

Liver Transplantation in a Monolung Patient: A Strategy of Sequential Treatments of Multiple Lung Tuberculosis Cavitations and Hepatocellular Carcinoma on Hepatitis B Related Virus Cirrhosis

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Abstract

The presence of extrahepatic infection is a contraindication for liver transplantation, even more if supported by an advanced pulmonary tuberculosis with persistent cavitation not curable with medical treatment. We report a case of a young patient with hepatocellular carcinoma on hepatitis B virus related liver cirrhosis and multiple lung tuberculosis cavitations. The patient was referred to our centre for liver transplantation. We adopted a strategy with sequential treatments. First a left extra-pericardial pneumonectomy was performed without opening the infected cavern, followed by a therapy with rifampicin, isoniazid and ethambutol for a period of nine months. After the cure of tuberculosis, the monolung patient eventually was listed for liver transplantation. An accurate planning of a multistep therapeutical strategy, an appropriate anesthetic management and a meticulous surgical technique allowed to successfully transplant a young patient suffering from three life-threatening diseases: cavitary tuberculosis, hepatitis B virus cirrhosis and hepatocellular carcinoma. Thirty months after liver transplantation the patient is in good health, with normal liver function, forced expiratory volume in one second of 42% (1.53 liters) and without any tuberculosis disease reactivation.

Keywords: Mycobacterium Tuberculosis, Infection, Pneumonectomy, Liver Disease, Liver Surgery

1. Introduction

Tuberculosis (TB) is a serious infection due to Mycobacterium Tuberculosis, with an estimated prevalence of 13.7 million cases world-wide [1]. The frequency of the disease varies geographically, with particular regions (Asia and Africa) having a higher prevalence than other areas of the world [2]. Several factors place transplanted patients at a greater risk of developing active TB. A previous TB infection increases the likelihood of TB developing after transplantation [3]. The number of pre-transplant patients with a positive tuberculin skin test (TST) underestimates the number of patients infected with TB

because end-stage liver disease may result in cutaneous anergy, which decreases the sensitivity of the TST. Patients with compensated cirrhosis should be considered for the treatment of TB. Patients with decompensated cirrhosis should defer therapy to the period after transplantation. Patients with active TB should not undergo transplantation; exceptions might be considered for patients with well-controlled infections. In general, active TB is an absolute contraindication for transplantation [4]. The presence of extrahepatic infection is a contraindication for liver transplantation, even more if supported by an advanced pulmonary tuberculosis with persistent cavitation not curable with medical treatment. The aim of

this study was to demonstrate that liver transplantation, usually contraindicated in presence of pulmonary tuberculosis with persistent cavitation, can be successfully performed using such sequential treatments strategy.

2. Case Report

A 30 years old black man, born in Sub Saharan Africa, with hepatocellular carcinoma (HCC) induced by hepatitis B virus (HBV) chronic liver disease was referred to our centre for liver transplantation in April 2006.

In 2003 the patient underwent cholecystectomy and at that time HBV related liver cirrhosis and active pulmonary tuberculosis were diagnosed. Subsequently, pulmonary TB was treated in Africa in 2003 with streptomycin (STP), isoniazid (INH) and pyrazinamide (PZA) for two months followed by INH and ethambutol (ETB) for one month. The reason for the withdrawal of the anti TB treatment was not clear. Two years later the patient was treated again due to a relapse of TB with rifampicin (RPM), ETB and ciprofloxacin (CIP) for eight months. At the end of the treatment, a chest tomography revealed

cavitory evolution in the left lung, the largest cavitation had a diameter of five centimeter with no signal of active infection.

In January 2006 liver cirrhosis was complicated by the detection of two masses of HCC (VII and VIII segments, both two centimeter in diameter) which were treated by percutaneous ethanol injections. Subsequently, the patient was evaluated for a liver transplantation. In June 2006 during the pre-transplant assessment, a chest computed tomography revealed a large parenchyma effusion in the left lung (**Figure 1**) suggesting an active infection that was a contraindication for liver transplantation.

In December 2006 a relapse of HCC (VII segment nodule) was treated by selective transarterial chemoembolization using embosphere-biosphere gauge of 100 - 300 micron.

In January 2007, a computed tomography of the liver revealed a residual of HCC (**Figure 2**); in addition, he suffered a decompensation of the liver cirrhosis with massive ascites, portal hypertension and esophageal varices. At this time the patient was reconsidered for liver transplantation with mayo end-stage liver disease



Figure 1. Chest computed tomography scan show pulmonary tuberculosis and left lung cavitation.

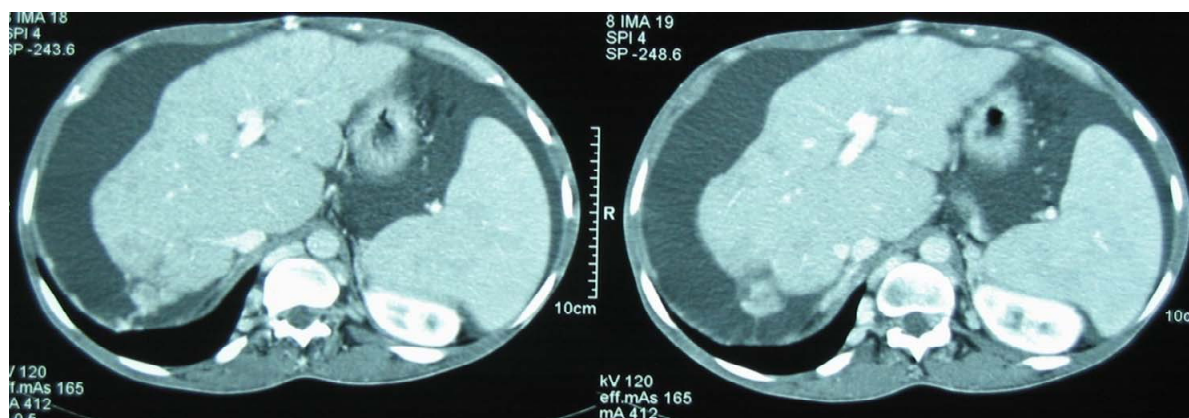


Figure 2. Abdomen computed tomography scan show liver cirrhosis and hepatocellular carcinoma.

(MELD) HCC 22.

While the sputum culture was negative for acid-alcohol resistant bacillus, based on a chest computed tomography TB infection of the major pulmonary cavitation was still present at lung framework. Therefore, we planned a pre-transplant surgical treatment of the end-stage pulmonary TB disease due to a major risk for relapse of infection in post-transplant period.

In May 2007 a left extrapericardial pneumonectomy was performed without opening the infected cavern and with covering the bronchial stump with intercostal muscle (**Figure 3**).

The histological examination described pulmonary emphysema, with interstitial fibrosis and multiple granulomatous giant cells lesions, sometimes necrotizing and calcified. The Ziehl-Neelsen stain did not reveal acid-fast bacilli.

Subsequently, a therapy with RPM, INH and ETB was begun in October 2007.

The rationale for the third treatment was the non conventional schedule of the previous treatments especially for patients listed for liver transplantation and the high suspicion of recurrence of disease despite the negative culture for Koch's bacillus. The treatment was well tolerated and prolonged until the liver transplantation for a total period of nine months.

The patient was listed for transplantation in February 2008 with mayo end-stage liver disease (MELD) HCC 22, mild pulmonary hypertension with systolic pulmonary artery pressure of 35 mmHg and diastolic pulmonary pressure of 18 mmHg. Forced expiratory volume in one second (FEV1) was 42% (1.53 liters), left ventricular ejection fraction (EF) 63%, estimated right ventricular telesystolic pressure 37 mmHg and the patient at high peri-operative risk (ASA IV).

Finally, the patient underwent liver transplantation in June 2008 with a whole size graft from a deceased donor. The liver transplantation was performed using a mini-

transplant procedure as described previously (**Figure 4**) [5]. The total hepatectomy was performed preserving the recipient's vena cava and the graft was implanted using a latero-lateral caval anastomosis.

The liver transplantation proceeded without any complications with peri-operative hemodynamic stability. Intra-operatively 3000 ml of crystalloid and 2000 ml of fresh-frozen-plasma were given. No red blood cells transfusions were infused during the surgical procedure. Cold ischemia time was 330 minutes and warm ischemia time 30 minutes.

The anesthesiologic management consisted of induction via TIVA method (propofol, remifentanyl, cisatracurium), cardiovascular monitoring via Swan-Ganz and VigileoTM catheter and a lung protective mechanical ventilation. The combined use of different hemodynamic monitoring enabled an accurate optimization of the volemic expansion by adapting it to operating phases. Central venous pressure (CVP) was 6 mmHg and pulmonary capillary wedge pressure (PCWP) 12 mmHg.

The histological examination described macro and micro nodular liver cirrhosis, with two poorly differentiated (G3) hepatocellular carcinoma, which measured three and two centimeter in diameter, respectively. These masses of HCC were partially capsulated, with extensive necrotic areas and vascular carcinomatous aspects.

The intensive care unit (ICU) stay lasted 4 days. The patient was extubated six hours after operation and started oral alimentation on the first post-operative day. The whole hospital stay lasted two months and ascites persisted for three months post-operatively.

After the transplantation we decided not to start with INH prophylaxis according to previous reports of transplanted patients well treated for TB before [6].

Immunosuppression was based on low doses tacrolimus (blood trough level of 5 ng/ml) and steroids.

After thirty months the patient is in good health with normal liver function and without any tuberculosis disease

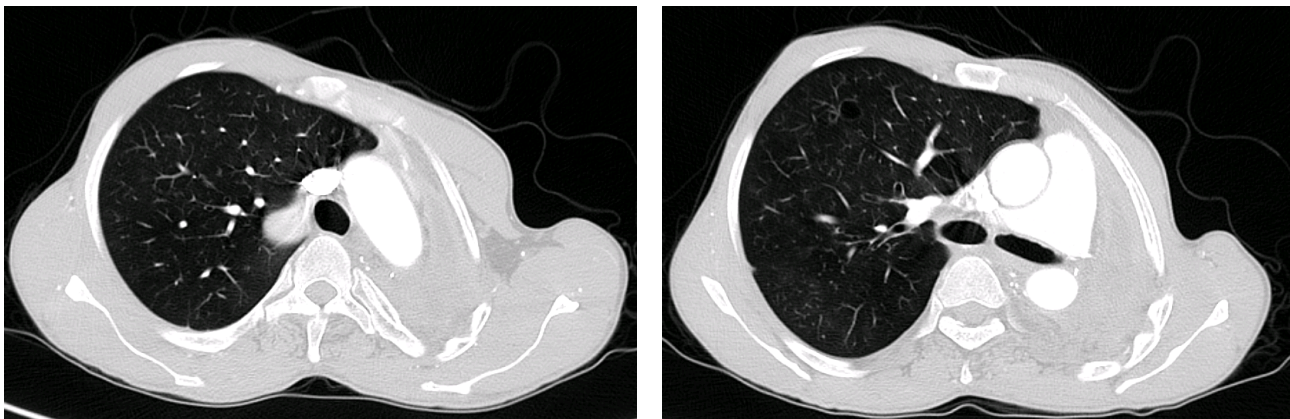


Figure 3. Chest computed tomography scan after left pneumonectomy and before liver transplantation.



Figure 4. Minitransplant procedure with right subcostal incision after 12 months of follow-up.

reactivation so far. No episodes of biopsy proven acute cellular rejection was recorded.

3. Discussion

The management of TB disease in patients with end-stage liver disease candidated for liver transplantation requires a multidisciplinary approach to minimize the risk of drug toxicity and relapse of disease in the post-transplant period.

Reports in literature regarding transplanted patients with recent history of active tuberculosis are scarce and only describe patients who underwent liver transplantation because of hepatic failure due to anti TB treatment [7,8]. Moreover, there is no universal consensus about the prophylactic regimen following a documented TB disease [6].

As reported in our case, the left lung was completely affected by cavernous evolution of TB as confirmed by histological report. Thus, the only possible treatment was the surgical approach with a left pneumonectomy. On the other hand, pneumonectomy involves important cardio-respiratory changes that affect surgical and anesthetic management of liver transplantation.

In our case, we have adopted an approach with sequential treatments, that combined with an appropriate anesthetic management and a meticulous surgical tech-

nique allowed to successfully transplant a young patient suffering from three life-threatening diseases: cavitary tuberculosis, HBV cirrhosis and hepatocellular carcinoma. Due to the concern of a possible reinfection, we used a low dose immunosuppressive regimen (tacrolimus dose of 1 mg per day with a blood trough level of 5 ng/ml, switched after two years to everolimus 1.5 mg per day with a blood trough level of 4 ng/ml, and steroids 2.5 mg per day). Furthermore, an active surveillance allowed us to preserve the patient from TB reinfection without post-transplant therapy after thirty months follow-up. Neither cases of liver transplantation in monolung patients nor similar cases have been reported in the literature so far.

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Abbreviations

TB: tuberculosis; TST: tuberculin skin test; HCC: hepa-

tocellular carcinoma; HBV: hepatitis B virus; STP: streptomycin; INH: isoniazid; PZA: pyrazinamide; ETB: ethambutol; RPM: rifampicin; CIP: ciprofloxacin.