Case report
Catheter directed hepatic artery thrombolysis following liver transplantation. Case report and review of the literature

Miguel Ángel Carrillo-Martínez MD, Carlos Rodríguez-Montalvo MD, Eduardo Flores-Villabá MD, Lucas Tijerina-Gómez MD, Francisco Edgardo Puente-Gallegos MD, Samuel Eugene Kettenhofen MD and Germán Alfonso Garza-García MD

Department of Interventional Radiology, Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Mexico
Department of Surgery, Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Mexico
Department of Diagnostic Radiology, Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Mexico
Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Mexico

Address correspondence to: Dr Samuel Eugene Kettenhofen
E-mail: sam.ketten@gmail.com

ABSTRACT

Hepatic artery thrombosis is the most frequent vascular complication following orthotopic liver transplantation, and often results in biliary complications, early graft loss and death. Surgical revascularization and retransplantation are considered the mainstay of treatment. However, intraarterial endovascular therapy is an alternative that has shown low morbidity and mortality, thereby avoiding the need for retransplantation. We describe a case of orthotopic liver transplantation complicated with hepatic artery thrombosis that was successfully treated with endovascular therapy.

BACKGROUND

Vascular complications following orthotopic liver transplantation have a direct influence on graft viability and patient mortality. Post-operative complications include hemorrhage, stenosis, and thrombosis at any vascular anastomosis, however, hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT) are considered the most common complications.

HAT and PVT interrupt adequate graft vascularization which leads to graft dysfunction, loss and even patient death, making this a serious complication requiring urgent revascularization.

Surgical revascularization and urgent retransplantation are considered the mainstay therapy, however endovascular therapy is an attractive alternative with a comparatively high success rate and low mortality and morbidity.

CLINICAL PRESENTATION

A 39 year-old male with a past medical history of sclerosing cholangitis and hepatic cirrhosis classified as Child-Pugh C was subjected to a cadaveric whole liver transplantation. Conventional surgical technique was performed with resection of the inferior vena cava and venovenous bypass with a total cold ischemic time of 460 min. Post-operative immunosuppression therapy included tacrolimus, myco-phenolate mofetil, and steroids. Anticoagulant therapy was not administered.

A Doppler ultrasound on post-transplant Day 2 (PTD) demonstrated absence of flow in the hepatic artery. An emergent exploratory laparotomy attributed this finding to thrombosis at the site of vascular anastomosis and an aorto-portal graft was placed with a No. six ringed Gore-TEX® vascular graft (W.L. Gore & Associates, Flagstaff, AZ).

On PTD three the patient developed hyperbilirubinemia secondary to an increase in the direct bilirubin (total bilirubin: 6.1 mg dl⁻¹, direct bilirubin: 4.74 mg dl⁻¹) with increased liver enzymes (aspartate transaminase: 172 U l⁻¹, alanine transaminase: 70 U l⁻¹ and alkaline phosphatase 414 U l⁻¹). A hepatic ultrasound reported absent flow in the hepatic artery at the hilum without evidence of intrahepatic arterial flow. Occlusion of the aorto-hepatic vascular graft was confirmed with angiography (Figure 1a). Although there was no contraindication for surgical revascularization, endovascular management was elected as an initial therapeutic option considering our teams experience...
on a previous case, reserving surgery for technical failures or complications. A Teflon® coated guidewire (Cordis, Santa Clara, CA) and a 4 Fr catheter were used to access the graft and perform catheter-directed thrombolysis with recombinant tissue plasminogen activator (rtPA) 4 mg initial dose followed by 4 mg continuous infusion for 20 min (Figure 1b,c,d). Post-thrombolysis control angiography demonstrated significant stenosis at the hepatic anastomosis of the graft and balloon dilatation was performed with 5 × 20 mm and 6 × 20 mm balloons with unfavorable results due to immediate elastic restenosis (Figure 2a,b). Subsequently, a 6 × 20 mm Hippocampus® stent (Medtronic, Minneapolis, MN) was placed, achieving adequate flow in the vascular graft and the main branches of the right hepatic artery. (Figure 3a,b). Proximal occlusion of the left hepatic artery with distal collateral circulation was observed.

The patient’s clinical condition deteriorated on PTD 14, presenting with lower extremity edema, dyspnea during rest, tachycardia, tachypnea and hypoxemia (89% pulse oximetry). Thrombosis of the inferior vena cava (IVC) was suspected and a cavography was performed, confirming occlusion of the infrarenal IVC with collateral filling (Figure 4a,b). A multipurpose catheter was inserted and a guidewire was used to recanalize the IVC. Pre-dilatation with a 10 mm balloon catheter was performed and a 14 × 80 mm self-expanding S.M.A.R.T.® stent (Cordis, Santa Clara, CA) was placed and expanded to 14 mm (stents of a greater caliber were unavailable) (Figure 4c). Control cavography demonstrated adequate recanalization of the IVC with anterograde flow and absence of collateral filling (Figure 5a,b). The patient had a favorable evolution and was discharged approximately 1 month post-transplant.

3 months after discharge, the patient developed an abscess at a previously detected site of focal hepatic necrosis, requiring percutaneous drainage with complete resolution after 3 weeks.

**DISCUSSION**

HAT is the most common and severe vascular complication following orthotopic hepatic transplantation, accounting for approximately 50% of vascular complications and with reported mortality as high as 75%. It is defined as a thrombotic occlusion of the hepatic artery and is classified as early or late depending on time of presentation following liver transplantation. Early HAT occurs within 30 days and is associated
Case report: Hepatic artery thrombolysis following liver transplantation.

with a rapid clinical deterioration, a high rate of graft loss and increased mortality rates. Late HAT occurs after 30 days post-transplantation and has a relatively mild clinical course. Because the hepatic artery is the only route by which oxygenated blood is supplied to the liver, its obstruction results in parenchymal and biliary ischemia. Clinically, its presentation varies from slight signs of parenchymal involvement to fulminating hepatic failure.

A determining factor that limits hepatic injury and graft loss is the early detection of arterial complications by means of Doppler ultrasound of the liver and angiography. Clinical markers that may indicate early HAT include fever, leukocytosis, elevation of hepatic enzymes, hyperbilirubinemia, and shock. Other patterns that may also suggest HAT include fulminant hepatic failure, late-onset biliary leakage, and recurrent bacteremia. Doppler ultrasound within the first 3 days post-transplantation provides the advantage of diagnosis of HAT before clinical manifestations become apparent.

Three treatment options have been described for HAT: surgical revascularization, urgent retransplantation and endovascular revascularization. Retransplantation is considered the first-line therapy, however, it often carries a higher mortality rate and is limited by a shortage of donors. Urgent endovascular revascularization therefore plays an important role in the management of HAT, potentially avoiding the need for retransplantation in cases where a diagnosis is made before signs and symptoms of graft dysfunction become apparent.

Intra-arterial thrombolysis for HAT was first described by Hidalgo et al in 1989. It is thought that thrombolysis is most effective in “fresh” thrombi due to a higher water content and a matrix relatively poor in fibrin. Literature on this particular topic varies greatly, some recommending thrombolysis as early as 4 h and others as late as 120 days post-transplantation. There are no current guidelines regarding the therapeutic window for thrombolysis. Nevertheless, the general consensus is that it should not be attempted more than 3 months post-transplantation.

Hepatic-artery thrombolysis is considered a safe treatment, with the most common and severe complication being hemorrhage reported in approximately 20% of patients. The main pitfall of thrombolysis is short-term recurrence of HAT if the conditions that favored its formation are not resolved (e.g. kinks, twist, dissection or stenosis at the site of anastomosis). Angioplasty and
stent placement after intraarterial thrombolysis have become a solution with more favorable results.\(^9,10\) It is important to mention that multiple points of stenosis as well as HAT in pediatric patients are not considered absolute contraindications for thrombolysis and angioplasty, particularly if retransplantation is not an option.

Our patient also presented with thrombosis of the IVC, a rare complication estimated to occur in 1–2% of transplants.\(^11\) It is most often related to surgical technique and generally occurs within the first month after transplantation. Without prompt diagnosis and therapeutic intervention, it is associated with high morbidity, mortality and graft failure. There are several reports of successful management of thrombosis of the IVC with thrombolysis and stent placement.\(^12\) Surgical repair may be unavoidable in cases of restenosis or kinking of the graft due to size mismatch between the donor and recipient.

**CONCLUSION**

HAT is a serious complication of liver transplantation and early detection is crucial to preserve function and viability of the graft and improve patient survival. Post-operative hepatic Doppler ultrasound is an important tool in early diagnosis, although angiography is currently the gold standard in the detection of this complication with the added benefit of permitting endovascular therapeutic options. Catheter directed thrombolysis is safe and effective, although restenosis is common if the predisposing factor is not corrected. However, when combined with post-thrombolysis balloon angioplasty and stent placement, therapeutic results and patient outcome may improve. Although the ideal treatment of symptomatic patients and those with severe graft dysfunction is urgent retransplantation, the shortage of donor livers makes endovascular therapy an attractive therapeutic option to save the graft and avoid retransplantation or facilitate it in an elective setting.

**LEARNING POINTS**

- Early detection of hepatic artery thrombosis is critical to conserve graft vitality.
- Doppler ultrasound assessment must be done by experienced sonographers and in case of doubt, an angiography or angiotomography must be performed.
- Thrombolysis of the hepatic artery is safe and effective.
- After thrombolysis, balloon angioplasty with or without stent placement may be needed.

**PATIENT CONSENT**

The authors obtained written informed consent from the patient for the publication of this case report, including accompanying images.

**REFERENCES**

1. Duffy JP, Hong JC, Farmer DG, Ghobrial RM, Yerisiz H, HIatt JR, et al. Vascular complications of orthotopic liver transplantation: experience in more than 4,200 patients. J Am Coll Surg 2009; 208: 896–903. doi: https://doi.org/10.1016/j. jamcolsurg.2008.12.032
2. Singhal A, Stokes K, Sebastian A, Wright HI, Kohli V. Endovascular treatment of hepatic artery thrombosis following liver transplantation. Transplant Int 2010; 23: 245–56. doi: https://doi.org/10.1111/j.1432-2277.2009.01037.x
3. Garcia-Criado A, Gilabert R, Berzigotti A, Brú C. Doppler ultrasound findings in the hepatic artery shortly after liver transplantation. AJR Am J Roentgenol 2009; 193: 128–35. doi: https://doi.org/10.2214/AJR.07.3919
4. Maruzzelli I, Miraglia R, Caruso S, Milazzo M, Mamone G, Gruttadauria S, et al. Percutaneous endovascular treatment of hepatic artery stenosis in adult and pediatric patients after liver transplantation. Cardiovasc Intervent Radiol 2010; 33: 1111–9. doi: https://doi.org/10.1007/s00270-010-9848-4
5. Tzakis AG, Gordon RD, Shaw BW, Iwatsuki S, Starzl TE. Clinical presentation of hepatic artery thrombosis after liver transplantation in the cyclosporine era. Transplantation 1985; 40: 667–71. doi: https://doi.org/10.1097/00007890-198512000-00019
6. Silva MA, Jambulingam PS, Gunson BK, Mayer D, Buckels JAC, Mirza DF, et al. Hepatic artery thrombosis following orthotopic liver transplantation: a 10-year experience from a single centre in the United Kingdom. Liver Transpl 2006; 12: 146–51. doi: https://doi.org/10.1002/lt.20566
7. Sheiner PA, Varma CV, Guerrera JV, Cooper J, Garatti M, Enre S, et al. Selective Revascularization improves patient and graft survival. Transplantation 1997; 64: 1295.
8. Hidalgo EG, Abad J, Cantarero JM, Fernández R, Parga G, lover JM, et al. High-dose intra-arterial urokinase for the treatment of hepatic artery thrombosis in liver transplantation. Hepatogastroenterology 1989; 36: 529.
9. Ueno T, Jones G, Martin A, Ikegami T, Sanchez EQ, Chinnakotla S, et al. Clinical outcomes from hepatic artery stenting in liver transplantation. Liver Transpl 2006; 12: 422–7. doi: https://doi.org/10.1002/lt.20628
10. Breguet R, Dondero F, Pupulim L, Goossens N, Sepulveda A, Francoz C, et al. Endovascular treatment of arterial complications after liver transplantation: long-term follow-up evaluated on Doppler ultrasound and magnetic resonance cholangiopancreatography. Cardiovasc Intervent Radiol 2019; 42: 381–8. doi: https://doi.org/10.1007/s00270-018-1408-0
11. Grodzicki M, Anysz-Grodzicka A, Remiszewski P, Cielak B, Kotelski M, Kalinowski P, et al. Treatment of early hepatic artery thrombosis after liver transplantation. Transplant Proc 2011; 43: 3039–42. doi: https://doi.org/10.1016/j.transproceed.2011.08.028
12. Abdelaziz O, Hosny K, Amin E, Emaddin S, Uemoto S, Mostafa M. Endovascular management of early hepatic artery thrombosis after living donor liver transplantation. Transpl Int 2012; 25: 847–56. doi: https://doi.org/10.1111/j.1432-2277.2012.01509.x