PRIMARY SCLEROSING CHOLANGITIS – A REPORT OF 2 CASES

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ABSTRACT

Primary Sclerosing Cholangitis (PSC) is a rare cholestatic condition seen locally. Its etiology is unknown and it is commonly associated with ulcerative colitis, another rare condition seen locally. In this report, 2 patients with PSC, both Indian males, had ulcerative colitis and in one PSC was diagnosed some 15 years later. An interesting feature common to both patients was that of intra-hepatic ductal involvement. Percutaneous transhepatic cholangiogram (PTC) and Endoscopic Retrograde Cholangio-Pancratogram (ERCP) showed characteristic stricturing and beading of the intra-hepatic ducts.

Keywords: PSC, Stricturing and beading of intra-hepatic bile ducts.

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INTRODUCTION

Cholestasis in Singapore is often caused by viral hepatitis, drug hepatitis and obstruction of the biliary system by stones or cancer of the head of the pancreas. Primary Biliary Cirrhosis (PBC) and PSC are rare causes in Singapore. 4 cases of PBC were described in an earlier report (1). We describe 2 cases of PSC confirmed by liver biopsy, PTC and ERCP. Both patients have ulcerative colitis.

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CASE 1

A 54-year old Indian man presented in 1969 with bloody diarrhoea. Subsequent investigations (Barium Enema and colonoscopy) confirmed the diagnosis of ulcerative colitis involving the whole colon (pancolitis). He was started on a course of steroids and salazopyrine and soon went into remission. He remained well on salazopyrine except for occasional mild exacerbations. In 1984, 15 years after initial diagnosis, he complained of anorexia, weight loss, intermittent low grade fever with generalised weakness and lethargy. Serial liver function tests revealed persistently raised levels of alkaline phosphatase with mildly elevated transaminases (see Table I). An ultrasonagraphic examination of the liver suggested cirrhosis and a liver biopsy confirmed cirrhosis. There were fibrous bands seen radiating from the portal triads with bridging fibrosis and ductular hyperplasia. HBsAG was not detected and he did not consume alcohol regularly. A repeat colonoscopy was done at this time and both the colonoscopy and colonic biopsies suggested quiescent colitis. The patient's symptoms however persisted throughout the next year of follow-up and this together with the persistently raised alkaline phosphatase raised the possibility of sclerosing cholangitis or cholangio-carcinoma. In view of these possibilities, a percutaneous transhepatic cholangiogram was done in 1986 (2 years later). This revealed a picture of sclerosing cholangitis (see figure 1). Multiple ectatic and narrowed segments were seen throughout the intra-hepatic biliary tree with sparing of the extra-hepatic ducts. A repeat liver biopsy supported this diagnosis of Primary Sclerosing Cholangitis (see figure 2, 3). Of significance also were the presence of anti-smooth muscle antibodies and generally raised immunoglobulins (see Table II). Patient was subsequently started on a short course of steroids with no improvement. He has however remained anicteric and has not required any other therapy other than salazopyrine for his ulcerative colitis.

Table I
SERIAL LIVER FUNCTION TESTS OF CASE 1

	6/4/84	2/5/85	31/10/85	8/3/86
Bil mg/dl	0.8	1.4	1.3	1.1
T protein gm/dl	7.5	8.2	7.9	7.9
Albumin gm/dl	3.8	3.5	3.3	3.6
SAP iu/dl	285	378	324	302
SGOT iu/dl	60	83	81	78
SGPT iu/dl	90	106	82	108

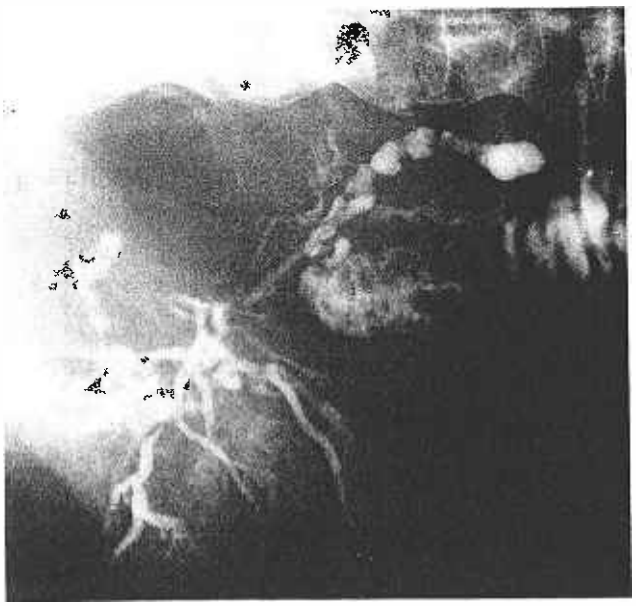

Figure 1

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAM OF CASE 1

Note presence of numerous intrahepatic strictures, an incidental finding of gallstones in the gall bladder but not in the common bile duct.

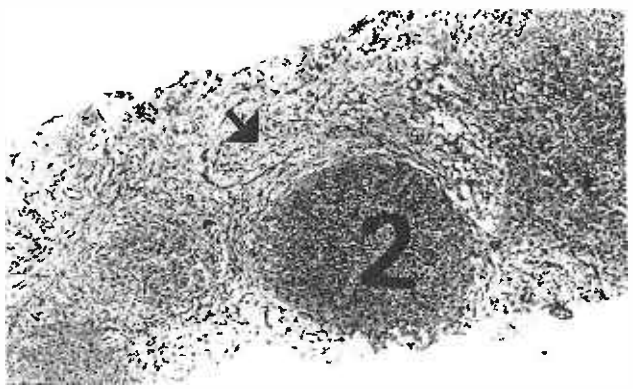

Figure 2

LIVER HISTORY OF CASE 1 (40X)

1) fibrosis around bile duct (arrowed)
2) cirrhotic nodule

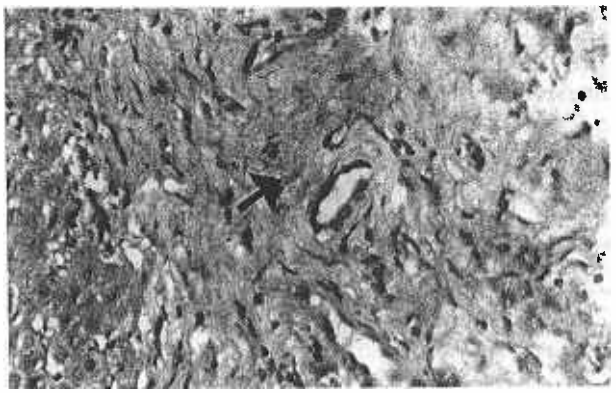

Figure 3

HIGH POWER VIEW OF SAME PATIENT (400X)
Dense fibrosis around the bile duct (arrowed)

Table II
OTHER SIGNIFICANT INVESTIGATIONS IN CASE 1

Anti smooth muscle antibodies positive

Anti mitochondrial antibodies negative

Immunoglobulins IgG 1965 mg% (760-1620)
IgA 532 mg% (70-380)
IgM 230 mg% (30-160)

CASE 2

The second case is a 32-year old Indian man who presented in June 1987 with a 1 week history of fever associated with diarrhoea and dark coloured urine. The stools were watery yellow and were not associated with mucous or blood. He was jaundiced. A course of Ampicillin and Gentamicin was started, the initial diagnosis being that of infective diarrhoea. Repeated stool cultures were persistently negative for enteric pathogens. The fever did subside with the antibiotics but the diarrhoea persisted.

He was subsequently transferred to the Communicable Disease Centre, Tan Tock Seng Hospital for further management. The diarrhoea lasted for a month but it finally resolved after a course of intra-venous hydrocortisone. His jaundice however persisted and got worse. Severe pruritus developed and he was started on cholestyramine. Serial liver function tests again revealed persistently raised alkaline phosphatase (see Table III). Hepatitis markers done were negative for HBsAg, Anti-HBc(IgM) and anti-HAV(IgM) thus excluding the possibility of cholestatic viral hepatis. A colonoscopy and colonic biopsies were done and these showed features of an inactive pancolitis. A liver biopsy revealed portal inflammation with cholestasis, a picture consistent with Primary Sclerosing Cholangitis. We pro-

ceeded with an endoscopic retrograde pancreatocholangiam (ERCP) which revealed a normal sized common bile duct with multiple intra-hepatic strictures. A percutaneous transhepatic cholangiogram was done which showed a picture very similar to that in patient 1. Serum immunoglobulins were again generally elevated but in this case, both the anti-smooth muscle and the anti-mitochondrial antibodies were absent (Table IV). Patient has remained icteric and is still on cholestyramine.

Table III
LIVER FUNCTION TESTS OF CASE 2

	Jun '87	Feb '88	Apr '88
Bil mg/dl	6.7	28.3	9.4
T Prot mg/dl	5.5	7.9	6.0
Alb mg/dl	2.4	2.2	1.9
SAP iu/dl	652	496	997
SGOT iu/dl	198	42	177
SGPT iu/dl	201	55	193

SAP — serum alkaline phosphatase, SGOT — aspartate transaminase, SGPT — alanine transaminase

Table IV
OTHER INVESTIGATIONS IN CASE 2

Anti smooth muscle antibody	negative	
Anti mitochondrial antibody	negative	
Serum immunoglobulins	IgG	2328 mg% (760-1600)
	IgA	636 mg% (70-380)
	IgM	211 mg% (30-160)

DISCUSSION

Primary sclerosing cholangitis (PSC), a condition first described by Delbert (2) in 1924 is a disease characterised by intense subepithelial fibrosis of both the intrahepatic and extrahepatic biliary tree (3). It was once thought to be a rare disease, up till just a decade ago (4 – 6). However, with the use of ERCP, the incidence of this condition has been shown to be much higher than originally expected (7). Its prevalence is closely related to that of inflammatory bowel disease, in particular ulcerative colitis. It is estimated that up to 4% of patients with ulcerative colitis have this condition (4). Conversely, about 54% – 100% of patients with PSC will have ulcerative colitis (4 – 7). It is therefore not surprising, given the low incidence of ulcerative colitis in Singapore (8), that PSC is an even rarer condition here.

The clinical presentation of PSC is varied ranging from an asymptomatic patient with abnormal liver function tests (usually a raised serum alkaline phosphatase), to one with jaundice and recurrent cholangitis (3 – 6). From previous studies done, jaundice, pruritus, abdominal pain and recurrent cholangitis are among the common presenting features of this condition whereas weight loss is uncommon (3 – 6). The symptoms when present should always raise the possibility of cholangiocarcinoma, a condition also known to be associated with ulcerative colitis. This differentiation is sometimes made more difficult when one recognises that cholangiocarcinoma can develop from PSC. While PSC usually involves both the intra and extrahepatic biliary ducts, involvement of only the intra or extrahepatic ducts has been reported (3, 4, 9). When this happens, differentiation from cholangiocarcinoma can be difficult and laparotomy may be needed (2). Our 2 patients had involvement of only the intrahepatic ducts. Cholangiocarcinoma is unlikely based on (a) the liver histology: case 1 being diagnostic and case 2 having features that could go with the diagnosis of PSC; (b) the course of illness in both our patients: case 1 survived four years since the onset of illness and case 2, one year. Two other features are interesting in our patients. Firstly, the time of diagnosis of PSC from the onset of ulcerative colitis was different in both our patients. PSC was diagnosed only 15 years after onset of the colitis in our first patient whereas the second patient developed jaundice from the onset of colitis. This was also reported in other studies where in some it was diagnosed even before the onset of colitis (3, 4). The second interesting feature was the poor correlation between liver histology obtained percutaneously and ERCP/PTC findings in our second patient. This we note was also seen in other studies where only 20-40% of patients with this condition had characteristic changes on percutaneous liver biopsy. This perhaps emphasises the need for cholangiography in all patients suspected of having this condition.

The course of PSC is extremely variable. While once thought to have a universally poor prognosis (3, 13), recent studies have shown that they may be stable for years (4, 5, 7) as in our first patient. As yet, no obvious prognostic factors have been found though Aadland et al in their study of 55 patients felt that the finding of widespread piecemeal necrosis correlated with a poorer prognosis (7).

The results of treatment of PSC have been disappointing. Steroids and immunosuppresives (azathioprine) have been tried without success (4-6, 14). The mainstay of treatment thus far has been symptomatic. On the horizon however, is the promising prospect of liver transplantation as a modality of treatment. Preliminary results of this mode of treatment have been encouraging (15, 16).

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