

BILIARY ASCARIASIS AND EXTRAHEPATIC CHOLANGIOCARCINOMA : A REPORT OF TWO CASES

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ABSTRACT

We report two cases of rural Malay women in Perak, Malaysia, with extrahepatic cholangiocarcinoma and coexistent biliary ascariasis. In both cases, the narrowed bile duct may have resulted in inability of the migratory nematode to return to the gastrointestinal tract. It may be reasonable, also, to postulate that chronic biliary tract infestation by *Ascaris lumbricoides* may have contributed to the development of cholangiocarcinoma; a situation similar to that observed in liver fluke infestation.

Keywords: *ascaris*, cholangiocarcinoma.

SINGAPORE MED J 1994; Vol 35: 400-402

INTRODUCTION

Primary biliary tract carcinoma is an uncommon form of gastrointestinal neoplasm accounting for only 1.3% of such malignancies in the University Hospital, Kuala Lumpur, Malaysia from 1981 to 1985⁽¹⁾. Gallbladder carcinoma accounted for 33% of these, extrahepatic tumours 29% and 13% were intrahepatic, while 25% were too extensive to classify.

A few conditions are incriminated in the aetiology of carcinoma of the biliary tree by association. It has been reported that 40-80% of patients having gallbladder carcinoma have gallstones^(2,3) and in about 1% of cholecystectomies, gallbladder carcinoma were found⁽⁴⁾. In Taiwan, it has been observed that gallstones in the intrahepatic biliary tree were associated with cholangiocarcinoma. Two percent of 850 patients operated for hepatolithiasis had cholangiocarcinoma while gallstone associated carcinoma formed 32% of cholangiocarcinoma⁽⁵⁾.

In Asia, parasitic infestation has been implicated in the aetiology of biliary tract malignancy. Two flukes, namely *Clonochis sinensis* and *Opisthochis viverrini*, are associated with cholangiocarcinoma. In Hong Kong, the prevalence of *C. sinensis* measured in unselected patients going to autopsy was found to be 32% or as high as 65% if painstaking parasitologic and anatomic techniques were used to detect mild parasitism⁽⁶⁾. In an autopsy review of patients with well-differentiated cholangiocarcinoma, over 90% had a moderate or severe degree of Clonorchiasis. A report from Korea suggested that this fluke is associated with a peripheral type of cholangiocarcinoma. Adenomatous hyperplasia found in such cases may predispose to carcinoma⁽⁷⁾. In North-east Thailand, where the prevalence of *O. viverrini* is as high as 80%⁽⁸⁾, this parasite can be found in more than 90% of patients with cholangiocarcinoma (Pausawasdi A. Personal communication). Similarly, in operated patients who are

jaundiced and have the fluke, about 60% had cholangiocarcinoma. These malignancies were of three patterns: intrahepatic peripherally, central and mixed.

The suggestion that ascariasis may also cause carcinoma of the extrahepatic bile ducts is not new⁽⁹⁾. However, evidence linking cholangiocarcinoma with *A. lumbricoides* is rather lacking. We are unaware of any such previous case reports. The scarcity of reports of cholangiocarcinoma seen with ascariasis from areas where there is high prevalence of the worm raises doubt of any association between the two. We wish to draw attention to two cases where co-existent extrahepatic cholangiocarcinoma were found.

CASE REPORTS

Case 1

A 58-year-old rural Malay woman was referred from a district hospital after having been treated for ascending cholangitis for 10 days with ampicillin and gentamicin. Although her right hypochondrial pain and fever settled, her jaundice had deepened.

The patient was thin and had features of obstructive jaundice. Her liver was enlarged, being palpable 6 cm below the right costal margin. The spleen was not palpable. She was pyrexial; her temperature ranged from 37°C to 39.5°C. Serum bilirubin was elevated at 276 µmol/L and prothrombin time was prolonged (31 sec) (normal range 11-15 sec). She was hepatitis B surface antigen (HBs Ag) negative. Ultrasound examination showed a normal echopattern of the liver parenchyma with gross dilatation of the intrahepatic ducts and common bile duct (15mm). There was a linear echogenic strip containing a central longitudinal anechoic 'tube'. This appearance was in keeping with an ascaris worm.

She was scheduled for cholecystectomy and bile duct exploration. At operation, a thin wall distended gallbladder was found together with a solid mass stricture encasing the cystic duct and the junction of the cystic duct and common hepatic duct. The normal sized common bile duct below it was opened into but did not permit instrumental dilatation of the stricture. Retrograde cholecystectomy was performed, after which the stricture was cut across and the proximal distended common hepatic duct opened. Mucoïd fluid (white bile) was aspirated together with a macerated black stained ascaris which was in two pieces. A T-tube was placed across the stricture and the bile duct repaired primarily over the tube.

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She made a good postoperative recovery. Bacterial cultures of bile taken at operation showed no growth. Histopathology of the excised specimen showed a moderately differentiated adenocarcinoma involving part of the resected cystic duct and the thickened gallbladder neck. Fig 1 shows the gross specimen and Fig 2 a photomicrograph of the tumour. Her jaundice resolved completely after discharge and as she was well she did not wish further treatment despite explanation of her condition.

Case 2

A frail 35 kg, 78-year-old Malay woman was referred from another district hospital. She gave a history of occasional

Fig 1 - Gallbladder with carcinoma in the cystic duct and neck of the gallbladder (arrowed).

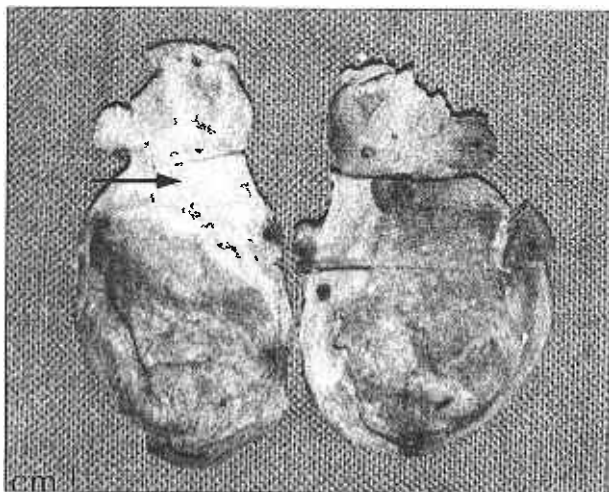
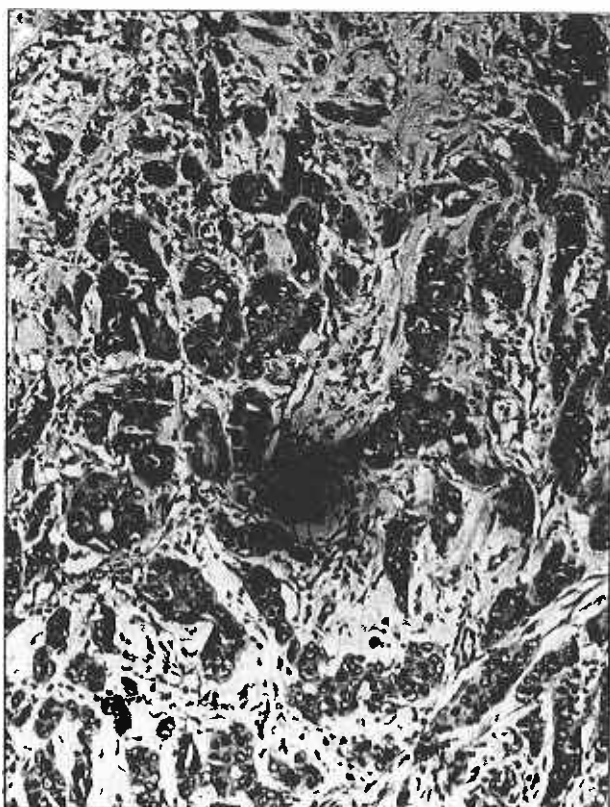


Fig 2 - Cholangiocarcinoma: an adenocarcinoma showing narrow tubular structure in the stroma. H&E x 100.



pain in the right hypochondrium for six months associated with loss of appetite and weight. One week before admission she developed jaundice, with pale stools and dark urine. Ultrasound examination showed gross dilatation of the intrahepatic ducts and the common bile duct (Fig 3). A linear echogenic strip with a central anechoic 'tube' was seen in the common bile duct, compatible with an ascaris worm. In addition, multiple echogenic foci were seen within the gallbladder indicating the presence of gallstones.

On examination, she was deeply jaundiced. She had a temperature of 38.5°C which settled in 2 days with antibiotic therapy. There was a 6 cm globular mass palpable below the right costal margin. Her bilirubin was 696 µmol/l and her prothrombin time was marginally prolonged at 18 secs. She was HBs Ag antigen negative.

Fig 3 - Ultrasonograph showing ascaris (arrowed) in the common bile duct. The portal vein is posterior to it.



Percutaneous transhepatic cholangiography (PTC) showed intrahepatic ducts and common bile duct dilation due to obstruction at the distal common bile duct but the worm could not be identified. At laparotomy a very dilated gallbladder was found. It was opened at the fundus and a few black flaky stones were removed. A hard tumour about 5 cm in its largest diameter was noted behind the first part of the duodenum. It was fixed to the head of the pancreas. The tumour was deemed irresectable and only a wedge biopsy was taken. A palliative cholecystojejunostomy was fashioned. The common bile duct was opened for exploration but the worm could not be found. An operative cholangiogram was done but no worm could be seen. Histology of the tumour showed that it was a cholangiocarcinoma.

Post-operatively, she developed acute renal failure which resolved with fluid and diuretic therapy. She however remained bedridden with faecal incontinence. T-tube cholangiogram on the tenth post-operative day showed a long filling defect within the left hepatic duct system (Fig 4). The appearance was that of an ascaris worm which had migrated proximally. Her general condition deteriorated, primarily due to poor oral intake and dehydration. Against medical advice, her relatives took her home on the 17th post-operative day.

DISCUSSION

Extrahepatic cholangiocarcinoma usually form just 0.1 - 0.45% of all cancers in developed countries^(10, 11). Longmire estimated that there were only about 4,500 such malignancies in the entire United States in 1976⁽¹²⁾. The known associations of cholangiocarcinoma include pre-existing diseases such as chronic inflammatory bowel disease with primary sclerosing

Fig 4 - T-tube radiograph of biliary tree with contrast. The ascaris in the left hepatic duct is arrowed.



cholangitis, typhoid carrier state, congenital anomalies of the biliary tree (eg Caroli's disease), cystic fibrosis, liver cysts, and choledochal cysts⁽¹³⁾. Exposure to some chemicals such as thorotrast⁽¹⁴⁾ puts patients at risk and rarely, women on oral contraceptive steroids and men on anabolic agents have been observed to develop the tumour. Some unknown carcinogen seem to affect workers in rubber factories and in the motor industry⁽¹³⁾.

More importantly, the high incidence of cholangiocarcinoma in Hong Kong and North-east Thailand implicates the presence of the flukes as a causal factor. These tumours are mainly intrahepatic. There is histological evidence of adenomatous hyperplasia in cases of clonorchiasis to support this association. However, the link between ascariasis, one of the commonest helminth infestations worldwide and cholangiocarcinoma, a rare tumour, is tenuous. If it had as much potential to cause cholangiocarcinoma as the flukes, we would expect to encounter the tumour more frequently than reported. However, the ascaris is a migratory worm mainly resident in the intestinal tract. It does not

commonly invade the biliary tree but when it does it can cause chronic cholangitis which could presumably lead to metaplasia and neoplastic change. Because of its migratory habit, these worms could have left the biliary tree by the time malignancy is diagnosed. Chronic inflammatory changes in the biliary epithelium is a predisposing cause of cholangiocarcinoma.

The direct causal relationship between ascariasis and cholangiocarcinoma in the tropics poses an interesting question. It may be rewarding to do careful pathological studies to identify the presence of chronic cholangitis and metaplasia in populations where ascariasis is prevalent, with special reference to the prevalence of biliary ascariasis. However, more evidence is required to postulate an aetiological role for *A. lumbricoides* in cholangiocarcinoma.

An alternative explanation for the two cases presented is that the narrowed bile duct prevented the return of these worms to the gastrointestinal tract. Biliary ascariasis, though uncommon, has been previously reported from our hospital⁽¹⁵⁾ and there has been one other unreported case in our records since. In the two reported cases although no carcinoma was identified, the biliary systems were dilated, indicating pathologic changes already occurring.

CONCLUSION

The possibility of a co-existent cholangiocarcinoma ought to be considered in cases of biliary ascariasis. Both are fairly uncommon conditions. Their co-existence may be just coincidental but it is possible that the two conditions are associated as a result of chronic cholangitis produced by biliary ascariasis.

ACKNOWLEDGEMENTS

We would like to thank Dr Robert P Jalleh for reviewing this paper critically, Liew Sin Wah for help with the illustrations and the Director General of the Ministry of Health Malaysia for permission to publish this paper.

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