

Cholangiocarcinoma: Morphology and biological behavior

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Based on growth characteristics, cholangiocarcinoma is classified as mass-forming, periductal-infiltrating, and intraductal-growing types. This classification is considered to be the most reasonable because it describes gross appearances, growing characteristics, biological behavior, and prognostic implication. It is also useful in radiologic interpretation.

Morphology of Cholangiocarcinoma

Mass-Forming Type

An intrahepatic cholangiocarcinoma forms a small or large mass, up to 15 cm in diameter. Grossly the tumor is firm and whitish-grey because of a large amount of fibrous stroma. The margin is well-circumscribed and wavy or lobulated. There may be central necrosis. Multicentricity, especially around the main tumor, is common and this is due to the propensity of formation of tumor emboli into the adjacent peripheral branches of the portal vein.

An extrahepatic cholangiocarcinoma forms a small nodule which is usually 1 cm in diameter. The tumor penetrates the wall and invades the periductal tissue, and obstructs the bile duct lumen. A mass-forming extrahepatic cholangiocarcinoma can be easily detected because the tumor occludes the bile duct resulting in dilatation of the proximal bile ducts. The bile ducts are usually completely obstructed at the time of diagnosis.

Periductal-Infiltrating Type

A periductal-infiltrating cholangiocarcinoma grows via the bile duct wall without formation of a sizable mass. The involved bile duct becomes thickened and narrow for a varying length resulting in eventual obstruction. The thickness of the wall increases up to 2 mm. Concentric layering of cellular stroma around the neoplastic glands is the most important identifying feature. The vast majority of hilar cholangiocarcinomas are of the periductal-infiltrating type, and it is therefore difficult or impossible to depict a sizable tumor mass on imaging. There may be combined tumor formation outside of the large bile ducts in the intrahepatic portion.

In the extrahepatic ducts, the tumor appears as a diffuse, firm, grey-white, annular thickening of the extrahepatic ducts with almost complete obstruction of the lumen. On imaging, the bile ducts may show two layers consisting of central enhancing and peripheral non-enhancing layers. The extent of the tumor varies, ranging

from 0.5 cm to 6 cm in length, sometimes involving all of the extrahepatic ducts and extending proximally as far as the intrahepatic ducts.

Intraductal-Growing Type

The majority of intraductal-growing cholangiocarcinomas are intraductal papillary mucinous neoplasm, comprising innumerable frondlike infoldings of proliferated columnar epithelial cells and slender fibrovascular cores. The tumors are usually small and sessile or polypoid in shape, but sometimes tumor spreads superficially along the mucosal surface and resulting in multiple tumors (papillomatosis) along varying segments of the bile ducts. Sometimes, the tumor forms a large cystic mass. Occasionally, the tumor produces a profuse amount of mucus, resulting in partial biliary obstruction. Usually a tumor is limited to the mucosa, but in the very late phase, it invades the wall as well as the surrounding tissue. The neoplasm occurs in any site of the bile ducts involving the intrahepatic, hilar and extrahepatic ducts. There are very few cases of intraductal-growing tubular cholangiocarcinoma or papillotubular cholangiocarcinomas.

Morphologic Types Depending upon Bile Duct Anatomy

Peripheral intrahepatic cholangiocarcinomas including bile ductular carcinoma (or cholangiocellular carcinoma) are mass-forming type. Central (large bile duct) intrahepatic cholangiocarcinomas are either mass-forming type or periductal-infiltrating, whereas hilar cholangiocarcinomas are mostly periductal-infiltrating type. Extrahepatic cholangiocarcinomas are either mass-forming or periductal infiltrating type. Intraductal-growing cholangiocarcinomas (including intraductal papillary neoplasms) arise in the large intrahepatic, hilar and extrahepatic ducts.

Clinical Significance

Morphologic classification of cholangiocarcinoma is useful for understanding biological behavior, planning and choosing appropriate treatment and for predicting prognosis. Surgical treatment should be tailored according to gross morphology of the cholangiocarcinoma. In order to achieve permanent cure, liver resection with a tumor-free margin should be performed in cases of mass-forming type, but for cholangiocarcinomas of periductal-infiltrating type, more aggressive surgery including extensive liver resection and lymph node dissection, and adjuvant anticancer therapy should be performed. For intraductal-growing cholangiocarcinomas, tumor resection with a tumor-free margin is sufficient and long-term patient survival can be expected.