

# BILHEMIA FOLLOWING TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT PLACEMENT (TIPS): LIVER TRANSPLANTATION AS A RESCUE PROCEDURE - CASE REPORT

*Hemobilia após colocação de anastomose portossistêmica intra-hepática transjugular (tips): transplante hepático de resgate – relato de caso*

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## INTRODUCTION

**T**ransjugular intrahepatic portosystemic shunt (TIPS) is an effective method of controlling portal hypertension and reducing its complications, such as collateral venous formation. It has been used to control bleeding from esophageal and gastric varices, management of refractory ascites, hepatic hydrothorax and hepatorenal syndrome<sup>1,3</sup>. The most frequent complications related to this procedure are: hepatic encephalopathy, bleeding, deterioration of liver function and occlusion of the stent<sup>11</sup>. Bilhemia, defined as the passage of bile into the bloodstream through a bile duct-venous fistula, is rarely observed but it has been reported following TIPS procedure<sup>5,7,13</sup>, liver biopsy<sup>17</sup>, liver trauma<sup>4</sup> and transhepatic percutaneous catheter placement<sup>12</sup>. The clinical scenario in these cases is associated with recurrent bacteremia, fever, jaundice and anemia. Here, it is presented an unusual case of a patient, who had clinical deterioration associated with sepsis and multiorgan failure after TIPS procedure, secondary to a fistula between the bile ducts and the TIPS shunt. This manuscript was approved by the institutional ethics committee.

## CASE REPORT

A 53 years old man, cirrhotic, diabetic (diabetes mellitus type II) with history of hepatitis C, alcohol abuse

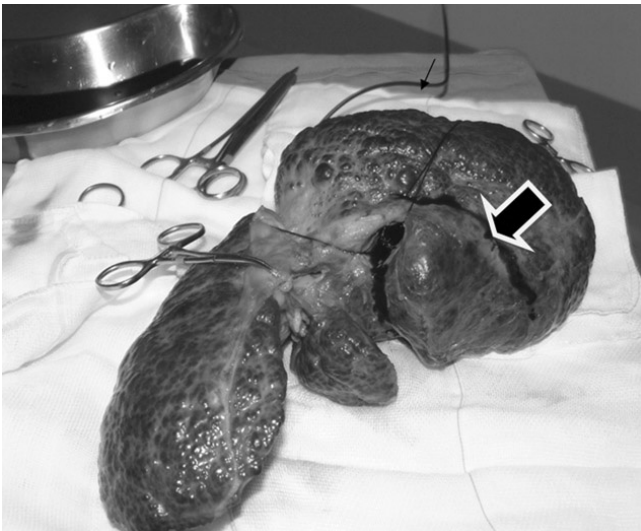
and multiple episodes of bleeding from esophageal and gastric varices, underwent a TIPS procedure in order to control refractory gastroesophageal hemorrhage and as a bridge to liver transplantation. On admission, he was clinically stable and had a model of end-stage liver disease score of 13 and an initial serum total bilirubin of 3.7 mg/dl. The TIPS procedure was performed through the right internal jugular vein using the standard technique<sup>9</sup>. The selected and available stent was a bare metal self-expandable stent Wallstent 10 X 68 mm (Boston Scientific Corporation, MA, USA), which was adequately deployed in the liver, creating a shunt between the right hepatic vein and one of the branches of the left portal vein. The tract was post stenting dilated with a 10 mm balloon and a control portal venogram demonstrated patency of the shunt and no significant opacification of the venous collateral circulation. There was reduction of portal venous pressure from 26 to 16 mmHg, and of the portosystemic gradient pressure from 19 to 9 mmHg. The procedure was uneventful overall and the patient remained at the hospital for observation.

Three days after the TIPS, the patient presented with sudden jaundice without any signals of hepatic failure (encephalopathy) or sepsis (fever or hypotension). At this point, laboratory evaluation showed total bilirubin level of 41.6 mg/dl (direct bilirubin of 28.1 mg/dl), international normalized ratio of 1.2, alkaline phosphatase of 151 IU/l, alanine aminotransferase of 60 IU/l, aspartate aminotransferase of 104 IU/l, creatinine of 1.0 mg/dl, and total leucocyte count of 6,800/ml. Liver Doppler ultrasound showed adequate stent placement, patency and antegrade flow, without evidence of biliary dilation. Abdominal computed tomography angiogram was performed and did not provide any additional information.

One week later, the patient was clinically unchanged, except for jaundice worsening. There was no evidence of infection, encephalopathy or hemobilia. Although the laboratory tests were

not compatible with colesthasis, the serum total bilirubin increased to 49 mg/dl. Three weeks after the TIPS procedure, the patient developed hypotension, fever, and mental confusion requiring intensive care unit admission. Septic shock was diagnosed and the management included large spectrum intravenous antibiotics such as Vancomicine/Piperacilin-Tazobactan. A control liver Doppler ultrasound did not reveal any significant abnormality. Blood culture was positive for *E. Coli.*, and clinical condition improved allowing intensive care unit discharge after six days. He recovered renal function and metal status but total bilirubin continued elevated (34.9 mg/dl).

During the following week, clinical scenario deteriorated again and another intensive care unit admission was necessary because of shock and mental confusion. At this time, blood culture sample grew *Candida parapsilosis* and anphotericin was introduced. Through a transjugular approach again, a 10 mm X 10 cm stent-graft (Viatorr; W.L. Gore & Associates, Flagstaff, AZ, USA) was placed coaxially inside the bare existing stent as an attempt to seal the biliary-venous fistula. Three days later, a compatible cadaveric donor was available and the patient underwent liver transplantation. Methylene blue was injected through the common the bile duct of the explanted liver and the blue dye was noted flowing through the right hepatic vein confirming the suspected communication between the biliary system and this vein through the bare stent mesh (Figure 1).



**FIGURE 1** -Injection of methylene blue after cannulation of the common bile duct with a 6 F silicone catheter (small arrow) demonstrated free passage of blue dye into the right hepatic vein (big arrow). The stent-graft had been removed and the dye injection was performed with the bare stent still in place. Middle and left hepatic veins were not colored by the blue dye (hemostatic clamp).

During the first postoperative week, the serum bilirubin levels decreased as expected, and in a few weeks the patient was discharged home under stable clinical conditions. After two months, clinical follow-up revealed total bilirubin level of 1.0 mg/dl. The patient did not present any liver transplantation complication during the last two years of close clinical follow-up.

## DISCUSSION

TIPS has been used to prevent variceal bleeding secondary to portal hypertension in the last two decades. Medical uncontrolled complications such as hepatic failure and hepatic encephalopathy typically occur in patients with model of end-stage liver disease score greater than 14, or when portosystemic gradient pressure is reduced to 5 mmHg or lower<sup>2</sup>. A TIPS related biliary-venous fistula is a rare complication that can result in intermittent hemobilia, sepsis, anemia and bilhemia<sup>6,7,13,15</sup>. The typical pressure within the common bile duct ranges between 12 and 14 mmHg. The clinical manifestations (bilhemia or hemobilia) will depend on which intra-hepatic blood vessel was injured during the TIPS procedure.

Biliary fistulas with the portal vein and/or hepatic artery are more likely to cause hemobilia, because portal system pressure in cirrhotic patients is frequently higher than 14 mmHg, even after TIPS procedure. On the other hand, fistulization between the bile ducts and a hepatic vein branch may result in an acute severe jaundice, as experienced by this patient, because the gradient between central venous pressure (mean of 7 mmHg) and common bile duct pressure (mean of 12-14 mmHg) favors bile to flow into the hepatic vein. However, it is not uncommon to have high central venous pressures in the patients who underwent TIPS due to the sudden porto-mesenteric venous decompression and subsequent increase in right atrium pressures. In this scenario, it is unlikely for the bilhemia to happen.

Few biliary-venous fistula case reports have been published in the literature and most of them are related to the TIPS creation. Anemia, hyperbilirubinemia and systemic sepsis are the most common clinical manifestations<sup>5,7,8,15</sup>. Total bilirubin levels have been reported to range between 5 and 8 mg/dl, without significant increase in transaminases and alkaline phosphatase. In this patient, acute increase in total bilirubin levels was observed right after the TIPS procedure, what has not been reported before. Despite the continuous increase in serum total bilirubin levels during the first two weeks, the patient had no evidence of hepatic failure or other significant organ dysfunction. Sepsis was the driving force that deteriorated clinical picture later on, and antibiotic treatment provided only temporary improvement.

The definite treatment of an infected

endoprosthesis involves withdrawn of the foreign body. However, infected TIPS can not be removed. In order to seal the fistula, endoscopic biliary stent placement has been described with successful decompression of the biliary system<sup>7,10</sup>. The insertion of a stent-graft inside the bare stent to seal-off the bile leak also has been used alternatively<sup>14,16</sup>. However, a more recent publication demonstrated that a combination of covered stent placement and antibiotic treatment was unable to control sepsis at long-term<sup>15</sup>, indicating that some patients will require removal of the stent.

The initial treatment management of this patient included a stent-graft placement in the attempt to control the deleterious effects bile leaking into the blood stream, while a liver graft was not available for liver transplantation. The true result of this procedure could not be appreciated because the patient underwent liver transplantation 72 hours later.

The orthotopic liver transplantation was a life saving procedure for this patient. Although, stent-grafts have replaced the bare stents for the TIPS procedures in most of the medical centers worldwide, biliary-venous communication still have been recently reported in the literature<sup>8</sup>. Thus, injury to the bile ducts may occur after any kind of liver invasive procedure or trauma, and a biliary-venous fistula should be always suspected whenever there is an unexpected rise in bilirubin levels soon after invasive liver procedures, mainly if no radiologic or biochemical evidence of cholestasis is detected. In this context, liver transplantation is an important and definite therapeutic option not only to cirrhotic patients with this morbid complication, but also for noncirrhotic cases in which sepsis is persistent or recurrent.

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