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Slide Seminar 5, HEPATOBILIARY AND PANCREATIC PATHOLOGY

Cystic tumors of the liver, biliary tract and pancreas

Comments concerning Intraductal Papillary Neoplasms of the Bile Duct (case 5)

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Precancerous lesions of the pancreas and biliary tract are uncommon. However, they are important to identify as adenocarcinomas occurring in such organs have a poor prognosis. In these 2 locations, precancerous lesions can occur under a pattern of papillary intraductal proliferation producing different amount of mucin. These tumors correspond to intraductal papillary mucinous neoplasm of the pancreas (IPMN-P) and traditionally to biliary papillomatosis. While the concept of IPMN-P is well-recognized, the pathological characteristics of intraductal biliary proliferation have more recently been revisited in different Japanese studies. Due to important morphological similarities between these 2 intraductal proliferations, it has been proposed to call the biliary papillary tumors, intraductal papillary neoplasms of the bile duct (IPN-BD) in analogy to their pancreatic counterpart [1, 2].

In regards to cholangiocarcinomas which may involved intrahepatic, perihilar or distal extrahepatic bile ducts, IPN-BD constitute a rare disease entity. They usually affect adults older than 60 years-old with a slight male predominance (male:female ratio of 2:1 to 3:2). The most common symptoms of IPN-BD at presentation consists of recurrent colicky abdominal pain, repeated episodes of acute cholangitis with fever and jaundice, due to partial or intermittent obstruction of the bile duct by mucus and tumor obstruction and/or fragmentations.

Like IPMN-P, IPN-BD are macroscopically detectable showing intraductal papillary lesions and focal or diffuse dilatation of ductal system. IPN-BD involves the extrahepatic ducts alone in 58% of cases, both extra- and intra-hepatic ducts in 33% and intrahepatic ducts alone in 9% [3]. While mass protruding and visible mucin secretion into the lumen appears less frequent than in IPMN-P, important and diffuse markedly dilated bile duct is usually observed. Exceptional cases involving both pancreas and bile duct have been reported.

Similarly to IPMN-P, intestinal, pancreatico-biliary, gastric and oncocytic types have recently been described in IPN-BD [1, 4]. However, the frequency of these tumor-cell types appear different and variable among series suggesting that it is perhaps less easy to distinguish them than in IPMN-P. The two most common are the intestinal and the pancreaticobiliary types. In contrast to IPMN-P, gastric type is rarely encountered. Although the same tendencies of overexpression of MUC2 in intestinal types and MUC1 in pancreaticobiliary types occur like in IPMN-P, some intestinal cases show both expression of these markers particularly when invasive component is present.

During progression of tumour, IPMN-P and IPN-BD could progress to two types of invasive cancers: tubular adenocarcinomas and colloid carcinomas. Around 50% of invasive carcinomas in IPMN-P are colloid carcinomas whereas tubular carcinomas appear to be more frequent in IPN-BD. Almost all colloid carcinomas occurring in these 2 locations are associated with intestinal-type proliferation.

The rate of invasive carcinoma is estimated to 30-40% in IPMN-P and 64-90% in IPN-BD [1, 5, 6]. The presence of such invasive component is critical predictor of clinical outcome in these 2 locations. IPMN-P and IPN-BD colloid carcinomas have a better prognosis as compared to tubular carcinomas [1, 4].

Concerning the differential diagnosis IPN-BD needs to be conceptually distinguished with biliary intraepithelial neoplasia (BilIn), the counterpart of precancerous lesion named PanIN (pancreatic intraepithelial neoplasia) in pancreas. This biliary precancerous lesion is microscopically detected in liver explants exhibiting cirrhosis. Its occurrence is rare in chronic hepatitis C and alcohol cirrhosis as it has been detected in only 1,8% of cases (19 of 1058 explants analysed) [7]. In contrast, BilIN appears much more frequent in other conditions such as hepatic stones, biliary tree infection by flat worms and mostly in primary sclerosing cholangitis (PSC). In this latter, biliary dysplasia is present in 50% of PSC liver explants, divided approximately equally between high-grade and low-grade [8]. Different data strongly support a metaplasia–low-grade dysplasia–high-grade dysplasia– carcinoma sequence in PSC. The differential diagnosis can also be raise with pure endobiliary colorectal metastasis [9]. Despite what it reported in the literature [10, 11] , such distinction is not always so easy in daily practice as the cytokeratine profile does not permit to distinguish accurately these 2 lesions.

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