Multidisciplinary approach in the long-term management of intrahepatic stones: Indian experience

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Background: Intrahepatic stones, though common in East Asia, are uncommon in India. There is paucity of data from India regarding the treatment and long-term outcome of patients with intrahepatic stones.

Methods: We retrospectively analyzed medical records of 35 patients with intrahepatic stones who had been treated surgically. Endoscopic biliary drainage had been used in patients who presented with acute cholangitis. Intraoperative stone clearance was confirmed by choledochoscopy and intraoperative cholangiography. Outcome of surgery, frequency and subsequent management of recurrent intrahepatic stones, and factors associated with stone recurrence and cholangitis were analyzed.

Results: Twenty-one (60%) patients had bilobar disease. Eight patients underwent hepatectomy and 16 hepatico-jejunostomy with access loop; 12 of these were jejuno-duodenal anastomoses. Postoperative morbidity was observed in 10 patients (29%). Recurrence of stones occurred in 12 patients (34%) and cholangitis in 9 patients (26%). Presence of bilobar disease and associated biliary strictures were associated with recurrent cholangitis (p<0.05). Two patients (6%) required re-operation for recurrent cholangitis. Complete removal of recurrent stones using conventional endoscope was possible through jejuno-duodenostomy in all 5 cases who had this type of access loop construction.

Conclusion: Surgical treatment for intrahepatic stones depends on the site of involvement. Construction of a jejuno-duodenal access loop in patients with bilobar disease and intrahepatic strictures is helpful in facilitating postoperative stone clearance. A multidisciplinary approach is beneficial especially when the disease is bilobar and recurrent in type. [Indian J Gastroenterol 2004;23:209-213]

Key words: Access loop, hepaticojejunostomy, recurrent pyogenic cholangitis

Intrahepatic stones are defined as calculi or concretions located proximal to the confluence of the right and left hepatic ducts. This disease is widely prevalent in East and Southeast Asian countries. It is infrequent in the Western population and India. Khuroo et al reported a close relationship between biliary ascariasis and recurrent pyogenic cholangitis from the Kashmir Valley in northern India. The first report from India of intrahepatic stones unassociated with biliary ascariasis was in 1988.

The factors responsible for intrahepatic stones are not exactly known, although recurrent bacterial infection, parasitic infestation, ethnic background, and stasis due to congenital abnormalities of the biliary tract have been postulated. Patients with intrahepatic stones usually present with recurrent cholangitis, sepsis and intrahepatic abscesses, and may develop liver atrophy and secondary biliary cirrhosis. The disease may progress to epithelial dysplasia and cholangiocarcinoma in 3%-8% of cases.

The main aim of treatment is to prevent liver damage by early clearance of stones and elimination of bile stasis. The principal approaches are surgical exploration of bile duct and intrahepatic ducts, hepatic resection, and percutaneous transhepatic cholangioscopic lithotomoy (PTSCL). The success rates with these range from 72% to 92%. However, recurrent stones and cholangitis are common, with frequency of 30%-35% after surgery, 31%-40% after PTSCL, and 50%-100% after PTSCL in patients with biliary strictures.

We reviewed our institution’s experience in the management of intrahepatic stones.

Methods

Between 1993 and September 2001, 35 patients with intrahepatic stones underwent surgical treatment at our center that treats around 50 cases of choledocholithiasis annually, with a large majority undergoing endoscopic extraction. All patients were residents of Kerala. Demographic data, details of operative findings, type of surgical procedure performed, follow up details, and treatment of recurrent cholangitis were analyzed retrospectively. Only cases with predominant intrahepatic calculi were included; those with associated extensive extrahepatic bile duct calculi or secondary biliary cirrhosis were excluded.

The patients’ demographic data and preoperative parameters are shown in Table 1. The diagnosis was based on clinical picture and imaging data (ultrasonography, CT scan and ERCP). Magnetic resonance cholangiography was performed in 4 selected cases during the
latter part of the study. Thirteen patients (37%) presented with cholangitis. The other presenting features were abdominal pain (n=33), recurrent fever (29), obstructive jaundice (15) and hepatomegaly (4).

Patients who presented with cholangitis were managed initially with intravenous antibiotic therapy and supportive care. They then underwent endoscopic biliary stent or nasobiliary catheter placement after attempted stone extraction. A mean of 1.8 ERCP sessions for attempted stone clearance had been performed in these patients. Surgery was done if the ERCP failed to clear stones and cholangitis persisted.

Nine patients had previously undergone some type of surgery prior to a definitive procedure. These included cholecystectomy in 4 patients, bile duct exploration and choledocho-duodenostomy in 2 cases, cholecystectomy and hepaticotomy (division of parenchyma to expose intrahepatic ducts) for stone removal in one, and bile duct exploration and T-tube drainage in one case. One patient had undergone seven interventions before the definitive procedure; these included bile duct explorations, transhepatic stone removal, and stone removal through T-tube tracts.

Surgical treatment

The first step was cholecystectomy, unless the gall bladder had already been removed, followed by bile duct exploration. Choledochotomy was sited close to the biliary confluence to allow easy extension to one or both hepatic ducts depending on the predominant location of the stones. Intrahepatic stones were removed using Desjardin’s forceps, saline flushing, and balloon extraction or metallic wire basketing. Stone clearance was confirmed using intraoperative choledochoscopy (CHF T20; Olympus, Tokyo, Japan), which was done in selected cases as per the surgeon’s discretion.

The nature of definitive surgery was guided by the presence or absence of the following factors: extrahepatic biliary ductal dilatation, intrahepatic strictures, unilobar or bilobar disease, atrophy of the entire liver or a liver lobe, and portal hypertension. Resection of the involved portion of the liver was chosen if the disease was unilobar and the liver atrophic. In patients with gross extrahepatic biliary dilatation and no strictures at or above the liver hilum, choledoco-duodenostomy was done. Roux-en-Y hepatico-jejunostomy was done in cases with bilobar disease without extrahepatic biliary dilatation. An access loop procedure was used when strictures or numerous stones made complete stone clearance difficult. In all, 16 patients underwent biliary access procedures. These included two patients with hepaticocutaneous jejunostomy, two with interposition of vascularised jejunal segment between hilum and duodenum, and 12 with in-continuity side-to-side jejunoo-duodenal access loops (JDA) in the descending limb of the Roux loop used for hepatico-jejunostomy. In the latter part of the study period, hepatico-jejunostomy with JDA was preferred in patients with bilobar disease, since it permitted easy access to intrahepatic ducts using conventional forward-viewing endoscope.

Follow-up and study end point

Patients were reviewed 6 weeks after surgery, at 3-month intervals thereafter for the first year, and at 6-month intervals thereafter, unless they became symptomatic. Liver biochemistry and ultrasonography were done during the first follow-up visit to detect residual stones. All patients who underwent jejuno-duodenal access loop construction underwent a check endoscopy using forward-viewing endoscopes to assess the feasibility of access of intrahepatic ducts at 6 weeks after the surgery. The mean follow up was 46 months. The end point of the study was the development of recurrent cholangitis; this was defined as the occurrence of two separate episodes of clinical and biochemical features of cholangitis during the postoperative period. Patients with recurrent cholangitis were managed with antibiotics, ursodeoxycholic acid and endoscopic stone extraction through an access loop, if present. Intervention was chosen only if recurrent stones caused symptoms such as cholangitis.

Statistical analysis

Univariate analysis was performed using the chi square test or the Mann-Whitney U test as appropriate. Ten clinicopathological variables were stratified and analyzed to identify factors associated with recurrent cholangitis.

Results

Surgical procedures and immediate complications

Eight patients (23%) underwent hepatic resection along with other biliary drainage procedures. Of these, two underwent common bile duct exploration (normal remnant liver ducts), one had choledoco-duodenostomy, and five had hepatico-jejunostomy. Access loops for
upper gastrointestinal access were constructed for 16 patients along with hepatico-jejunostomy. The surgical procedures could be divided into four groups according to the type of biliary drainage procedure used, viz., common bile duct exploration (n=2), choledochoduodenostomy (6), hepaticojejunostomy (11) and hepaticojejunostomy with access loop construction (16). No patient required emergency surgery. The mean operation time, including that for cholangiography and choledochoscopy, was 6.2 hours and mean blood loss was 420 mL.

A positive bile culture was obtained in 32 (91%) cases. The cultured organisms were *Escherichia coli* in 12 patients (38%), *Klebsiella* in 9 (28%), pseudomonas species in 7 (22%), and multiple organisms in 4 (13%) patients. Wound infection was the commonest complication, occurring in 15 (43%) patients; in 6 patients, it was severe, requiring prolongation of hospital stay. Pulmonary complications occurred in 7 (20%) patients, and intra-abdominal collections in 5 (14%) patients; 3 (8%) patients had biliary leak that responded to conservative treatment. Postoperative morbidity was observed in 9 patients (26%). One patient (3%) died of postoperative pulmonary embolism. There were no specific complications attributable to the construction of the access loop.

**Long-term follow up and treatment of recurrent cholangitis**

In patients who had a hepaticocutaneous stoma, access to the intrahepatic biliary system was easily achieved under radiological control. It was difficult in those who had interposition of jejunal segment; this was due to redundancy of the jejunal segment, resulting in failure to negotiate the endoscope to the hepatic hilus. Endoscopic access to the hepaticojejunostomy and intrahepatic ducts, using the forward-viewing endoscope, was possible in all 12 patients after JDA.

Residual stones were observed in 12 (34%) patients. Recurrent cholangitis occurred in 9 (26%) patients; it occurred in one patient after common bile duct exploration, 1 patient after choledocho-duodenostomy, 2 patients following previous hepatico-jejunostomy, and 5 patients after hepatico-jejunostomy with access loop construction. Recurrence of cholangitis occurred at a mean period of 11 months after the initial surgical procedure, was always associated with recurrent stones, and required 2.25 hospital admissions per patient.

Five patients who had JDA underwent endoscopic stone clearance (Table 2). Six endoscopy sessions (1.2 procedures per patient) were required to remove intrahepatic stones. All these patients are asymptomatic on long-term follow up (mean 46 months). Two patients who had hepatico-jejunostomy required re-operation due to obstruction of hepatico-jejunostomy by recurrent stones; in these cases, stones were cleared and jejuno-duodenal anastomosis constructed. Both patients remain symptom-free at the end of the study. The patient who had choledocho-duodenostomy had endoscopic stone clearance through the anastomosis. Another patient with recurrent symptoms was advised long-term antibiotics and ursodeoxycholic acid prophylaxis as he was unwilling for re-operation.

**Factors associated with recurrent cholangitis**

Presence of bilobar disease and intrahepatic strictures were associated with recurrent cholangitis (Table 3). Recurrence of cholangitis was observed in only one of 14 patients (7%) with unilateral disease, and in 8 of 21 (38%) patients with bilobar disease (p<0.05). Intrahepatic strictures were observed in 67% of cases with recurrent cholangitis. Hyperbilirubinemia, presence of extrahaepatic bile duct stones, liver atrophy and hepatic resection were not related to development of recurrent cholangitis.

Four patients (13%) required re-operation. In two, hepatico-jejunostomy stoma was obstructed by recur-

### Table 2: Details of patients who had recurrent cholangitis and their management

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>Disease</th>
<th>Surgery</th>
<th>Recurrent cholangitis (months)</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 F</td>
<td>Bilobar</td>
<td>HJ-JDA</td>
<td>9</td>
<td>Endoscopic clearance</td>
</tr>
<tr>
<td>32 M</td>
<td>Bilobar</td>
<td>HJ-JDA</td>
<td>10</td>
<td>Endoscopic clearance</td>
</tr>
<tr>
<td>31 M</td>
<td>Bilobar</td>
<td>HJ</td>
<td>8</td>
<td>Revision HJ-JDA</td>
</tr>
<tr>
<td>29 F</td>
<td>Bilobar</td>
<td>CDD</td>
<td>21</td>
<td>Endoscopic clearance</td>
</tr>
<tr>
<td>34 F</td>
<td>Bilobar</td>
<td>CBD clearance</td>
<td>6</td>
<td>Antibiotics, UDCA</td>
</tr>
<tr>
<td>36 F</td>
<td>Unilobar</td>
<td>H-HJ-JDA</td>
<td>14</td>
<td>Endoscopic clearance</td>
</tr>
<tr>
<td>34 M</td>
<td>Bilobar</td>
<td>HJ</td>
<td>12</td>
<td>Revision HJ-JDA</td>
</tr>
<tr>
<td>27 F</td>
<td>Bilobar</td>
<td>H-HJ-JDA</td>
<td>11</td>
<td>Endoscopic clearance</td>
</tr>
<tr>
<td>37 M</td>
<td>Bilobar</td>
<td>H-JJ-JDA</td>
<td>8</td>
<td>Endoscopic clearance</td>
</tr>
</tbody>
</table>

IHJ-JDA: hepatico-jejunostomy with jejuno-duodenal access loop; CDD: choledocho-duodenostomy; HJ: hepatico-jejunostomy, H-HJ-JDA: hepatectomy with hepatico-jejunostomy and access loop; UDCA: ursodeoxycholic acid

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### Table 3: Univariate analyses of clinicopathological variables associated with recurrent cholangitis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Asymptomatic (n=26)</th>
<th>Recurrent cholangitis (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male:female)</td>
<td>9:17</td>
<td>4:5</td>
</tr>
<tr>
<td>Dilated bile duct</td>
<td>12 (46%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>Common bile duct calculi</td>
<td>13 (5%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>Non-visualization of IHBR on ERCP</td>
<td>4 (15%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>13 (50%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Atrophy of liver</td>
<td>6 (23%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Bilobar disease*</td>
<td>12 (46%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Associated intrahepatic strictures**</td>
<td>4 (15%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Hepatic resection</td>
<td>6 (23%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Access loop</td>
<td>10 (39%)</td>
<td>6 (67%)</td>
</tr>
</tbody>
</table>

p*<0.05, **<0.01

IHBR: intrahepatic biliary radicles
rent stones; in them, an incision was made in the Roux loop 5-7 cm below the stoma, stones were cleared, and the opening in the Roux loop was anastomosed to the side of the duodenum to achieve a JDA. The other two required surgical intervention for closure of previously created hepaticocutaneous stoma. These patients had complained of troublesome discharge of bile and skin excoriation prior to closure of the access stoma.

Discussion
Treatment of intrahepatic stones is difficult and the disease progresses in most patients even after adequate treatment.4,11 The experience from India is limited and long-term results of surgical treatment of this disease are not available.8,9,10 The major approaches to intrahepatic stones are: hepatic resection,18 exploration of bile duct and intrahepatic ducts for stone removal with biliary drainage or hepatico-jejunostomy (with or without access loop construction), and percutaneous treatment. However, selection of cases for individual treatment modalities is often difficult. Bilobar disease, presence of multiple intrahepatic strictures, presence of atrophy-hypertrophy complex, and secondary biliary cirrhosis are responsible for poor results.5,19

Hepatic resection constitutes definitive treatment in patients with intrahepatic calculi confined to one lobe of the liver. It removes not only calculi, but also associated lesions like bile duct strictures, periductal fibrosis, intrahepatic abscesses, and occasionally cholangiocarcinoma.1,5,12 It is particularly useful when the stones lie proximal to an intrahepatic stricture.12,14 However, this technique is not applicable to patients with bilobar disease and its use in livers without atrophic changes remains controversial.3,5

Hepatic resection is also used in cases where strictures involve predominantly one lobe and a bilio-enteric anastomosis is constructed at the confluence to allow drainage of the opposite lobe. In selected cases with bilobar stones, left hepatectomy and prolonged stenting of the right-sided strictures has yielded good results.5,14 However, such an approach may require placement of multiple tubes in the liver as tracts for stone removal, which may need to be retained for 6-12 months or even longer,7,6 and multiple treatment sessions (up to 20). Similarly, bilobar hepatolithiasis may be treated with hepatic resection and postoperative cholangioscopic removal with a clearance rate of 84%.18

In our series, hepatic resection with hepatico-jejunostomy was performed only for patients with predominant unilobar disease associated with atrophy. Seventy-five percent of the cases that underwent hepatic resection remain symptom-free. There was significant association between recurrent cholangitis and bilobar disease and intrahepatic strictures. Fourteen patients (40%) had predominant unilateral disease and 7 patients among them underwent hepatectomy. Recurrence of cholangitis was seen in only one patient (7%) with unilateral disease, whereas 8 of 21 patients (38%) with bilobar disease developed recurrent cholangitis (p<0.05). Our experience with hepatic resection for bilobar disease is limited. Our policy in such patients is to perform dilatation of strictures followed by stone clearance and construction of hepatico-jejunostomy with a JDA for biliary interventions in future, should patients develop cholangitis.

PTSCL is being increasingly used with the advent of the four-angled choledochoscope.11 It has the advantage of providing a tract for repeated access to the biliary system for management of recurrent stones. Our experience with PTSCL was limited to two patients. In a long-term follow-up study, Jan et al15 compared patients who had percutaneous treatment with those who underwent surgery; though the stone clearance rates were similar (85.6% and 83.3%, respectively), 22.5% of those who had PTSCL required surgical intervention.

The factors responsible for the failure of PTSCL were bilobar strictures, multiple right hepatic duct strictures, intrahepatic angulations, and variations in the drainage of the right posterior sectoral duct. These factors are also associated with failure of treatment and recurrent cholangitis with other treatment modalities.5,14 Moreover, Lee et al13 recently reported stone clearance as being significantly lower (58% versus 85%) and recurrence rates higher (100% versus 28%) in those with severe strictures as compared to mild and moderate strictures. This has been the experience in other series too.5,16 Jeng et al20 also reported severe pain in 14%, bleeding in 14%, and a failure rate of 22% in patients undergoing PTSCL. Therefore PTSCL has limitations as the sole therapeutic modality and is the most useful as an adjunct to surgery.

Stone recurrence and recurrent cholangitis occur more commonly in patients with intrahepatic duct strictures. Jan and Chen16 reported residual or recurrent stones in 20.5% of patients with strictures as compared to no stones in those without stricture. Various techniques have been used for postoperative access of biliary system in the treatment of recurrent stone with cholangitis.21-25 Postoperative cholangioscopic removal of stones through a T-tube tract was popular earlier; however Cheung et al21 reported poor overall success rate (50%) and technical difficulties like inaccessibility of the ducts, failed manipulation due to strictures, losing the tract during dilatation, and difficulties in extracting large stones. Permanent-access loop hepatico-jejunostomy, either as a stoma22 or as a subparietal access loop23 where the closed end of the Roux limb is kept subcutaneously, has also been widely used. Clearance
of intrahepatic residual stones is performed under radiological control and success rates are good in units that utilize this method routinely.22,23 Similarly, the end of the Roux loop has been anastomosed to the duodenum or stomach for endoscopic access to the biliary system.24,25

Our experience with modified JDA17 was excellent. It was possible to access the intrahepatic system in all the patients during check endoscopy. Five patients who underwent JDA and developed recurrent stones/cholangitis needed 1.2 endoscopic sessions per patient for stone removal and hospitalization for a mean of 2.3 days for treatment of recurrent cholangitis. Both these techniques – percutaneous access hepatico-jejunostomy or endoscopic access hepatico-jejunalstomy – are effective for repeated access of the intrahepatic biliary system, and the choice of a particular approach may depend on the available expertise (radiology or endoscopy). In any case, selection of a judicious combination of therapeutic options according to the site of involvement has been shown to improve results.6,18

In conclusion, patients with intrahepatic stones need individualized treatment according to the site of involvement and location of intrahepatic strictures. In patients with bilobar disease and multiple intrahepatic strictures, no single treatment modality suffices, and long-term management of such patients requires a multidisciplinary approach including surgical, endoscopic and interventional radiological techniques.

References