Biliary Abnormalities Associated with Extrahepatic Portal Venous Obstruction

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We prospectively studied 21 consecutive patients with extrahepatic portal venous obstruction for evidence of biliary tract disease. Two patients were first seen with extrahepatic cholestasis; another had recurrent cholangitis. All three patients with clinically manifest biliary disease were adults. Another five patients had icterus on clinical examination. Liver function tests revealed elevated bilirubin levels in 14 patients (66.6%), elevated alkaline phosphatase levels in 17 (80.9%) and elevated serum ALT levels in 8 (38.0%). Endoscopic retrograde cholangiography revealed abnormal findings in 17 patients (80.9%). The changes involved the common bile duct (66.6%) more often than they did the hepatic bile ducts (38.1%). Cholangiographic abnormalities included strictures (52.4%), caliber irregularity (23.8%), segmental upstream dilatation (42.8%), ectasia (9.5%), collateral veins causing extraluminal bile duct impressions (14.3%), displacement of ducts (9.5%), angulation of ducts (4.7%) and pruning of intrahepatic ducts (9.5%). The pathogenesis of such cholangiographic abnormalities is unknown. However, possible factors in such changes include collateral veins bridging the blocked portal vein, causing bile duct impressions; fibrous scarring of porta hepatis, causing angulation of bile duct; and ischemic injury to bile duct, leading to stricture formation and caliber irregularity. Biliary disease is important in the clinical outcome of patients with extrahepatic portal venous obstruction because variceal sclerotherapy has prolonged the life expectancies of such patients. (HEPATOLOGY 1993;17:807-813.)

Extrahepatic portal venous obstruction (EHPVO) is a common cause of portal hypertension. Thirty percent of cases of portal hypertension in all age groups are due to EHPVO (1), whereas in children EHPVO is the most common cause of portal hypertension (2). Known childhood causes are omphalitis, umbilical vein catheterization and intraabdominal sepsis (2, 3). Association of other congenital abnormalities suggests that some cases of EHPVO are congenital (4). Nearly half of all patients with EHPVO experience onset in adulthood (2). In adults known causes are myeloproliferative disorders, local tumor invasion and chronic pancreatitis (1). In India, thrombosis of portal vein is the main cause of EHPVO. The thrombosis may extend into intrahepatic portal venous branches, giving rise to combined extrahepatic and intrahepatic portal venous obstruction (5). As many as half of all patients with EHPVO (children and adults) have no predisposing cause (1-5).

Gastrointestinal bleeding is the most common symptom of EHPVO in both the adult and childhood forms of disease. Splenomegaly is a prominent clinical finding giving rise to abdominal distension. Ascites is usually absent or mild. It may follow gastrointestinal bleeding and is responsive to treatment. Portal systemic encephalopathy is a rare occurrence. Other clinical features may include anemia, hypersplenism, abdominal pain and abdominal infections (1-6).

Biliary disease is not a recognized clinical manifestation of EHPVO. In this paper we report clinical, biochemical, sonographic and radiologic findings in the biliary tracts of 21 consecutive patients with EHPVO.

TABLE 1. Clinical parameters of the study group

Clinical parameter	No. of patients
Age (yr)[a]	14.0 ± 8.8
Sex (M/F)	13/8
Bleeding episodes (no./patient)[a]	18 (1.7 ± 1.0)
Splenomegaly (cm below costal margin)[a]	18 (13.0 ± 3.5)[b]
Hypersplenism	13
Jaundice	3
Esophageal varices (variceal score/patient)[a]	21 (7.2 ± 4.0)
Gastric varices	7
Hypertensive gastropathy	6
Transfusions (no./patient)[a]	16 (3.4 ± 2.5)
Esophageal variceal sclerotherapy (no./patient)[a]	17 (4.0 ± 2.8)
Surgery	4

[a]Data expressed as mean ± S.D.
[b]Another three patients underwent splenectomy.

PATIENTS AND METHODS

From December 1989 to November 1991, we prospectively studied 21 consecutive patients with EHPVO. Clinical parameters are given in Table 1. Of the 21 patients, 13 were children

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TABLE 2. Laboratory results in 21 patients with EHPVO

Test	Mean ± S.D.	Range	Abnormal value (%)
Serum bilirubin	2.5 ± 1.5	0.6-8.7	14 (66.6)
Serum ALT	47 ± 18	13-120	8 (38.0)
Serum alkaline phosphatase	859 ± 250	274-3381	17 (80.9)
Serum albumin	3.9 ± 0.5	3.3-4.5	1 (4.7)

Normal values: serum bilirubin, < 1 mg/dl; serum ALT, < 40 IU/L; serum alkaline phosphatase, 90-270 U/L; serum albumin, 3.5-4.5 gm/dl.

younger than 15 yr. All patients had portal hypertension evidenced by splenomegaly, esophageal varices and portal systemic collateral veins at other sites. The dominant symptom was gastrointestinal bleeding necessitating multiple blood transfusions and emergency variceal sclerotherapy. Elective variceal sclerotherapy was performed after the emergency procedure to obliterate varices. Surgery had been performed in four patients before their entry into the study. These patients underwent splenectomy with devascularization (n = 2), splenectomy with splenorenal shunt (n = 1) or devascularization (n = 1).

The diagnosis of EHPVO was based on findings obtained on abdominal ultrasonography (US), splenoportovenography (SPV) and liver biopsy (7).

Abdominal US was performed with linear US apparatus SSD 256 (Aloka Co., Japan). The findings on portal hypertension and portal venous obstruction were reported according to the method of Kane et al. (7).

Patients underwent esophagogastroduodenoscopy, limited left-side colonoscopy and endoscopic retrograde cholangiopancreatography (ERCP). Endoscopies were performed in children younger than 15 yr with intravenous ketamine anesthesia (Ketalar, Parke-Davis, India) (2 mg/kg body wt). Adults underwent endoscopy while under light sedation with 5 to 10 mg diazepam (Diazepam Biological E. Ltd., India). Esophagogastroduodenoscopy was performed with fiberoptic panendoscopes (GIF QW, GIF P2; Olympus Co., Tokyo, Japan). Esophageal varices were graded on a scale of 1 to 4 as reported earlier (8). Standard definitions were used to report findings of gastric varices and hypertensive gastropathy (9). Endoscopic variceal sclerotherapy was performed with intravariceal injection of 1% polidocanol (Aethoxysklerol; Kreussler and Co., GmbH) into varices about 5 cm above the gastroesophageal junction. Sclerotherapy was repeated every 3 wk until varices were obliterated (10).

Colonoscopy was performed with a pediatric fiberoptic colonoscope (PCF10; Olympus Co.), and findings were reported as described earlier (11). At least two punch biopsy specimens from the colon were taken, processed, stained and examined. Specimens were studied in particular, for changes indicative of inflammatory bowel disease.

ERCP was performed with a side-view fiberoptic duodenoscope (JIF 1 T; Olympus Co.). Ducts were opacified, and care was taken not to overfill or underfill them. Multiple x-ray films were taken with patients in various positions. Films were read by two experienced gastroenterologists without knowledge of the clinical details of the patients. ERCP results obtained from 10 subjects (eight men, two women; mean age, 15.0 ± 2.5 yr) without gastrointestinal disease were included with the ERCP results of 21 patients as controls; findings were recorded on a proforma. Discrepancies between the reports of the two gastroenterologists were cleared by mutual consultation. The diameters of the ducts were corrected for magnification by referring to the diameter of the endoscope. Cholangiographical abnormalities were reported as described earlier (12).

SPV was performed by injection of 20 to 40 cm^3 of meglumine iothalamate (Conray-280; May & Baker Pharmaceuticals, India) into the splenic pulp; x-rays were exposed at a rate of 1/sec for 6 sec. The films were assessed for evidence of portal hypertension and site of blockage in the portal venous system, as described earlier (5).

Liver biopsy was performed with a Menghini needle. Specimens were processed, stained and assessed as described earlier (13).

RESULTS

Of the 21 patients, 3 (14.3%) had clinical manifestation of biliary disease. All three patients were adults and had extrahepatic bile duct obstruction first noted as cholestasis (two patients) or cholangitis (one patient). Two of these three patients died after biliary surgery. In one patient, cholangitis, septicemia and endotoxic shock developed. Another patient had surgery to relieve biliary obstruction. At laparotomy, the porta hepatis had been replaced by a fibrotic mass containing multiple tortuous collateral veins. An attempt at biliary exploration led to exsanguination and death due to hypovolemic shock. Of the remaining 18 patients, 5 had icterus on clinical examination. Liver function test results are shown in Table 2. Most (80% to 90%) of the patients had elevated serum alkaline phosphatase levels suggestive of biliary obstruction. Serum bilirubin levels were elevated in 14 (66.77%) patients. However, serum albumin levels were within normal limits in nearly all the patients.

US. Abdominal US was performed in all 21 patients; it revealed enlarged spleens in 18 patients (mean diameter, 13.0 ± 3.5 cm). The splenic vein was patent and dilated in all patients, and multiple collateral veins were seen in the splenic hilum and around the pancreas and left kidney. Livers demonstrated normal echogenicity with patent, normal-sized hepatic veins. The portal vein could not be visualized in 18 patients, and the porta hepatis in all these patients contained diamond-shaped bands of high-level echoes (portal cavernoma). Multiple tubular anechoic structures were seen passing through the echogenic band; these were collateral veins entering the hepatic parenchyma (Fig. 1). In three patients the portal vein was thick walled, with irregular lumen. Multiple tubular anechoic structures were seen around the portal vein; these were collateral veins around the thrombotic portal vein (7, 14, 15). Hepatobiliary ultrasound also revealed distended gall bladders in two patients. Gallstones were seen in one patient. The common bile duct could not be visualized in any of the patients because of high-level echoes in the porta hepatis and multiple

FIG. 1. US: subcostal oblique view, from a 12-yr-old girl with multiple attacks of variceal bleeding. The portal hepatis contained a large echogenic structure containing multiple anechoic tubes (portal cavernoma).

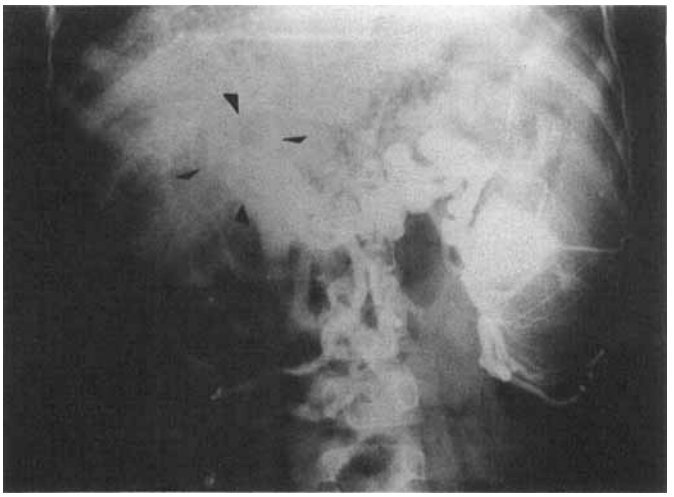

FIG. 2. SPV in an 8-yr-old boy with multiple attacks of variceal bleeding. The intrasplenic contrast is drained by tortuous splenic vein, with multiple collateral veins in perisplenic region and around the pancreas. The portal vein is not filled; however, multiple vessels running parallel to each other are seen in the region of porta hepatis and entering the hepatic parenchyma (portal cavernoma).

TABLE 3. Cholangiographic findings in 21 patients studied

Abnormalities	No. of patients	
	Common duct	Hepatic ducts
Strictures	11	2
Single	9	1
Multiple	2	1
Short	4	1
Long	7	1
Caliber irregularity	3	2
Upstream dilatation	9	2
Ectasia	1	2
Varices	3	–
Displacement	2	1
Angulation	1	–
"Pruning"	–	2
Normal	5	13

anechoic tubular structures that distorted normal anatomical relationships and concealed the bile duct. Hepatic ducts were dilated in two patients first seen with cholestasis. In the remaining 19 patients, hepatic ducts were of normal size.

SPV. Splenoportovenograms were obtained in 18 patients with intact spleens; they revealed dilated splenic veins with collateral veins around the spleen, pancreas, left kidney and lower end of the esophagus. The portal vein had been replaced by a bunch of vessels entering the liver (portal cavernoma) (Fig. 2) (5).

ERCP. Pancreatograms were available in 10 patients; none revealed abnormalities. Cholangiographical findings are shown in Table 3. Seventeen cholangiograms revealed abnormal findings, whereas four revealed no abnormalities. The disease was limited to the common bile duct in nine patients and to the hepatic bile duct in three patients; it involved the common bile duct and hepatic bile ducts in five patients. The dominant finding in the cholangiograms was strictures, mostly involving extrahepatic bile ducts (Fig. 3). Strictures were typically smooth taperings. They involved short (1- to 2-cm) segments in five patients and long, confluent segments in eight patients. Upstream dilatation of the bile duct was frequent. Multiple strictures and short dilated segments produced a characteristic beaded appearance (Fig. 4). Localized saccular dilatation of the common bile duct or hepatic bile duct not associated with strictures occurred in three patients (Fig. 5). Extraluminal smooth impressions were seen in three patients. These were localized and crossed transversally across the common bile duct in two patients. Multiple serpiginous impressions were found all along the common bile duct length in one patient. Smooth impressions displacing the common duct or hepatic duct were seen in three patients, suggesting an extraluminal mass effect (Fig. 6). In two patients the common bile duct was angulated, possibly as a result of fibrous scars in the porta hepatis; in another two patients, ERCP revealed sparsity and abrupt termination of intrahepatic duct branches resulting in a typical "pruned-tree" appearance.

Of the 17 patients with abnormal ERCPs, 15 had received esophageal variceal sclerotherapy; the re-

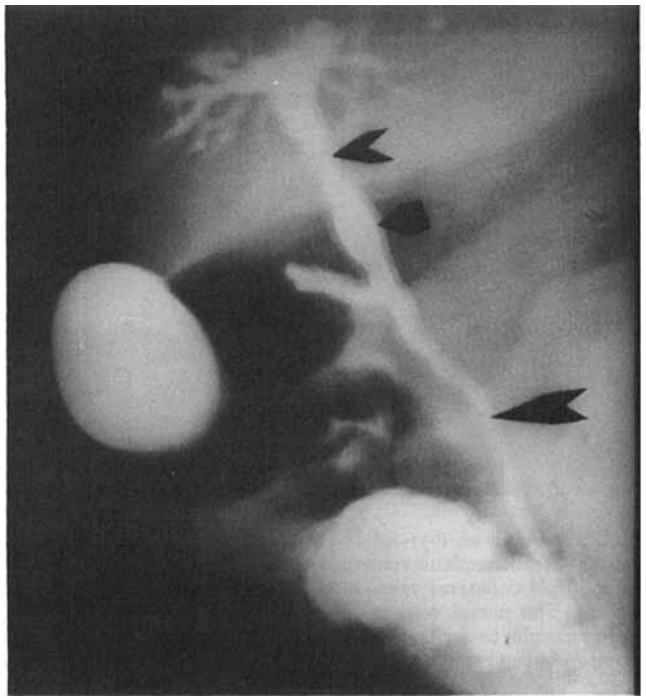

FIG. 3. ERCP in a 6-yr-old boy with EHPVO and multiple attacks of variceal bleeding. The common bile duct *(long arrowhead)* had a long stricture with segmental upstream dilatation of the common hepatic duct *(thick arrowhead)*. Above the dilated segment of the common hepatic bile duct, a localized stricture *(short arrowhead)* was evident. The gallbladder was filled normally.

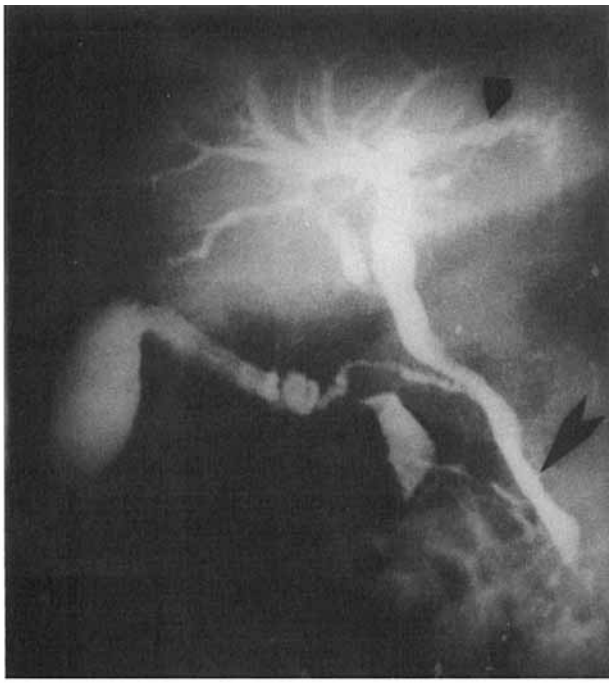

FIG. 4. ERCP in a 9-yr-old with EHPVO. The common bile duct *(long arrowhead)* displays marginal irregularity. The entire duct has lost its parallelism. The left hepatic duct walls *(short arrowhead)* were shaggy. The cystic duct and gallbladder were filled normally.

maining 2 patients, without previous variceal bleeding, had not. Only one of the three patients with clinically manifest biliary disease had undergone sclerotherapy previously. All three patients in whom US did not show portal cavernoma had abnormal ERCPs.

Colonoscopy. Colonoscopic findings and rectal biopsy specimens were normal in all 21 patients, and none had evidence of active or healed ulcerative colitis. All patients were negative for immune markers (antinuclear antibody, antimitochondrial antibody and smooth muscle antibody). One patient was positive for rheumatoid factor, in a low titer.

Liver Biopsy. Liver biopsy was performed in all 21 patients; none had evidence of cirrhosis or portal fibrosis that could have caused portal hypertension. Liver biopsies in two patients with clinically manifest biliary disease revealed evidence of hepatocellular and intracanalicular cholestasis. None of the patients demonstrated evidence of loss of ducts, portal triaditis, ductular proliferation or cirrhosis.

DISCUSSION

We prospectively studied 21 consecutive patients with EHPVO. The diagnosis of EHPVO was made on the basis of multiple criteria. The manifestations of portal hypertension were dominant symptoms in the clinical courses of these patients. The manifestations in our patients resembled those of other patients reported in India and other countries (1-6). Cholangiographic abnormalities were seen in many of these patients. Because our study group comprised a random selection of consecutive patients, we believe that the data are truly representative of bile duct changes in EHPVO.

Cholangiographic abnormalities in sclerosing cholangitis include irregular strictures of extrahepatic and intrahepatic bile ducts, segmental dilated segments and strictures with a beaded appearance, ectasia and "pruning" of the intrahepatic bile ducts (12, 16). All these changes were seen in the cholangiograms obtained from patients with EHPVO in this study. However, the strictures in patients with EHPVO differed from those seen in sclerosing cholangitis because they displayed smooth taperings rather than irregular ones. Three other cholangiographic findings seen in our patients were extraluminal impressions of collateral veins on the bile duct, mass effect causing displacement of bile and hepatic ducts and angulation of the bile duct. Such changes have not been reported in patients with sclerosing cholangitis and were peculiar to patients with EHPVO.

Sclerosing cholangitis is known to have two anatomic disease components: large-duct and small-duct disease (12, 17). Large-duct disease involves extrahepatic or intrahepatic bile ducts and is best diagnosed on cholangiography (12). Small-duct disease involves septal or interlobular bile ducts and characteristically spares

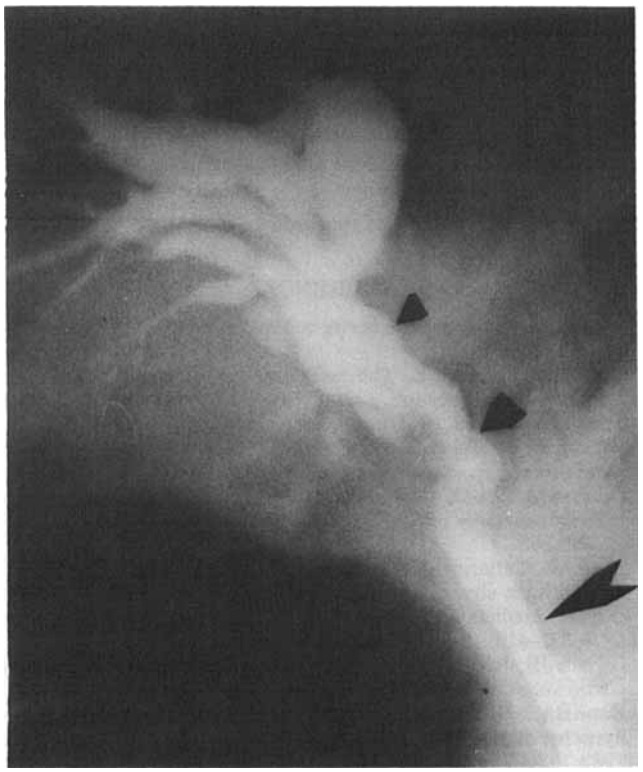

FIG. 5. EHPVO in a 25-yr-old man with EHPVO manifested as multiple attacks of variceal bleeding. He was first seen with recurrent cholangitis and died of septicemia and endotoxic shock. The common bile duct *(long arrowhead)* was noted to have marginal irregularity. The common duct *(thick arrowhead)* was angulated; it and the intrahepatic duct branches revealed saccular dilatations without downstream strictures, suggestive of cholangiectasia.

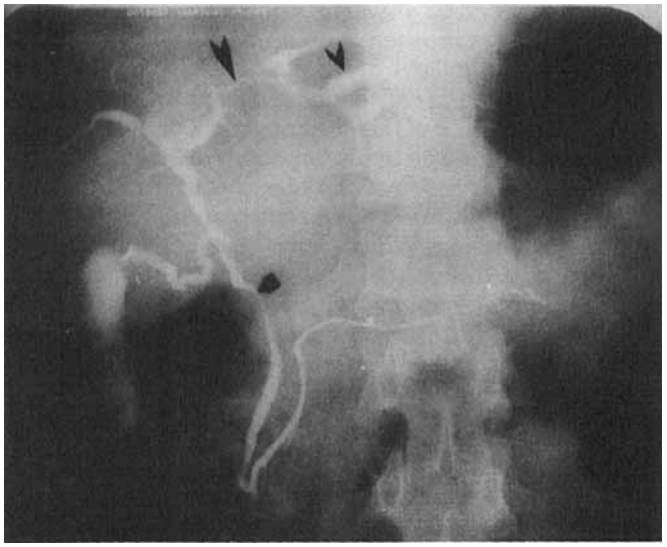

FIG. 6. ERCP in a 4-yr-old child with EHPVO manifested as multiple attacks of variceal bleeding. The common bile duct *(thick arrowhead)* had a localized area of narrowing and medial displacement without upstream dilatation. The entire left hepatic bile duct *(long arrowhead)* was narrowed and exhibited smooth displacement upwards. The left intrahepatic bile duct branches *(short arrowhead)* were dilated.

ductules. Diagnosis is made at liver biopsy, which reveals loss of bile ducts (so-called ductopenia) (17). However, this histological abnormality may be obscured by ductular proliferation. The histological component of small-duct disease was lacking in all the patients in this study. Thus we believe that biliary abnormalities in patients with EHPVO are limited to large bile ducts and characteristically spare small bile ducts.

Although cholangiographic changes were common in patients with EHPVO in this study, only three patients had clinical symptoms of biliary disease. All three of these patients were adults. None of the children had clinical manifestations of biliary disease. However, abnormal liver function caused by partial biliary obstruction was commonly seen and pointed to the occurrence of cholangiographic abnormalities. The bile duct disease in EHPVO may be progressive in nature and would manifest clinically only in those patients who survive to adulthood.

No well-documented reports of biliary disease in patients with EHPVO have come from other studies; the reasons for this are unknown. However, some studies have excluded patients with biliary disease from their series of patients with EHPVO (2). In a study of 97 patients with EHPVO, Web and Sherlock (2) observed that 13 patients were clinically jaundiced. In six patients hyperbilirubinemia followed major gastrointestinal bleeding. In five, serum bilirubin levels were permanently elevated. However, the authors did not study their patients further to determine the causes of jaundice (2). Other authors have observed that jaundice may be the initial feature of portal vein occlusion and have postulated that it occurs as a result of spread of infection from the portal vein to bile ducts or compression of bile ducts by collateral veins (3, 6). Recently Dilawari and Chawla (18) studied cholangiographic changes in 20 patients with EHPVO and found focal narrowing, dilatations and cholangitis changes affecting the main bile ducts and hepatic bile ducts. The authors believe these changes are caused by choledochal varices (18).

Sclerosing cholangitis of the small-duct or large-duct type can occur as a primary syndrome of unknown pathogenesis, and more than 50% of such patients have inflammatory bowel disease (19). Small-duct disease is known to occur in allograft rejection, graft-vs.-host disease and drug-induced cholangitis (20, 21). Patients with AIDS are sometimes first seen with sclerosing cholangitis, which may be caused by human papillomavirus, *Cryptosporidium* or the human immunodeficiency virus itself (22). Of course, large-duct disease can occur in choledocholithiasis or surgical injury to the bile duct (20). Our patients had none of the above-mentioned entities. None had colonoscopic or histopathologic evidence of inflammatory bowel

disease, had received any drug known to cause bile duct strictures or had other conditions known to cause sclerosing cholangitis.

The pathogenesis of cholangiographic changes in patients with EHPVO is unknown. We believe that fibrous scarring in the porta hepatis (portal cavernoma) in EHPVO is the cause of the bile duct angulation seen in the cholangiograms. The fibrous scarring could cause localized narrowing, which may appear as strictures. However, it is difficult to explain how long, confluent strictures; caliber irregularity; and cholangiectasis could be caused by fibrous scarring in the porta hepatis. Moreover, none of the three patients who did not have portal cavernoma on US had cholangiographic abnormalities. Recently, great interest has been shown in the vascular supply of the bile ducts (23) and the ischemic nature of sclerosing cholangitis after liver transplantation, after administration of intraarterial floxuridine and after other surgical procedures (20, 21, 24). We believe that vascular injury at the time of portal vein thrombosis might cause ischemic necrosis of the bile ducts and subsequent stricture formation, caliber irregularity and cholangiectasis. The vascular injury could occur as a result of thrombosis of the veins draining the bile duct or extension of thrombosis to the arterial network supplying bile duct. The bile duct displacement in the cholangiograms of two of our patients are more difficult to explain. Such displacement can be caused by extraluminal masses. Portal cavernoma formed by thrombosis of the portal vein, collateral vessels and fibrous scarring can appear as a mass effect (9). It is possible that it caused cholangiographic abnormalities.

Most of our patients had undergone repeated esophageal variceal sclerotherapy. Bile duct scarring has been shown to follow ethanol embolization of the hepatic artery in experimental studies in monkeys (25). We believe that intravariceal sclerosant injection was not the cause of biliary abnormalities in our study. Two of the patients with clinically manifest biliary disease had never undergone sclerotherapy. The sclerosant, after injection into varices, flows into the azygous venous system and can cause pulmonary damage (26-28). Even if the sclerosant flows toward the liver, it will reach hepatic parenchyma rather than the bile duct. The bile ducts draw their blood supply from the hepatic artery; and intraarterial sclerosant injection must be given to cause biliary changes.

In the past, the major concern in the management of patients with EHPVO has been control of gastrointestinal bleeding (1-6). Variceal bleeding was a major cause of death in such patients. However, esophageal variceal sclerotherapy has changed the outlook of management of such patients and, the procedure has drastically reduced mortality from variceal bleeding (10). Patients are expected to have prolonged survival; thus they may be seen with problems other than variceal bleeding. Biliary disease caused by sclerosing cholangitis may be one such important entity. Our study showed that biliary disease in EHPVO can appear in adulthood and may contribute significantly to morbidity and mortality. Surgical management of biliary strictures in sclerosing cholangitis is difficult, and the presence of collateral veins around the bile duct in patients with EHPVO carries high mortality in biliary approach and exploration. Endoscopic balloon dilatation might be an attractive form of therapy for such strictures, especially if strictures are single and localized.

REFERENCES

1. Triger DR. Extra hepatic portal venous obstruction. Gut 1987;28: 1193-1197.
2. Webb LJ, Sherlock S. The aetiology, presentation and natural history of extrahepatic portal venous obstruction. Q J Med 1979;192:627-639.
3. O'Donnell B, Moloney HA. Development and course of extrahepatic portal hypertension in children. Lancet 1968;1:789-791.
4. Odievre M, Pige G, Alagille D. Congenital abnormalities associated with extrahepatic portal hypertension. Arch Dis Childhood 1977; 52:383-385.
5. Basu AK, Guharay BN. Profile of portal hypertension in India with and without cirrhosis of liver. In: Ahuja MMS, ed. Progress in clinical medicine in India. New Delhi: Arnold Hernemann, 1974:373-419.
6. Gibson JB, Johnston GW, Fulton TT, Rogders HW. Extrahepatic portal venous obstruction. Br J Surg 1965;52:120.
7. Kane RA, Katz SG. The spectrum of sonographic findings in portal hypertension: a subject review and new observations. Radiology 1982;142:453-458.
8. Paquet KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices: a prospective controlled randomized trial. Endoscopy 1982;14:4-5.
9. Quintero E, Pique JM, Bombi JA, et al. Gastric mucosal vascular ectasia causing bleeding in cirrhosis: a distinct entity associated with hypergastrinemia and low serum levels of pepsinogen 1. Gastroenterology 1987;93:1054-1061.
10. Howard ER, Stringer MD, Mowat AP. Assessment of injection sclerotherapy in the management of 152 children with oesophageal varices. Br J Surg 1988;75:404-408.
11. Khuroo MS, Mahajan R, Zargar SA, et al. Colon in shigellosis: serial colonoscopic appearances in shigella dysentarae type I. Endoscopy 1990;22:35-38.
12. MacCarty RL, LaRusso NF, Wiesner RH, Ludwig J. Primary sclerosing cholangitis: findings on cholangiography and pancreatography. Radiology 1983;149:39-44.
13. Scheuer PJ. Liver biopsy interpretations. 3rd ed. London: Baillière Tindall, 1980.
14. Webb LJ, Berger LA, Sherlock S. Gray-scale ultrasonography of the portal vein. Lancet 1977;2:675-677.
15. Kauzlaric D, Petrovic M, Barmeir E. Sonography of cavernous transformation of the portal vein. AJR Am J Roentgenol 1984; 142:383-384.
16. Ludwig J, MacCarty RL, LaRusso NF, Krom RAF, Wiesner RH. Intrahepatic cholangiectasis and large duct obliteration in primary sclerosing cholangitis. HEPATOLOGY 1986;6:560-568.
17. Wee A, Ludwig J. Pericholangitis in chronic ulcerative colitis: primary sclerosing cholangitis of the small bile duct? Ann Intern Med 1985;102:581-587.
18. Dilawari JB, Chawla VK. Pseudosclerosing cholangitis in extrahepatic portal venous obstruction. Gut 1992;33:272-276.
19. Wiesner RH, LaRusso NF. Clinicopathologic features of the syndrome of primary sclerosing cholangitis. Gastroenterology 1980;79:200-206.
20. Ludwig J. New concepts in biliary cirrhosis. Semin Liver Dis 1987;7:293-301.
21. Dikengil A, Siskind BN, Morse SS, et al. Sclerosing cholangitis from intraarterial floxuridine. J Clin Gastroenterol 1986;8: 690-693.
22. Dowsett JF, Miller R, Davidson R, et al. Sclerosing cholangitis in

acquired immunodeficiency syndrome. Scand J Gastroenterol 1988;23:1267-1274.
23. Cho KJ, Lunderquist A. The peribiliary vascular plexus: the microvascular architecture of the bile duct in the rabbit and in clinical cases. Radiology 1983;147:357-364.
24. Terblanche J, Allison F, Northover JMA. An ischemic basis for biliary stricture. Surgery 1983;94:52-57.
25. Doppman JL, Griton ME. Bile duct scarring following ethanol embolization of the hepatic artery: an experimental study in monkeys. Radiology 1984;152:621-626.
26. Connors AF, Bacon BR, Miron SD. Sodium morrhuate delivery to the lung during endoscopic variceal sclerotherapy. Ann Intern Med 1986;105:539-542.
27. Monroe P, Morrow CF, Millen JE, Fairman RP, Glauser FL. Acute respiratory failure after sodium morrhuate esophageal sclerotherapy. Gastroenterology 1983;85:893-899.
28. Kahn D, Terblanche J, Kitano S, Bornman P. Injection sclerotherapy in adult patients with extrahepatic portal venous obstruction. Br J Surg 1987;74:600-602.