Liver Resection for Primary Intrahepatic Stones

A Single-Center Experience

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Hypothesis: Primary intrahepatic lithiasis occurs frequently in East Asia but is rare in Western countries. Biliary pain and episodes of cholangitis are the most common presenting symptoms, whereas intrahepatic cholangiocarcinoma represents a long-term unfavorable complication of the disease. When a single liver lobe or segment is involved, partial hepatectomy may be regarded today as an effective method of treatment.

Design: Retrospective study.

Setting: Hepatobiliary unit in a tertiary care hospital.

Patients: The clinical records of 35 patients treated for primary intrahepatic lithiasis between January 1, 1992, and December 31, 2005, were reviewed and clinical data, cholangiograms, operative procedures, and early and late results were examined.

Interventions: Thirty-four patients underwent liver resection; left hepatectomy (18 patients) and left lateral segmentectomy (10 patients) were the most frequently performed procedures. A cholangiocarcinoma was found in 3 patients (8.6%): 2 underwent liver resection and 1, who was found unresectable at surgery, underwent only explorative laparotomy.

Main Outcome Measures: Survival, quality of life, laboratory data, and need for further treatments.

Results: There was no postoperative mortality. Morbidity was 20.0% with a prevalence of infectious complications related to bile leakage. Long-term results, assessed in 26 patients with follow-up longer than 12 months (range, 12-170 months; mean, 63 months), were good or fair in 24 patients (92.3%), including 3 patients who needed subsequent endoscopic removal of biliary stones.

Conclusions: Primary intrahepatic lithiasis more commonly involves 1 single liver segment or lobe. Partial hepatectomy is a safe and effective procedure, allowing definitive treatment of the disease and prevention of cancer.

Arch Surg. 2008;143(6):570-573

INTRAHEPATIC LITHIASIS IS PREVALENT in Japan and East Asia and is much less common in Western countries. In Western patients, intrahepatic stones usually result from the migration of gallbladder or common bile duct (CBD) stones into intrahepatic ducts or may develop proximal to strictures related to previous biliary surgery. In these cases, the disease is caused by an extrabiliary factor and the stones can be defined as secondary stones.

More rarely, stones originate inside the liver at the level of single or multiple cystic dilatations of the intrahepatic biliary tree, proximal to strictures of hilar ducts. In these cases, an intrahepatic factor is responsible for the development of stones, which can be considered primary stones. Primary intrahepatic lithiasis (PIL) is defined by the presence of primary stones in intrahepatic ducts. Abdominal pain, fever, and jaundice are typical presenting symptoms, whereas cholangiocarcinoma represents a long-term unfavorable complication of the disease. In Eastern patients, primary stones occur more commonly than secondary stones and recurrent pyogenic cholangitis represents the well-recognized clinical manifestation of the disease.

See Invited Critique at end of article

The most appropriate treatment for intrahepatic stones is not yet established and several surgical or nonsurgical procedures can be used. Nevertheless, the complete removal of stones and the elimination of bile stasis and infection should be the main goals. In patients with PIL, which is usually limited to 1 single liver segment or lobe, partial hepatectomy is re-
garded today as an effective means of treatment and prevention of recurrence.2,3

We have reviewed a series of patients selected for partial hepatectomy for PIL in our hepatobiliary surgery unit and have evaluated early and late results with an assessment of indications, methods, and long-term outcomes.

**METHODS**

Detailed clinical records of patients treated for PIL in our unit between January 1, 1992, and December 31, 2005, were reviewed. The following data were considered: sex and age of the patients; presenting symptoms and previous treatments; preoperative radiological investigations (with careful assessment of the location of strictures and dilatations in each cholangiographic study); surgical procedures (extension of resections) with macroscopic findings (bile duct dilatation, parenchymal atrophy) and type of stones; postoperative course (morbidity and mortality); findings at pathological examination (inflammation, dysplasia or malignant neoplasm at the level of hepatic bile ducts, and, in the case of malignant neoplasm, stage of tumor according to the TNM classification).4

Follow-up data were obtained by direct clinical evaluation, laboratory findings, ultrasonography, and magnetic resonance cholangiography. Long-term results were classified as the following: good if patients remained asymptomatic with normal levels of bilirubin, transaminases, alkaline phosphatase, and γ-glutamyltransferase; fair if patients had up to 2 episodes of cholangitis per year, not affecting daily activities; and poor if patients had more than 2 episodes of cholangitis per year, with persistent alteration of laboratory data.

**RESULTS**

Thirty-five patients, including 25 men and 10 women with a mean age of 51 years (range, 28-74 years), underwent surgery for PIL in our unit in the aforementioned period. The most common presenting symptoms were recurrent biliary pain (18 patients [51.4%]) and episodes of cholangitis with pain, jaundice, and fever (13 patients [37.1%]). The presentation was with simple jaundice in 2 patients and with gallstone pancreatitis in 2 other patients. Twenty-nine patients (82.9%) had received 1 or more treatments during the period from the initial onset of symptoms to admission, which ranged from 6 months to 30 years. These treatments included 20 cholecystectomies, 4 CBD explorations, 3 papillotomies, 2 biliary-digestive anastomoses, 1 explorative laparoscopy, and 51 sessions of endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy and stone extraction. A choledochal cyst had been detected in 2 cases at the time of cholecystectomy, and a cystojejunostomy had been performed in 1 of them. Therefore, a total of 82 procedures had been performed, without long-lasting benefit, in 29 patients (mean, 2.8 procedures/patient).

After admission, ultrasonography was performed in all of the patients, magnetic resonance cholangiography was performed in 30 patients, and computed tomography was performed in 24 patients.

Most or all of the biliary stones were located proximally to strictures of the left liver ducts in 30 patients and of the right liver ducts in 5 patients. In 4 cases, some stones were also present in the opposite hemiliver. Stones in the CBD were found preoperatively in 2 patients and extracted by endoscopic retrograde cholangiopancreatography with endoscopic sphincterotomy. A patient with PIL involving liver segments 2 and 3 also had a left liver lobe mass.

Liver resection was performed in 34 patients according to the site of biliary stricture and dilatation. Intraoperative ultrasonography was used for a more accurate localization of stones and dilatations. Most strictures were located at the root of the left hepatic duct, just above the bifurcation of the left and right ducts, and left hepatectomy was the most frequently performed procedure. This was performed in 18 patients, and in 5 cases with dilatations also involving the ducts of segment 1, it was associated with caudate lobe resection. The gallbladder was removed in all of the 15 patients who had not previously been selected for cholecystectomy, and stones in the gallbladder were found in 5 cases. Choledochotomy with choledochoscopy was performed in 4 patients to remove stones from the intrahepatic ducts of the remnant liver. The excision of a choledochal cyst with hepaticojejunostomy was associated with liver resection in 2 patients. Intraoperative cholangiography was performed in most cases at the end of the procedure to verify the absence of residual stones or to determine the anatomical details of the biliary tree. Twenty-one patients received T-tube biliary drainage at the end of the surgical procedure; the tube was removed 2 months later. Common macroscopic findings on the resected liver were a varying degree of atrophy and fibrosis, with abscesses and dilated ducts filled with stones.

Details on location of the strictures, surgical procedures, and type of stones are reported in the Table. Interestingly, in patients with or without history of cholangitis, there was a similar incidence of cholesterol stones (6 vs 10 cases, respectively) and of calcium bilirubinate stones (7 vs 10 cases, respectively).

A 66-year-old man with a preoperatively undiagnosed unresectable cholangiocarcinoma complicating PIL of the left lobe underwent only explorative laparotomy. The patient with a mass in the left hemiliver underwent a left hepatectomy: histological examination revealed a poorly differentiated T3 cholangiocarcinoma with microscopic involvement of the resection margin and metastases in 3 hilar lymph nodes. In addition, a small (T1) cholangiocarcinoma of the left hepatic duct was found in the surgical specimen of a 71-year-old woman selected for left hepatectomy; in this case, a negative-margin resection was performed and there was no lymph node involvement.

A neoplasm was found in 3 of 35 patients (8.6%) with PIL. However, multiple erosions of the biliary epithelium and some degree of inflammatory reaction were commonly found at histological examination in all of the cases.

There was no postoperative mortality. Specific complications occurred in 7 patients (20.0%): 4 had a subdiaphragmatic abscess requiring percutaneous drainage, 2 had a biliary fistula that was treated conservatively, and 1 had a choleperitoneum requiring relaparotomy.

The patient with an unresectable neoplasm and the patient with T3 cholangiocarcinoma died 6 months after surgery; the patient with a T1 neoplasm is alive at 58 months from surgery. In 26 patients with a follow-up
PIL, only liver resection allows the complete removal of cutaneous procedures. On the contrary, in patients with irreversible biliary stricture of bilioenteric anastomoses, at least in patients unfit for redo hepaticojejunostomy. Furthermore, the stricture of bilioenteric anastomoses, at least in patients with intrahepatic stones proximal to bile duct strictures. Poor results were also reported by Uchiyama et al.3 After transcatheter liver resection, patients may undergo multiple inappropriate treatments before a correct diagnosis is established.

Various methods of treatment have been proposed for intrahepatic lithiasis, and no consensus has been reached on the ideal therapy. Intracorporeal lithotripsy by percutaneous approach as a nonsurgical method was used by Bonnel et al, who treated 53 patients with a 9% recurrence rate at 5 years. On the contrary, poor results with a 31.4% recurrence rate were reported by Kusano et al using extracorporeal lithotripsy associated with hepaticojejunostomy. Okugawa et al used peroral cholangioscopy and lithotomy in patients with intrahepatic stones proximal to bile duct strictures. Poor results were also reported by Uchiyama et al after conservative surgical treatment (cholangiojejunosotomy or T-tube insertion).

In our opinion, intrahepatic lithiasis includes different types of disease, and the choice of treatment should be based on the accurate assessment of the intrahepatic biliary tree, bile duct strictures, and the location of stones. For instance, peroral endoscopy may be a successful treatment for migrating stones in the absence of bile duct strictures. Similarly, interventional radiology by percutaneous approach may treat intrahepatic lithiasis secondary to the stricture of bilaenteric anastomoses, at least in patients unfit for redo hepaticojejunostomy. Furthermore, intracorporeal or extracorporeal shock-wave lithotripsy can be a useful tool when associated with endoscopic or percutaneous procedures. On the contrary, in patients with PIL, only liver resection allows the complete removal of stones and the elimination of strictures, bile stasis, infection, and risk of cancer. Indeed, cholangiocarcinoma is reported as a consequence of epithelial changes caused by stones and inflammation.2,3 Cholangiocarcinoma was found in 3 of 35 patients (8.6%) in our series; it remained undiagnosed before admission (in 2 cases even before surgery), and in 2 patients it caused death within 6 months. The risk of development of cancer cannot be predicted from the duration or the clinical history of the disease because cancer may also be the first presenting symptom.12 Unfortunately, the relative rarity of PIL in Western countries is often responsible for a delay in recognition of the disease, and patients may undergo multiple inappropriate treatments before a correct diagnosis is established.

Tsunoda et al described 119 patients with intrahepatic stones divided into cases with secondary stones (type I, migrating stones; type II, stones proximal to biliary strictures) and with primary stones (type III, intrahepatic unilateral strictures and cystic dilatations containing stones; type IV, bilateral disease). Liver resection was performed in 57 patients having primary stones, with good or fair results in 33 of 39 patients (84.6%) included in the follow-up. Choi et al reported the results of 4 modalities of treatment in 115 patients: CBD exploration in 74 patients, transhepatic intubation in 10, hepatotomy in 5, and partial hepatectomy in 26. The rate of failure, mostly related to recurrence of stones, in each group was 23.6%, 37.5%, 75.0%, and 4.2%, respectively, thus contributing to developing the concepts that simple stone removal cannot be the definitive treatment and that excision of the involved ducts by liver resection produces the best results. Indeed, strictures and dilatations are known to cause bile stasis, cholangitis, and formation of stones. When the diseased ducts are not removed, the rate of recurrence of stones proximal to strictures is very high because the predisposing factors remain unaltered.10,11 As mentioned already, the chronic epithelial changes caused by stones and inflammation significantly increase the risk of cholangiocarcinoma, which has an incidence reported to range between 5.8% and 17.0%.2,3,5,13 Therefore, liver resection has gained ground in the treatment of PIL. In a large Chinese series,16 excellent or good results were found in 87.9% of

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a Plus caudate lobe resection in 5 cases.
b Plus choledochal cyst excision with hepaticojejunostomy in 2 cases.

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cases selected for partial hepectomy for PIL; in a large series of consecutive partial hepectomies reported by Poon et al., PIL was the most common benign indication.

The nature of the biliary strictures that occur at the liver hilum and are held responsible for the development of PIL remains controversial. In some authors’ opinions, these could be the consequence of inflammation and passage of stones rather than the primary cause of dilatation. Nevertheless, the observation of cases of stricture without PIL and the location of strictures in proximity to the hepatic hilum imply that strictures may develop congenitally. Matsumoto et al. reported a series of patients with intrahepatic bile duct dilatations caused by congenital strictures of the upper portion of the biliary tract and discussed the pathogenesis and clinical significance of these strictures. Because intrahepatic bile ducts do not develop embryologically as an extension of the extrahepatic duct but differentiate from hepatic cells and subsequently join the extrahepatic duct, discrepancies in size between intrahepatic and extrahepatic ducts may result in congenital biliary strictures near the hilum.

In this article, we report a series of patients with PIL treated by partial hepectomy. This series is of considerable size given the rarity of PIL in Western countries. The history of the patients before admission repropuses the challenges of a difficult diagnosis, with multiple failed attempts at treatment and 3 cases already having cancer. The complexity of liver resection was slightly increased by the presence of adhesions from previous cholangitis (or previous treatments) or by the rotation of the liver and the portal pedicle as a consequence of atrophy of the affected segments with hypertrophy of the other segments. Useful complements to resection were intraoperative ultrasonography and, at the end of the procedure, intraoperative cholangiography. The results were good, with no mortality and a 20.0% morbidity that was mostly related to infectious complications of a bile leakage (and thus to factors that might become preventable by a more careful surgical technique); liver insufficiency was not an issue as the resected liver segments were often already atrophic. Furthermore, good or fair long-term results were achieved in 92.3% of cases. These data support the concept that hepectomy is an adequate treatment with very good clinical results in Western patients with PIL. It is a safe and effective procedure allowing the removal of the involved segments with strictures, dilatations, and stones as well as the prevention of cancer.

In conclusion, PIL is a condition that, because of its rarity, may long remain undiagnosed with dismal consequences. Its diagnosis requires particular attention and has recently become more frequent owing to the improvement in imaging techniques. It should be evaluated and treated in dedicated centers where adequate expertise is available. Liver resection is the treatment of choice. The resection does not carry an increased risk and is associated with satisfactory long-term results.

Accepted for Publication: March 7, 2007.

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Financial Disclosure: None reported.

Funding/Support: This work was supported by a contribution from the Catholic University of the Sacred Heart and the Italian Ministry for University and Scientific Research (D.I. funds).

REFERENCES