Primary sclerosing cholangitis associated with inflammatory bowel disease in Cape Town, 1975 - 1981

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Summary

Patients with inflammatory bowel disease and serum akaline phosphatase persistently raised to more than twice the normal level were investigated to assess the frequency of primary sclerosing cholangitis (PSC) in the Gastro-intestinal Clinic from 1975 to 1981. Twelve patients had a persistently raised alkaline phosphatase level of hepatic origin, 9 out of 250 with ulcerative colitis and 3 out of 164 with Crohn's disease. PSC was demonstrated in 8 (3%) of the patients with ulcerative colitis, and carcinoma of the pancreas in the remaining 1. Three of the patients with PSC also had gallstones. The colitis antedated the biliary symptoms and signs in all but 1 patient. There was no correlation between the duration, extent and activity of the colitis and the development and outcome of the liver involvement. Investigations in the 3 patients with Crohn's disease revealed the presence of PSC in 2 (1,2%) and chronic active hepatitis in the 3rd. Of the 2 with PSC, one had cholelithiasis and has had recurrent episodes of cholangitis. The other has had only mild symptoms.

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It has long been apparent that hepatic disease may be associated with inflammatory bowel disease and that fatty change, pericholangitis, nonspecific reactive infiltration, cirrhosis and chronic active hepatitis are the commonest changes encountered. More rarely, viral hepatitis, amyloidosis and bile duct carcinoma have also been described. With the advent of endoscopic retrograde cholangiography, primary sclerosing cholangitis (PSC) is becoming increasingly recognized in association with inflammatory bowel disease. This paper reports on patients with PSC who were seen at Groote Schuur Hospital between 1975 and 1981.

Patients and methods

All patients with inflammatory bowel disease who attended the Gastro-intestinal Clinic at Groote Schuur Hospital from 1975 to 1981 were screened for a persistently raised serum akaline phosphatase level of hepatic origin. In order for patients to be accepted into the study, their levels had to be raised to more than twice normal for at least 1 month. Patients were then subjected to endoscopic retrograde cholangiopancreatography (ERCP) and liver biopsy. Total and conjugated bilirubin, glutamic oxaloacetic transaminase (SGOT), antinuclear factor and smooth muscle and mitochondrial antibodies were measured in serum and the presence of hepatitis B surface antigen was determined by radio-immunoassay. The duration, activity and extent of the inflammatory bowel disease were assessed by the patient's history, double-contrast radiological study of the large bowel, and/or colonoscopy and barium follow-through examination.

Results

Out of 250 patients with ulcerative colitis and 164 with Crohn's disease, 12 had a raised alkaline phosphatase level, 9 with ulcerative colitis and 3 with Crohn's disease. A pancreatic carcinoma was found in 1 of those with ulcerative colitis and chronic active hepatitis in 1 with Crohn's disease. The remaining 10 were all shown to have PSC; in 8 this was associated with ulcerative colitis and in 2 with Crohn's disease. The results in Tables I-III apply to the former cases only.

Biochemical findings (Table I)

Although a minimum level of twice normal was used to screen these patients, all had markedly elevated alkaline phosphatase levels, the lowest level recorded being three times normal. The SGOT level was also raised in all but 1 patient, while the bilirubin level was often normal. Two patients had smooth-muscle antibody titres positive to 1:10, and 1 of these also had a positive antinuclear factor titre of 1:500, but all had negative mitochondrial antibody titres. Hepatitis B surface antigen was absent in all patients.

TABLE I. BIOCHEMICAL FINDINGS

Patient	Alk. phos. (U)	Total/ conjugated bilirubin (μmol/l)	SGOT (U/l)	SMA, M.Ab., ANF
1	1 650	27/19	125	—
2	504	8/3	40	—
3	1 100	146/145	225	—
4	285	13/6	148	—
5	470	20/12	182	—
6	1 200	40/26	290	ANF 1:500 SMA 1:10
7	840	32/17	184	SMA 1:10
8	400	300/250	160	—

SMA = smooth-muscle antibodies; M.Ab. = mitochondrial antibodies; ANF = antinuclear factor.

Clinical features (Table II)

The 8 patients with ulcerative colitis were aged 21 to 61 years, with an equal number of males and females. The extent and activity of the colitis varied at the time the diagnosis of PSC was made. Five patients had total colitis, whereas in the remaining 3 the colon distal to the hepatic flexure, the mid-transverse colon and the descending colon were involved. In 2 patients the disease was inactive while 1 patient had had two episodes of toxic dilatation, and 1 had had a colectomy 22 years after the onset of colitic symptoms. The duration of colitis before diagnosis of PSC varied from 2 to 25 years.

Morbidity and mortality

Two patients (Nos 2 and 7) have remained free of symptoms of liver disease, despite varying degrees of colitis. Of particular interest is a 3rd patient (No. 6) who presented initially with attacks of substernal and right hypochondrial pain. Investigations included oral cholecystography and intravenous pyelography, both of which failed to opacify the gallbladder. Subsequent laparotomy did not demonstrate calculi. Four months after his initial symptoms, he developed watery diarrhoea, but the diagnosis of ulcerative colitis was made only 3 months later. Over the next 6 years he was troubled by intermittent pruritus and colitis. He then became icteric; liver biopsy and ERCP confirmed the presence of PSC. For the last 5 years he has suffered from intermittent pruritus responding to cholestyramine and has remained chronically jaundiced, without episodes of cholangitis. Despite relapsing bouts of colitis he has managed to lead a very active life.

Gallstones were documented in 3 patients. Patient 1 presented with jaundice, pruritus and staccato attacks of right hypochondrial pain 3 years after the onset of colitis. ERCP (Fig. 1) revealed PSC and calculi in the gallbladder. The latter could not be excluded as a cause of his attacks of pain, but were considered unlikely to account for his jaundice at this stage of duct abnormality. It was decided to postpone cholecystectomy and he has remained pain-free but persistently jaundiced over the past year. Patient 4 presented with biliary colic, 8 years after the onset of colitis. Laparotomy revealed a gallbladder full of stones and a stricture in the supraduodenal portion of the common bile duct, which had multiple pigment stones and 'biliary mud'. Cholecystectomy, excision of the stricture with end-to-end anastomosis, and transduodenal sphincterotomy were performed. After this operation she developed intermittent attacks of cholangitis and was referred a year later for opinion. ERCP revealed features of sclerosing cholangitis (Fig. 2). Over the last 3 years she has been treated with antibiotics and intermittent courses of corticosteroids, with improvement in her symptoms. Patient 3 perforated his gallbladder during an attack of cholecystitis. At elective cholecystectomy 2 months later, a lower common bile duct stricture was noted, necessitating a choledochoduodenostomy. In view of a persistently raised alkaline phosphatase level and intermittent hyperbilirubinaemia, ERCP was performed 2 years later and revealed changes of sclerosing cholangitis (Fig. 3).

There have been 3 deaths to date. The first was the patient with the choledochoduodenostomy. Despite inactive colitis, he

TABLE II. DETAILS OF 8 PATIENTS WITH ULCERATIVE COLITIS AND PSC

Patient	Sex	Age	Extent	Ulcerative colitis activity	Duration before diagnosis of PSC (yrs)	Morbidity and mortality
1	M	60	Descending	Active	3	Cholelithiasis; pruritus; jaundice
2	F	40	Mid-transverse	Active	2	Asymptomatic
3	M	61	Hepatic flexure	Inactive	10	Cholelithiasis, CBD surgery, cholangitis. Died
4	F	23	Total	Inactive	9	Choledocholithiasis; CBD surgery; cholangitis
5	F	21	Total	Active	2	Died
6	M	27	Total	Active	6	Jaundice; pruritus
7	M	51	Total	Active	7	Toxic dilatation (twice); PSC asymptomatic
8	F	35	Total	Active	25	Colectomy. Died. PSC at autopsy

CBD = common bile duct.

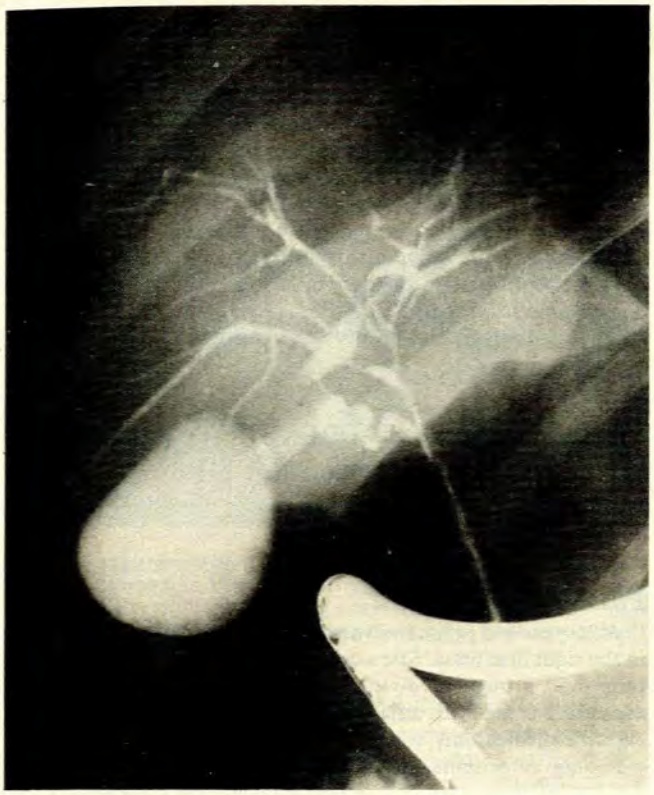

Fig. 1. Patient 1. Marked stenosis of the extrahepatic ducts and stenosis, ectasia and pruning of the intrahepatic ducts. Gallbladder calculi are seen.

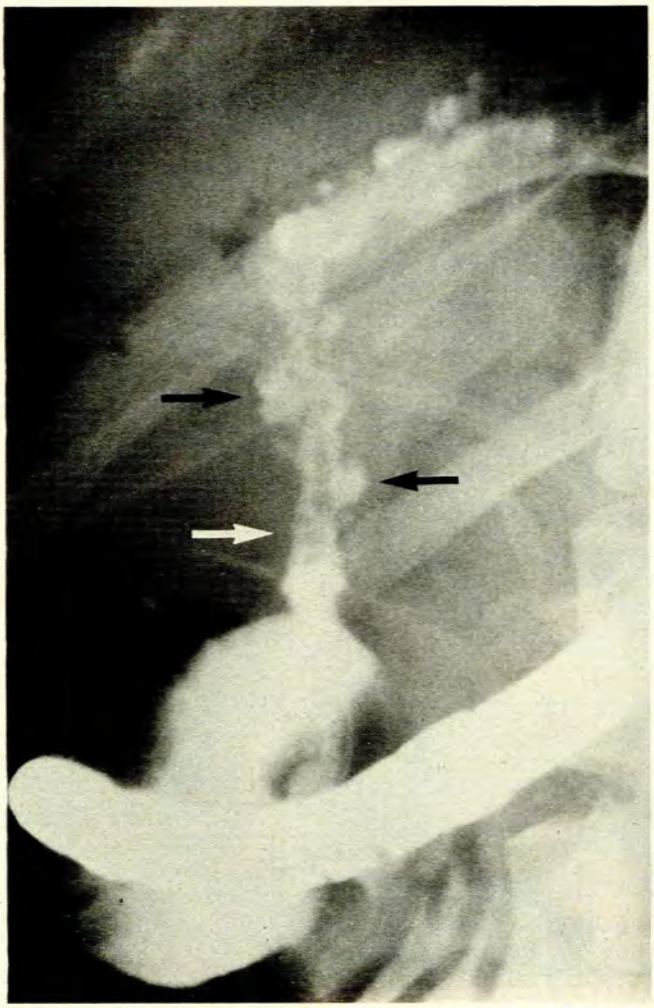

Fig. 2. Patient 4. Beading and pruning of the intrahepatic system, as well as sacculation (black arrows) **and nodules** (white arrow) **in the common bile duct.**

suffered for 5 years after the operation from repeated episodes of cholangitis, became progressively jaundiced and eventually died in liver failure. The second death was that of the 35-year-old woman who had had a colectomy, at which time she was noted to have a cirrhotic liver. Over the next 3 years she suffered from numerous stomal variceal bleeds, became progressively jaundiced and died in liver failure. At autopsy, the diagnosis of PSC was made, with biliary cirrhosis secondary to a stricture in the common bile duct and each of the main hepatic ducts. The third death was in a 21-year-old girl who developed septicaemia and an irreversible shock-like state during a flare-up of her colitis.

Radiological findings (Table III)

ERCP was performed in 7 patients. One had changes only in the intrahepatic ducts, while the rest had involvement of both intra- and extrahepatic systems. Stenosis was present in all patients. In the intrahepatic ducts, this was associated with ectasia in 4 patients (Figs 1-4), giving a beaded appearance in 2 (Figs 2 and 4). When severe enough, the stenosis caused tapering of the ducts, with resultant diminished branching and eventual pruning of the intrahepatic system. An additional feature in the extrahepatic ducts was mural irregularity, with sacculation in 2 patients (Figs 2 and 4) and with intraluminal nodules in 1 (Fig. 2). The gallbladder was visualized in 3 patients and, except for gallstones in patient 1, appeared normal.

Histological findings

Percutaneous liver biopsy, using either a Menghini or a True-cut needle, was successful in 5 of the patients. Orcein staining was used to detect copper-associated protein. Patient 2 showed enlarged portal tracts with excess lymphocytes and histiocytes, but there was no bile duct loss, reduplication, or periductal

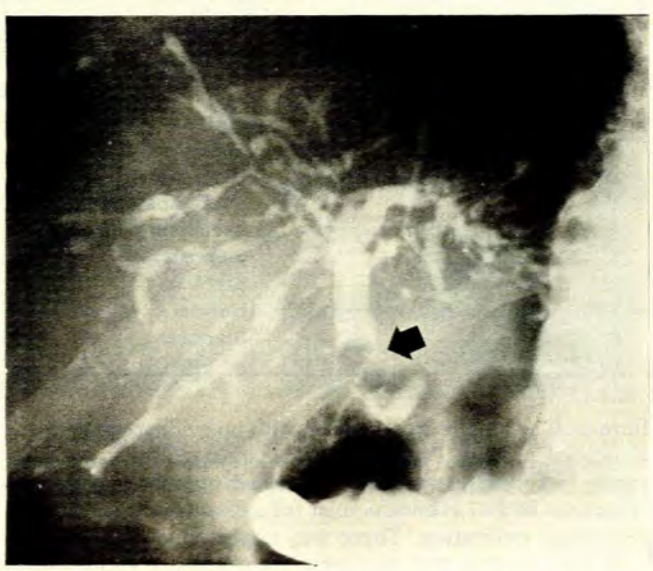

Fig. 3. Patient 3. Widespread intrahepatic stenosis and ectasia. The filling defect (arrow) **is an inflated balloon catheter, used to prevent reflux of contrast medium through the choledochoduodenostomy anastomosis.**

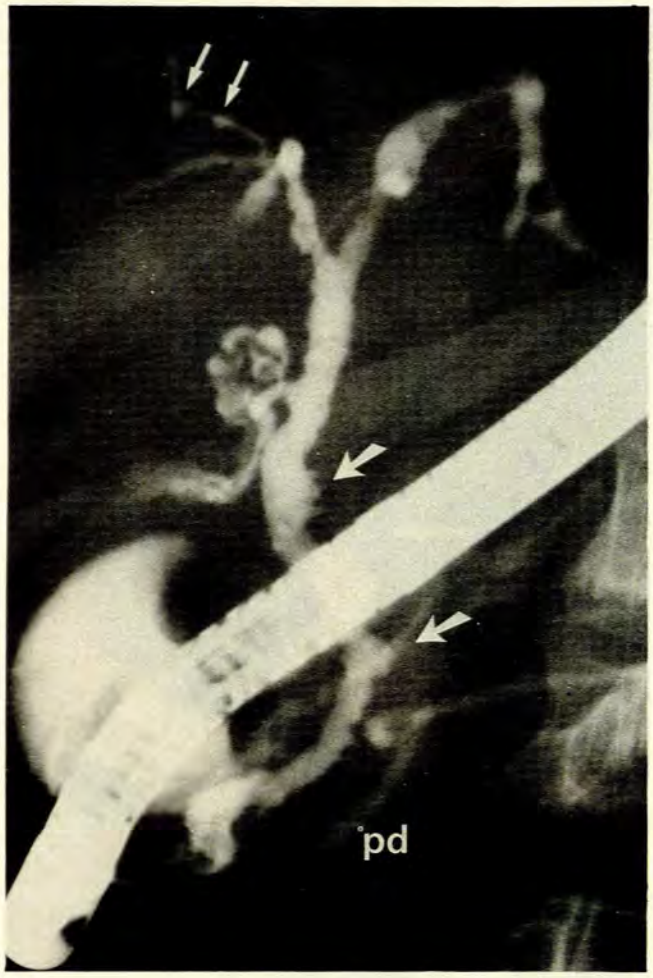

Fig. 4. Patient 2. Intrahepatic duct stenosis, beading (small arrows) **and pruning. The common bile duct shows characteristic sacculation** (large arrows) **(pd = pancreatic duct).**

TABLE III. INTRA- AND EXTRAHEPATIC CHANGES SEEN ON ERCP

Patient	Intrahepatic	Extrahepatic
1	**Stenosis, ectasia, pruning**	**Stenosis, cholelithiasis**
2	**Stenosis, beading, pruning**	**Sacculation**
3	**Stenosis, ectasia, pruning**	**Stenosis, choledochoduodenostomy**
4	**Beading, pruning**	**Sacculation, nodules**
5	**Pruning**	**Stenosis**
6	**Pruning**	**Stenosis**
7	**Stenosis, pruning**	**Normal**
8	**Stenosis**	**Stenosis**

fibrosis. The lobules were normal with no evidence of copper-associated protein. Patient 4 had enlarged portal tracts with excess lymphocytes and histiocytes and occasional lymphoid aggregates as well as bile ductular reduplication associated with neutrophil infiltration. There was neither bile duct loss nor periductal fibrosis, but piecemeal necrosis was present. Stains for copper-associated protein were weakly positive. The initial liver biopsy on patient 5 was normal. One year later, a second biopsy showed scattered mononuclear portal tract infiltration with periductal fibrosis. Stains for copper-associated protein were weakly positive. The slides of patient 6, who was biopsied elsewhere, were unavailable for review. Initial biopsy, 2 years after diagnosis of ulcerative colitis, was reported as showing features of pericholangitis. After 6 years of colitis, a second liver biopsy was reported as showing enlarged fibrotic portal tracts infiltrated by lymphocytes and plasma cells in a periductal distribution. Micronodular cirrhosis was demonstrated in patient 8, 2 years before she died. At autopsy, however, all the extrahepatic ducts were affected by extensive fibrosis and a mild patchy periductal chronic inflammatory cell infiltrate. Examination of the liver confirmed a secondary biliary cirrhosis associated with dense concentric periductal fibrosis, ductular proliferation, marked cholestasis and positive staining for copper-associated protein.

Findings in patients with Crohn's disease

Since the occurrence of PSC is rare in Crohn's disease, it would seem appropriate to report the clinical features of the 2 patients individually.

Patient 1

A 26-year-old pregnant woman presented in 1956 with a mass in the right iliac fossa. She was submitted to a diagnostic laparotomy and a mass involving the terminal ileum, caecum and ascending colon with adjacent node involvement was noted. A right hemicolectomy was performed. Histologically the specimen showed oedema, submucosal lymphoid hyperplasia and a diffuse inflammatory cell infiltrate involving all layers of the bowel, thought to be due to chronic nonspecific inflammation of long duration. The nodes showed chronic nonspecific reactive hyperplasia. For the next 15 years intermittent symptoms of abdominal cramps, diarrhoea and fever persisted. Only in 1972 was a diagnosis of Crohn's ileocolitis made on the basis of a barium enema showing features of colitis with rectal sparing and abnormality of the ileum proximal to the anastomosis.

She presented again in April 1980 with the onset of jaundice and fever. Biochemical investigations revealed cholestasis, with the alkaline phosphatase level raised to 1 809 U, the SGOT 266 U/l, and a total bilirubin level of 150 μmol/l (conjugated 144 μmol/l). Antibody tests were negative. Both percutaneous transhepatic cholangiography and ERCP demonstrated a stenosed lower common bile duct as well as features of PSC involving the intrahepatic system. Despite the use of intermittent corticosteroids and antibiotics she had frequent attacks of fever, jaundice and right hypochondrial pain. She was admitted to Groote Schuur Hospital in February 1981.

Examination revealed a 51-year-old woman who was not acutely ill but was pyrexial and jaundiced. Her abdomen was soft and non-tender, with a palpable gallbladder. Investigations were similar to those done previously. ERCP was repeated and demonstrated a normal pancreatic duct, with a long stricture in the common bile and hepatic ducts (Fig. 5). The intrahepatic ducts in the right lobe varied in calibre and there was an abscess cavity in the left system.

At laparotomy the liver was macroscopically cirrhotic, with marked atrophy of the left lobe. The gallbladder was removed and a segment of remaining cystic duct was sent for histological examination, as was a portion of the common bile duct, which had been opened longitudinally. Via this opening the surgeon was able to dilate the left abscess cavity and gain entry to the right-sided ducts. With difficulty he also dilated the lower common bile duct via a duodenotomy through the ampulla. He was then able to insert a U-tube drainage system (Fig. 6). Bile from the gallbladder and abscess cavity grew *Escherichia coli*.

The common bile duct and cystic ducts showed fibrosis and nonspecific chronic inflammation with regenerating epithelium. The gallbladder, which contained a 5 mm calculus, showed

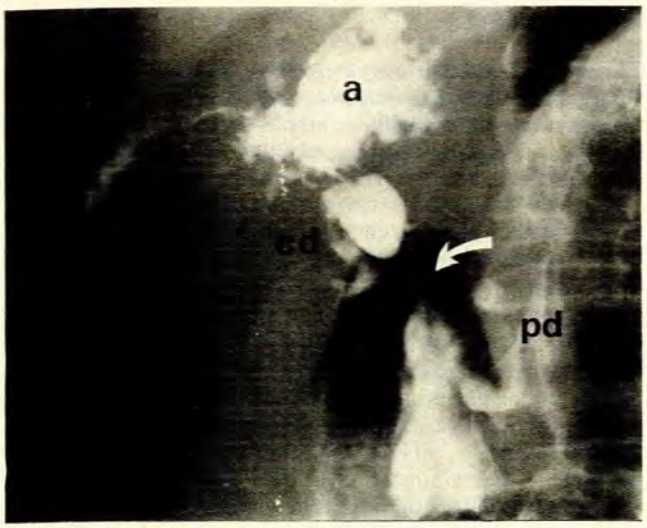

Fig. 5. First patient with Crohn's disease, demonstrating stenosis of the common bile and common hepatic ducts (arrow), varying calibres of the right intrahepatic ducts and a large abscess (a) in the left lobe of the liver (cd = cystic duct; pd = pancreatic duct).

oedema and nonspecific chronic inflammation. Wedge biopsy specimens of liver (Fig. 7) showed features of active cirrhosis, lymphoid aggregates, bile duct loss with replacement and periductal fibrosis, as well as ductular reduplication. Cholestasis was marked and stains for copper-associated protein were strongly positive.

After the U-tube insertion she improved, but still required intermittent antibiotic therapy for recurrent cholangitis; the U-tube has been resited on two occasions, the last being March 1982.

Patient 2

A 57-year-old man came to his doctor in December 1978 complaining of general malaise, epigastric fullness and anorexia. In view of abnormal liver enzyme values, a diagnosis of hepatitis was made. He improved but subsequently relapsed on a number of occasions with similar symptoms over the next 10 months and was admitted for investigation in September 1979. Of significance was a history of mild diarrhoea about 30 years previously, diagnosed at the time as 'colitis'. This settled with diet and had not recurred. Examination revealed a fit, healthy man with no stigmata of chronic liver disease. Relevant biochemical investigation showed a raised alkaline phosphatase level (540 U), an SGOT value of 90 U/l, and a normal bilirubin level. Antibody titres were not raised.

ERCP demonstrated a normal pancreatic system, but the biliary system was abnormal with a stricture of the lower common bile duct and varying calibre of the intrahepatic ducts, consistent with PSC (Fig. 8). Liver biopsy revealed preservation of the overall architecture, mild portal fibrosis and oedema, with focal destruction of the limiting plate. Bile duct proliferation was present, with an inflammatory infiltrate of lymphocytes, plasma cells and a few neutrophils surrounding the ducts. There was no bile plugging, but stains for copper-associated protein were weakly positive. A barium enema showed three separate narrowed areas on either side of the splenic flexure and the mucosa in these areas appeared abnormally granular (Fig. 9.). The rest of the colon was normal. Colonoscopy to the mid-transverse colon confirmed the areas of narrowing, with normal intervening mucosa. The affected areas appeared inflamed with small ulcers. Biopsy showed nonspecific active colitis with no granulomas. The small bowel on enema examination was normal except for an unusually featureless, amorphous and slightly dilated terminal ileum.

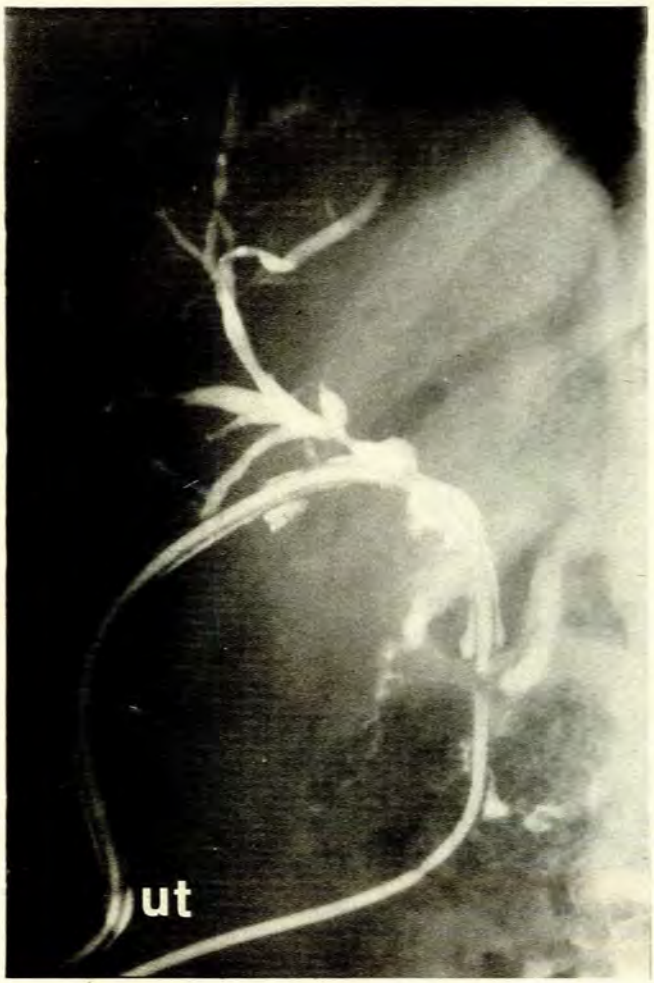

Fig. 6. Postoperative tubogram on the same patient as in Fig. 5. An U-tube drainage system (ut) has been passed through skin, the right intrahepatic ducts, the common bile duct and the duodenum.

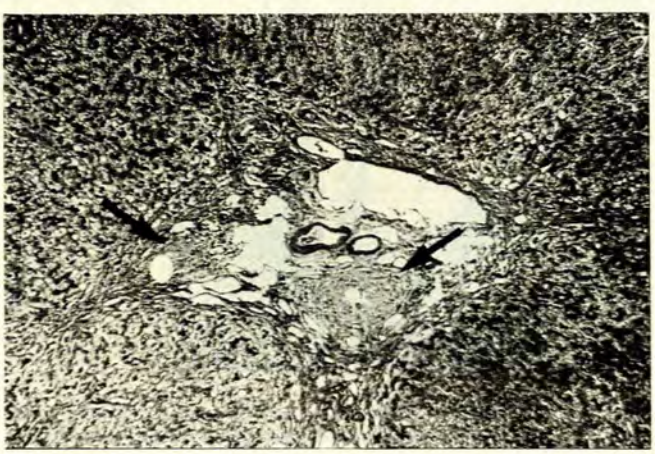

Fig. 7. Wedge biopsy specimen from first patient with Crohn's disease demonstrating cirrhosis with two areas of concentric periductal fibrosis (arrows) in an enlarged portal tract (H and E x 40).

Although the association of inflammatory bowel disease and sclerosing cholangitis can be made in this instance, the nature of the bowel lesion is not absolutely clear. However, taking into

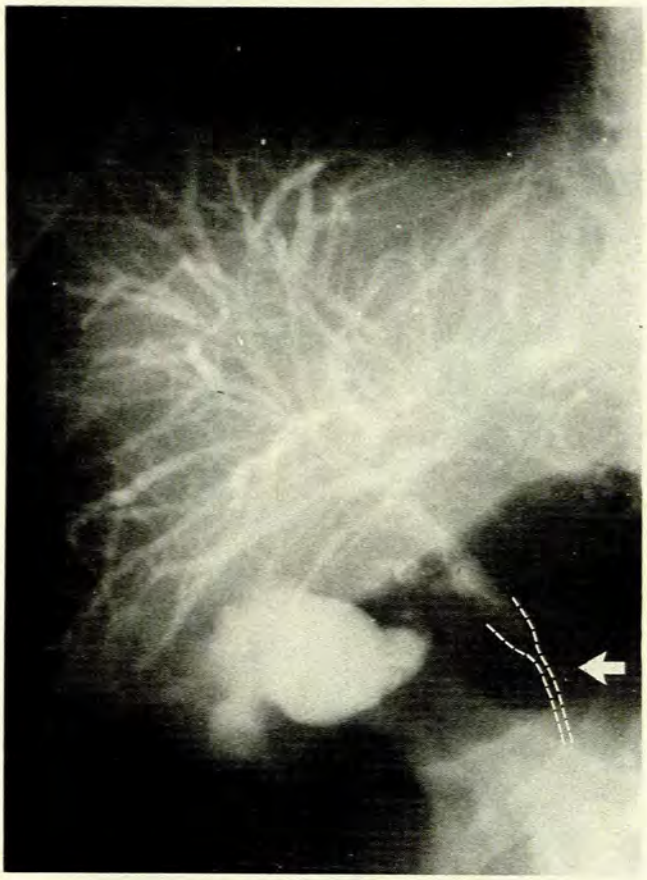

Fig. 8. Second patient with Crohn's disease demonstrating varying calibre of the intrahepatic ducts and a stricture of the lower common bile duct (dotted lines, arrow).

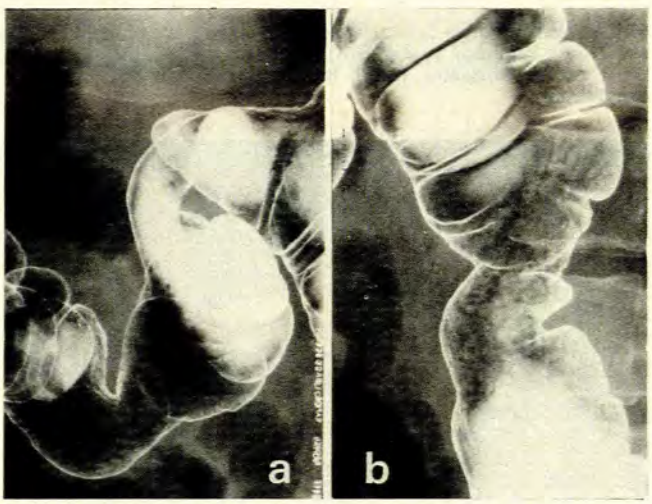

Fig. 9. Double-contrast barium enema study in the patient shown in Fig. 8. There are two areas of narrowing in the transverse colon (a) and one in the descending colon (b).

account the radiological features of the terminal ileum and colonic skip lesions with stenoses, the most likely diagnosis is that of Crohn's disease. Since diagnosis he has had similar recurrent symptoms and in January 1981 asymptomatic haematuria was noted. An intravenous pyelogram revealed a calculus in the right renal pelvis and at operation an oxalate stone was removed. He has since remained well, with the serum alkaline phosphatase level dropping to 294 U in May 1982.

Discussion

PSC was first described by Delbert[1] in 1924 and has been the subject of numerous reports since then. The whole of the biliary tree including the gallbladder may be involved in the chronic fibrosing inflammatory process, resulting in thickening and varying calibre of the ducts. The condition must be distinguished from similar changes secondary to biliary calculi, previous duct surgery, a slow-growing cholangiocarcinoma or congenital biliary duct abnormalities.[2]

The aetiology of PSC is unknown. The majority of cases are associated with inflammatory bowel disease, particularly ulcerative colitis. It is suggested that portal bacteraemia and toxaemia from the diseased colon is responsible, but there is no correlation between the histological picture of the liver and the presence of a positive bacteriological culture from portal blood.[3] Viral agents and drug ingestion, especially of sulphonamides, have also been implicated.[4] The inhibition of leucocyte migration in the presence of a bile antigen derived from bile duct epithelium adds to the suggestion of an immune mechanism.[5] An increase in hepatic copper deposition has also been noted in PSC,[2] although this is a nonspecific finding present in chronic cholestasis. Finally, PSC may be associated with other fibrosing conditions of obscure aetiology, such as Riedel's thyroiditis, mediastinal and retroperitoneal fibrosis, orbital pseudotumour and Peyronie's disease.

The frequency with which ulcerative colitis is associated with PSC varies from 28% to 72%.[6,7] Conversely, the frequency of PSC in patients with ulcerative colitis is only of the order of 1% or less,[6] so that our figure of 8 out of 250 (3%) is a little higher than expected. Crohn's disease, however, has rarely been reported[2,8,9] as the associated condition and the association is even disputed by some,[10] although our 2 cases (1,2%) do substantiate a possible occurrence. PSC bears no relationship to the duration, extent or activity of the inflammatory bowel disease. In 1 of the patients, symptoms and signs referable to biliary involvement appeared 4 months before the onset of diarrhoea, while in the rest there was a lapse of 2-25 years before diagnosis. Even colectomy in 1 patient did not prevent progression to biliary cirrhosis and death.

Many authors consider that gallstones invalidate the diagnosis of PSC, since the changes seen may be secondary to cholelithiasis. Warren *et al.*,[6] however, feel that many cases will be excluded if this criterion is applied indiscriminately. In their group of 12 patients with colitis, 1 had common duct stones, while 3 had both gallbladder and common duct stones. In 2 of these, the changes of PSC were noted at the first operation, suggesting that the calculi developed secondary to obstruction, bile stasis and infection. In addition, they maintain that the extent of stricture due to gallstones is less than with PSC. Wiesner and La Russo[2] excluded only those cases with choledocholithiasis but not if stones were present in the gallbladder, whereas Chapman *et al.*[7] excluded patients with stones irrespective of where the gallstones were sited. Calculi were noted in 4 of our patients, but in only 1 was there evidence of choledocholithiasis. Even in this case the changes of PSC were noted at the initial operation and the pigment stones and 'biliary mud' may well have been secondary to chronic stasis. The calculus found in the woman with Crohn's disease is even more interesting in view of the recognized higher incidence of gallstones in patients with this condition.[10]

Patients may vary from being totally asymptomatic[11] to having repeated attacks of cholangitis with fever, rigors and jaundice. Other milder symptoms such as pruritus, right hypochondrial discomfort and weight loss may also feature. As the condition progresses, biliary cirrhosis with resultant portal hypertension and liver failure with all its sequelae may supervene. The prognosis is extremely variable, many patients remaining well for years,[12] while some may die within a few months.[10] Although not yet evident in this series, cholangiocarcinoma may supervene many years later.[7]

Consequent on the cholestatic nature of the underlying lesion, the serum alkaline phosphatase level is the most sensitive biochemical test, and as in many of our patients, may rise to more than 10 times normal. This elevated level may also reflect active bowel disease but, if persistent, is highly suggestive of underlying PSC and further investigation is warranted. The choice of a value increased to twice the normal obviously excluded patients with less elevated levels and therefore led to a lower incidence of other hepatic diseases than one might have expected. Serum transaminase and bilirubin levels are frequently more variable. The occurrence of a positive antinuclear factor titre and smooth muscle antibodies in 2 patients was nonspecific and these tests as well as those for antimitochondrial antibodies are usually negative. The total serum immunoglobulin levels are usually normal but the IgM level may be raised.[7]

The histological appearance of the liver in PSC is nonspecific and there is considerable overlap between PSC and pericholangitis, which may not be a separate entity.[7,13] In addition to portal tract oedema and fibrosis, ductular proliferation in association with a portal infiltrate of lymphocytes, histiocytes, plasma cells and neutrophils, one looks for concentric periductal fibrosis (Fig. 7), but even this may not distinguish the primary type from chronic large-duct obstruction.[14] In an effort to increase diagnostic accuracy, Chapman *et al.*[7] reviewed additional features. As many as 19 (60%) of their patients showed piecemeal necrosis, suggestive of chronic active hepatitis, but in the absence of a raised IgG level or smooth muscle antibodies, the latter diagnosis was unlikely. Similar changes were seen in 2 of our patients. Diminution of small bile ducts in the portal tracts was noted in the majority of Chapman *et al.*'s[7] patients, but was difficult to assess and only positively identified on wedge biopsy and at autopsy in 2 cases. Accumulation of copper and copper-associated protein are features of chronic cholestasis and may even occur in the absence of bile pigment deposition. Orcein staining for copper-associated protein was positive in 5 of our cases, although only 2 demonstrated cholestasis, both having features of secondary biliary cirrhosis.

The diagnosis of PSC has in the past depended on rather unsatisfactory parameters. Liver biopsy often showed nonspecific changes and percutaneous cholangiography frequently failed because of the inaccessibility of non-dilated intrahepatic ducts.

The advent of ERCP, however, has facilitated adequate visualization of the biliary system, allowing a firm morphological diagnosis to be made without resorting to laparotomy. Rarely, changes may be segmental,[15] but more commonly intra- and extrahepatic ducts are diffusely affected. The predominant feature is stenosis, which may ultimately progress to occlude the lumen. In the intrahepatic system diffuse stenosis with ectasia is commonest. If severe, beading (i.e. an ectatic segment between two stenotic areas) may occur.

The appearance of diminished branching or pruning of ducts results from underfilling of the system when the lumen is occluded. Marked dilatation is not a feature. The extrahepatic ducts are also affected by stenosis, but in addition mural irregularities such as nodules and sacculation (small pockets) have been described[16] and were seen in 2 patients in this series. The gallbladder is rarely abnormal. In view of its availability, ERCP is strongly recommended in cases of inflammatory bowel disease and a markedly raised alkaline phosphatase level. PSC may otherwise be overlooked.

Treatment of PSC is chiefly symptomatic. As with other diseases of unknown aetiology and highly variable natural history, therapy has often been empirical, anecdotal and frequently unsatisfactory. Since there are no controlled data, no single line of action can be recommended. Where there is segmental involvement, surgical repair may be successful[15] but in diffuse disease this is not possible. Suggested drugs for therapy include antibiotics for attacks of cholangitis, corticosteroids, either short-term or long-term,[17] penicillamine in view of the heavy copper deposition in the liver,[2] and cholestyramine.[18] As in 1 of our patients, the introduction transhepatically of intraductal stents to provide adequate drainage and decompression has proved beneficial.[17,19] It must be emphasized that despite earlier reports[6] removal of the offending colon will not necessarily alter the course of the PSC.[9]

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