

# INTRAHEPATIC CYSTIC DISEASE WITH CONGENITAL FIBROSIS (CAROLI'S COMPLEX DISEASE). A CASE REPORT AND REVIEW OF THE LITERATURE

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**SUMMARY** – A female patient affected by Caroli's disease with congenital fibrosis (Caroli's complex), aged 27 years, is described. Caroli's disease had been asymptomatic to the present. It was recognized as an intraoperative finding during the left hepatectomy procedure after an acute abdominal crisis episode. The main reason for this surgery was the incidence of malignant transformation to cholangiocarcinoma of the cells of the cystic walls. The complex Caroli's disease is more common than other forms. The case report is supplemented with literature review and discussion on the etiopathogenetic mechanisms hypothesized.

**Key words:** *Caroli's disease, etiology; Caroli's disease, diagnosis; Caroli's disease, complications; Hepatectomy; Case reports*

## Introduction

Although Caroli's disease generally involves the entire liver, it may be segmental or lobar. The inheritance is autosomal recessive. Clinically, patients suffer from bouts of recurrent fever and pain. Jaundice occurs only when a stone blocks the common bile duct<sup>1,2</sup>. Leukocytosis is observed typically when acute cholangitis develops. Liver tests are generally normal except during the episodes of obstructive jaundice. The diagnosis is established by cholangiography (intravenous, transhepatic), endoscopic retrograde cholangiopancreatography, ultrasonography, and computed tomography (CT). The complications include recurrent cholangitis, abscess formation, septicemia or pyemia, intrahepatic lithiasis, and amyloidosis. Adenocarcinomas, including some arising in cases with a lobar distribution, have also been reported<sup>3,4</sup>. Surgical treatment is by internal or external drainage procedures. Segmental or lobar forms of Caroli's disease can be treated by partial hepatectomy.

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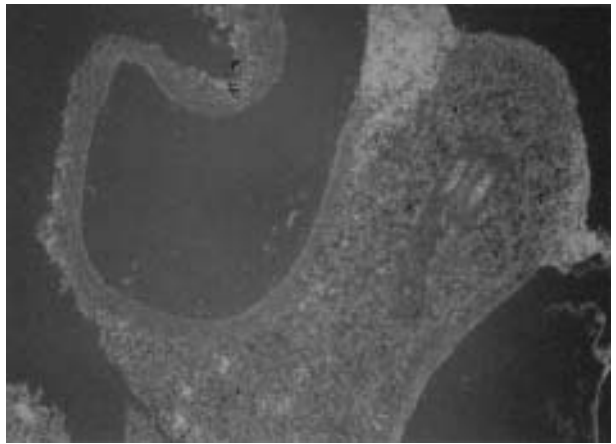
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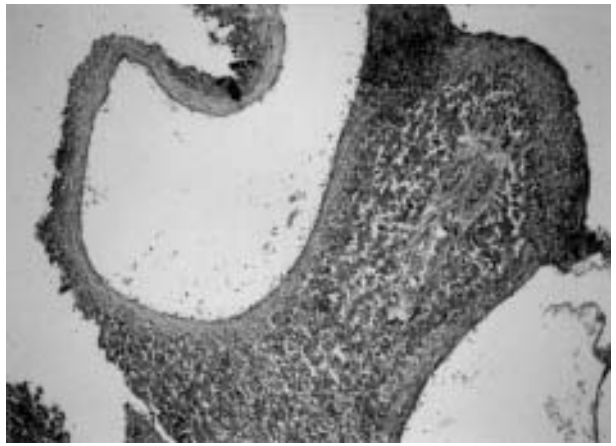
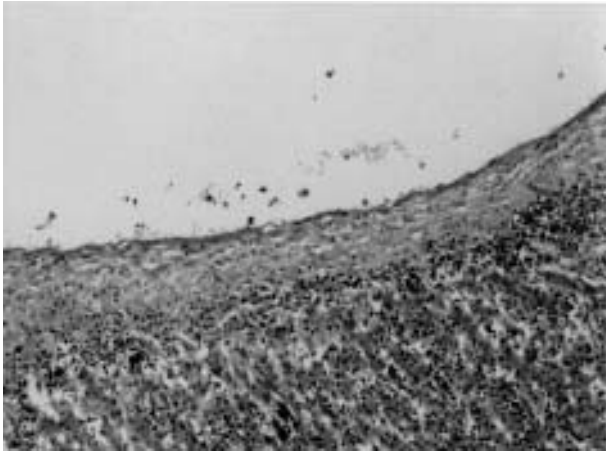
According to Desmet<sup>5</sup>, the pathogenesis of Caroli's disease seems to involve total or partial arrest of remodeling of the ductal plate of the larger intrahepatic bile ducts. In Caroli's syndrome (Caroli's disease with congenital hepatic fibrosis) the hereditary factor causing the arrest of remodeling seems to exert its influence not only during the early period of bile duct embryogenesis, but also later during development of the more peripheral biliary ramifications (the interlobular bile ducts).

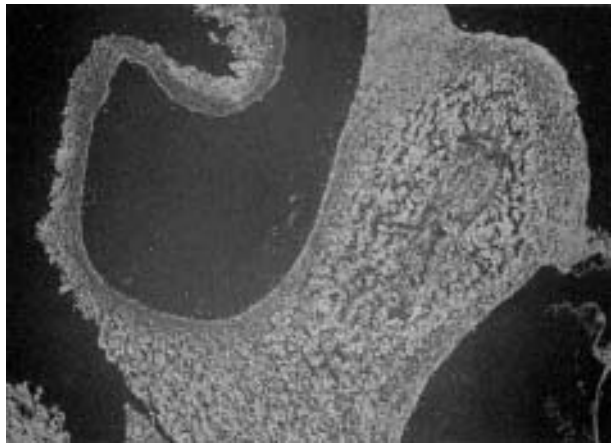
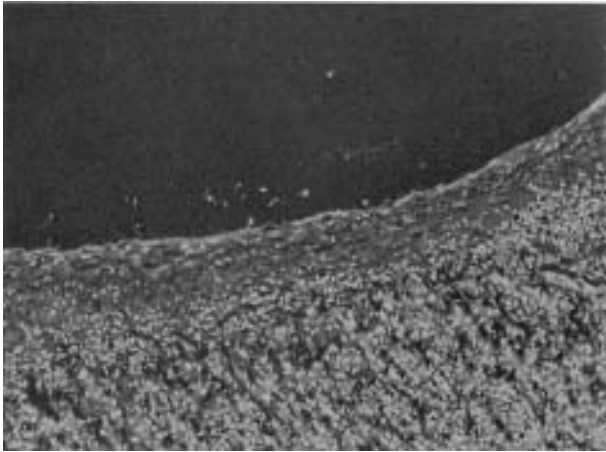
## Case Report

A 27-year-old female was referred to our hospital with an acute abdominal crisis. On clinical examination there was hepatomegaly. Serologic testing showed leukocytosis and normal levels of the tumor associated antigens CEA and CA 19-9. Indirect hemagglutination test was negative.

Ultrasound revealed multiple small and large unilocular cysts involving the left hepatic lobe. Most appeared anechoic due to clear fluid content with posterior acoustic enhancement, and had a smooth regular wall. There were also some cysts containing internal echoes, and the largest ones produced mass effect with pericystic biliary dilatation. One cyst showed a discontinuity in the wall







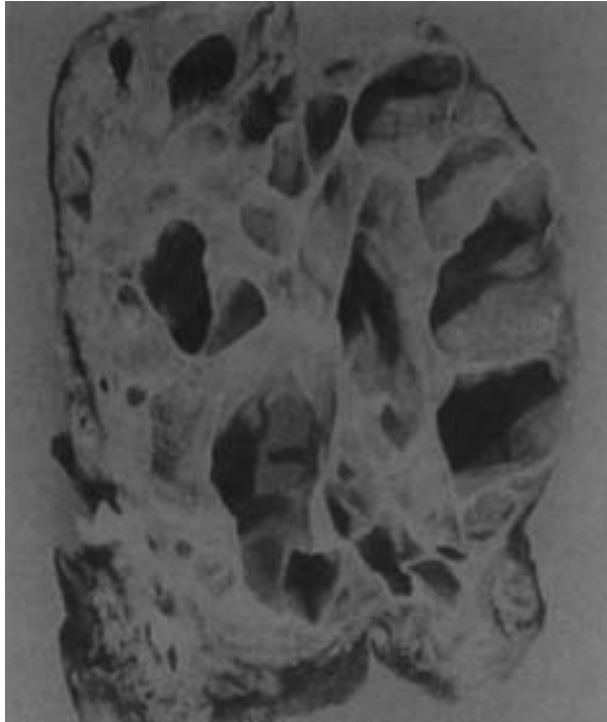


Fig. 1. Surgical specimen of left hepatectomy.

(ruptured cyst). CT appearance of the cysts with respect to ultrasonography was as follows: anechoic ones consisted of a well-circumscribed, homogeneous mass with no discernible wall. They had attenuation value (range from -5.8 HU to 20 HU), and showed no enhancement after intravenous contrast medium administration. Those producing mass effect showed contrast enhancement (evi-

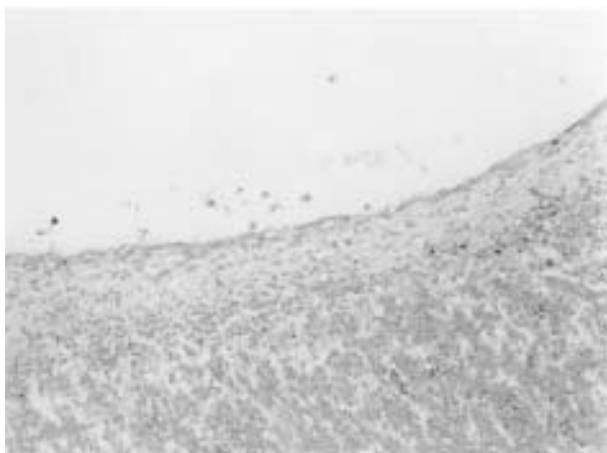


Fig. 2. Parietal tissue of the intrahepatic cyst lined by flattened epithelium. (H&E X100)

dence of pericycstic biliary radicle dilatation). Left hepatectomy was subsequently performed and the surgical specimen was submitted to routine histologic analysis.

On gross examination multiple cysts (of greatest diameter ranging from 1 to 4.5 cm) were found (Fig. 1). The cysts were round to oval and were encapsulated. They contained several liters of clear fluid. Some of them were hemorrhagic and one was ruptured. The lining of the cysts consisted of a single layer of flat or cuboidal epithelium (Fig. 2). The cells rested on a basement membrane and were supported by a variably dense fibrous connective tissue. The hepatic parenchyma was intersected by sinuous bands of dense fibrous connective tissue that involved portal areas, isolating single or several lobules (Fig. 3). The lobular architecture was partly disturbed. The hepatocytes showed no abnormalities. Our findings were consistent with congenital cystic disease and hepatic fibrosis (Caroli's syndrome).

## Discussion

Cystic and dysplastic lesions of the liver are a complex group of disorders, the relating classification and terminology being quite confused. The dilatations may be extrahepatic or intrahepatic but may affect the entire biliary system, either diffusely or focally. Some consist of cystic dilatations of the biliary tract that communicates with the bowel (e.g., choledochal cyst, Caroli's disease). The classifications proposed by Longmire *et al.*<sup>6</sup> in 1971 and by Hadad *et al.*<sup>7</sup> in 1976, which in turn was partly based on the classification of Alonso-Lej *et al.*<sup>8</sup> from 1959, have helped

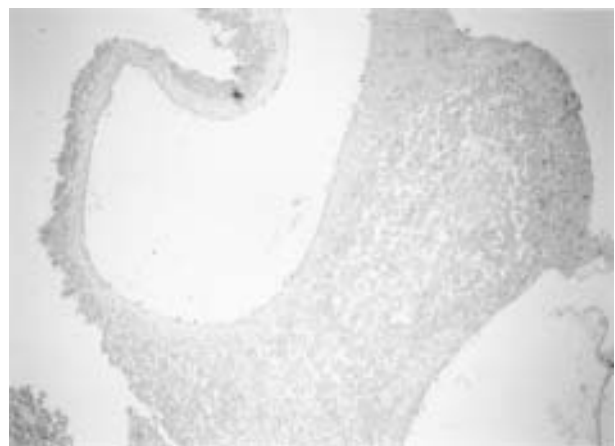


Fig. 3. Bands of dense fibrous connective tissue involving hepatic lobules. (H&E X100)

clarify the issue. Whether the solitary (non-parasitic) bile duct cyst fits into this group of disorders remains to be determined. The cystic dilatations, however, are by no means 'pure', i. e. limited to dilatation of one form or another, since some may also be associated with proximal and/or distal atresia<sup>9</sup>, or with congenital hepatic fibrosis<sup>10</sup>. Landing<sup>11</sup> has proposed a unifying hypothesis for neonatal hepatitis, biliary atresia and choledochal cyst.

Congenital polycystic disease clearly exists in two forms, the infantile and the adult, which have different modes of inheritance; von Meyenburg complexes fall into the spectrum of adult polycystic disease. Congenital hepatic fibrosis is regarded by some as morphologically indistinguishable from infantile polycystic disease<sup>12</sup>, although others consider the renal changes to be different<sup>13</sup>. Formidable arguments have been advanced against the very existence of congenital hepatic fibrosis as an entity<sup>14</sup>. The relationship of congenital hepatic fibrosis to other diseases such as Ivemark's familial dysplasia and Meckel's syndrome requires clarification, as pointed out by Lieberman *et al.*<sup>13</sup> and Murray-Lyon *et al.*<sup>14</sup> The hepatic changes in Potter's type III cystic disease of the kidney also appear identical to those of congenital hepatic fibrosis<sup>15</sup>. A classification based on the renal abnormalities may perhaps prove more useful than the one emphasizing liver changes<sup>14</sup>. A unifying concept of all congenital cystic and dysplastic liver diseases has yet to be formulated.

The current classification includes five types:

- type 1 – choledochal cyst, a localized cystic dilatation of the extrahepatic bile duct;
- type 2 – diverticulum of the common bile duct or gallbladder;
- type 3 – choledochele, a lesion that extends into the wall of the duodenum;
- type 4 – multiple dilatations of extra- and intrahepatic ducts (Caroli's syndrome); and
- type 5 – fusiform extra- and intrahepatic dilatation.

Our case was consistent with type 4 lesion (Caroli's syndrome). Hypertension in these patients is said to be presinusoidal and may be related to the hypoplasia of the portal veins. It can be treated by portal system shunt. In a series of 27 children with congenital hepatic fibrosis, portasystemic shunt was carried out in 16 children between 3 and 16 years of age. No impairment of hepatic function or sign of hepatic encephalopathy was apparent during follow-up examinations over periods ranging from 3 months to 12 years<sup>16</sup>. The infantile form has a favorable prognosis<sup>17</sup>. As far as the adult form is concerned, the treatment of

choice is hepatic resection due to the high incidence of malignant transformation to cholangiocarcinoma of the cells of the cystic walls<sup>18-20</sup>. Simple Caroli's disease (without congenital fibrosis) is less common than other forms<sup>21</sup>.

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#### Sažetak

### INTRAHEPATIČNA CISTIČNA BOLEST S KONGENITALNOM FIBROZOM (CAROLIJEV KOMPLEKS). PRIKAZ SLUČAJA I PREGLED LITERATURE

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Opisan je slučaj 27-godišnje bolesnice s Carolijevom bolešću i kongenitalnom fibrozom (Carolijev kompleks). Carolijeva bolest dotad je bila asimptomatska. Prepoznata je kao intraoperacijski nalaz tijekom postupka lijevostrane hepatektomije nakon akutne epizode abdominalne krize. Glavni razlog za operacijski zahvat bila je maligna pretvorba u kolangiokarcinom stanica cističnih stijenka. Carolijev kompleks češći je od drugih oblika bolesti. Prikaz slučaja je dopunjen pregledom literature i raspravom o pretpostavljenim etiopatogenetskim mehanizmima.

*Ključne riječi: Carolijeva bolest, etiologija; Carolijeva bolest, dijagnostika; Carolijeva bolest, komplikacije; Hepatektomija; Prikaz slučaja*