010.

Keywords

HIV, liver transplantation, cirrhosis, hepatocellular carcinoma.

INTRODUCTION

Human immunodeficiency virus (HIV) has become an important public health problem. According to statistics from the World Health Organization, about 40 million people were living with the infection as of December 2015. (1) Improved survival with highly active antiretroviral therapy (HAART) has led to more and more HIV-infected patients who are prone to chronic diseases including advanced liver failure. This has produced a need for liver transplantation in selected cases, and these patients currently have survival rates similar to those with other indications for transplantation. (2, 3)

Before HAART began to be used, HIV infection was considered to be an absolute contraindication for liver transplantation in most centers because of the poor results obtained. One year survival rates were only 45%, and the main cause of death was the acquired immunodeficiency syndrome (AIDS) and associated opportunistic infections and neoplasias due to the immunosuppression received by the transplant recipient. (3, 4).

Since HAART was introduced in 1996, it has changed the landscape of the natural history of HIV-infected patients. It has restored immune function and improved the efficiency of liver transplantation, thus HIV is no longer a contraindication to liver transplantation. However, in many countries, this alternative is still not considered for management of these patients because of fear of drug interactions that can lead to loss of HIV control and because of the additional burden of immunosuppressants that may increase the risk of disease progression. (5) HAART has significantly prolonged the survival of patients infected with the human immunodeficiency virus and opportunistic infections and neoplasms caused by AIDS since these primary causes of morbidity and mortality have been set aside. Thus, hepatic disease related to chronic hepatitis B virus (HBV) and hepatitis C virus (HCV), hepatotoxicity, and alcohol con-

sumption have now become significant diseases in these patients. (2 , 6, 7) In particular, chronic HBV and HCV infections have natural histories that are accelerated by HIV coinfection, and they develop more rapidly into cirrhosis and/or hepatocellular carcinoma than they do in patients without the HIV coinfection. (7, 8)

Patients with HCV and HIV coinfections represent an additional challenge because of recurrence rates and because poor post-transplant results were still considered a contraindication for transplantation. However, with the advent of direct action antivirals against HCV, the outlook has changed, and there are now pretransplant and post-transplant treatment options that have brought post-transplant survival rates of patients with HCV and HIV coinfections into line with those of other transplant patients. In addition, prophylaxis of HBV reinfection and management with new high resistance barrier antivirals such as entecavir and tenofovir ensure better prognoses for the organ in transplanted patients who have chronic HBV infections.

In this report, we present our experience from 2010 with the first HIV patient ever to receive a liver transplant at the Hospital Pablo Tobón Uribe and in Colombia. We will also comment on the patient's post-transplant evolution and review the literature.

CLINICAL CASE

The patient was a 41-year-old man who had had a history of HIV and HBV coinfection since 1996. He also had had other opportunistic infections including pulmonary TB in 2003 and herpes zoster in 2008. Antiretroviral therapy was initiated in 2008 with lamivudine/zidovudine + efavirenz. The patient was evaluated by the hepatology department in January 2009 for HBV coinfection. Child-Pugh A hepatic cirrhosis secondary to chronic HBV infection was detected with real-time PCR (COBAS AmpliPrep/COBAS TaqMan HBV-Test [ROCHE]) which showed a viral load of 43,855,324 IU/mL. The patient tested negative for HBeAg and anti-HBe antibodies. The HBV virus was suspected to have resistance to lamivudine.

At the time of the evaluation, the patient's CD4 count was 440 and PCR did not detect any viral load for HIV. The fact that HIV viral load was negative allowed initiation of entecavir at 1 mg/day against the HB virus infection. The patient was followed up by the hepatology department. Eight months after initiation of entecavir, the patient's real-time viral load was 5,389 IU/mL of HBV (COBAS Taqman [Roche]). An upper abdominal ultrasound reported a solid nodular focal lesion in the right hepatic lobe that measured 32 x 19 x 28 mm. A simple and contrast-enhanced MRI of the abdomen showed a cirrhotic liver with a 37-mm segment VI lesion that met the criteria for hepatocellular carcinoma (Figure 1). The patient's alpha-fetoprotein level was 11 ng/mL.

This case was presented to the liver transplant staff. The patient had virological and immunological control of HIV infection, without current opportunistic infections and with indication of Child-Pugh A liver cirrhosis with focal hepatocellular carcinoma. The transplant protocol was performed without contraindications for the intervention. The patient was placed on a waiting list. On March 23, 2010, he was transplanted with a cadaveric donor liver without complications during the intraoperative period with the usual vascular anastomosis and choledochotomy. Laboratory findings from the explant confirmed the diagnosis of moderately differentiated hepatocellular carcinoma with a solid brachial pattern (Figure 2). The patient's post-transplant evolution was very good, and the patient was discharged

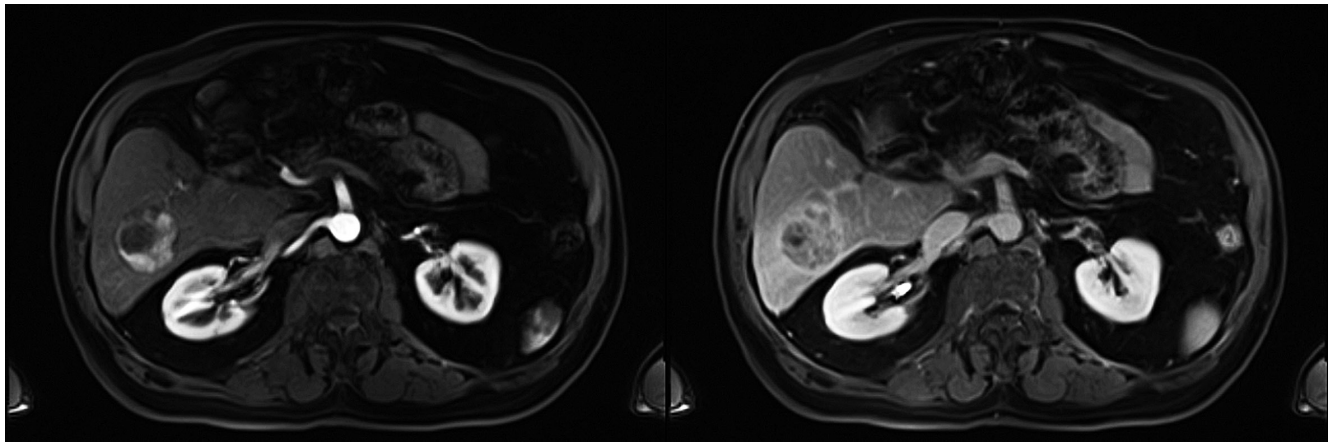

Figure 1. Magnetic resonance imaging with gadolinium showing a 3.7 cm lesion in the right hepatic lobe which meets the criteria for hepatocellular carcinoma. Enhancement of arterial phase and portal phase lavage.

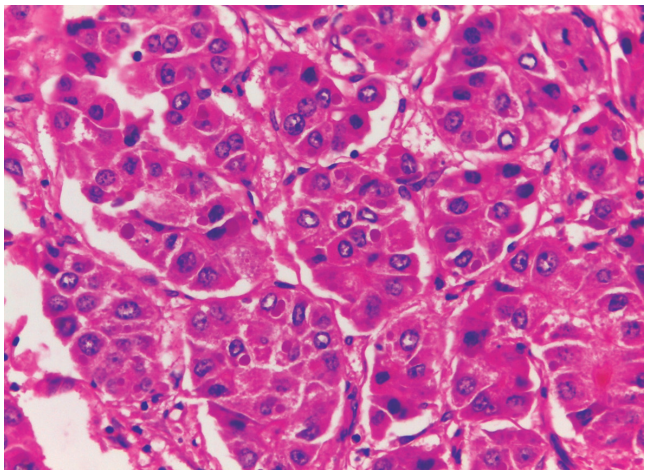

Figure 2. Neoplastic proliferation of moderately differentiated hepatocytes with eosinophil cytoplasm and oval nuclei. Hepatocellular carcinoma with a solid tracheal pattern. Grade II, Edmonton classification.

on the sixth postoperative day. The only post-transplant complication was a surgical site infection with methicillin-resistant staphylococcus aureus. The site was reentered and treated with clindamycin. The immunosuppression scheme used was steroid + cyclosporine + azathioprine. Reinfection by HBV was prevented by administration of an intramuscular hepatitis B immunoglobulin scheme for one week followed by monthly administration for two years after transplantation. At that time the patient was vaccinated with a double dose regimen and subsequently achieved an adequate concentration of anti-HBV antibodies. In addition, he is receiving entecavir indefinitely. At the time of publication, the patient had survived for more than 7 years and had been reintegrated into normal life. He receives management 100 mg of cyclosporine every 12 hours, 50 mg of azathioprine every 24 hours, and 1 mg of entecavir of every 24 hours.

DISCUSSION

Throughout the world, treatment and follow-up of patients with human immunodeficiency virus (HIV) have changed since 1996 when HAART was introduced. HAART has reduced the number of acquired immunodeficiency syndrome (AIDS) cases as well as deaths directly related to it. (9) So great has the success of antiretroviral therapy been, that at present, more than 50% of deaths in HIV-positive patients receiving HAART are not directly related to HIV infections or to AIDS. (9,10,11) However, there has been an increase in mortality from other causes over the rates in the general population. The increase in non-AIDS morbidity, compared to the general population, appears to be multifactorial. HIV infections lead to a state of immune dysregulation and inflammation whereas HAART therapy predisposes patients to dyslipidemia and diabetes. (12)

The D.A.D study has compiled data on the adverse effects of anti-HIV drugs and has shown that liver disease is the second most common cause of non-AIDS related deaths. (13) Taking into account similar transmission routes, coinfections with hepatitis B virus (HBV) and hepatitis C virus (HCV) are common. (14) Prior to this, there was a high mortality rate of presumed infectious origin secondary to the immunosuppression of disease that allowed colonization and pathogenesis of different opportunistic microorganisms. Currently, the prognosis for these patients is no longer determined by HIV infection, but by coexisting diseases, including liver damage. Liver disease is associated with 7.1% of the deaths in patients with HIV and hepatic alterations, and of these, hepatitis accounts for 55.8%. Depending on the population studied, the most frequent etiology is due to coinfections, especially with HBV or HCV which have prevalences of 10% and 30%, respectively. Other liver diseases among HIV-positive people include hepatotoxicity, alcohol-induced liver disease, non-alcoholic steatohepatitis (NASH), and hepatocellular carcinoma (HCC).

Manifestations of liver damage in HIV patients are similar to those in patients who are HIV-negative, but HIV patients present these events earlier, and the survival rate is markedly reduced after the first episode of decompensation. (15) In HIV-positive patients with compensated cirrhosis, a high mortality rate is associated with ages over 50 years, MELD scores greater than 11, and poor control of HIV disease. (16) Indications for liver transplantation are the same as for other patients. At the beginning of the 1990s, this therapy was questioned because of its poor initial results, but later series have demonstrated post-transplant survival rates and times for these patients that are similar to other patients who undergo transplantation. (15, 16) At this point in time, most medical centers throughout the world consider liver transplantation to be standard therapy for patients with HIV infections who have indications for the intervention and who meet criteria for immunological and virological control of the HIV infection.

In this report, we have presented the first case of liver transplantation in Colombia in a patient with an HIV infection and a diagnosis of liver cirrhosis associated with HBV coinfection and hepatocellular carcinoma. The transplantation took place in March 2010 and has been followed by survival of the patient and the graft to this date. The patient continues to have good immune and virological control of HIV and has no evidence of recurrence of hepatocellular carcinoma.

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