Caustic Sclerosing Cholangitis treated with Orthotopic Liver Transplantation

Gilles Morali MD[1], Rifaat Safadi MD[2], Orit Pappo MD[3], Oded Jurim MD[4] and Daniel Shouval MD[2]

[1]Department of Gastroenterology, Shaare Zedek Medical Center, Jerusalem, Israel
[2]Liver Unit, Division of Medicine, [3]Department of Pathology, and [4]Division of Surgery, Hadassah University Hospital, Jerusalem, Israel

Key words: secondary sclerosing cholangitis, formaldehyde, liver histology, liver transplantation

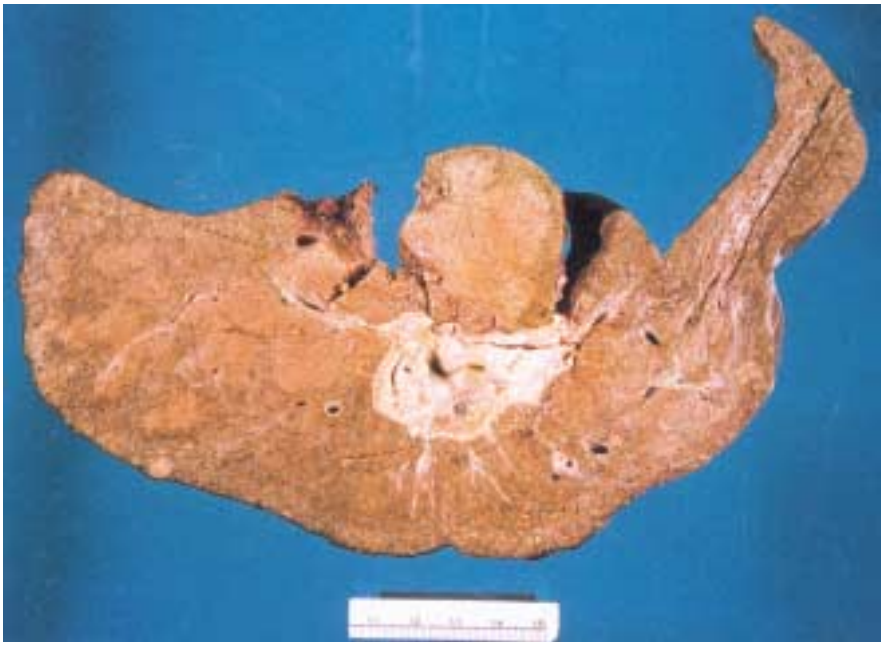
IMAJ 2002;4:1152–1153

Caustic sclerosing cholangitis, so named by Belghiti et al. in 1986 [1], is a rare entity caused by injection of a scolicidal solution into hydatid cysts during surgery. Until now, only 40 cases have been reported in the world medical literature [2], and the histologjc features are not well described. We report a case of a teenage girl with formaldehyde-induced sclerosing cholangitis who was treated by orthotopic liver transplantation. This enabled us to study in detail the macroscopic and microscopic features of this entity.

To the best of our knowledge, this is the first reported case of caustic sclerosing cholangitis in a patient who had previously undergone liver transplantation. We describe the unique macroscopic features, characterized by severe scarring with a calcified mass in the area of previous injection of formaldehyde.

Patient Description

A 16 year old girl had undergone surgery at the age of 12 for an echinococcal cyst of the liver. A 2% formaldehyde solution was injected into the cyst, the cyst was removed and the residual cavity was drained with a catheter. Postoperatively a biliary-cutaneous fistula developed with recurrent episodes of ascending cholangitis. Endoscopic retrograde cholangiopancreatography demonstrated intrahepatic bile duct strictures compatible with sclerosing cholangitis. The common bile duct was spared. Following antibiotic treatment, papillotomy and stenting by ERCP, the fistula was closed. Subsequently, over a period of one year, the patient became jaundiced, hepatosplenomegaly developed, and cholestatic features were dominant: Alkaline phosphatase 770 IU/ml, gamma-glutamyl transferase 190 IU, total bilirubin 150 μmol/L, aspartate aminotransferase and alanine aminotransferase levels were elevated to twice normal limits. Serum albumin was 32 gl and INR of the prothrombin time was 2.3. Leukocyte count was 3,800/ml, hemoglobin 1.3 g/dl and platelet count 90,000/ml. Antineutrophil cytoplasmic antibodies as well as other autoimmune antibodies and viral serology were all negative. Liver biopsy revealed cholestasis and secondary biliary cirrhosis. The patient did not develop ascites but had asymptomatic esophageal varices. Treatment with ursodeoxycholic acid and propranolol led to a decreased rate of cholestasis. However, due to the clinical and laboratory assessment of secondary biliary cirrhosis with portal hypertension and synthetic dysfunction, together with severe fatigue that confined her at home, an orthotopic liver transplantation was performed 4 years after the initial injection of formaldehyde. Macroscopic examination of the explant revealed an enlarged, greenish brown liver that was firm in texture. The capsular surface was nodular with little variation in size and shape of the nodules. At the hilum, the area of the previous surgical procedure, a 4 cm grey calcified mass was noted with incarcerated stones in the area of previous surgery [Figure]. The main intrahepatic bile ducts were dilated and contained sludge. Microscopic examination revealed irregular cirrhosis that was



Macroscopic picture of the explanted liver showing a 4 cm calcified mass at the site of the previous formaldehyde injection.

ERCP = endoscopic retrograde cholangiopancreatography

mildly active, with cholate stasis and cholangiolar proliferation. There was also moderate mixed inflammatory cell infiltrate in portal tracts and septae. Septal and interlobular bile ducts were noted in some of the portal tracts and seemed normal in appearance. In the parenchyma, hepatocanalicular cholestasis was present along with feathery degeneration of hepatocytes. At the hilum a broad fibrosis scar was noted with coarse calcification. Within the scar the large bile ducts showed a fibrous thickening of their wall.

Comment

Injection of a scolicidal solution into hydatid cysts is used to sterilize the cysts and prevent intraabdominal dissemination of the parasite during surgery. Caustic sclerosing cholangitis, which develops after surgical treatment of hydatid cyst of the liver using formaldehyde, 20% saline, or alcohol, has been reported [1–5]. Four basic factors are thought to cause this disease [2]: a) scolicide agent injection into the cyst cavity, b) cysto-biliary communication, c) a condition that prolongs the exposure of the biliary tree to the scolicidal solution, and d) individual sensitivity to the scolicidal agent

Our case fulfilled all these conditions: after formaldehyde was injected, the patient developed a biliary-cutaneous fistula secondary to biliary damage produced during the surgery. Thus, a cysto-biliary communication, which frequently occurs in hydatid disease of the liver [1], might have occurred during the operation. Since the damage to the biliary tree increased the time of exposure to the scolicidal agent, the patient developed a severe caustic sclerosing cholangitis that evolved into end-stage liver disease within 4 years, necessitating liver transplantation.

Our case is compatible with caustic sclerosing cholangitis and not with primary sclerosing cholangitis for two reasons: The first is the rapid course of the disease compared to primary SC. In primary SC, the time from diagnosis to the stage of liver transplantation takes an average of 10–14 years, whereas in our case the evolution was more rapid. Second, in most patients with primary SC, strictures affect the whole biliary tree; in caustic sclerosing cholangitis they are localized to only a part of it, as in our case.

The tie between the injection of formaldehyde and the development of sclerosing cholangitis is based on the following: the patient developed cholangitis after the operation, the biliary strictures were localized, and other causes were excluded such as gallstones and primary SC.

A caustic lesion caused by the scolicidal solution having passed from the cyst into the biliary tree is a much more plausible explanation. This mechanism is consistent with the early development of the strictures after surgery and with the distribution of the bile duct lesions not in proximity to the hydatid cyst. The passage of the scolicidal solution from the cyst into the biliary tree is most likely the consequence of a cystic-biliary communication. The solution might be deleterious to the biliary epithelium.

Our patient developed secondary biliary cirrhosis necessitating liver transplantation. This indication for transplantation was unique to our patient. Moreover, this enabled us to describe the pathologic features that were unknown previously.

SC = sclerosing cholangitis

References

1. Belghiti J, Benhamou JP, Houry S, Grenier P, Huguier M, Fekete F. Caustic sclerosing cholangitis: a complication of the surgical treatment of hydatid disease of the liver. *Arch Surg* 1986;121:1162–5.
2. Castellano G, Moreno-Sanchez D, Outierrez J, Moreno-Gonzalez E, Colina F, Solis-Herruzo JA. Caustic sclerosing cholangitis. Report of four cases and a cumulative review of the literature. *Hepatogastroenterology* 1994;41:458–70.
3. Khodadadi DJ, Kurgan A, Scmidt B. Sclerosing cholangitis following the treatment of echinococcosis of the liver. *Int Surg* 1981;66:361–2.
4. Polo Melero J, Teres J, Gomez-Moli J, Bruguera M. Sclerosing cholangitis after surgical treatment of hepatic echinococcal cysts: report of three cases. *Am J Surg* 1984;148:694–7.
5. Mirouze D, Bories P, Pommier-Layargues G, et al. Cholangite sclerosante secondaire a une formolisation accidentelle des voies biliaires chez 5 malades porteurs d'un kyste hydatique du foie. *Gastroenterol Clin Biol* 1983;7:200–1.

Correspondence: Dr. G. Morali, Dept. of Gastroenterology, Shaare Zedek Medical Center, Jerusalem 97342, Israel.
Phone: (972-2) 676-5180
Fax: (972-2) 676-5147
email: gilles@bezeqint.net

Capsule

Neurotrypsin and mental retardation

Inherited mental retardation (MR) is often linked to abnormalities on the X chromosome or to abnormalities in brain development or other clinically identifiable features, but in most cases none of these attributes is present. An analysis of such non-syndromic MR patients by Molinari et al. revealed an association with the mutation of the serine protease neurotrypsin. *In situ* hybridization studies of the expression of neurotrypsin during normal development revealed that it is expressed in parts of the brain associated with learning and memory and first appears at 44 days of development. Immunoelectron microscopy localized neurotrypsin at presynaptic nerve endings. Although this mutation does not appear to be a common cause of MR, further studies may yield insights into the pathways leading to these diseases.

Science 2002;298:1779