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Case Report

Paclitaxel coated-stent for early-onset thrombosis after liver transplantation

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Abstract

Hepatic artery thrombosis (HAT) is the most common vascular complication of orthotopic liver transplantation (OLT) and constitutes a potential emergency during the postoperative period. Surgical revascularization and retransplantation are the treatments of choice for this condition. The aim of this report is to present long-term follow-up on survival and graft function of three patients with paclitaxel-coated hepatic artery stents placed percutaneously after early-onset HAT. Three patients developed early onset HAT after cadaveric-donor OLT in a tertiary care center in Mexico. These patients were treated percutaneously with balloon angioplasty and paclitaxel-coated stents. After 24 months or more of follow-up, 2 patients present total occlusion of the stent and one patient, intra-stent stenosis; interestingly, all patients have normal graft function and excellent quality of life. In conclusion, although balloon angioplasty and stent placement may be a therapeutic option for suitable patients with early-onset HAT after OLT, long-term patency is unlikely even with the use of paclitaxel-coated materials.

Key words: Liver transplantation, hepatic artery thrombosis, balloon angioplasty, stent.

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Case series

Hepatic artery thrombosis (HAT) is the most frequent vascular complication after orthotopic liver transplantation (OLT) and represents a life-threatening complication in the early postoperative course (i.e. < 4 weeks).[1,2] Urgent retransplantation or surgical reconstruction has been considered mainstay therapy for survival after early-onset HAT;[3] however, percutaneous therapy has shown encouraging results.[4-6] We report our experience using endovascular therapy with paclitaxel-coated stents for HAT after cadaveric-donor OLT.

Patient # 1

A 53-year old female with primary biliary cirrhosis (PBC) was submitted to our hospital as a transplantation candidate. She had history of 2 episodes of variceal bleeding, treated by endoscopic ligation and at the time of transplantation she was classified as a Child-Pugh B (7 points).[7] OLT through a piggy-back technique and end-to-end hepatic artery anastomosis was performed without intraoperative complications. Eight days after OLT the patient developed abnormal liver function tests (LFT) due to HAT (documented through Doppler Ultrasound (US) and MRI). Hepatic angiogram showed total occlusion at HA origin due to an organized thrombus without interventional possibilities; thrombectomy was performed the next day with a Fogarty catheter.

One week later, the patient presented with abdominal pain and HA rethrombosis was documented. Balloon angioplasty was used to remove multiple thrombi on both hepatic arteries and to relieve a 90% stenosis identified at the anastomosis. An abciximab infusion was started and a 7 X 19 mm Express SD Biliary Stent was impacted at 14 atm in the hepatic artery with a complete restitution of blood flow, afterwards, a 90% stenosis was identified proximal to the stent and a second Liberté 5 X 15 mm stent was impacted at 14 atm. A Maverick 3 X 15 mm balloon was introduced to the right hepatic artery and a distal to proximal angioplasty was performed successfully. During a follow-up Doppler four months later, an asymptomatic obstruction at the hepatic artery origin due to an organized thrombus was documented. A balloon

was successfully passed to the distal portion of the proximal stent, however, angioplasty was unsuccessful and the procedure was aborted. At 27 months of follow-up the patient is alive with normal liver enzymes, albumin, bilirubin and INR and an excellent quality of life.

Patient #2

A 30-year old female with cirrhosis incidentally discovered during cholecystectomy was referred to our Unit. After extensive laboratory work-up, a diagnosis of primary biliary cirrhosis and autoimmune hepatitis overlap syndrome was established. At the time of transplantation she was classified as Child-Pugh C (15 points).[7] The patient was treated with acyclovir and isoniazid prior to OLT because of active genital herpes (HSV-1) and a positive Mantoux test (22 mm) without other evidence of active tuberculosis. OLT was performed using aorto-safenous vein-hepatic artery graft for reconstruction of the hepatic artery. Due to technical difficulties, a cavo-caval anastomosis was performed with a 15-liter blood loss. Eight days later, HA rethrombosis was documented by Doppler US and MRI. After angiographic confirmation, a balloon angioplasty was performed and an Ultrathin Diamond 7 X 20 mm was advanced and dilated to 12 atm, observing distal thrombus; a 10 X 94 mm uncoated Wallstent was impacted to 12 atm, obtaining a normal flow. The right hepatic artery exhibited tandem lesions and a 3.5 X 20 mm Maverick balloon was impacted to 8 atm and a 3.5 X 32 mm Liberté Stent was placed to 10 atm, without residual lesions and normal blood flow *(Figure 1)*. Despite total occlusion of the hepatic artery due to rethrombosis, at 26 months of follow-up the patient is alive with normal liver enzymes, albumin, bilirubin and INR and an excellent quality of life.

Patient # 3

A 37 year-old male who received a blood transfusion at birth developed liver hepatitis C virus-related cirrhosis in adulthood. The patient had a previous history of mild ascites and grade I-II hepatic encephalopathy, however at the time of OLT he was classified as Child-Pugh A (5 points).[7] OLT through a piggy-back technique with end-to-end hepatic artery anastomosis was performed without intraoperative complications. Two days after OLT, periportal edema was identified by US; abdominal CT scan showed extensive hypodense areas and HAT was docu-

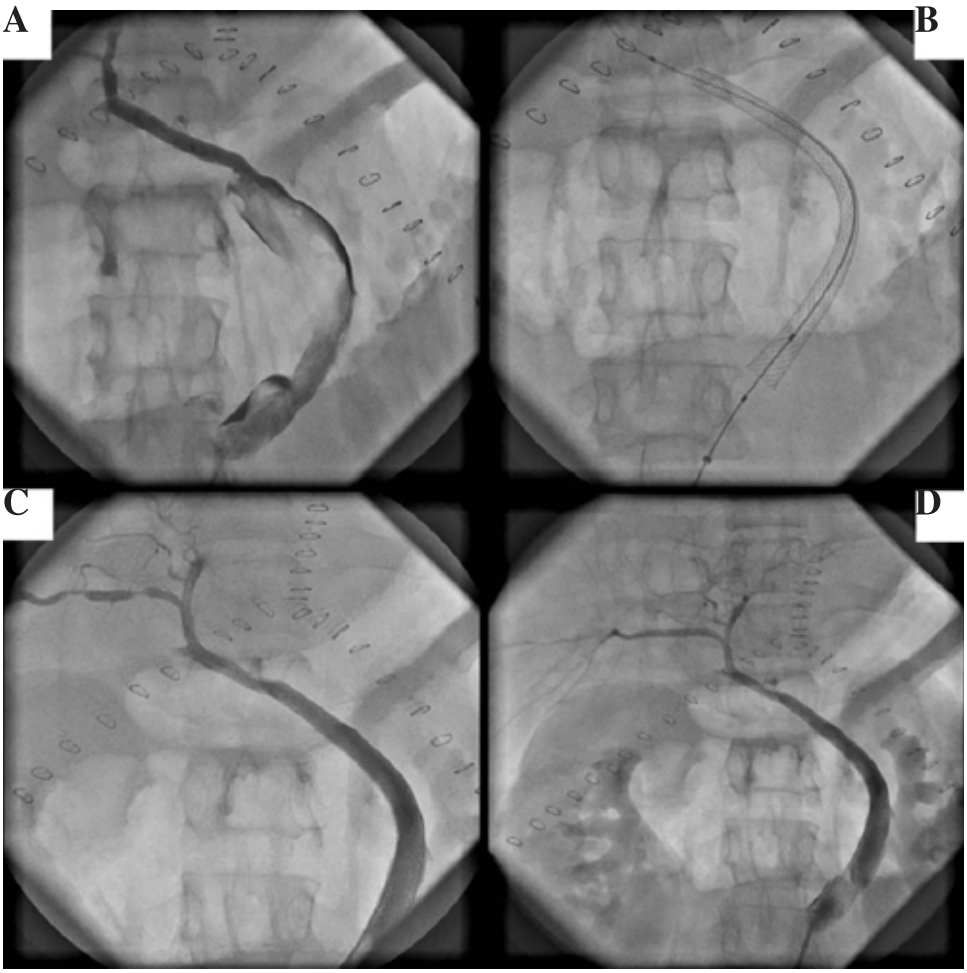

Figure 1. Representative pictures from the angiographic procedure performed in patient # 2. A) Organized thrombus in safenous vein allograft. B) Stent placement in venous graft. C) Graft reperfusion; tandem lesions are noted in the right hepatic artery. D) Final result.

mented by MRI. Hepatic angiogram showed total occlusion at the origin of the hepatic artery and a balloon angioplasty was performed obtaining adequate flow. Selective hepatic angiogram showed total occlusion at the origin of the hepatic artery and a 3.5 X 20 mm Maverick balloon was passed through the obstruction and dilated distal-to-proximal to 8, 10 and 14 atm, obtaining adequate anterograde flow. A 3.5 X 16 mm B-Braun data coroflex Stent was placed distally and a 4 X 19 mm B-Braun Stent was placed proximally; lastly a 4 X 19 mm B-Braun Stent was impacted at the ostium of the hepatic artery, obtaining a normal blood flow. The left hepatic artery was also obstructed and the distal Stent was postdilated using a 2.5 X 20 mm Maverick balloon. The patient developed insulin-requiring diabetes mellitus at the ICU and was discharged after a month. Eight months later, progressive rising in alkaline phosphatase was detected and abdominal MRI showed stenosis at bile duct anastomosis with pre-stenotic dilation; a biliary-digestive derivation was performed. Although Doppler US shows hepatic artery stenosis at the stent placement site; at 24 months of follow-up the patient is alive with and an excellent quality of life. His albumin, bilirubin and INR are normal. A liver biopsy was performed because of abnormal liver enzymes which revealed nonalcoholic steatohepatitis and no evidence of HCV reactivation.

Discussion

Hepatic artery blood flow is crucial for the donor extrahepatic bile ducts and its patency is mandatory for liver engraftment.[8] Closed Doppler US surveillance is recommended, even transoperatively, in order to confirm adequate flow.[9] MRI is useful in the postoperative state to confirm obstruction, prior to an invasive hepatic artery angiography, considered as the gold standard to diagnose this condition.[8]

HAT is the most frequent vascular complication after OLT and a major cause of graft loss; its morbidity and mortality are high among all series (~50%).[2] HAT incidence is approximately 7% (range 5-25%), while for hepatic artery stenosis is lies between 5 to 10%.[1] Early HAT after OLT produces graft and biliary tract ischemia, presenting as acute graft failure or as biliary complications (biliary stenosis, bile leak, cholangitis and hepatic abscesses or even sepsis).

Risk factors for early-onset HAT include internal flaps, kinking of a long artery, donor or recipient multiple and/or aberrant hepatic arteries, use of vascular extension grafts, vascular diameter and severe hypotension.[8] Other nonsurgical risk factors have been described,[2] however, these findings have been inconsistent among series.

Early-onset HAT usually requires urgent retransplantation due to the rapid deterioration in liver function and the patient's condition. Within the first 10 days after transplantation, thrombectomy can be an alternative to retransplantation with a success rate of 50–88% in adults.[3] Interventional percutaneous revascularization is a growing option for HAT and stenosis after OLT.[10] First reported in 1989 for the treatment of hepatic artery stenosis by Abad et al.,[11] percutaneous transluminal angioplasty was performed in our patients with the application of paclitaxel-coated coronary artery stents for patency insurance and prevention of recurrent thrombosis; however, two of three patients developed recurrent thrombosis.

The use of prophylactic acetylsalicylic acid has been suggested for late-onset HAT prevention, with a relative risk reduction of 82% found in a retrospective study.[12] We believe that the use of platelet aggregation inhibitors agents such as acetylsalicylic acid and clopidogrel are promising in the care of patients with hepatic artery stents placed to treat HAT. The three patients presented in this series are on AAS and clopidogrel therapy from the time of diagnosis with no anticoagulation.

The use of coated-stents has been suggested for HAT therapy by large case series using bare-stents.[13] This brief report describes our experience with paclitaxel-coated stents, an antiproliferative drug that induces tubulin polymerization, preventing smooth muscle proliferation and neointimal hyperplasia.[14] Despite the potential benefits of paclitaxel-coating, the lack of blood flow patency at long-term in these patients fails to support the use of coated-stents for early-onset HAT.

HAT might be a major but temporal issue, as patients with total occlusion during follow-up shows normal graft function. In this scenario, percutaneous angioplasty might act as a bridge for biliary revascularization, providing enough critical blood flow for a short period of time that allows graft survival while collateral flow develops. Definitively, further well-designed clinical studies are needed to evaluate the impact of percutaneous revascularization in this setting.

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