Transplant Hepatic Artery Stenosis: Endovascular Treatment and Complications

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Abstract

Keywords

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Hepatic artery stenosis (HAS) is an infrequent complication of liver transplant; if left untreated, it can lead to hepatic artery thrombosis with high risk of biliary necrosis and graft loss. HAS is diagnosed with screening Doppler ultrasound, together with computed tomography angiography and magnetic resonance angiography. Endovascular treatment with angioplasty ± stent placement is safe and effective with infrequent major complications; however, when complications occur, they can devastate long-term graft survival. Herein, we present two cases of HAS treated with balloon angioplasty with resultant major complications requiring operative intervention.

Case 1

A 37-year-old man with alcoholic cirrhosis developed low resistive indices in his right and left hepatic arteries (0.29–0.34) on a screening Doppler ultrasound (US) 4 weeks after orthotopic liver transplant. Subsequent CTA and conventional angiogram showed tortuosity of the hepatic artery with a focal high grade (>75%) narrowing of the donor hepatic artery spanning ~1 cm (►Fig. 1a). The patient was started on full-dose aspirin and clopidogrel, but follow-up US 3 weeks later showed a rising peak systolic velocity in the donor hepatic artery (210 cm/s), and a *tardus parvus* waveform in both right and left branches. Moreover, serum bilirubin and liver enzyme levels were mildly elevated. As a result, repeat conventional angiogram was performed, now 10 weeks after liver transplant.

Angiography revealed interval progression of stenosis within the donor hepatic artery, with high-grade stenosis spanning 2 cm. Via a femoral approach, 3-mm balloon angioplasty of the stenosis was performed (►Fig. 1b). Subsequent angiography showed mild improvement in luminal caliber with persistent 50% luminal narrowing (►Fig. 1c). Initial attempts at passing a larger balloon were unsuccessful due to proximal tortuosity, and as such, vascular access was shifted to the left brachial artery for improved pushability;

4-mm balloon angioplasty of the lesion yielded satisfactory improvement in luminal caliber, though focal mild narrowing was present at the distal margin of the aforementioned stenosis (►Fig. 1d). This residual stenosis was treated with additional 4-mm balloon angioplasty, and immediately brisk contrast extravasation was evident (►Fig. 2). Multiple attempts to regain hemostasis were made with balloon tamponade; however, these were unsuccessful, and the patient was immediately taken to the operating room with the balloon inflated at the site of injury. Of note, an appropriately sized stent graft was not available at the time of the angioplasty procedure.

The transplant surgical team identified complete dehiscence of the donor hepatic artery at the proximal margin of the stenotic lesion, distal to the anastomosis. The stenosed segment was resected and a new primary anastomosis was made. His hospital course was unremarkable, and follow-up laboratory and imaging studies, over the past 12 months, showed a full recovery of graft function.

Case 2

A 64-year-old man with hepatitis B and alcoholic cirrhosis developed rising liver enzymes 3.5 weeks after orthotopic liver transplantation. Image-guided transplant liver biopsy

Fig. 1 (a) Conventional diagnostic angiography performed 1 month after orthotopic liver transplantation demonstrates high-grade segmental stenosis of the donor hepatic artery, spanning 1 cm (white arrow), and tortuosity. (b) Repeat angiography, 6 weeks after diagnostic angiography, shows progression of stenosis, now doubling in length, at 2 cm (black arrows). (c) Angiographic images, after 3-mm balloon angioplasty, identify persistent 50% residual stenosis (white arrows). (d) Therefore, 4-mm balloon angioplasty was performed via left brachial approach, given caudal orientation of the celiac trunk and desired improved pushability. After angioplasty, residual focal narrow is seen at the distal margin (white arrow).

was negative for acute rejection; CTA showed focal stenosis of the donor hepatic artery, just proximal to its bifurcation into left and right hepatic arteries (►Fig. 3a). In addition, the aortohepatic artery conduit had a prominent kink (►Fig. 3b). Liver enzymes continued to rise (alanine transaminase 296 IU/L, aspartate transaminase 109 IU/L, normal <45 IU/L), and US identified an elevated peak systolic velocity in the donor hepatic artery of 220 cm/s. Conventional hepatic angiography was performed 32 days after transplant.

Angiography showed a high-grade stenosis spanning 1 cm within the donor hepatic artery (►Fig. 3c). Four-millimeter balloon angioplasty of the lesion was performed, and immediately after, wire access was lost due to built-up tension from the aforementioned vascular conduit kink and hepatic

artery tortuosity. Subsequent angiography demonstrated sluggish flow with dissections extending from the lesion into the right and left hepatic arteries (►Fig. 4a). This progressed to occlusion of the RHA (►Fig. 4b). Attempted guidewire access of the true vascular lumen, distal to dissections, was unsuccessful, and included administration of heparin, tissue plasminogen activator, and nitroglycerine. The patient was placed on a heparin drip and US identified diminished flow in the right and left hepatic arteries with resistive indices of 0.30 to 0.39. Within 24 hours of the angioplasty procedure, the patient became markedly hypotensive requiring vasopressors, transfusion, and intubation. A large hematoma was found at his right femoral access site. The hemoglobin level dropped from 12.0 to 6.8 g/dL.

Fig. 2 (a, b) Immediately after additional 4-mm balloon angioplasty of residual focal stenosis, brisk contrast extravasation is visualized (black arrows).

Over the following week, the patient developed worsening acidosis and renal failure. Serial US and CT examinations showed enlarging areas of cystic necrosis in both hepatic lobes (→Fig. 5). On postprocedure day 10, his total serum bilirubin peaked at 8.3 mg/dL, with a MELD score of 31. On day 11 after angioplasty, he underwent repeat orthotopic liver transplantation. Complete thrombosis of the hepatic artery was noted in the operative report, and reconstruction was performed utilizing the existing aortohepatic conduit.

Post-retransplant US showed normal hepatic vascular flow and serum liver enzymes began to normalize. He no longer required vasopressor support, though continued to receive hemodialysis for renal failure. On postoperative day 6, the patient was reintubated for respiratory distress. Radiographs showed left lung consolidation and bronchoalveolar lavage cultures grew staphylococcus. The patient developed hypotension with progressively worsening metabolic and respiratory acidosis. He died 32 days after the angioplasty procedure.

Discussion

Transplant hepatic artery stenosis (HAS) complicates 4 to 10% of adult cases, and if left untreated, it progresses to hepatic artery thrombosis in > 50% of patients.^{1–4} The actual incidence of HAS is largely unknown as many patients are asymptomatic, screening protocols are variable, and different HAS criteria are described. Common causes are operative technique, graft rejection, and microvascular injury.¹ HAS typically occurs at the anastomosis and may manifest as insidious graft dysfunction.^{2,5}

HAS causes reversible biliary ischemia followed by irreversible biliary necrosis, which leads to graft dysfunction, incompatible with long-term graft survival.^{1,3} As such, early diagnosis and treatment are paramount. HAS is often diagnosed by color Doppler US. Normal hepatic artery US find-

ings show a rapid systolic upstroke, with continuous diastolic flow, and a resistive index (RI; peak systolic velocity – end diastolic velocity/peak systolic velocity) of 0.55 to 0.80.⁶ HAS yields distal compensatory vasodilation; therefore, diastolic flow increases and the RI is diminished. With severe stenosis, distal flow is blunted, resulting in a *tardus parvus* waveform. Importantly, a normal waveform in a hepatic artery distal to the anastomosis is nearly 100% specific in excluding a flow-limiting anastomotic stricture; and on the other hand, a RI < 0.55 is nearly 100% sensitive for significant stenosis.⁶ A peak systolic velocity of > 200 cm/s is highly suggestive of a stenosis (specificity of 96%), yet its absence poorly excludes stenosis (sensitivity of 30%).⁷

CTA and MRA often overestimate significant HAS (≥ 50% diameter reduction) compared with catheter angiography. CTA has a sensitivity of 88 to 100% and a specificity of 89% in identifying extrahepatic HAS.⁸ MRA is 100% sensitive and 74% specific, and a normal MRA definitively excludes a significant stenosis with a 100% negative predictive value.⁹

Treatment options for HAS are surgical and endovascular. Surgical options include resection of the stenotic segment with reanastomosis, aortic conduit graft, interposition vein or artery graft, or vein patch angioplasty.² These traditional surgical techniques have been replaced by endovascular therapy, including angioplasty with or without stent placement, except for very early stenosis (<7 days from liver transplant).^{2,5,10}

The efficacy of hepatic artery angioplasty, for the treatment of HAS, was described 30 years ago, and a larger retrospective study of 37 patients was reported in 2005.^{1,11} In this study, primary balloon angioplasty was considered technically successful if luminal diameter was restored (< 30% residual stenosis) without immediate complication. The overall technical success rate was 81%, and solitary stenoses, without associated hepatic arterial kinks, had a technical success rate of 95% with no complications.

Fig. 3 (a) Three-dimensional volume rendering of a computed tomographic angiography (CTA) demonstrates stenosis (white arrow) of the donor hepatic artery immediately proximal to its bifurcation. (b) CTA also identifies prominent kink within the aortohepatic artery conduit (white arrow). (c) Initial angiographic imaging shows high-grade segmental stenosis of the donor hepatic artery spanning 1 cm (white arrow). Kinking of the aortohepatic conduit is evident (white arrowhead).

The 1-year primary patency rate was $44\% \pm 12\%$ and the primary assisted patency rate was $60\% \pm 11\%$. The hepatic artery thrombosis rate, at 6 months, was threefold higher with untreated HAS, as compared with technically successful angioplasty treatment, thus highlighting the importance of timely intervention. The intraprocedural complication rate of angioplasty was 7%, namely dissection and arterial rupture, and all complications were managed surgically.¹

An improved patency rate of endovascular therapy was identified by Sabri et al. Specifically, HAS without associated kinks, treated with primary angioplasty, and selective use of stents, resulted in a 12-month assisted patency rate of 81%. Major complications occurred in 12% of patients.¹⁰

Major complications of endovascular therapy for HAS include rupture and dissection, along with thrombosis. Active

contrast extravasation from a ruptured hepatic artery is treated with balloon tamponade, stent graft placement, embolization, and/or surgery. A coronary stent graft is sometimes the only endovascular option for hepatic artery rupture, and its use is off-label, on an emergent compassionate basis.¹² Hepatic artery dissection treatment includes medical management with anticoagulation and antiplatelet therapy, endovascular treatment with stent, and balloon tacking of the dissection flap, along with surgical revascularization.¹ In the study of Sabri et al, 16% of patients required stent placement for HAS of which 50% were for iatrogenic dissection.¹⁰ Hepatic artery thrombosis is treated by catheter-directed thrombolysis with subsequent therapy for underlying HAS.

The long-term outcomes of angioplasty $\pm$ stent placement for HAS was reported in 2016.⁵ Critical HAS was

Fig. 4 (a) After balloon angioplasty, guidewire access across the lesion was lost, and complex dissection extends from the treatment site into both the left and right hepatic arterial branches (white arrows) with (b) subsequent occlusion of the right hepatic artery (arrowhead).

defined by $> 50\%$ narrowing of the hepatic artery on CTA, and symptomatic HAS was defined by either biological abnormalities (i.e., cholestasis) or biliary complications (i.e., biliary stenosis). Noncritical HAS was treated with antiplatelet agents and serial imaging follow-up, while critical HAS was treated with endovascular techniques. Thirty patients underwent endovascular treatment, which was technically successful in 90% (27 patients); specifically, 23 patients were treated with angioplasty and stent placement, while 4 patients were treated with angioplasty alone. The overall complication rate was 10%. The 1-, 3-, and 5-year hepatic artery patency rates were 68, 63, and 63%, respectively. Hepatic artery patency rates were not significantly different with angioplasty alone versus angioplasty + stent.

Fig. 5 Non-contrast-enhanced CT 8 days after angioplasty demonstrates large regions of cystic necrosis in the right and left hepatic lobes (white arrows).

No significant difference in patient, or graft survival, was seen between symptomatic and asymptomatic patients, after endovascular therapy. Retransplantation for ischemic cholangitis was observed in 67% of patients with failed angioplasty versus 19% with successful angioplasty. The authors indicate that endovascular therapy for critical HAS should be offered to all patients, including symptomatic patients with established biliary ischemia, to reduce retransplantation for ischemic cholangitis.⁵

A meta-analysis compared percutaneous balloon angioplasty versus stenting for the treatment of HAS after liver transplant.¹³ Pooled technical success for both techniques was similar at 90%, and pooled complications rates were not statistically different (16 vs. 19%). Complications at the site of intervention were thrombosis, perforation, and dissection. Hepatic artery patency at greater than 6 months of follow-up was not significantly different, that is, 76% with angioplasty and 68% with stents. Need for retransplant was also similar in both cohorts: 25% with angioplasty versus 20% with stent. The authors indicate angioplasty and stenting are equally effective and safe for treatment of transplant HAS. Moreover, technical failures are uncommon and, when encountered, are due to a kinked or tortuous hepatic artery.¹³

Significant HAS, left untreated, may progress to thrombosis, which leads to additional risk of biliary stricture and graft dysfunction/loss. Pulitano et al sought to define patients who will benefit from HAS endovascular therapy.¹⁴ HAS was defined as $\geq 70\%$ stenosis on CTA or catheter angiography, and treatment strategies incorporated conservative therapy with aspirin versus angioplasty $\pm$ stent placement. Twenty-three patients received endovascular therapy (15 patients with angioplasty, and angioplasty with stent in 8 patients), and 31 patients were managed conservatively. Conservative therapy was motivated by severe hepatic artery kinks (7 patients), right HAS (3 patients), presence of collaterals (8 patients), and normal

liver function tests (13 patients). Overall, 35% of endovascular patients and 29% of conservative patients developed new biliary strictures. No asymptomatic HAS patient with normal LFTs developed a biliary stricture. Propensity score-matched analysis was used to compare the endovascular treatment group with the conservative management group. Early-onset HAS (<6 months after LT) benefited from endovascular treatment with improved biliary stricture-free survival. Interestingly, no significant difference was identified for patients with late-onset HAS (≥ 6 months). The authors indicated asymptomatic HAS and late-onset HAS do not benefit from endovascular therapy.¹⁴ This statement is in contradistinction to the aforementioned study of Rajakannu et al, in which endovascular therapy benefited all patients, regardless of onset and symptoms.⁵ As neither of these studies is a prospective randomized trial comparing endovascular therapy with conservative management, the triage of asymptomatic and late-onset patients is unanswered.

In a recent study, long-term patency of the transplant hepatic artery, after endovascular treatment, along with delayed bile duct abnormalities, was reported.¹⁵ The technical success rate was 94% and hepatic artery patency at 5 years was 81%. After a median follow-up of nearly 5 years, 32% of patients developed radiological features of ischemic cholangiopathy. Diagnosis with HAS within 3 months of transplant was the only risk factor associated with ischemic cholangitis. This supports the finding of Pulitano et al, whereby late-onset HAS does not benefit from endovascular therapy, possibly due to collateral formation.¹⁴

Risks of endovascular therapy for HAS were detailed by the highest volume transplant center in the United States, over a 79-month period, encompassing 106 angiograms in 79 patients with HAS.¹⁶ Major complications occurred in eight cases (7.5%), consisting of artery dissection and rupture. Most complications were treated with a stent or stent graft (rupture cases) and no surgical intervention was required. However, 50% of these cases progressed to hepatic artery thrombosis, compared with 1.4% undergoing intervention without a major complication. Severe tortuosity of the hepatic artery, and presence of a second liver transplant, yielded a twofold and threefold increased risk of a major complication, respectively. Although vessel tortuosity and retransplant produced more complications, technical success was achieved in most patients with these risk factors. Similarly, Saad et al reported more complications with hepatic artery angioplasty for HAS in the setting of arterial kinks. Specifically, the technical success and complication rates in cases with arterial kinks was 14 and 29%, respectively, compared with 94 and 10% without arterial kinks.¹

The aforementioned case vignettes have several common features. Both patients developed symptomatic HAS (elevated liver function tests) less than 3 months after liver transplant, and hence, considered early-onset HAS. Endovascular therapy for symptomatic early-onset HAS has universal support in the reviewed literature. CTA and conventional angiography revealed tortuosity of the donor hepatic artery in both patients, along with a kinked aorto-

hepatic conduit. The presence of tortuosity and kinking is known to limit technical success and increase complication rates. Endovascular rescue therapy was unsuccessful in these cases and operative management was required, including retransplantation. These vignettes highlight the importance of case selection in setting procedural expectations and mitigating adverse events.

Conclusion

Transplant HAS progressing to hepatic artery thrombosis is associated with a high risk (47%) of graft loss; hence, timely diagnosis and treatment are paramount.¹⁷ Diagnosis of a hemodynamically significant stenosis is made with noninvasive imaging, which also identifies kinks and tortuosity of transplant hepatic arterial supply. Endovascular treatment is agreed upon for symptomatic early-onset HAS, while treatment of asymptomatic and late-onset HAS is debated. Angioplasty and stenting are equally effective and safe for the treatment of transplant HAS. Technical failures are uncommon unless kinked or tortuous hepatic arterial supply is present.

Disclosure Statement

The authors have no disclosures.

Conflict of Interest

None.

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