Cutting balloon treatment of anastomotic biliary stenosis after liver transplantation: Report of two cases

Fan Ding, Hui Tang, Chi Xu, Zai-Bo Jiang, Shu-Hong Yi, Hua Li, Nan Jiang, Wen-Jie Chen, Qing Yang, Yang Yang, Gui-Hua Chen

Abstract

Biliary stenosis is a common complication after liver transplantation, and has an incidence rate ranging from 4.7% to 12.5% based on our previous study. Three types of biliary stenosis (anastomotic stenosis, non-anastomotic peripheral stenosis and non-anastomotic central hilar stenosis) have been identified. We report the outcome of two patients with anastomotic stricture after liver transplantation who underwent successful cutting balloon treatment.

Institutional review board statement: This case report was exempt from Institutional Review Board review [(2016)2-114] at The Third Affiliated Hospital of Sun Yat-Sen University in Guangzhou, China.

Informed consent statement: The patients involved in this report gave their written informed consent for the use and disclosure of their health information.

Conflict-of-interest statement: The authors declare that there is no conflict of interest related to this report.

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CASE REPORT

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Cutting balloon treatment. Case 1 was a 40-year-old male transplanted due to subacute fulminant hepatitis C. Case 2 was a 57-year-old male transplanted due to hepatitis B virus-related end-stage cirrhosis associated with hepatocellular carcinoma. Both patients had similar clinical scenarios: refractory anastomotic stenosis after orthotopic liver transplantation and failure of balloon dilation of the common bile duct to alleviate biliary stricture.

Key words: Liver transplantation; Cutting balloon; Anastomotic; Biliary stenosis; Cholangiography; Balloon dilation

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Core tip: Biliary stenosis is the relatively common complication after liver transplantation. Our case report represents one of few documenting evidence of the cutting balloon treatment as a safe and effective procedure in refractory anastomotic stenosis after orthotopic liver transplantation. The cutting balloon treatment could be an alternative therapy to the endoscopic application or the surgical application.

INTRODUCTION

Cutting balloon is an angioplasty device, which appropriately combines microsurgical incision with mechanical dilation. The system was invented by Barath et al[1] and was initially used in percutaneous coronary interventions. Compared with traditional balloon dilation technology, cutting balloon can effectively incise the vascular wall with concentrated and low-dilated pressure.

Cutting balloon technology plays an important role in complex coronary artery lesions[2], but is rarely reported in the field of biliary stenosis after orthotopic liver transplantation[3,4]. This report summarizes the application of cutting balloon treatment in two cases with anastomotic biliary stenosis after liver transplantation.

CASE REPORT

Case 1 was a 40-year-old male with hepatitis C virus (HCV)-related end-stage cirrhosis associated with portal hypertension. The patient, who weighed 71.5 kg, had undergone splenectomy 5 years previously and had no clinical history of other systemic diseases. Laboratory examinations revealed high levels of hepatobiliary enzymes, coagulation factors and quantitative HCV RNA: aspartate aminotransferase (AST) was 123.0 U/L, alanine aminotransferase (ALT) was 64 U/L, albumin (ALB) was 34.1 g/L, total bilirubin (TBILI) was 91.62 µmol/L, direct bilirubin (DBILI) was 36.87 µmol/L, prothrombin time (PT) was 15.1 s, the international normalized ratio of prothrombin time (PT-INR) was 1.25, and HCV RNA was 1.21 × 10^6 IU/mL. Case 2 was a 57-year-old male with hepatitis B virus (HBV)-related end-stage cirrhosis associated with hepatocellular carcinoma (HCC). The patient, who weighed 69.0 kg, was diagnosed with type II diabetes 12 years previously and had not undergone abdominal surgery. Blood examination results were as follows: AST 41.0 U/L, ALT 33 U/L, ALB 39.6 g/L, TBILI 73.7 µmol/L, DBILI 49 µmol/L, PT 19.0 s, PT-INR 1.59, and HBV DNA 270 IU/mL. The clinical characteristics of these two patients are described in Table 1.

Case 1

Due to the failure of medical therapy, Case 1 underwent orthotopic liver transplantation (OLT) on June 6, 2012 (the liver graft warm ischemia time was 6 min and cold ischemia time was 7 h). Biliary anastomoses were performed by continuous anastomosis with absorbable suture (6-0 PDS suture). Postoperative pathology revealed nodular cirrhosis associated with cholestasis in hepatocytes and capillaries (Figure 1). Immunosuppressive therapy consisting of cyclosporine and mycophenolate mofetil was administered. Five months later, the patient was readmitted due to xanthochromia and pruritus. Re-examination of hepatic enzymes, coagulation factors and quantitative HCV RNA: aspartate aminotransferase (AST) was 129.0 U/L, alanine aminotransferase (ALT) was 64 U/L, albumin (ALB) was 34.1 g/L, total bilirubin (TBILI) was 52 µmol/L, direct bilirubin (DBILI) was 36.87 µmol/L, prothrombin time (PT) was 15.1 s, the international normalized ratio of prothrombin time (PT-INR) was 1.25, and HCV RNA was 1.21 × 10^6 IU/mL. Case 2 was a 57-year-old male with hepatitis B virus (HBV)-related end-stage cirrhosis associated with hepatocellular carcinoma (HCC). The patient, who weighed 69.0 kg, was diagnosed with type II diabetes 12 years previously and had not undergone abdominal surgery. Blood examination results were as follows: AST 41.0 U/L, ALT 33 U/L, ALB 39.6 g/L, TBILI 73.7 µmol/L, DBILI 49 µmol/L, PT 19.0 s, PT-INR 1.59, and HBV DNA 270 IU/mL. The clinical characteristics of these two patients are described in Table 1.

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ALP 4895 µmol/L. On November 22, 2013, based on the clinical history and out-patient examinations, we performed cutting balloon treatment (Figure 5). The key surgical procedures were: the patient was placed in the left position and his abdominal skin was sterilized. The guidewire was then successfully placed in the correct position and the surgeon implanted the cutting balloon into the stenosis site and inflated the balloon (diameter 6 mm, length 4 cm; inflated pressure 6 atm, dilatation time 3 min). The surgeon subsequently consolidated the cutting site with conventional balloon dilatation (diameter 8 mm, length 4 cm). The operation was successful. Complications included abdominal pain, nausea and emesis, which were minor and tolerable. On January 7, 2014, cholangiography indicated that the anastomotic stenosis was resolved (Figure 6). Liver function gradually recovered to physiological level within the 3-year follow-up period.

**Case 2**

Having met the standard of the "Milan criteria", OLT was performed in Case 2 on September 14, 2014 (the liver graft warm ischemia time was 0 min and cold ischemia time was 6 h). Biliary anastomosis was performed by continuous anastomosis with absorbable suture (7-0 PDS suture). Postoperative pathology indicated moderately differentiated HCC and nodular cirrhosis.

**Table 1** Patient characteristics

| Case No. | Age, yr | Sex | Diagnosis                              | Child-Pugh scores | MELD scores |
|----------|---------|-----|----------------------------------------|-------------------|-------------|
| Case 1   | 40      | Male | Subacute fulminant hepatitis C          | 9                 | 15          |
| Case 2   | 57      | Male | Hepatitis B virus-related end-stage cirrhosis associated with HCC | 6                 | 17          |

HCC: Hepatocellular carcinoma.

Figure 1 Postoperative pathology. Nodular cirrhosis associated with hepatocyte and capillary bile cholestasis.

Figure 2 Magnetic resonance cholangiopancreatography findings. Post-orthotopic liver transplantation anastomotic stenosis of the choledochal duct, intra-hepatic bile duct dilation, and biliary sludge in the common hepatic duct and bilateral hepatic ducts; patient diagnosed with transplantation-related ischemic injury involving the biliary tract.

Figure 3 Percutaneous transhepatic cholangial drainage combined with balloon dilation. A: Anastomotic stenosis of the choledochal duct (straight arrow); B: The inflated balloon (diameter 8 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilatation (straight arrow).
pathological changes in peripheral hepatic tissues (Figure 7). Immunosuppressive therapy consisting of tacrolimus and mycophenolate mofetil was administered. Fifteen days after surgery, the patient developed cutaneous or sclera icterus, and emergency examination results were: AST 33 U/L, ALT 41 U/L, TBILI 74.50 µmol/L, DBILI 47.1 µmol/L, GGT 470.0 µmol/L, ALP 537 µmol/L; MRCP revealed severe anastomotic stenosis of the choledochal duct, and severe choledochectasia involving the intrahepatic bile ducts and left-right hepatic bile ducts above the anastomotic stomas. The patient was diagnosed with biliary anastomotic stenosis (Figure

Figure 4 Cholangiography findings. The anastomotic stenosis was reduced by about 20 % (straight arrow).

Figure 5 Cutting balloon therapy. A: Cholangiography showed the development of anastomotic stenosis (straight arrow); B: The inflated cutting balloon (diameter 6 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight arrow).

Figure 6 Cholangiography findings. The anastomotic stenosis was resolved (straight arrow).

Figure 7 Postoperative pathology. A: Moderately differentiated hepatocellular carcinoma; B: Peripheral hepatic tissues revealed nodular cirrhosis pathologic changes.
8). On October 4, 2014, PTCD was performed without severe complications (Figure 9). Five months later, cholangiography revealed the presence of anastomotic stenosis, hence cutting balloon treatment was carried out (Figure 10). The surgical procedures were as follows. The patient was placed in the left position and his abdominal skin was sterilized. The guidewire was successfully placed in the correct position. The surgeon implanted the cutting balloon into the stenosis site and inflated the balloon (diameter 5 mm, length 2 cm; inflated pressure 6 atm, dilatation time 3 min). The surgeon subsequently consolidated the cutting site with conventional balloon dilatation (diameter 8 mm, length 4 cm). The surgery was successful. The patient had transient hemorrhage on the first night after surgery. Emergency blood examinations showed no change. Under the standardized management of

Figure 8  Magnetic resonance cholangiopancreatography findings. Severe anastomotic stenosis of the choledochal duct, severe choledochectasia involving the intrahepatic bile ducts and left-right hepatic bile ducts above the anastomotic stomas; Patient diagnosed with biliary anastomotic stenosis.

Figure 9  Percutaneous transhepatic cholangial drainage combined with balloon dilation. A: Severe anastomotic stenosis of the choledochal duct (straight arrow); B: The inflated balloon (diameter 8 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight arrow).

Figure 10  Cutting balloon therapy. A: Cholangiography showed that the anastomotic stenosis had resolved; B: The inflated cutting balloon (diameter 5 mm, length 2 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight arrow).
The anastomotic stenosis was reduced by about 30% (straight arrow). Figure 11 Cholangiography findings.

Postoperative anastomotic biliary stenosis can occur after surgery in the bile ducts of transplanted or non-transplanted liver. The majority of postoperative anastomotic stenosis encountered by the organ transplantation team are most often seen in liver transplant recipients. Three types of biliary stenosis (anastomotic, peripheral, and central) have been reported. The causes of biliary stenosis are shown in Table 2. In addition to ischemia and fibrosis, immunological processes and ABO blood type incompatibility are suspected to contribute to biliary stenosis after liver transplantation.

The cutting balloon system, which incorporates three or four radially-directed microsurgical blades on the surface of the balloon, is an alternative device that has been used in calcified or rigid lesions. Compared with conventional angioplasty, by creating endovascular micro-incisions during dilatation, the cutting balloon reduces vascular tone, yielding a greater luminal diameter and lower incidence of residual stenosis, which is conducive for lower inflation pressure and a reduced incidence of postoperative complications. This device is particularly suitable for biliary stenosis, which is characterized by a high concentration of elastic and muscle fibers that can generate substantial recoil following balloon inflation. We have used cutting balloon treatment in patients who have a high risk of refractory anastomotic stenosis and this treatment has yielded satisfactory results, with no severe postoperative complications, such as bile leakage or catheter-related complications.

In conclusion, cutting balloon treatment for biliary anastomotic stenosis after liver transplantation may be an alternative therapy to endoscopic or surgical treatment, and avoids unnecessary routine stents, directly incising stenosis scars, and has a favorable long-term prognosis.

Table 2  Etiologies of biliary stenosis

| Procedure-related factors | Non-procedure-related factors |
|---------------------------|-----------------------------|
| Biliary anastomosis       | Chronic pancreatitis        |
| Cholecystectomy           | Inflammation and infections |
| Ischemic injury           | Primary sclerosing cholangitis |
| Choledocholithiasis       | Radiation therapy           |
| Post-endoscopic biliary sphincterotomy | Autoimmune cholangiopathy |
| Trauma                    | Sphincter of Oddi dysfunction |

Outcomes described in previous reports of endoscopic treatment.

In conclusion, cutting balloon treatment for biliary anastomotic stenosis after liver transplantation may be an alternative therapy to endoscopic or surgical treatment, and avoids unnecessary routine stents, directly incising stenosis scars, and has a favorable long-term prognosis.

**DISCUSSION**

**Case characteristics**

Two patients were diagnosed with biliary stricture after liver transplantation. Both patients were treated immediately by percutaneous transhepatic biliary drainage combined with balloon dilatation. However, cholangiography revealed postoperative restenosis (Case 1 approximately 2 mo later, Case 2 approximately 5 mo later). Both patients underwent cutting balloon treatment with a good prognosis.

**Clinical diagnosis**

Case 1: Initial diagnosis was subacute fulminant hepatitis C complicated by post-orthotopic liver transplantation (OLT) anastomotic stenosis of the choledochal duct. Case 2: Initial diagnosis was hepatitis B virus-related end-stage cirrhosis associated with hepatocellular carcinoma, complicated by severe anastomotic stenosis of the choledochal duct.

**Differential diagnosis**

Biliary infection; hepatic insufficiency; ischemic cholangitis.

**Laboratory diagnosis**

Hyperbilirubinemia.
Imaging diagnosis
Case 1: Magnetic resonance cholangiopancreatography (MRCP) showed post-OLT anastomotic stenosis of the choledochal duct (Figure 2). Case 2: MRCP revealed severe anastomotic stenosis of the choledochal duct (Figure 8).

Pathological diagnosis
Case 1: Nodular cirrhosis associated with hepatocyte and capillary bile duct cholestasis (Figure 1). Case 2: Moderately differentiated hepatocellular carcinoma and peripheral hepatic tissues revealed nodular cirrhosis pathologic changes (Figure 7).

Treatment
Cutting balloon treatment with the aim of resolving anastomotic biliary stenosis.

Related reports
The safety and efficacy of cutting balloon treatment in vascular surgery has been widely reported. Hence, this technology has gradually been used to treat biliary or ureteral stenosis. In the few reports on post-OLT biliary stenosis, although the efficacy requires further clinical evidence, this technology shows huge potential according to the findings in the two cases reported.

Term explanation
Cutting balloon treatment and refractory anastomotic stenosis after OLT.

Experiences and lessons
Cutting balloon treatment may be an alternative therapy to endoscopic or surgical treatment.

Peer-review
The report provides clinical support for the safety and efficacy of cutting balloon treatment used in post-OLT refractory anastomotic stenosis.

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