

Hepatolithiasis—A Case Series

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Abstract

Introduction: Hepatolithiasis is an uncommon entity in Singapore. We reviewed the cases presented to our institution (a 1200-bedded restructured hospital) over a 5-year period. **Materials and Methods:** Twelve cases of hepatolithiasis were treated between December 1995 and July 2000 representing 0.77% of gallstone disease operated on in the same period. The clinical presentation, investigations, treatment and subsequent progress are presented. **Results:** The patients' ages ranged from 28 to 82 years. There was a male to female ratio of 5:7. All patients had upper abdominal pain at presentation; 10 patients had clinical evidence of cholangitis. Ultrasound was the commonest first line investigation but additional investigations, such as computed tomographic (CT) scan and various forms of cholangiography, were frequently necessary for complete delineation of the biliary disease. The intrahepatic stones were located predominantly in the left lobe of the liver. Parenchymal atrophy was seen in 83% of patients. Two patients underwent a biliary bypass operation only, 5 had a hepatic resection only, and 5 had combined procedures. Follow-up ranged from 4 to 50 months. Postoperative recovery was generally unremarkable. Complications included subphrenic abscess (1 patient), recurrent stricture (1 patient) and recurrent stones (1 patient). One patient had an elevated serum CA 19-9 preoperatively; a small villous adenoma was noted at the biliary stricture in the resected left lateral segment of the liver. There was no operative mortality. **Conclusion:** Hepatolithiasis is uncommon in Singapore. Complete diagnosis requires a combination of imaging modalities. Surgery remains the mainstay of definitive treatment. With adequate treatment, good outcome is possible.

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Key words: Cholangiography, Intrahepatic stones, Parenchymal atrophy, Villous adenoma of bile duct

Introduction

Intrahepatic biliary stone or hepatolithiasis is an uncommon entity worldwide, with a higher incidence in East Asia in comparison to the West. As yet, the aetiology remains to be clearly defined. Due to its rarity and attendant intrahepatic biliary infections, hepatolithiasis continues to pose both a diagnostic and management challenge. In this paper, we reviewed the incidence of hepatolithiasis in our institution (a 1200-bedded restructured hospital), its clinical presentation, the recommended diagnostic methods and treatment modalities.

Materials and Methods

We reviewed all patients who received treatment for hepatolithiasis over a period of 55 months. Their case records were traced and analysed; the clinical presentation, modes of investigation, primary management as well as subsequent progress are presented.

Results

Twelve patients were treated for hepatolithiasis between December 1995 and July 2000. This represents 0.77% of 1554 patients treated for gallstone disease during the same period. Their ages ranged from 28 to 82 years (mean age 46.3 years) and there was a female preponderance of 7 to 5. The patients' profiles are summarised in Table I.

Upper abdominal pain was the commonest symptom, occurring in all patients at the time of presentation. Nine had fever, 7 had elevated serum bilirubin (Bil) levels and 7 had raised serum alkaline phosphatase (ALP) levels. Ten of the 12 patients presented with clinical evidence of cholangitis, with 4 (33%) having the classical Charcot's triad of symptoms. Blood cultures were positive for gram-negative gut-related organisms in 5 patients, with *Escherichia coli* cultured in 40%. CA 19-9 was done in 5 patients; only 1 patient had elevated levels.

Ultrasound (US) scan of the hepatobiliary system was

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TABLE I: SUMMARY OF CLINICAL FEATURES AND TREATMENT FOR EACH PATIENT

No.	Age	Sex	Symptoms*	Bil (umol/L)#	ALP (umol/L)#	CA 19-9 (U/mL)	Imaging**	Distribution of stones	Segmental atrophy	Surgical treatment##
1	55	F	P	9	53	-	U + E + C	left lobe	yes	L-lateral segmentectomy + HJ
2	32	F	P, F, J	32	519	12.8	U + E + C + P	right lobe	no	HJ + jejunal access loop
3	45	M	P	18	77	4.1	U + E + C	left lobe	yes	L-lateral segmentectomy
4	41	F	P, F, J	104	810	-	U + E + C	left lobe	yes	L-lateral segmentectomy + HJ
5	82	F	P, F	20	123	36	U + E + C	left lobe	yes	L-lateral segmentectomy + HJ
6	27	F	P, F, J	65	500	-	U + E + C + Mg	global	yes	Ext L-hepatectomy + HJ + jejunal access loop
7	71	M	P, F, J	32	96	333	E + C + Mg	left lobe	yes	L-lateral segmentectomy
8	33	M	P, F	15	141	-	E + C	global	yes	L-lateral segmentectomy + Segment V resection + HJ
9	52	F	P, F	18	64	2	U + E + C + Mg	segment VI	yes	Segment VI resection
10	36	F	P, F, J	53	153	-	U + E + C + Mg	global	no	HJ
11	33	M	P, F, J	48	402	-	Mg	left lobe	yes	L hepatectomy
12	49	M	P, F, J	40	105	-	U + Mg	left lobe	yes	L-lateral segmentectomy

* F: fever; J: jaundice; P: epigastric or right hypochondrial pain

ALP: serum alkaline phosphatase at diagnosis; Bil: serum bilirubin at diagnosis

** C: computed tomography; E: endoscopic retrograde cholangiogram; P: percutaneous cholangiogram; Mg: magnetic resonance cholangiogram; U: ultrasound

HJ: hepatico-jejunostomy; L: left

often the first investigation in view of hepatobiliary sepsis. Combinations of computed tomographic (CT) scan and cholangiography, such as endoscopic retrograde cholangiopancreatogram (ERCP), percutaneous transhepatic cholangiogram (PTC) and magnetic resonance cholangiogram (MRCP), were often necessary for definitive diagnosis (Figs. 1a to 2b). Eight patients (66%) required up to 3 imaging modalities for a complete delineation of the biliary tree and the remaining 4 (33%) had more than 3 investigations.

There was left lobe predominance in stones location. Seven patients (58%) had left-sided involvement only, 2 had right-sided involvement only and 3 had bilateral disease. Parenchymal atrophy of the affected segments was seen in 10 patients. Four had concomitant common bile duct (CBD) stones and 4 had concomitant gallbladder stones.

Five patients underwent hepatic resection only (3 left-lateral segmentectomies, 1 segment VI resection and 1 left hepatectomy), 2 patients underwent a biliary bypass procedure only and 5 patients had combined procedures (3 had left-lateral segmentectomy + biliary bypass, 1 had combination of left-lateral segmentectomy + segment V resection + bypass and 1 had extended left-hepatectomy + bypass to separate right sectoral ducts). A subcutaneous jejunal access loop (using the Roux loop of the hepatico-jejunostomy) was created in 2 patients for easy access to the biliary tree in the future.

The follow-up period ranged from 4 to 50 months. One patient had a small subphrenic abscess after extended left hepatectomy and biliary bypass to separate right sectoral bile ducts. This resolved with percutaneous drainage. This

same patient developed recurrent stricture in the right posterior sectoral duct bypass subsequently; this was managed successfully with percutaneous balloon dilatation. She is currently symptom-free and well. All patients with previously elevated serum bilirubin levels normalised after operation. One patient who had an elevated preoperative CA 19-9 level underwent a left lateral segmentectomy for stones and stricture in the left lateral segments; a small (<5 mm) villous adenoma was noted at the biliary stricture on histology. The level of CA 19-9 returned to normal after operation. One patient returned to his home country and was lost to follow-up; however, he was well and symptom-free when last reviewed at 4 months after combined resection and bypass procedure. One patient developed recurrent stones 3 years after initial bypass procedure and is currently being worked up for repeat operation. There was no operative mortality in our series.

Discussion

Hepatolithiasis is prevalent in East Asia, where incidence of up to 53% of all patients undergoing surgery for gallstone disease have been reported,¹ in contrast to the low figures in the West.^{2,3} This difference has been attributed to the prevalence of Asiatic or Oriental cholangitis (recurrent pyogenic cholangitis). Our low incidence of 0.77% of gallstone operations is consistent with previous findings of a low incidence in Singapore when compared with Hong Kong or Taiwan, which are of ethnically similar populations,¹ lending strength to the postulate that environmental factors play a significant role in its aetiology. Postulated mechanisms include poor general nutrition predisposing to recurrent gastroenteritis and portal

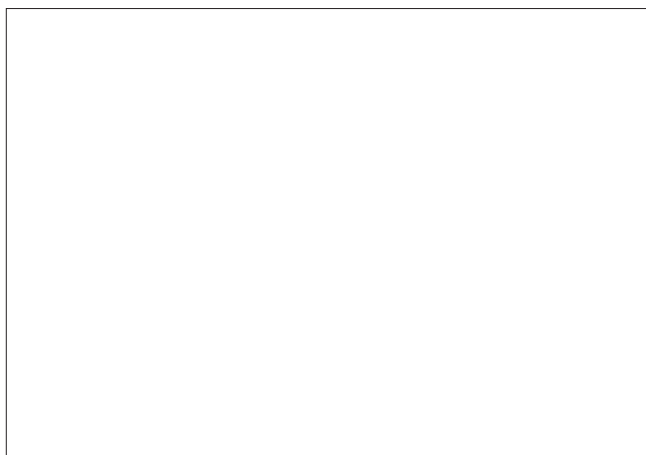


Fig. 1a. PTC showing normal left hepatic duct and the right anterior sectoral duct. The right posterior sectoral duct is not visualised. Figures 1a and 1b are of the same patient.

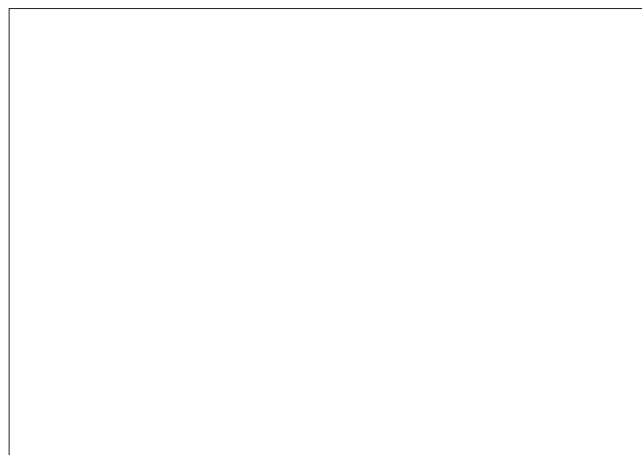


Fig. 1b. Subsequent CT scan reveals a dilated aberrant posterior sectoral duct filled with multiple stones, completing the cholangiogram findings of the PTC.

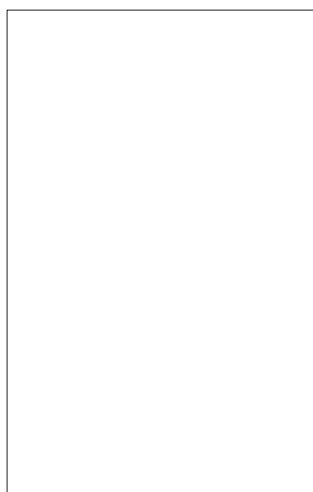


Fig. 2a.

Fig. 2a. ERCP showing the common bile duct dilated and packed with stones. The intrahepatic biliary tree is inadequately filled.

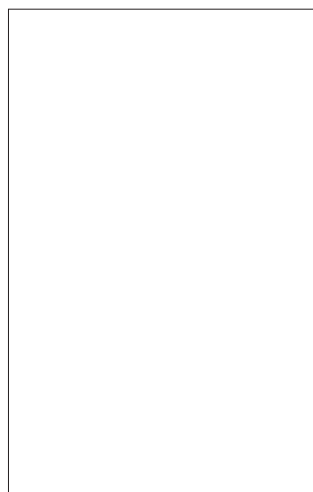


Fig. 2b.

Fig. 2b. Follow-up MRCP reveals the presence of global disease with multiple intrahepatic stones, as well as common bile duct stones.

Figures 2a and 2b are of the same patient.

bacteraemia, food such as pickled vegetables, parasitic (*Clonorchis*) infections,⁴ and ascending infections from a patulous duodenal papilla.¹

Stone Distribution

There is a concurrent presence of gallstones in 45% to 76% of cases.¹ In our series, 33.3% of patients had concomitant gallbladder stones. Cholangitis is the major problem and presentation of hepatolithiasis; recurrent attacks are common with 55% of patients having had more than 2 cholangitic attacks.⁴ In our study, 10 patients had clinical picture of cholangitis at presentation, with 7 having had at least 2 attacks and 4 presenting with the classical Charcot's triad of fever, upper abdominal pain and jaundice. Blood cultures were positive in 50% of those with

cholangitis; this is comparable to figures in a study by Fan et al⁵ which showed a positive blood culture rate of 47 %.

Diagnostic Modalities

The diagnosis is usually reached through a combination of soft-tissue imaging (US scan and CT scan) and cholangiography (ERCP, PTC and MRCP). Ultrasound of the liver is frequently the first investigation; it is non-invasive, easily available and inexpensive. However, it is limited in not being able to delineate segmental bile ducts well and is also heavily operator-dependent. In our study, CT scan was the most commonly used modality. Not only is it able to overcome the shortcomings of US scan, it also provides a topographic picture of the liver, allowing for an accurate assessment of the liver parenchyma (including abscesses and atrophy) and associated extrahepatic pathologies,⁶ which is crucial for surgical planning. It can also better differentiate pneumobilia from calculi. Contrast cholangiograms, such as ERCP and PTC, delineate the biliary anatomy as well as provide a means of biliary decompression in obstructed systems. However, these methods are invasive and fall short when ducts are obstructed.

MRCP is non-invasive and is not limited by ductal obstruction. It also has the added advantages of being tri-planar and its images can be reconstructed to provide a 3-dimensional picture of the hepatobiliary system. Kubo et al⁷ showed that MR cholangiography is better at detecting the presence and location of stones as well as showing ductal dilatation and stenoses when compared to ultrasonography, ERCP and CT scan, making it an important tool in the planning of treatment. Finally, imaging of the liver parenchyma can be acquired on magnetic resonance imaging (MRI) as well.⁸ In addition to providing the surgeon with adequate information for preoperative

planning, being non-invasive, MRCP has the added advantage of avoiding the risk of causing a flare up of sepsis in an obstructed biliary system. With improvement in the quality of MRI and the software for their reconstitution, there has been increasing recognition of the advantages of MRI/MRCP in the diagnostic workup of biliary disease. We believe that MRCP will eventually be the investigation of choice for hepatolithiasis. It was the principal investigative modality in our last 2 patients (cases 11 and 12) when MRCP became available at our institution.

Disease Pattern

The predominance of left-sided involvement is believed to be attributed to the fact that the left hepatic duct courses more horizontally in relation to the common hepatic duct and enters the latter at a more acute angle, resulting in a less efficient drainage system.⁹ The left lobe is also more susceptible to atrophy.¹⁰ Lam et al⁹ also noted a higher rate of manifestation of the left intrahepatic ducts by *Clonorchis*. In our study, 10 of the 12 patients had left-sided involvement, with 4 having global disease and 8 had associated left-sided parenchymal atrophy.

The principles in the management of hepatolithiasis include complete delineation of the biliary tree and its pathology, followed by the removal of all stones, strictures and destroyed liver segments.¹¹ Treatment remains primarily surgical. Residual or recurrent stones are the most troublesome problem after surgery, with the potential for causing recurrent cholangitis and sepsis, secondary biliary cirrhosis with attendant problems of portal hypertension and liver failure, as well as the association of cholangiocarcinoma in long-standing biliary strictures. Chijiwa et al¹² advocate complete relief from calculi and cholangitis at an early stage of the disease to prevent progressive liver damage leading to an increased rate of mortality.

Intrahepatic strictures are the main cause of retained or recurrent stones in hepatolithiasis.^{13,14} Up to three-quarters of patients with hepatolithiasis in Asia have associated biliary strictures.^{1,6} Jan et al¹⁵ reported a recurrent stone rate of 29.6% in a 4- to 10-year follow-up period. Chijiwa et al¹² gave a mean time of stone recurrence of 4.2 years from initial surgery. Jan et al¹⁵ showed that patients who underwent hepatectomy had fewer recurrent symptoms and recurrent stones than those treated with other methods. Even before the introduction of non-surgical modalities such as ERCP and PTC, hepatic resection gave the lowest rates of recurrent symptoms requiring repeat operations when compared with other operations such as transhepatic intubation and irrigation, hepatotomy and CBD exploration, thus it is the best operative procedure for this condition.^{15,16} However, this is only ideal in patients whom the disease is

localised to part of the liver. Repeat operation in patients with previous biliary bypass can often be hazardous with increasing difficulty in exposure of the bile ducts in subsequent operation. This can be overcome by the construction of a hepaticocutaneous jejunal access loop for percutaneous access to the biliary tree in the event of recurrent disease.¹⁷ The indication for the latter procedure is not yet well defined, but Fan et al¹¹ suggest this as a valuable though not definitive procedure in patients with severe or bilateral intrahepatic disease, in whom recurrence is anticipated and in those where hepatic resection is not the appropriate treatment. Alternatively, in those patients in whom a hepatic resection is not possible or not warranted, biliary dilatation via a matured T-tube track or percutaneous transhepatic biliary drainage track can provide a high stone clearance rate,¹³ and this may be augmented by stenting of longer strictures.¹⁸

In our series, liver resection was performed in 10 patients; 5 of whom also had biliary bypass. This allowed us to achieve a high stone clearance rate. The 1 patient who developed recurrent stones had biliary bypass only in the first operation. The indications for liver resection have been described by Ker et al¹⁹ as: 1) stones and strictures localised at one or two segments, 2) fibrotic changes in the affected segment and 3) stricture site at least 10 mm away from the bifurcation of the left and right hepatic ducts. We have found this to be a useful guide. Liver resection provides by far the best results and is our preferred surgical option where appropriate.

Concomitant CBD pathology, such as stones and stricture, should be adequately treated during the management of hepatolithiasis. The aim is to completely eradicate the stones in the CBD and to ensure good drainage of the bile duct. CBD stones can be removed via endoscopic means after adequate sphincterotomy or formal surgical exploration of the CBD during operation. Biliary drainage procedure such as trans-duodenal sphincteroplasty, choledochoduodenostomy or choledochojejunostomy is necessary to bypass a stricture when present. In patients with global or bilateral disease, ancillary biliary drainage procedures are often performed with the hope that residual or newly-formed stones can pass spontaneously into the bowel.

The association of cholangiocarcinoma with intrahepatic calculi and long-standing biliary stricture is well recognised and this is believed to be secondary to chemical irritation of prolonged bile stasis and bacterial infection, together with mechanical irritation by calculi. Studies suggest the associated rate of cholangiocarcinoma to be from 5% (based on operative findings)²⁰ to 10% (based on autopsy reports).²¹ Even with complete removal of intrahepatic calculi, Chijiwa et al²² reported an incidence rate of 6.4% 4 to 10 years post-surgery. As such, they recommend the

careful evaluation for the presence of cholangiocarcinoma in patients with recurrent cholangitis. The presence of mucobilia found on CBD exploration was also significant for the early diagnosis of intrahepatic ductal carcinomas.²⁰ In our study, no patients had cholangio-carcinoma on final histology, although one with elevated preoperative CA 19-9 was found to have an intrahepatic ductal adenoma in the resected specimen.

Conclusion

Hepatolithiasis is an uncommon condition in Singapore, and the aetiology as yet remains unclear. In the planning of management, complete delineation of the biliary tree is essential; this may involve multiple imaging studies. MRCP may play an increasing role as a single modality investigation. Surgery remains the standard mode of definitive treatment. When the disease or stricture is intrahepatic or segmental, liver resection gives the best outcome in terms of clearance of stones and a low stone recurrence rate and is therefore the treatment of choice, especially when there is associated parenchymal atrophy or destruction. Biliary bypass is indicated when the disease process involves the extrahepatic bile duct.

With a systematic approach involving complete delineation of the full extent of the disease process and careful planning and tailoring of the surgical procedure for each patient, good treatment outcome can be achieved. However, long-term follow-up is necessary in view of the high rate of recurrent symptoms and stones. Radiological and endoscopic interventions are useful adjuncts in the management of hepatolithiasis.

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