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SCLEROSING CHOLANGITIS IN A SIX-YEAR-OLD BOY*

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This unusual condition is characterized by progressive obstructive jaundice and generalized thickening and stenosis of the biliary tree, without intraductal pathology. Constriction of the intra- and extrahepatic biliary tree, secondary to inflammation and fibrosis of the submucosa, is the main abnormality in obstructive jaundice. Recently the cases of two children with this syndrome, both under 16 years of age, were described[1]. Here we would like to present the case of a very young patient with sclerosing cholangitis in whom the diagnosis was made by operative cholangiographic and microscopic examination of the several parts of the biliary tree.

Case Report

The patient, a boy, was first brought to Hacettepe University Children's Hospital in September 1979, when he was five years old, with the complaint of a protuberant abdomen. His height was 93 cm and the weight was 12 kg (both under 3. percentile) indicating severe growth retardation. Diabetes insipidus had developed following head trauma in a car accident in the year preceding his first admission to our hospital; this responded to pitressin treatment. On physical examination hepatomegaly was found to be present (the liver was palpable 6 cm below the right costal margin); other findings, including those of a neurologic examination, were not contributory. Blood pressure was 110/70 mmHg. Laboratory findings revealed no anemia (hemoglobin 12 g/dl), mild leukocytosis (WBC 14.000/µl), slightly elevated transaminases (SGOT: 92 U, SGPT: 120 U) and

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alkaline phosphatase (16 Bodansky Units; normal < 10 BU). The results of bone marrow examination, prothrombin time, partial thromboplastin time, alpha-1-antitrypsin (5.12 mg/ml; control 2 mg/ml) did not disclose any abnormality; serum amylase (162 U) was at the upper limit of normal. Liver needle biopsy showed slight proliferation of the bile canaliculi with mild portal fibrosis and mononuclear cell infiltration.

The general condition of the patient deteriorated and anemia with jaundice appeared with marked elevation of alkaline phosphatase activity (25 BU) within two months, but HBsAg and anti HBs remained negative. Bilirubinuria and urobilinogenuria persisted and a marked elevation of transaminases (SGOT: 475 U, SGPT: 375 U) was observed. After eight months the bilirubine (35.5 mg/dl, conjugated 24.3 mg/dl), alkaline phosphatase (35 BU), total lipids (1520 mg/dl) and cholesterol (470 mg/dl) levels were markedly elevated and the spleen was enlarged and palpable 5 cm below the left costal margin. Repeated liver needle biopsy indicated an increase in the number of bile canaliculi with some round cell infiltration and periportal fibrosis (Figure 1). Plasmocytoid cell islands were observed in microscopic examination of splenic needle aspiration (Figure 2). Although the IgG was found to be markedly elevated (1520 mg/dl, normal < 1300 mg/dl); IgA (122 mg/dl) and IgM (199 mg/dl) levels were within normal limits.

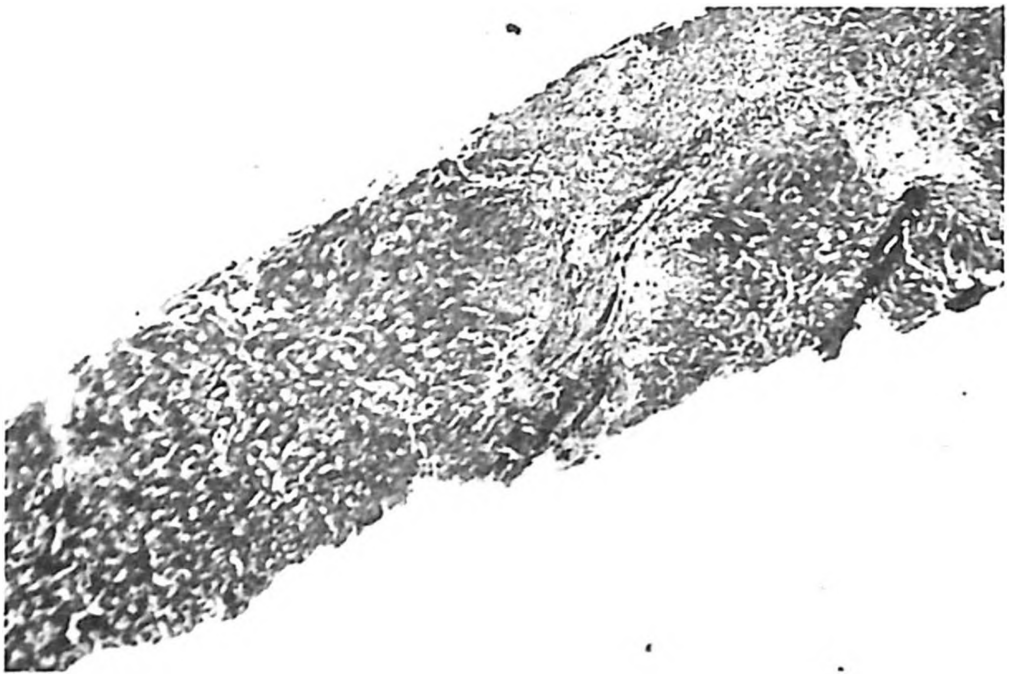

Figure 1

Preoperative liver needle biopsy shows periportal fibrosis.

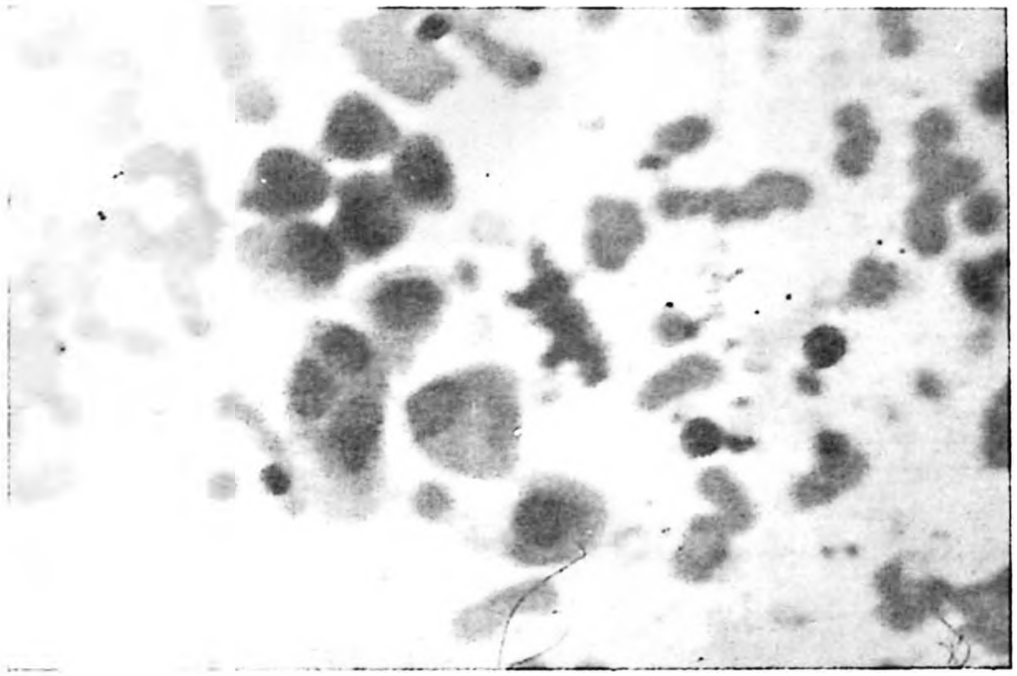

Figure 2

The cluster of plasmocytoid cells in the splenic needle aspiration.

Prior to the operation medical treatment was tried and phenobarbital (5 mg/kg) and prednisone (2 mg/kg) were given, each for a period of one month, but no change in the bilirubin, cholesterol or total lipid levels resulted. The drainage of bile through the insertion of a T tube into the choledochal duct did not effect the bilirubinemia either, and no changes were obsered in the general condition. The patient expired 25 days after the operation; an autopsy was not granted.

Exploratory laparotomy revealed a green colored nodular liver and hydropic gallbladder. The ductus cysticus was found to be very narrow and bead appearances were observed in the ductus choledocus which had narrow and enlarged parts.

The macroscopic changes of the bile ducts were clearly shown by the operative cholangiography (Figure 3) which was characteristic for sclerosing cholangitis. Submucosal round cell infiltration with very marked fibrotic bands was shown in microscopic examination of the bile canaliculi (Figure 4 a and b). Operative liver biopsies indicated intracellular and intraductal cholestasis with proliferation of bile canaliculi with mononuclear round cell infiltration and increased fibrotic tissue in the periportal spaces.

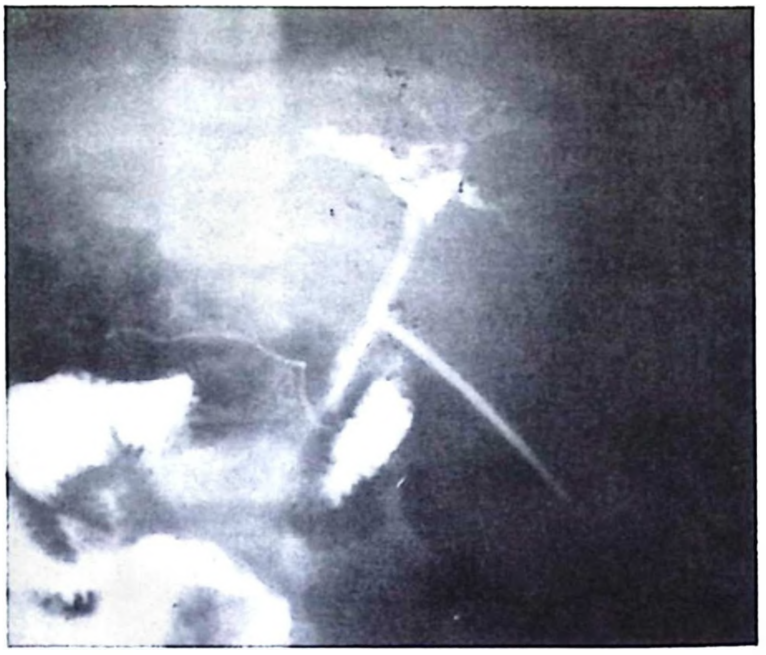

Figure 3
Operative cholangiography shows bead appearance of bile ducts.

Discussion

The most common causes of progressive obstructive jaundice in infancy are neonatal hepatitis and biliary atresia. The bile plug syndrome, choledochal cyst, bile duct hypoplasia, α_1-antitrypsin deficiency, and different types of hereditary recurrent intrahepatic cholestasis and Byler's disease should also be kept in mind in the differential diagnosis of obstructive jaundice[23]. Sclerosing cholangitis is the rarest form of obstructive jaundice in childhood. Liver cirrhosis which is a frequent cause of prolonged jaundice with bilirubinuria among Turkish children very rarely presents with obstructive jaundice[4,5]. Acquired bile duct stricture related to blunt trauma has also been reported as an infrequent cause of obstructive jaundice[6]. The main pathological finding in this condition is the presence of a fibrotic band, without any evidence of inflammation about the portahepatis[5]. More recently, fibrosing pancreatitis, another rare cause of obstructive jaundice, was observed in a previously asymptomatic three-year-old boy during laparotomy[7].

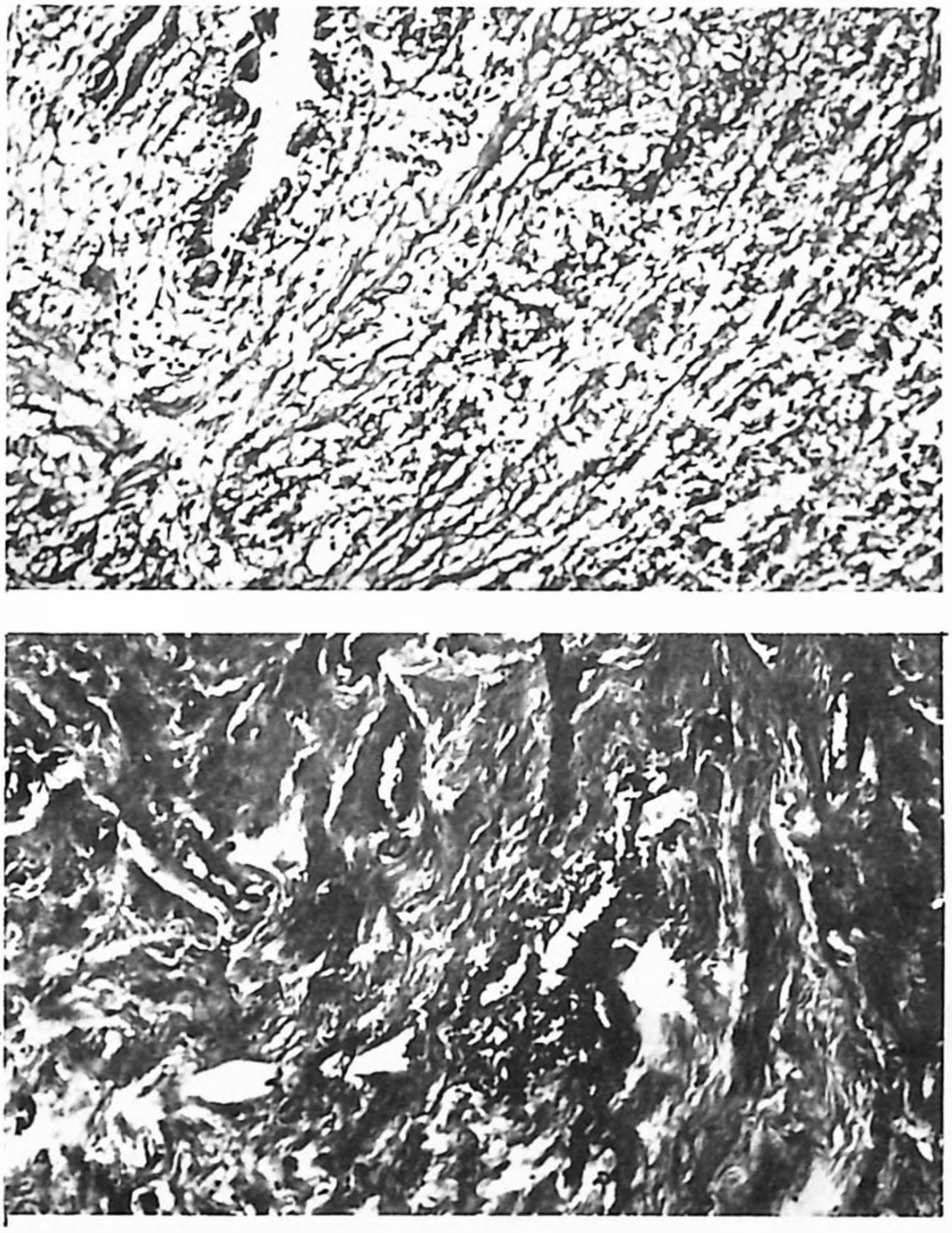

Figure 4

Microscopical examination of the bile duct. a) Round cell infiltration in the submucosa, b) Fibrotic bands of the bile ducts.

Sclerosing cholangitis has been reported with a variety of seemingly unrelated conditions such as tyroiditis, ulcerative colitis, Crohn disease, retroperitoneal fibrosis, orbital pseudotumor and sickle-cell anemia[1]. Although prolonged obstructive-type jaundice may occasionally occur in patients with sickle-cell anemia as in hepatic crises[8], it should be differentiated from the sclerosing cholangitis in which typical cholangiographic findings are observed[1]. As in our patient, the liver histological findings are not diagnostic in this syndrome, though portal fibrosis, mild portal inflammation and intracellular and intraductal cholestasis are observed. Intrahepatic ductal cholangiography usually does not visualize

the biliary tree. Transhepatic and operative cholangiography are the most important diagnostic procedures as in this case (Figure 3). Fibrosing pancreatitis was ruled out in our case by these studies.

If medical therapy is of no benefit, surgical intervention may be necessary for the diagnosis and the partial relief of obstruction in patients with sclerosing cholangitis. However, the complications of surgery should be considered and not attempted if at all avoidable. At present, the prognosis of this syndrome is guarded and treatment should be directed to the underlining disease if it can be found.

The plasmacytoid cells seen in the spleen of our patient have not, as far as we know, been previously reported in patients with sclerosing cholangitis. The morphologic findings in our patient might indicate some kind of immunologic response as the IgG level was also found to be elevated. However we could not substantiate the stimulatory factor for this immunologic response. The documentation of this syndrome in two adolescents with inflammatory bowel disease[9] and very recently in an infant with immunodeficiency[10] in whom hemolytic anemia was also documented, may also be taken as suggesting that some immunologic responses could be the underlying factor in the development of this pathological condition[11].

Acquired bile duct stricture related to blunt trauma was seriously considered in the case of our patient because of the history of a car accident a year prior to admission and the fibrotic band over the ductus cysticus. But because of the cholangiographic findings and submucosal round cell infiltration in the bile canaliculi, it seems more likely that this is an instance of sclerosing cholangitis.

Summary

The case of a six-year-old boy with sclerosing cholangitis is presented. The diagnosis was verified by cholangiographic and pathological studies. Despite surgical intervention, the jaundice and the course of the disease could not be altered. The plasmocytoid cell clusters in the spleen and marked IgG elevation in the serum suggest that the immunologic mechanism might account for the pathogenesis of this syndrome.

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