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CME Article

Clinics in diagnostic imaging (115)

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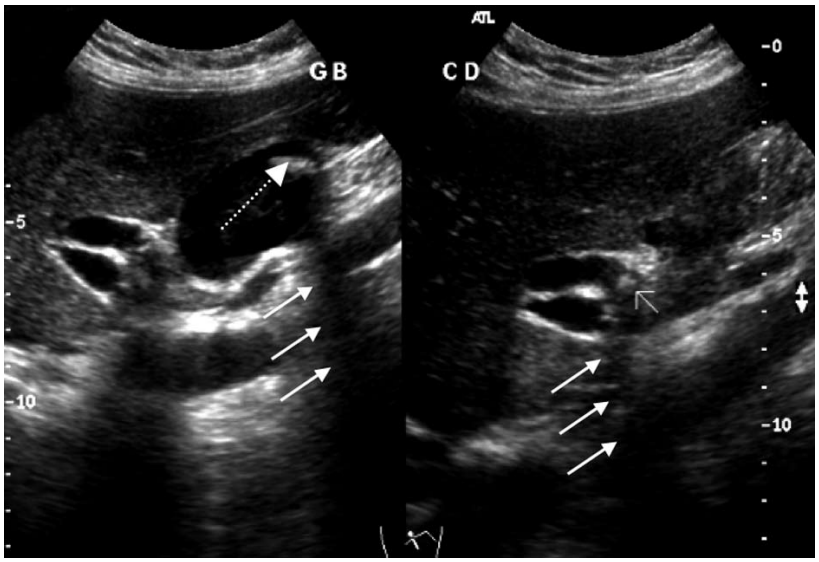

Fig. 1 US images of the upper right abdomen acquired on admission.

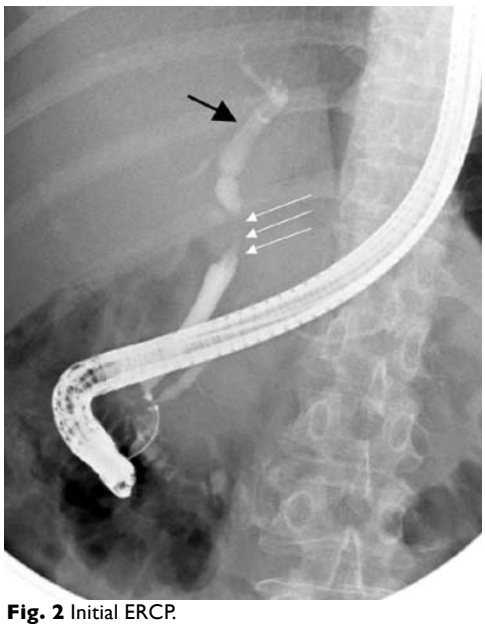

Fig. 2 Initial ERCP.

CASE PRESENTATION

A 58-year-old Chinese woman was admitted for two days for jaundice, right-sided upper abdominal pain, and nausea. Physical examination showed clinical jaundice and mild hepatomegaly. Her initial liver panel showed bilirubin of 161 μM (normal < 30), alanine aminotransferase (ALT) of 1,140 U/L (normal < 70), aspartate aminotransferase (AST) of 387 U/L (normal < 50), and alkaline phosphatase (ALP) of 288 U/L (normal < 130). Acute viral hepatitis A and B markers, anti-HAV IgM and anti-HBc IgM, were negative. Ultrasonography (US) of the upper abdomen was performed the following day (Fig. 1). Endoscopic retrograde cholangiopancreatography (ERCP) was performed five days later (Fig. 2). What is the likely cause of obstructive jaundice and the likely diagnosis? What should the endoscopical and subsequent management be?

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IMAGE INTERPRETATION

US showed a calculus within the gallbladder (dotted white arrow), and another echogenic calculus within the common bile duct (CBD) (short white arrow) and a dilated biliary tree. Both calculi were accompanied by echogenic shadows (triple white arrows), which were typical of calcified calculi (Fig. 1) Together with the patient's right hypochondrial pain and jaundice, the initial clinical diagnosis was obstructive jaundice that was most likely due to a CBD calculus. ERCP showed compression of the proximal CBD by an extrinsic lesion (triple black arrows). The common hepatic duct (white arrow) was mildly dilated (Fig. 2). As the compression was extrinsic, a biliary stent was inserted to decompress the proximal biliary system. Subsequent computed tomography (CT) of the abdomen performed during the same admission showed a gallstone at the neck of gallbladder and the position of the biliary stent (Fig. 3). The initial clinical diagnosis was Mirizzi syndrome, i.e. extrinsic compression of the biliary system by a cystic duct stone. However, as a 1.5 cm mass was also noted at the head of the pancreas (Fig. 4), a differential diagnosis of pancreatic carcinoma was also considered.

DIAGNOSIS

Extraluminal biliary tree obstruction due to compression by pancreatic head tumour.

CLINICAL COURSE

The patient's jaundice improved two days after biliary stent placement, with the bilirubin and ALT levels dropping to 39 μM and 206 U/L, respectively. CA19-9 level was within the normal range. She was discharged a few days later, and was assessed by a hepatobiliary surgeon. Initial management plan was to consider elective open cholecystectomy after resolution of jaundice. However, while open surgery was being considered, she was re-admitted two months later for recurrent jaundice and fever, presumably due to stent blockage. Repeat ERCP showed a blocked stent, with a 4 cm long stricture at the proximal CBD. (Fig. 5) Brushing and biopsy of the stricture were performed, and a new biliary stent was inserted for drainage. Subsequent bile duct brushing cytology showed atypical cells but bile duct biopsy was normal. Repeat CT of the abdomen showed similar findings to the first CT but a 1 cm diameter lymph node was noted at the level of the coeliac axis. Endoscopical US showed a 2 cm diameter mass in the head of the pancreas, and a 3 cm mass at the gallbladder. Clinical diagnosis was carcinoma of the gallbladder with extension to the pancreas.

After extensive preoperative evaluation and family conferences, the patient and family agreed on exploratory laparotomy, which was subsequently performed three

Fig. 3 Axial CT image taken at the level of the coeliac axis (white dotted arrow), shows a calculus at the neck of the gallbladder (black arrow) and a biliary stent (white arrow). Bifurcation of the coeliac axis into splenic artery (double white arrow) and common hepatic artery (black dotted arrow) is seen at this level.

Fig. 4 Axial CT of the abdomen shows the biliary stent (white arrow) and a non-specific mass at head of pancreas (white dotted arrow).

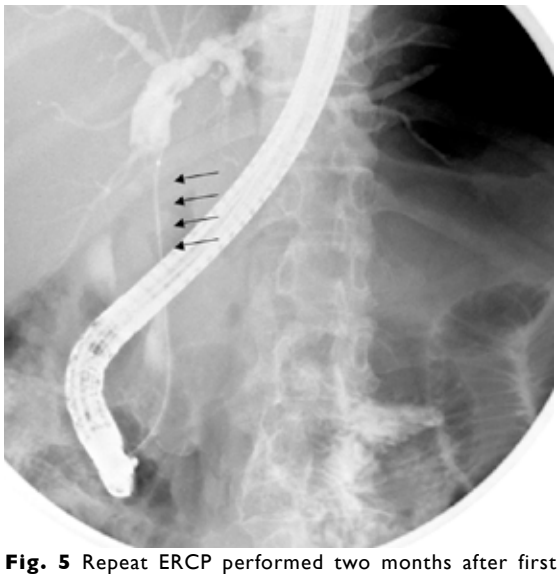

Fig. 5 Repeat ERCP performed two months after first admission shows a long, irregular stricture (white arrows) along the common bile duct. The cholangiogram was taken after the old stent has been removed, and a new biliary stent was inserted after the stricture was noted on the cholangiogram.

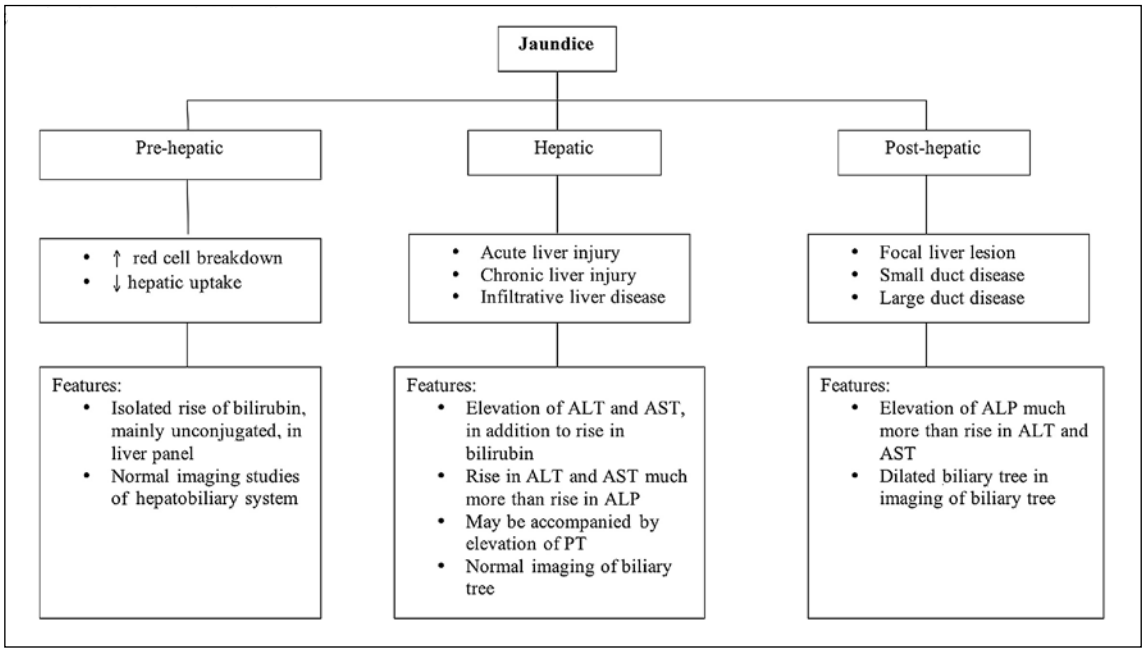

Fig. 6 Algorithmic approach to the evaluation of patients with jaundice.

weeks after her second admission. Intraoperatively, masses in the gallbladder and head of pancreas, with infiltration to segment IV of the liver, and multiple lymphadenopathy at portocaval and coeliac axis, were found. Frozen section of portocaval lymph nodes showed metastatic adenocarcinoma. In view of the extensive loco-regional involvement of the tumour, resection was not performed. The patient was subsequently admitted three times for recurrent cholangitis, and was managed palliatively with internal biliary metallic stenting. Patient was last reviewed four months since laparotomy, and had stable disease on CT.

DISCUSSION

The differential diagnosis of jaundice can be divided into pre-hepatic, hepatic, and post-hepatic causes.[1] (Fig. 6) Common pre-hepatic causes include haemolytic anaemia such as thalassaemia, or reduced hepatic uptake such as Gilbert's syndrome. Common hepatic causes include acute viral hepatitis, drug-induced liver injury, or chronic viral hepatitis B or C. Common post-hepatic causes include choledocholithiasis, liver abscesses or hepatocellular carcinoma, or other obstructive lesions at the biliary system. Our patient demonstrated typical features of post-hepatic causes of jaundice, with right upper abdominal colicky pain, elevated bilirubin and dilated biliary system on US. Patients with acute biliary obstruction often complain of acute right hypochondrial pain, and initial liver panel often first shows elevation of ALT and AST. Elevation of ALP often comes later in the course, as shown in our patient.

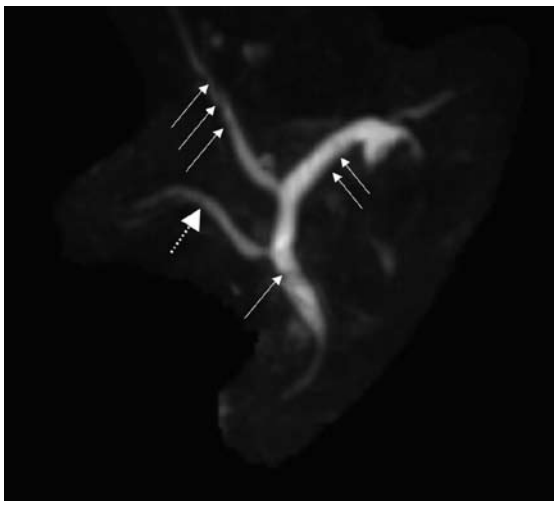

Fig. 7 Patient who presented with fever two weeks after open cholecystectomy and choledocotomy for choledocholithiasis. Liver panel showed obstructive picture with bilirubin 38 μM, ALT 166 U/L,AST 97 U/L,ALP 213 U/L. MRCP shows no residual stone in the biliary tree, with normal common bile duct (white arrow), left (double white arrow) and right hepatic ducts (triple white arrow), and presence of a T-tube (dotted white arrow). His jaundice resolved with antibiotics.

The follow-up investigation of choice for post-hepatic jaundice is a cholangiogram, either endoscopically by ERCP, or non-invasively by magnetic resonance cholangiopancreatography (MRCP).[2] The upper portion of the common duct is usually less than 4 mm in diameter on US, which may become slightly dilated with age. A common duct with diameter greater than 10 mm on US is certainly considered as being dilated.[3]

Fig. 8 ERCP of a patient who presented with biliary colic shows a dilated common bile duct with a filling defect (black arrow), most likely a calculus, inside the common bile duct. A guidewire (white arrow) was inserted to bypass the calculus.

Fig. 9 ERCP of a post-liver transplant patient who presented with sudden onset of jaundice shows a stricture at common hepatic duct (white arrow). Subsequent CT and angiogram showed that the cause of the biliary stricture was due to acute hepatic artery thrombosis. As the biliary tree was mainly supplied by the hepatic artery, hepatic artery thrombosis could lead to ischaemic biliary stricture.

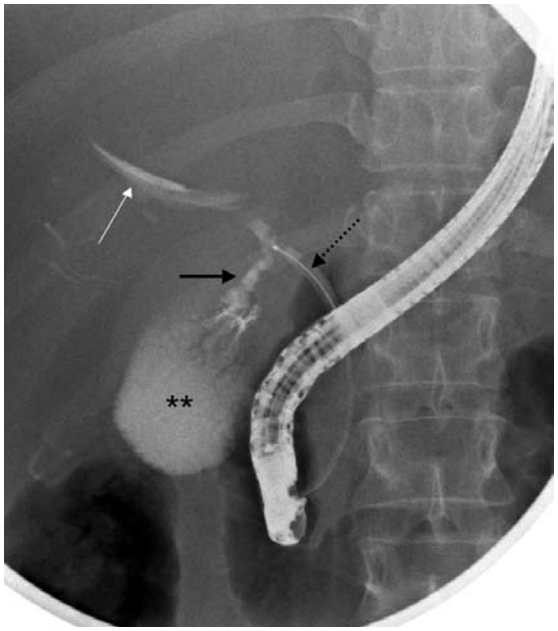

Fig. 10 ERCP of a patient with a large left lobe hepatocellular carcinoma shows an extrinsic compression at the common hepatic duct (white arrow), cystic duct (black arrow) and gallbladder (double asterisks) were seen on the cholangiogram. The dotted black arrow indicates the ERCP cannula.

As ERCP is invasive and associated with potentially serious complications such as acute pancreatitis, it should be reserved for when therapy is expected.[4] In our patient, the initial clinical diagnosis was choledocholithiasis and hence, ERCP was done with a view to follow with sphincterotomy and stone removal. On the other hand, in patients with a low pre-test likelihood of endoscopical therapy or high risk for ERCP, MRCP is the appropriate initial modality for cholangiography as it is non-invasive[5] (Fig. 7). ERCP can be planned only when significant findings are found on MRCP.

Obstruction of biliary system can further be divided into intraluminal lesions such as calculus or rarely, parasites such as *Clonorchis sinensis*; luminal lesions such as stricture; and extraluminal lesions such as lymphadenopathy, stone at the neck of the gallbladder, acute pancreas, carcinoma of the pancreas or carcinoma of the gallbladder.[6] The origin of obstruction can usually be demonstrated by cholangiography. Intraluminal lesions are seen as a filling defect inside the biliary tree (Fig. 8). In the absence of any filling defect within a dilated biliary tree, biliary stricture or extraluminal lesions should be considered, with differentiation between these two being difficult in some cases.

Luminal lesions, such as strictures, usually manifest as an irregular narrowing on cholangiogram, although smooth strictures can also be seen in some patients. The imaging features of another patient with post-liver transplant ischaemic biliary stricture, due to acute hepatic artery thrombosis, are shown in Fig. 9. Extraluminal lesions can manifest as a smooth narrowing with its borders showing the perimeter of the external lesion (Fig. 10), and should be further evaluated with CT,

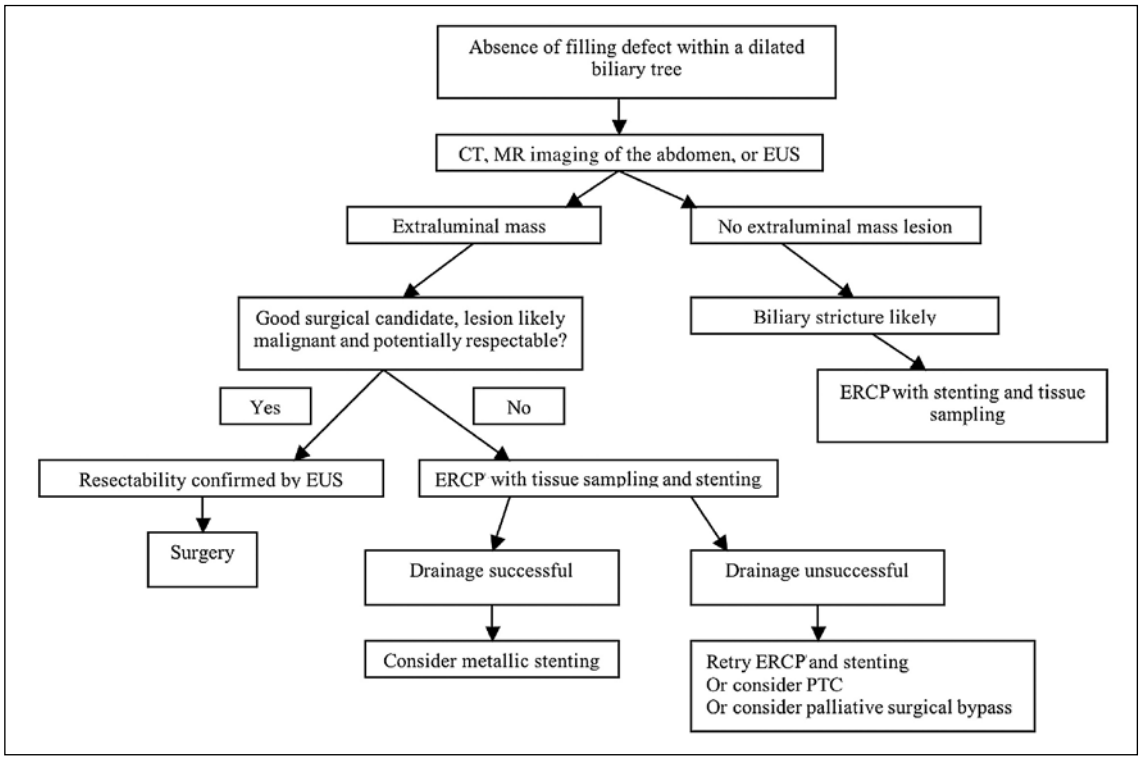

Fig. 11 Management workflow for patients with either biliary tree stricture or extraluminal biliary obstruction.

MR imaging, or endoscopical US (EUS). Patients with intraluminal calculus should be undergo ERCP with sphincterectomy and stone removal. Patients with biliary stricture or extraluminal obstruction should be further evaluated with either CT, MR imaging of the abdomen, or EUS. A proposed management workflow for patients with suspected malignant biliary tree obstruction is shown in Fig. 11. Yield of tissue sampling at time of ERCP can be increased by performing both brushings and biopsy of the stricture, as done in our patient. [4]

Gallbladder carcinoma is an aggressive disease with poor prognosis, with less than 10% five-year survival rates in most series.[7] Its poor prognosis is due to its vague and non-specific presenting symptoms, and a high proportion of cases being diagnosed at an advanced stage. As seen in our patient, who initially presented with obstructive jaundice and subsequently with cholangitis, she was deemed inoperable at laparotomy. Risk factors for development of gallbladder carcinoma include gallstones, calcified gallbladder, gallbladder polyp larger than 1 cm, anomalous pancreaticobiliary duct junction, and exposure to carcinogens such as nitrosamines. Although surgical resection is the only curative option, only 10%–30% of patients at presentation are considered to be surgical candidates. Results from external beam radiation therapy and systemic chemotherapy are also disappointing. The mainstay of management is palliative, which includes relief of biliary (and occasionally gastric outlet) obstruction by either stent placement or surgical bypass.

ABSTRACT

A 58-year-old Chinese woman presented initially with obstructive jaundice. Initial ultrasonography showed gallstones, calculus in common bile duct, and obstructed biliary system. Endoscopic retrograde cholangio-pancreatography showed an extrinsic compression at common bile duct, and subsequent computed tomography scan showed a mass in the head of the pancreas. Endoscopical ultrasonography revealed masses in the gallbladder and pancreas. An exploratory laparotomy confirmed gallbladder cancer with spread to pancreas, segment IV of the liver, and regional lymph nodes. The patient was treated palliatively with metallic biliary stent for biliary drainage.

Keywords: cholangiography, endoscopic retrograde cholangiopancreatography, gallbladder cancer, jaundice, magnetic resonance imaging, obstructive jaundice

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REFERENCES

1. American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of liver chemistry tests. Gastroenterology 2002; 123:1364-6. Comment in: Gastroenterology 2003; 125:279-80; author reply 280.
2. Oikarinen H. Diagnostic imaging of carcinomas of the gallbladder and the bile ducts. Acta Radiol 2006; 47:345-58.
3. Ralls PW, Jeffrey RB Jr, Kane RA, Robbin M. Ultrasonography. Gastroenterol Clin North Am 2002; 31:801-25.
4. Adler DG, Baron TH, Davila RE, et al. ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. Gastrointest Endosc 2005; 62:1-8.
5. Domagk D, Wessling J, Reimer P, et al. Endoscopic retrograde cholangiopancreatography, intraductal ultrasonography, and magnetic resonance cholangiopancreatography in bile duct strictures: a prospective comparison of imaging diagnostics with histopathological correlation. Am J Gastroenterol 2004; 99:1684-9. Comment in: Am J Gastroenterol 2004; 99: 1690-1.
6. Ahrendt SA, Pitt HA. Biliary tract. In: Sabiston Textbook of Surgery. 17th ed. Philadelphia: Saunders, 2004: 1602-3.
7. Misra S, Chaturvedi A, Misra NC, Sharma ID. Carcinoma of the gallbladder. Lancet Oncol 2003; 4:167-76. Comment in: Lancet Oncol 2003; 4:393-4.

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 200704A)

	True	False
Question 1. Regarding causes of jaundice in adults:		
(a) Gilbert's syndrome is a common cause.	☐	☐
(b) History of intake of any medications including herbs should always be sought.	☐	☐
(c) Acute hepatitis E is a common cause among Singaporean patients.	☐	☐
(d) Choledocholithiasis typically presents with painless jaundice.	☐	☐
Question 2. Regarding obstructive jaundice:		
(a) CT of the abdomen is the initial imaging of choice.	☐	☐
(b) It can be safely ruled out by liver panel if both ALT and AST levels are elevated.	☐	☐
(c) Unless endoscopic therapy such as sphincterectomy is expected, cholangiogram should be performed non-invasively by magnetic resonance imaging.	☐	☐
(d) Common complications of endoscopic retrograde cholangiogram include acute pancreatitis and post-sphincterectomy bleeding.	☐	☐
Question 3. Regarding biliary obstruction:		
(a) Parasites such as *Clonorchis sinensis* are commonly seen among local patients.	☐	☐
(b) Strictures always present as a smooth narrowing on cholangiogram.	☐	☐
(c) Yield of positive diagnosis in patients with suspected malignant obstruction from biliary tree brushing is the same whether it is done with or without stricture biopsy.	☐	☐
(d) Cholecystectomy should be performed after bile duct stone removal in fit patients to prevent a second episode of choledocholithiasis.	☐	☐
Question 4. Regarding malignant biliary obstruction:		
(a) Common causes include cholangiocarcinoma and carcinoma of head of pancreas.	☐	☐
(b) Endoscopic retrograde cholangiogram should be done in all patients prior to surgical exploration.	☐	☐
(c) Percutaneous transhepatic cholangiogram (PTC) is a better choice than endoscopic retrograde cholangiogram as PTC is not associated with acute pancreatitis.	☐	☐
(d) Jaundice should always be relieved by stent insertion prior to surgical exploration.	☐	☐
Question 5. The following statements are correct regarding gallbladder carcinoma:		
(a) Most are diagnosed at a resectable stage.	☐	☐
(b) Weight loss and painless jaundice are common presentations.	☐	☐
(c) Chronic alcohol consumption is a recognised risk factor for its development.	☐	☐
(d) Combined external beam radiation therapy with systemic chemotherapy is the standard of care for most patients with advanced disease.	☐	☐

Doctor's particulars:

Name in full: _____

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SUBMISSION INSTRUCTIONS:
(1) Log on at the SMJ website: **www.sma.org.sg/cme/smj** and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

RESULTS:
(1) Answers will be published in the SMJ June 2007 issue. (2) The MCR numbers of successful candidates will be posted online at **www.sma.org.sg/cme/smj** by 15 June 2007. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

Deadline for submission: (April 2007 SMJ 3B CME programme): 12 noon, 25 May 2007