Chapter 5
Hamster Models of Biliary Carcinoma

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A. Pancreaticobiliary Maljunction Model

5.1 Introduction

Pancreaticobiliary maljunction (PBM) is a congenital anomaly characterized by a union of the pancreatic and biliary ducts, located outside the duodenal wall [1]. This anomalous condition has recently been recognized as a high risk factor for the development of biliary carcinomas later in life [2,3]. Two-way regurgitation occurs in this disorder, as the reflux of pancreatic juice up to the biliary tree and/or of bile up to pancreatic duct, because the sphincter muscle of Oddi does not act functionally in this anomalous union. Therefore, patients with PBM are prone to the development of various pathological conditions of the biliary tract and pancreas, including cholangitis, pancreatitis, biliary and pancreatic calculi, and eventually biliary carcinoma [2–6].

Different animal models have been developed to investigate the pathogenesis of PBM, using dogs [7–9], cats [10], goats [11], lambs [12], and rats [13], and the important documented findings of these studies may contribute to clinical practice. Since the pathogenesis of PBM-related diseases is broad, a variety of species and preparatory methods have been studied. In particular, the association between PBM and biliary carcinogenesis has been investigated extensively; however, few animal experiments have successfully induced biliary carcinoma.

The most important pathophysiological condition in PBM is “pancreatic juice regurgitation into the biliary tract”. We performed cholecystoduodenostomy with dissection of the extrahepatic bile duct in the distal end of the common duct (CDDB) in hamsters. Despite the reported difficulties, we induced carcinoma of the gallbladder and extrahepatic duct with marked dilatation of the extrahepatic bile duct in hamsters, by administering a carcinogenic agent, N-nitrosobis(2-oxopropyl) amine (BOP) [14]. In this hamster model, pancreatic juice regurgitates into the biliary tract, and then flows into the duodenum through the gallbladder. On the other hand, the duodenal contents flow readily into the biliary tract. The CDDB model is based on the following clinical data: the risk of PBM-related biliary carcinogenesis is extremely high in patients undergoing an internal bilioenterostomy such as cystoduodenostomy or cholecystoduodenostomy [15–17]; and biliary
carcinoma develops in patients with a bilioenterostomy 15 years earlier than in those who have not been subjected to this procedure [17]. We explain our method for the successful induction of biliary carcinoma in hamsters, and describe the histopathological characteristics of the induced tumors.

5.2 Preparation of the Model

Under general anesthesia, 7-week-old female Syrian golden hamsters are subjected to cholecystoduodenostomy with dissection of the extrahepatic bile duct at the distal end of the common duct (CDDB) [14]. The schema of the completed surgical procedure of CDDB is illustrated in Figure 5.1. After anesthetization with sodium pentobarbital (50 mg/kg of body weight) an upper abdominal midline incision is made. First, the distal end of the common duct is doubly ligated with 6-0 nylon and dissected (Figures 5.2 and 5.3). The ligation of the common duct will cause distension of the gallbladder. Next, one 5 mm-long incision is made in the duodenal wall, approximately 10 mm distal to the pyloric ring of the stomach (Figure 5.4), and one

Fig. 5.1 Cholecystoduodenostomy with dissection of the distant common duct end (CDDB model) in the hamster. GB, gallbladder; Du, duodenum (modified from [14], with permission)