Case report

Primary biliary cirrhosis with cancer of the ampulla of Vater

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A test for the detection of antimitochondrial antibodies has led many physicians to accept the diagnosis of primary biliary cirrhosis without laparotomy; however, the coexistence of biliary tract malignancy in primary biliary cirrhosis is a definite possibility and has been reported on one occasion.[1] We report a case of carcinoma of the ampulla of Vater occurring with primary biliary cirrhosis, and discuss the value of the antimitochondrial antibody as well as the potential role of endoscopic retrograde cholangiopancreatography (ERCP) in establishing a correct diagnosis.

Case report

A 57-year-old white woman was referred to the Cleveland Clinic on September 18, 1970, because of jaundice and diarrhea of 8 to 9 months' duration. She described her stools as gray, bulky, and foul smelling. Other complaints were mild right upper quadrant abdominal discomfort, generalized bone pain, and a 3.6-kg weight loss. There was no history of pruritus, alcohol ingestion, exposure to toxins or drugs, or previous liver or biliary tract disease. On physical examination, the patient was thin and emaciated. She had scleral icterus, multiple spider angioma on face and neck, but no xanthelasma or xanthomas. The liver span was 30 cm and the spleen was palpable 2 cm below the left costal margin. There was no ascites or ankle edema. The physical examination was otherwise normal.

Table 1. Results of liver function tests

Date	Bilirubin		SGOT	Alkaline phosphatase	β-globulin	γ-globulin	Albumin	Prothrombin time
	Total mg/100 ml	Direct mg/100 ml	KU	KA units	g/100 ml	g/100 ml	g/100 ml	sec
Sept 1970	7.2	4.6	130	106	1.3	2.5	2.5	13/13
Feb 1971	8.5	6.3	370	630	1.2	2.3	2.7	14/13
Feb 1972	8.5	4.6	170	150	1.0	3.0	2.6	12/12
Aug 1973	14.8	...	250	160	...	3.5	2.2	16/12

Table 2. Additional laboratory tests

	Sept 1970	Feb 1971	Feb 1972	Aug 1973
Hemoglobin (g/100 ml)	11.6	14.5	10.6	9.2
Cholesterol (mg/100 ml)	700	700	320	310
Triglyceride (mg/100 ml)	300	332	320	282
Chylomicron	2+	2+	±	...
β-lipoprotein	4+	4+	3+	...
Total protein (g/100 ml)	7.7	7.3	7.5	6.2
IgM (mg/100 ml)	520	...	350	...
IgG (mg/100 ml)	3500	...	2000	...
IgA (mg/100 ml)	400	...	635	...

The results of the initial laboratory tests are listed in *Tables 1 and 2*. Antimitochondrial antibody was positive at greater than 1:160 serum dilution. Smooth muscle antibody and antinuclear factor were negative.

Barium enema and upper gastrointestinal series were normal. The intravenous cholangiogram did not show any abnormalities. Peritoneoscopy was performed and showed the liver to be deep green and finely nodular. The gallbladder was identified and appeared large and distended; the spleen was also identified and appeared enlarged. There was no evidence of primary or metastatic tumor. Cork bore biopsy of the liver was obtained. Microscopically, the liver biopsy specimens showed portal fibrosis and chronic inflammatory infiltrate comprised of lymphocytes and plasma cells (*Figs. 1 and 2*). Ducts were reduced and replaced by ill-defined lymphoid aggregates. The lobules were intact with no parenchymal necrosis. These findings were interpreted as compatible with primary biliary cirrhosis. She was discharged from the hospital with the diagnosis of primary biliary cirrhosis; a high protein diet and diphenoxylate hydrochloride (Lomotil) were prescribed for control of the diarrhea.

During the next 6 months pruritus appeared for the first time, and the patient continued to have diarrhea and weight loss. She was readmitted to the hospital in February 1971. Results of physical examination were unchanged from her previous admission, except for the presence of bilateral periorbital xanthelasma. Findings from studies are included in *Tables 1 and 2*. Despite the clinical and laboratory studies, and the fact that this patient had been deteriorating without exclusion of an obstructive process, it was decided that laparotomy was necessary. At laparotomy a 3.5-cm firm, rubbery mass was found in the head of the pancreas. Operative cholangiogram showed complete obstruction

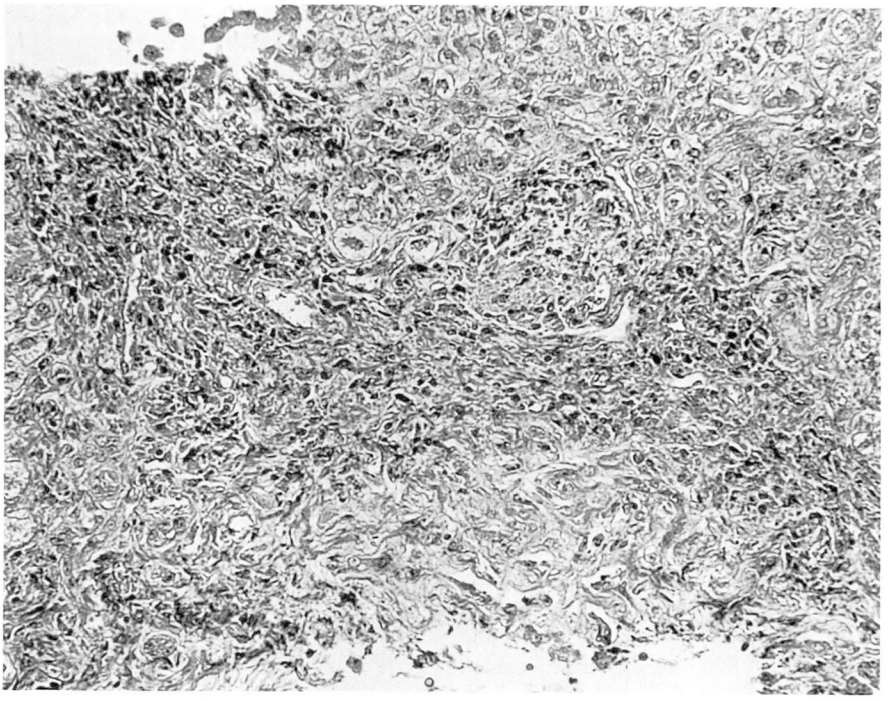

Fig. 1. Photomicrograph of portal triad (Masson-trichrome, ×204).

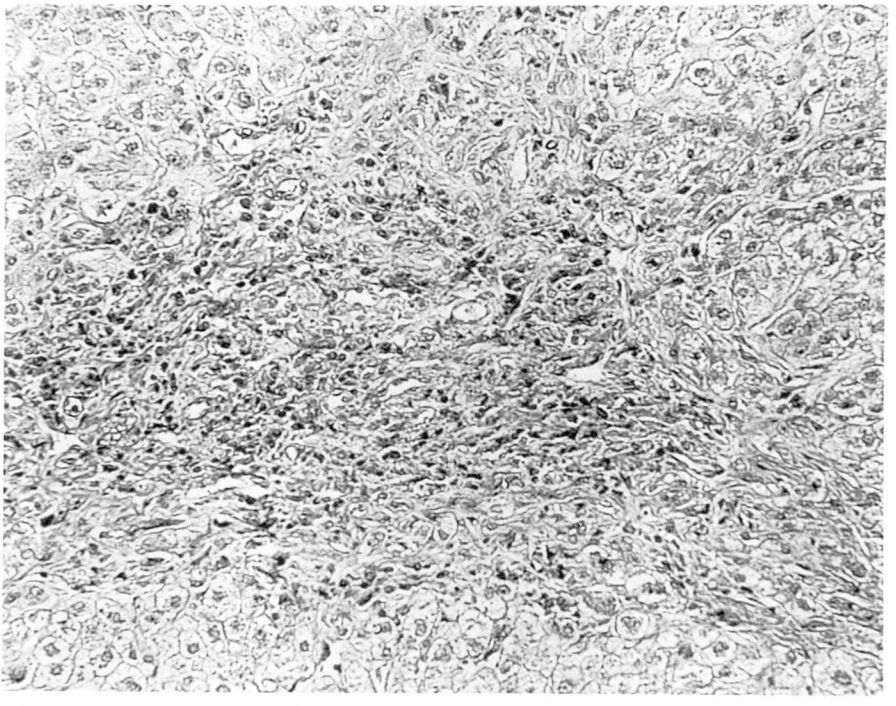

Fig. 2. Photomicrograph of portal triad (Masson-trichrome, ×204).

of the distal common duct with proximal dilatation. No stones were seen at exploration of the common bile duct, and several specimens of needle biopsies of the pancreatic mass indicated pancreatitis. The ampulla of Vater was identified and, although it showed no gross pathology, transduodenal biopsy of the ampulla showed well-differentiated adenocarcinoma. Three weeks later a Whipple's procedure was performed. The patient tolerated the procedure well and was discharged on a regimen of pancreatin, 10 to 12 tablets a day; cholestyramine, 4 g every 6 hours; and diphenoxylate hydrochloride, 6 to 8 tablets a day. For the next 30 months she continued to have severe diarrhea, and generalized bone pain developed due to demineralization of all bony structures. Her stool fat was 272 g/72 hr (normal, 18 g/72 hr). She received appropriate treatment with calcium orally and vitamin D injections.

The patient was readmitted to the hospital in September 1973, because of fatigue, weakness, and steatorrhea. Results of laboratory studies (*Tables 1 and 2*) were compatible with severe hepatocellular failure. By the 3rd hospital day, the patient's level of consciousness had declined and hepatoencephalopathy progressed to Grade IV. She died on the 4th day.

At autopsy the capsular surface of the liver was finely nodular and the entire liver parenchyma was deep green. There was no evidence of recurrence of metastatic tumor. However, a small calculus found in the pancreatic duct probably caused the chronic pancreatitis noted on histologic study.

Discussion

The association of primary biliary cirrhosis in carcinoma of the liver and biliary tree is interesting and raises certain questions concerning (1) the reliability of antimitochondrial antibodies in determining primary biliary cirrhosis, and (2) the role of laparotomy in patients considered to have primary biliary cirrhosis. A review of the literature indicates that the antimitochondrial antibody is an accurate, sensitive test that is positive in 80% to 85% of all patients with primary biliary cirrhosis and falsely positive in only 2% to 4%. Fifteen percent of these patients have findings compatible with primary biliary cirrhosis but with a negative antimitochondrial antibody. In one study 40 of 41 patients with primary biliary cirrhosis had positive antimitochondrial antibodies, but only 2 of 28 with common bile duct obstruction had positive antimitochondrial antibodies.[2] At a later date, other investigators reported a larger series of cases in which antimitochondrial antibody was positive in 83% of 213 patients with primary biliary cirrhosis and less than 1% of 253 patients who had common bile duct obstruction.[3] In another study,[1] 84% of 188 patients with primary biliary cirrhosis, 11% of 77 patients with chronic active hepatitis, and 6% of 33 with cryptogenic cirrhosis also had positive antimitochondrial antibodies. In this same series 180 patients with extrahepatic bile duct obstruction were studied, and 83 of these patients had carcinoma of the pancreas or bile duct. Two of the patients with carcinoma of the pancreas had positive antimitochondrial antibodies, and the only other two positive antimitochondrial antibodies were present in a patient with carcinoma of the gallbladder and transverse colon. Three of the four patients had metastatic disease to the liver or biliary tree, and the fourth had a history of jaundice and xanthelasma, increased alkaline phosphatase level, and elevated serum choles-

terol level. Six months after the onset of symptoms, a needle biopsy of the liver showed lesions which were consistent with primary biliary cirrhosis. Eighteen months after the onset, the patient died, and an autopsy revealed a carcinoma of the pancreas. The authors concluded that the patient probably had both diseases simultaneously. Obviously their case is similar to the one reported here, wherein the patient had clinical, laboratory, and histologic findings compatible with primary biliary cirrhosis 6 months prior to discovery of the carcinoma of the ampulla of Vater. Her symptoms had preceded the laparotomy by almost 18 months. Despite the removal of the obstructing lesion, her condition continued to deteriorate and she died 33 months after the operation. At autopsy, there was no evidence of recurrent tumor or obstruction of the common duct. We believe that this individual had primary biliary cirrhosis concomitant with carcinoma of the ampulla of Vater. Although the antimitochondrial antibody is a sensitive test, lesions of the biliary tract can produce a false positive test result, and these lesions can coexist with primary biliary cirrhosis.

Since the intravenous cholangiogram does not visualize the biliary tree in most cases, diagnostic studies are limited to the transhepatic cholangiogram or ERCP. Percutaneous transhepatic cholangiogram is now regarded as one of the most reliable techniques in differentiating between surgical and nonsurgical jaundice. In a recent report, visualization of the biliary tract was achieved in 67.5% of 314 patients with hepatobiliary problems.[4] With this technique, even if it fails, the failure in itself is meaningful, because it suggests the absence of bile duct dilatation. The complications reported in this study, however, have been as high as 2.6%.[4] Because of this, some physicians are reluctant to use percutaneous transhepatic cholangiography as a routine procedure. ERCP has been used successfully to exclude obstruction in the biliary tree and conditions such as sclerosing cholangitis.[5] The procedure is probably the safest one available at present, and we feel that this tool should be used routinely in patients with primary biliary cirrhosis in order to visualize the biliary tree and to rule out a correctable surgical lesion. If ERCP fails, we believe that laparotomy might become mandatory for (1) the female patient with clinical and laboratory tests compatible with primary biliary cirrhosis but negative antimitochondrial antibody, (2) the male patient with positive antimitochondrial antibody, and (3) the patient with a positive antimitochondrial antibody but rapid deterioration clinically and biochemically.

References

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