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ORIGINAL ARTICLE

Surgical management of patients with post-cholecystectomy benign biliary stricture complicated by atrophy–hypertrophy complex of the liver

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Abstract

Background: Atrophy–hypertrophy complex (AHC) of the liver rarely complicates post-cholecystectomy benign biliary strictures (BBS). This study aimed to analyse the effect of AHC on the surgical management of patients with BBS.

Methods: Between 1989 and 2005, 362 patients underwent surgical repair for BBS at a tertiary referral centre in northern India. A total of 36 (10%) patients had AHC. Patients with AHC ($n = 36$) were compared with those without ($n = 336$) to define the factors associated with the development of AHC.

Results: Overall, 35 patients with AHC underwent Roux-en-Y hepaticojejunostomy; right hepatectomy was performed in one patient. The interval between bile duct injury and stricture repair did not influence the development of AHC (mean 24 months in AHC patients vs. 19 months in non-AHC patients; $P = 0.522$). Of the 36 patients with AHC, 26 (72%) had hilar strictures (Bismuth's types III, IV, V), as did 163 of the 326 (50%) patients without AHC ($P = 0.012$). Patients with AHC had more blood loss at surgery (mean blood loss 340 ml in the AHC group vs. 190 ml in the non-AHC group; $P = 0.004$) and required more blood transfusion (mean blood transfused 300 ml vs. 120 ml; $P = 0.001$). Surgery was prolonged in AHC patients (mean duration of operation 4.2 hours in the AHC group vs. 2.8 hours in the non-AHC group; $P = 0.001$). Over a mean follow-up of 43 months (range 6–163 months), three of 36 (8%) AHC patients required re-intervention for recurrent strictures, compared with nine of 326 (3%) non-AHC patients ($P = 0.006$).

Conclusions: Iatrogenic injury at the hepatic hilum predisposes for the development of AHC. Surgery is more difficult and blood transfusion requirements are higher in patients with AHC during surgical repair of BBS. Atrophy–hypertrophy complex is a risk factor for recurrent stricture formation after hepaticojejunostomy.

Keywords

bile duct injury, biliary stricture, hepaticojejunostomy, liver atrophy

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Introduction

Atrophy of the hemiliver or a segment is usually a sequel of vascular occlusion, especially of the portal vein, or of prolonged biliary obstruction. Atrophy of the hemiliver along with compensatory hyperplasia of the non-affected part, termed 'atrophy–hypertrophy complex' (AHC), causes rotation of the liver with the hilum as the axis. Patients who sustain bile duct injury (BDI) during cholecystectomy occasionally present with AHC along with benign biliary stricture (BBS) and the gross deformation of normal anatomical relations at the hepatic hilum adds to the difficulty of surgical repair of the post-cholecystectomy BBS in an

already injured, inflamed and scarred area. These difficulties may eventually affect the final outcome of BBS repair. As most vascular injuries go undetected and because atrophy develops within a few weeks following the injury, AHC may be fully established by the time the patient presents for repair of BBS. We have previously published our longterm results of surgical repair of BBS.[1] Here, we review our experience with surgical repair of BBS complicated by AHC.

Materials and methods

Between 1989 and 2005, 362 patients were operated for BBS at a tertiary care referral hospital in northern India. The details of these patients were maintained prospectively in a database. Patients referred immediately after BDI with bile leak underwent emergency non-surgical (endoscopic and/or percutaneous) interventions to drain bile collections or to control bile leak. Elective surgical repairs were delayed, usually for a minimum of 6 weeks. Patients with BBS who were definitively managed with endoscopic or percutaneous intervention were excluded from the study. Liver function tests (LFT) and ultrasonography (US) of the abdomen were performed in all patients before the surgical repair. Preoperative stricture evaluation was undertaken with percutaneous transhepatic cholangiography (PTC), magnetic resonance cholangiography (MRC) or endoscopic retrograde cholangiography (ERC). Strictures were classified according to Bismuth's types. Preoperative insertion of catheters into the biliary system was required in some patients with high biliary strictures and ductal separation, either in anticipation of difficulty in intraoperative ductal identification or as part of biliary drainage in patients with severe uncontrolled cholangitis.

Intraoperatively, the liver was inspected for atrophy, hypertrophy and cirrhosis. Atrophy was defined as a reduction of at least 50% in the size of a segment (segmental atrophy) or a hemiliver (hemiliver atrophy).[2] Tissue for liver biopsy was taken in patients with suspicion of cirrhosis. Roux-en-Y hepaticojejunostomy (RYHJ) with anastomosis extended to the left hepatic duct (Hepp–Couinaud approach) was the standard surgical procedure. Anastomosis was stented in selected patients depending upon the stricture type, ductal diameter, technical difficulty at operation and the anticipated need for future percutaneous intervention.

Follow-up information was collected by outpatient visits, postal questionnaires and telephone interviews. Follow-up evaluation was carried out by investigating the clinical history, physical examination, LFT and US. Mebrofenin nuclear scintigraphy was performed to demonstrate the patency of bilio-enteric anastomosis in the presence of abnormal LFT or US findings. Cholangiography (PTC or MRC) was undertaken if there was biliary dilatation on US or delayed clearance and pooling of the radioactivity above the anastomosis on Mebrofenin scan. Those who had demonstrable stricture of the hepaticojejunostomy on cholangiography were offered re-intervention. The outcome of the surgical repair was graded as per the categories suggested by McDonald and colleagues,[3] where: grade A = asymptomatic, normal LFT; grade B = asymptomatic, mild LFT derangement or occasional episodes of pain or fever; grade C = pain, cholangitis defined as fever with jaundice and abnormal LFT, and D = surgical revision or dilatation required. Patients with McDonald grades A and B were classified as treatment successes and those with grades C and D were classified as treatment failures.

Detailed analysis of patients who had AHC along with BBS was performed retrospectively. In an attempt to identify the differences between patients with and without AHC, various factors were compared using univariate analysis. Chi-square test, Fisher's exact test or Student's *t*-test were used for univariate analysis as appropriate.

Results

The 362 patients included 303 (84%) males and 59 (16%) females with a median age of 37 years (range 10–70 years). Patients were referred after injuries sustained during laparoscopic cholecystectomy in 52 (14%) cases and during open cholecystectomy in 310 (86%). In 13 patients, the laparoscopic procedure had been converted to an open procedure once the BDI had been detected. A total of 88 (24%) patients had undergone emergency re-explorations before they were referred to our centre, mainly to control bile extravasation. By the time patients were referred, 15 (4%) had cirrhosis and 13 (4%) had portal hypertension. A total of 142 (39 %) patients were referred to our department after ERC. Percutaneous transhepatic cholangiography was performed in 174 (48%) patients and MRC in 89 (25%) patients. Fifty (14%) patients had undergone preoperative biliary drainage to control cholangitis that was unresponsive to antibiotics. Stricture types were type I in 37 (10%), type II in 137 (38%), type III in 148 (41%), type IV in 24 (7%) and type V in 16 (4%) patients.

Thirty-six of 362 (10%) patients with BBS were found to have AHC at operation. In 12 patients, preoperative US or cholangiography could not detect AHC although it was evident at operation. A total of 33 (91%) patients had right hemiliver atrophy and left hemiliver hypertrophy. Two patients had left hemiliver atrophy and another had isolated atrophy of segment 4. These 36 patients with AHC were referred to us after a median delay of 7 months (range 7 weeks to 16 years) after the BDI. Six (17%) patients had sustained injuries during laparoscopic cholecystectomy and the remaining 30 (83%) during open cholecystectomy. Nine patients had undergone re-exploration for bile extravasation, four had undergone attempted primary repair of the BDI and two had undergone stricture repair at a later date before referral to us. Four (11%) patients had Bismuth's type I, six (17%) had type II, 20 (56%) had type III and six (17%) had type IV strictures. Five (14%) patients required percutaneous transhepatic biliary drainage (PTBD) before operation to control cholangitis. Two patients had portal hypertension. Sixteen (44%) patients had spontaneous internal fistula to the duodenum. Fifteen (42%) patients underwent preoperative percutaneous

transhepatic catheterization into the ductal system in order to identify the ducts at operation.

A total of 34 patients underwent RYHJ; in one patient, two separate stomas were created during HJ and three separate stomas were required in another patient to drain the left, the right anterior and the right posterior ducts. In one patient, right hepatectomy was performed because of the severe atrophy of the right hemiliver and extension of the stricture into the segmental branches on the right side. Another patient with right hemiliver atrophy, operated in the earlier part of the period covered by this study, underwent HJ to the left duct and a porto-enterostomy to the right hemiliver (Table 1). Nine (25%) patients required stenting of the anastomosis because of difficulties during surgery and the anticipated need for future intervention. Mean blood loss was 340 ml (range 50–2500 ml) and mean blood transfusion requirement was 300 ml (range 0–2700 ml). The mean duration of the operation was 4.2 hours (range 3.0–9.9 hours). Liver biopsy revealed cirrhosis in six patients, fibrosis in four, cholangiohepatitis in five and zonal necrosis in one. Overall, 15 (42%) patients had postoperative complications. Two (6%) patients had anastomotic leak, which spontaneously resolved in both. There was no mortality.

Patients were followed for a median of 61 months (range 24–164 months) after stricture repair. Two patients were lost to follow-up. Three (8%) patients developed recurrent stricture during follow-up (McDonald's grade D). Right hepatectomy was performed after 6 years in the patient who underwent left HJ and right porto-enterostomy because of recurrent cholangitis and biliary dilatation in the right hemiliver. Percutaneous transhepatic biliary dilatation of the recurrent stricture was performed in another patient 12 months after HJ. Both these patients were doing well at last follow-up 6 and 5 years after re-intervention, respectively. The third patient, who was initially operated for a type III BBS, developed a recurrent BBS (type IV) 7 years later, but refused to undergo a planned balloon dilatation of the stricture. Among the six patients who had cirrhosis on liver biopsy, one was lost to follow-up, three had gradually deteriorating liver function and two had stable liver function at 7 and 2 years follow-up, respectively. A summary of the outcome in patients with BBS complicated by AHC is given in Table 2.

Associations between AHC and various preoperative, intraoperative and postoperative factors were analysed. Patients with AHC ($n = 36$) were compared with those without AHC ($n = 326$). The results are given in Table 3.

Table 1 Management of patients with benign biliary stricture complicated by atrophy–hypertrophy complex of the liver

BBS and AHC	$n = 36$
RYHJ	34
Right hepatectomy	1
RYHJ + portoenterostomy	1

BBS, benign biliary stricture; AHC, atrophy–hypertrophy complex; RYHJ, Roux-en-Y hepaticojejunostomy

Table 2 Outcome after surgical management in patients with benign biliary stricture (BBS) complicated by atrophy–hypertrophy complex (AHC) of the liver

BBS and AHC	$n = 36$
Successful outcome	27 (75%)
Recurrent cholangitis on medical therapy	1 (3%)
Progressive cirrhosis	3 (8%)
Right hepatectomy for re-stricture	1 (3%)
Balloon dilatation for re-stricture	1 (3%)
Refused intervention for re-stricture	1 (3%)
Lost to follow-up	2 (6%)

Discussion

Bile duct injury is a serious sequel of cholecystectomy and its incidence is increasing as laparoscopic cholecystectomy becomes more and more common. Centres which have sufficient

Table 3 Factors associated with atrophy–hypertrophy complex (AHC) of the liver in patients with post-cholecystectomy benign biliary stricture (BBS)

Factor	AHC ($n = 36$)	No AHC ($n = 326$)	P-value
History of laparoscopic cholecystectomy	6 (17%)	46 (14%)	0.837
History of attempted stricture repair	6 (17%)	47 (14%)	0.723
Mean cholecystectomy–stricture repair interval, months	24	19	0.517
High strictures (Bismuth types III, IV, V)	26 (72%)	163 (50%)	0.012*
Mean blood loss at operation, ml	340	190	0.004*
Mean blood transfusion, ml	300	120	0.001*
Mean duration of operation, hours	4.2	2.8	0.000*
Cirrhosis	6 (17%)	13 (4%)	0.001*
Postoperative morbidity	15 (42%)	110 (34%)	0.303
Re-stricture	3 (8%)	9 (3%)	0.006*

*Significant at $P < 0.05$

experience in the management of patients with BDI report success rates of >90% following surgical repair of BDI and BBS.[1,4] Bile duct injury is often associated with vascular injury.[5] In a study by Hatakeyama *et al.*[6] regarding the regional and general effects of hemilivers with impaired blood flow, hepatic artery ligation alone showed no obvious changes in either ligated or non-ligated hemilivers, whereas portal vein ligation resulted in atrophy–hypertrophy. Most vascular injuries associated with BDI are hepatic arterial injuries. Portal vein injury during cholecystectomy is less common. Even partial occlusion of the portal vein is enough to cause atrophy.[7] Prolonged hemiliver or segmental bile duct obstruction can also result in atrophy. Post-cholecystectomy BBS heads the list of benign causes, with an incidence of atrophy of 10–15%.[8] A total of 10% of our patients with BBS had AHC.

The mechanism by which AHC develops is poorly understood. Portal blood flow controls the hepatocyte size through hepatotrophic factors. In portal vein occlusion, gross atrophy occurs as a result of decreased cytoplasmic mass. An alternative mechanism is postulated for the atrophy, resulting from prolonged biliary obstruction. Hadjis *et al.* reported that the development of atrophy consequent to biliary obstruction is probably the result of the destruction of whole cells rather than cytoplasmic mass.[9] In the series reported by Fansto *et al.*,[10] the shortest interval reported between BDI and atrophy detection was 1 year, but we have noticed atrophy as early as 7 weeks after cholecystectomy. Gross atrophy and proportional hypertrophy can be observed as early as 2 weeks after preoperative portal vein embolization for liver resection.[11]

Awareness of AHC is required to enable its detection, both preoperatively and at operation. Ultrasonography can detect the presence of atrophy. Contrast-enhanced computer tomography (CT) and nuclear scintigraphy are valuable non-invasive means of diagnosing atrophy,[12] which may also be detected by MRC or PTC.[13] In patients with post-cholecystectomy BBS, absence of the gall bladder (which is used to differentiate between the right and left hemilivers) may make the diagnosis of AHC difficult on cross-sectional imaging such as contrast-enhanced CT.

An association between high biliary injury and AHC has been reported in the literature.[14] Three-quarters of our patients with AHC had high BBS. None of our patients with AHC had an isolated sectoral duct injury. It is not our routine practice to perform vascular evaluation in patients with BBS before surgical repair and therefore we could not assess the exact incidence of vascular injury in these patients. Performance of a high bilio-enteric anastomosis is difficult in patients with AHC. Right hemiliver atrophy causes rotation of the hepatic hilum in an anti-clockwise manner, with displacement of the bile duct posteriorly and the portal vein anteriorly. In addition, the entire hilum is pulled upwards. Hypertrophied segment 4 overhangs, thus masking the hilum, which further complicates access for repair. Identification of the healthy proximal bile ducts may be extremely difficult in these situations. Preoperative insertion of catheters by a percutaneous transhepatic route helped us to identify the ducts intraoperatively in half our patients. Crowding and distortion of the intrahepatic biliary radicles consequent to atrophy may cause difficulty for the interventional radiologist during transhepatic puncture. The duration of operation was significantly longer in our patients with AHC compared with those without, and blood loss and blood transfusion requirements were also increased (Table 3).

Secondary biliary cirrhosis was present in 19 of 362 (5%) of our patients with BBS, six of whom also had associated AHC. The histopathological feature of biliary atrophy has been previously described. Loss of hepatocytes and a reduction in their overall

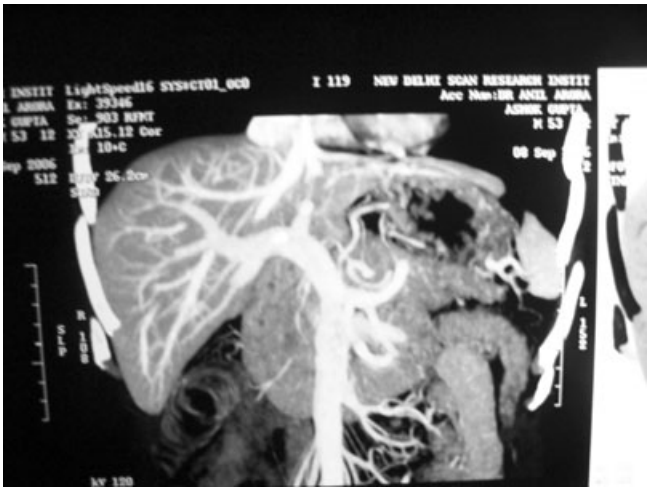

Figure 1 CT portography of a patient with left hepatic duct stricture showing left portal vein occlusion and an atrophied left hemiliver

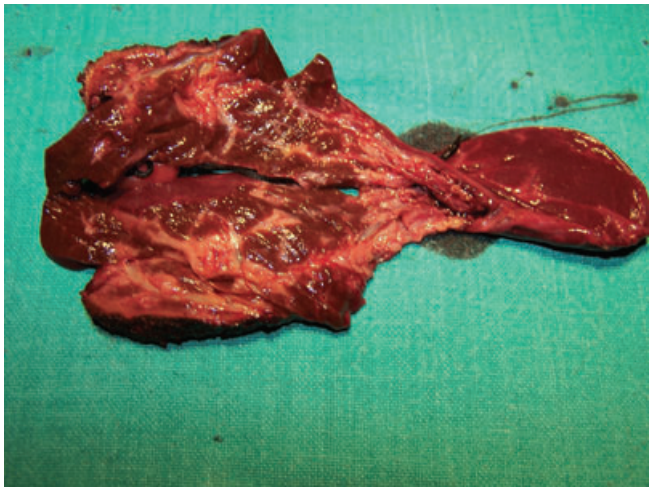

Figure 2 Left hepatectomy specimen of the same patient as shown in figure 1

number together with fibrosis rather than hepatocyte atrophy is the feature commonly observed.[9] Our patients exhibited a varied picture on histopathology.

The optimal management of patients with AHC associated with BBS is controversial. Most patients present with cholangitis and major centres have resorted to a combined radiological and surgical approach.[14] Expectant management with antibiotics is advised by some authors in patients with unilateral hepatic duct obstruction with atrophy, provided that the contralateral hemiliver functions normally.[10]

In patients with BBS, AHC may be caused by more than one factor. In our experience, the majority of AHC was seen in patients with bile duct obstruction to both hemilivers. Hidden vascular injury to the affected hemiliver may be sought in these patients. The extent of biliary obstruction to each hemiliver may also play a role in the disproportional unilateral atrophy. Secondary biliary cirrhosis can also contribute to the atrophy. In patients with BBS and AHC, the clinical picture of recurrent jaundice and cholangitis may partly reflect inadequate draining of ducts in the atrophied hemiliver. We resorted to right hepatectomy in two patients as Mebrofenin scintigraphy showed pooling of the activity and delayed excretion in the atrophied hemiliver. Both these patients presented with recurrent cholangitis and the strictures in both extended to the subsegmental systems. It is our policy to perform drainage even in the atrophied hemiliver if an adequate duct to mucosa biliary-enteric anastomosis can be achieved and we advise hemihepatectomy if anastomosis is not possible in the atrophied hemiliver (Figs 1 and 2). Although it has been suggested that the relief of segmental biliary obstruction does not reverse atrophy and the affected hemiliver continues to atrophy[10] even in the absence of obstruction, we think that undrained dilated segmental ducts in the atrophied hemiliver may cause problems in the future. A significant proportion of patients with AHC and secondary biliary cirrhosis may improve after adequate biliary decompression, as we saw in three of six patients.

Awareness of AHC in patients with BBS increases the proportion of cases detected. Biliary surgeons must be aware that the atrophied hemiliver may contribute to the patient's symptoms. Atrophied hemiliver must be drained to relieve cholangitis. Atrophy–hypertrophy complex is a risk factor for failure of surgical repair of BBS. Hemihepatectomy may be required in selected patients presenting with cholangitis if adequate drainage of the atrophied hemiliver is not possible.

Conflicts of interest

None declared.

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