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CASE REPORT

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

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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. 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

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.

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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 function showed the following results: AST 76 U/L, ALT 52 U/L, TBILI 90.8 μmol/L, DBILI 66.7 μmol/L, γ-glutamyl transpeptidase (GGT) 179.0 μmol/L and alkaline phosphatase (ALP) 315 μmol/L. Magnetic resonance cholangiopancreatography (MRCP) revealed post-OLT anastomotic stenosis of the choledochal duct, intra-hepatic bile duct dilation, and biliary sludge in the common hepatic duct and bilateral hepatic ducts; the patient was diagnosed with transplantation-related ischemic injury involving the biliary tract (Figure 2). On November 16, 2012, percutaneous transhepatic cholangial drainage (PTCD) was performed (Figure 3). Minor complications occurred during and after surgery, all of which were resolved following appropriate treatment and nursing. On January 15, 2013, re-examination by cholangiography showed that the anastomotic stenosis was reduced by nearly 20% (Figure 4); thus, we decided to remove the biliary drainage. One year later, the patient was referred to the Clinical Center again because of xanthochromia and pruritus. Clinical laboratory examination results were as follows: AST 129.0 U/L, ALT 42 U/L, TBILI 47.2 μmol/L, DBILI 35 μmol/L, GGT 755 μmol/L, and

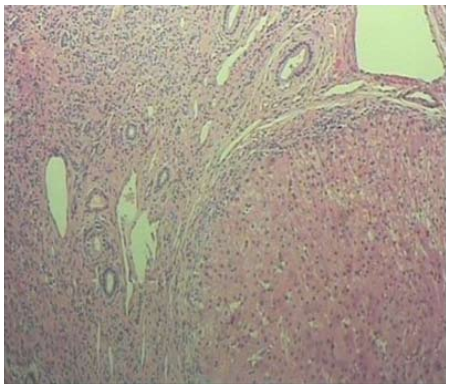

Figure 1 Postoperative pathology. Nodular cirrhosis associated with hepatocyte and capillary bile cholestasis.

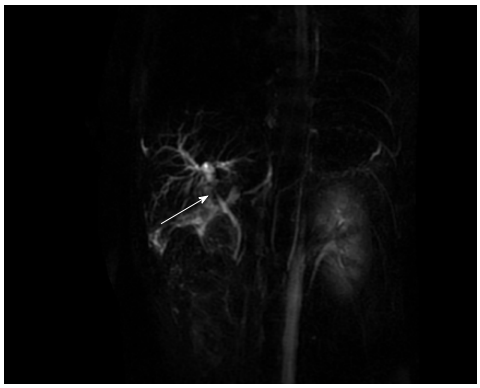

Figure 2 Magnetic resonance cholangiopancreatography findings. Post-orthotopic liver transplantation anastomotic stenosis of the choledochal duct, intra-hepatic bile duct dilation, and biliary sludge in the common hepatic duct and bilateral hepatic ducts; patient diagnosed with transplantation-related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

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.

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

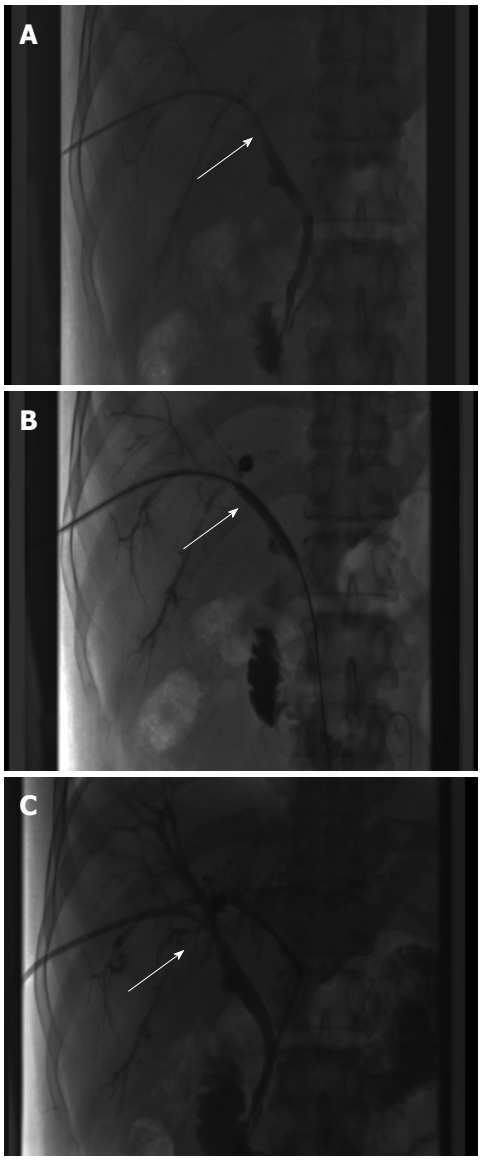

Figure 3 Percutaneous transhepatic cholangial drainage combined with balloon dilation. A: Anastomotic stenosis of the choledochal duct (straight arrow); B: The inflated balloon (diameter 8 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight arrow).

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

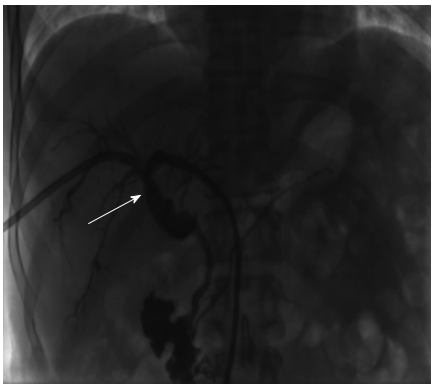

Figure 4 Cholangiography findings. The anastomotic stenosis was reduced by about 20 % (straight arrow).

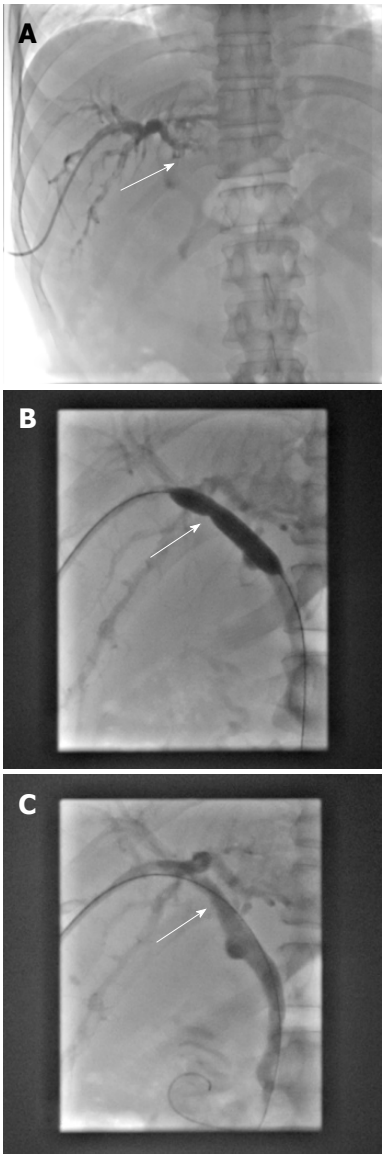

Figure 5 Cutting balloon therapy. A: Cholangiography showed the development of anastomotic stenosis (straight arrow); B: The inflated cutting balloon (diameter 6 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight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

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

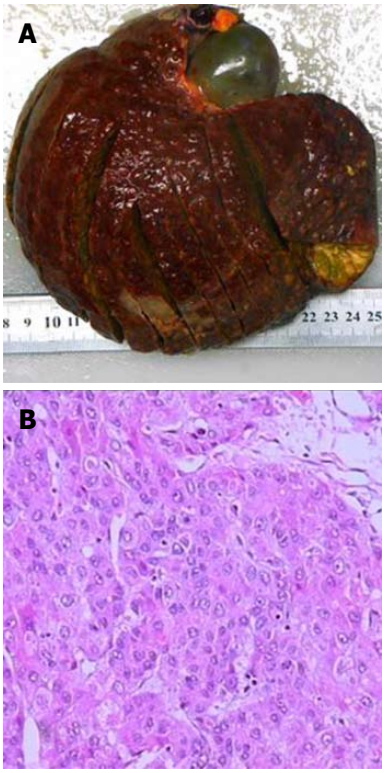

Figure 7 Postoperative pathology. A: Moderately differentiated hepatocellular carcinoma; B: Peripheral hepatic tissues revealed nodular cirrhosis pathologic changes.

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

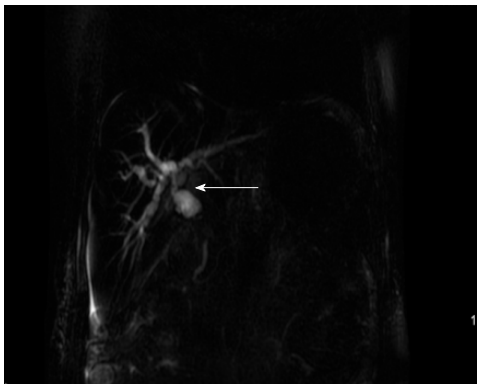

Figure 8 Magnetic resonance cholangiopancreatography findings. Severe anastomotic stenosis of the choledochal duct, severe choledochectasia involving the intrahepatic bile ducts and left-right hepatic bile ducts above the anastomotic stomas; Patient diagnosed with biliary anastomotic stenosis.

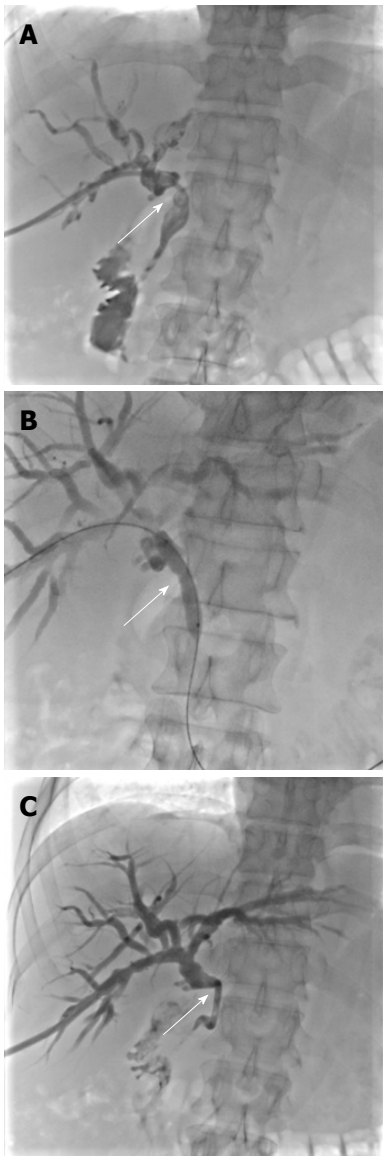

Figure 9 Percutaneous transhepatic cholangial drainage combined with balloon dilation. A: Severe anastomotic stenosis of the choledochal duct (straight arrow); B: The inflated balloon (diameter 8 mm, length 4 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the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

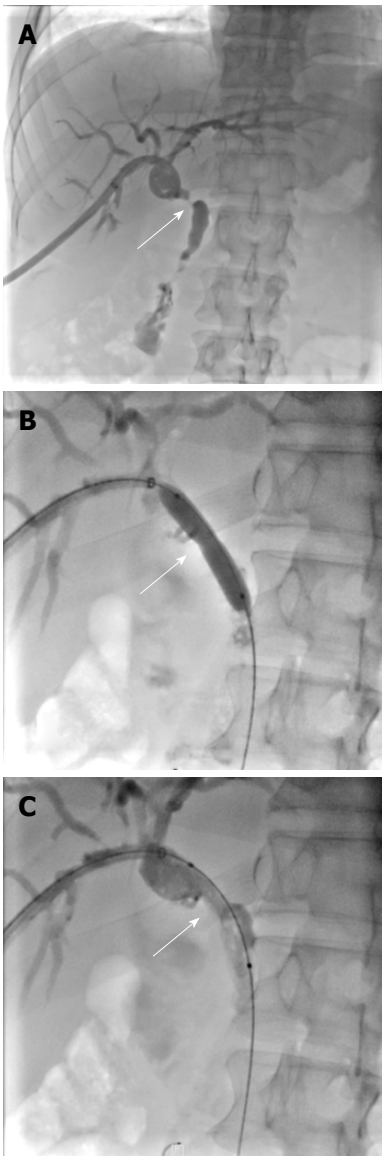

Figure 10 Cutting balloon therapy. A: Cholangiography showed that the anastomotic stenosis had resolved; B: The inflated cutting balloon (diameter 5 mm, length 2 cm) has a waist at the narrowest part of the stenosis (straight arrow); C: Resolution of the stenosis after balloon dilation (straight arrow).

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

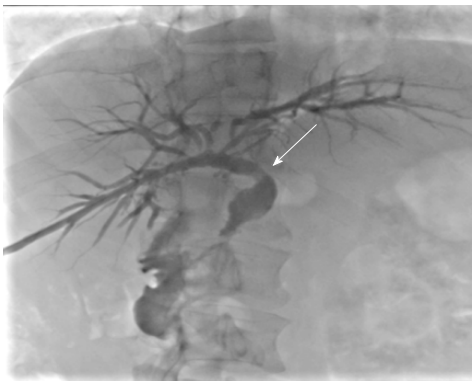

Figure 11 Cholangiography findings. The anastomotic stenosis was reduced by about 30% (straight arrow).

styptic measures, the prognosis was favorable. On March 10, 2015, cholangiography revealed that the anastomotic stenosis was reduced by 30% (Figure 11), and therefore biliary drainage was immediately removed. The clinical indicators gradually recovered and were maintained within the physiological range during the 10-mo follow-up period.

DISCUSSION

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[5,6]. 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[7-9].

Over the past two decades, with the development of technology and endoscopic treatment, the surgical management of biliary stenosis has undergone a rapid decline. Endoscopic treatment has the obvious advantage of high efficiency and a low incidence of procedure-related complications[10]. ERCP was first reported in 1968, and has been used for endoscopic visualization of the ampulla of Vater and minimally invasive cannulation of the pancreatic duct or biliary duct[11]. In 1974, Kawai *et al*[12] reported their clinical experience of endoscopic electrosurgical sphincterotomy of the ampulla of Vater to remove gallstones in the common bile duct. This new application in the field of surgical endoscopy was soon accepted as a safe, direct technique for evaluating biliary and pancreatic disease. ERCP has evolved from a diagnostic tool to an almost exclusively therapeutic technique[13]. While ERCP combined with balloon dilation or stent placement is generally effective for biliary stenosis after liver transplantation, uncertainties regarding the optimal therapy remain and can be seen in the variable outcomes described in previous reports of endoscopic treatment[14-17].

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

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[18]. 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[19]. 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[20,21]. 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.

COMMENTS

Case characteristics

Two patients were diagnosed with biliary stricture after liver transplantation. Both patients were treated immediately by percutaneous transhepatic cholangial 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 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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