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Original contribution

Choledochal cysts: a clinicopathologic study of 36 cases with emphasis on the morphologic and the immunohistochemical features of premalignant and malignant alterations☆

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Summary Choledochal cysts (CDCs) are believed to represent a risk factor for the development of neoplasia. However, the frequency and morphology of neoplastic changes have not been systematically studied, especially in North America. Our aims were to study the frequency and morphology of preneoplastic/neoplastic changes of CDCs. Thirty-six cysts were subjected to clinicopathological analyses. Metaplasia was found in 14 of 35, of which 9 had biliary intraepithelial neoplasia (BilIN). Of the 14 with metaplasia, 13 showed pyloric gland; 5, intestinal; and 2, squamous. BilINs included 6 BilIN-1, 2 BilIN-2, and 2 BilIN-3. Carcinoma was identified in 5 cases of which 3 were associated with metaplasia and BilIN. Only 1 of 18 cases without metaplasia had BilIN, and none had carcinoma (P = .0008). There was a trend toward more BilIN and carcinoma with intestinal rather than with pyloric gland metaplasia. All cases with metaplasia or/and BilIN were negative for MUC1. All cases with intestinal metaplasia were positive for CK20, CDX2, and MUC2, whereas cases with pyloric gland were positive for MUC6. MUC1, CEA, and B72.3 were positive only in carcinoma. There was a trend toward increasing p53 and Ki-67 from metaplasia to BilIN to carcinoma. Four of 5 patients with carcinoma died, and one was alive with disease. All others were free of disease except for one who developed new cysts. CDCs are associated with a high rate of BilIN (28.5%) and carcinoma (14.3%). CDCs show a sequence of tumor progression from metaplasia to BilIN and carcinoma.

1. Introduction

Choledochal cysts (CDCs) are rare pathologic dilatations of the biliary tract. They predominantly present in children, with only 20% to 30% of the patients being older than 20 years [1]. However, the diagnosis of CDCs has become more frequent in adults, most likely because of improvements in noninvasive hepatobiliary imaging [2].

CDCs are very rare in Western countries, with an estimated incidence of 1 in 13 500 in the United States. They are far more common in the Asian population, with a reported incidence of 1 per 1000 in Japan [3,4]. They are also

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more common in females, with a female-to-male ratio of 3.5 to 1 [1].

CDCs are predominantly extrahepatic, in the common bile duct; but they can also involve any part of the biliary tract, including the intrahepatic bile ducts [1].

They are classified based on their anatomic location and the extent and shape of the cystic lesion. In 1959, Alonso-Lej et al [5] proposed a classification for extrahepatic bile ducts cysts, which was later modified by Todani et al [6] to incorporate the intrahepatic dilatations. According to the Todani classification, which is a widely used classification, there are 5 types of CDCs (Fig. 1) [1,6], as follows: type I, solitary extrahepatic cyst (Ic, cystic type; If, fusiform type); type II, extrahepatic supraduodenal diverticulum; type III, intraduodenal diverticulum; type IV, extrahepatic and intrahepatic dilatation (IVa, fusiform extrahepatic and intrahepatic cysts; IVb, multiple extrahepatic cysts); and type V, multiple intrahepatic cysts (Caroli disease). Except for type IV cysts, which are seen more frequently in adults, the cyst types are equally distributed among children and adults [7–9]. Type I is the most common (79%), followed by type IV (13%), type III (4%), type II (3%), and type V (1%) [10].

Nevertheless, the Todani classification puts together different diseases with different etiology and pathogenesis and might be oversimplified. In 2004, Visser et al [11] suggested that the distinction between Todani type I and type IV cysts is arbitrary because the intrahepatic ducts are never completely normal and that types I and IV are the same process, type III is choledochocele, and type V is Caroli disease.

The classic triad of jaundice, abdominal mass, and pain occurs less commonly in adults with CDCs than in children. Adults usually present with vague symptoms; however, the symptoms in adults appear to be more serious, with a higher rate of cholangitis, pancreatitis, and cholecystitis than in pediatric patients [3,12]. CDCs may be associated with a variety of complications such as stones, inflammation, infections, and obstruction [3]. Moreover, they have been associated with increased risk of malignancy both in the bile ducts and in the gallbladder [4,13]. Presumably, the evolution of carcinoma in CDCs follows a similar sequence of dysplasia (biliary intraepithelial neoplasia [BilIN]) as described in the noncystic bile ducts [7,14]; but extensive pathologic studies have not been performed.

In this study, we examined 36 cases of CDC resected at a single North American institution, focusing on the morphologic features of these lesions including different types of metaplasia, BilIN, and carcinoma. We also analyzed the immunohistochemical features of the premalignant and malignant alterations in these lesions.

2. Materials and methods

After obtaining Institutional Review Board approval on September 2008, all identifiable cases of CDCs were retrieved from the files of the Department of Pathology at Memorial Sloan-Kettering Cancer Center, dating from 1990 to 2008. Hematoxylin and eosin–stained sections were available in 36 cases. The cystic lesions were well sampled: 88% of the cysts had at least 1 sampled section per

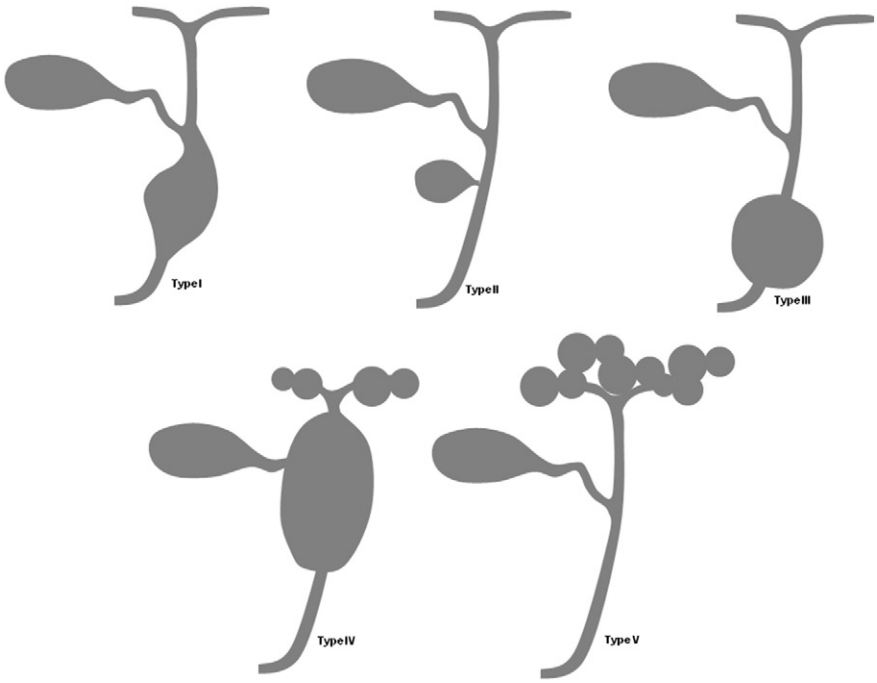

Fig. 1 Illustration of different type of CDCs described by Todani et al [6].