Diffuse biliary papillomatosis (IPNB) associated with IPNM: a case report

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Introduction
Biliary papillomatosis is a rare event. It concerns the biliary epithelium. The definition of the World Health Organization is the presence of multifocal papillary lesions on intra hepatic and/or extrahepatic bile ducts. There is a risk of malignant transformation. The papillary lesions are producing mucus conducting to biliary obstruction. Right hypochondrium pain and jaundice are the more frequent symptoms. Some common points have been described between IPNB and IPNM. IPNB can be a diffuse disease of all the biliary tree, with a real risk of neoplastic transformation and it could be a therapeutic challenge. We report the case of a patient suffering from diffuse IPNB associated with mixt IPNM who underwent pancreaticoduodenectomy and liver transplantation.

Presentation of the case
A 60 years old man was followed and treated in our hospital since 3 years for a presumed IgG 4 related disease because he has an history of repeated acute pancreatitis and CT scan features of notches on the two kydneys. However, the rate of circulating IgG4 was normal. In april 2021, he was admitted with a jaundice. CT scan demonstrated an extra hepatic biliary stenosis with above a biliary dilatation (Fig.1). ERCP and spy glass examination found a stenosis and several bilateral defects in the biliary lumen in all the extra hepatic biliary common bile duct and in the right and left bile ducts (Fig. 2). Spy glass biopsies found low grade dysplasia on the left duct, high grade dysplasia on the right duct and the common bile duct. We decided to perform a pancreaticoduodenectomy (PD) with endoscopic peroperative examination of intra hepatic bile ducts and biopsies. During PD, we resected all the extra hepatic biliary tree and we noticed that the left pancreas had completely disappeared with thrombosis of the splenic vein and segmental portal hypertension due probably to the multiple episodes of acute pancreatitis. Biliary anastomosis was done on the upper biliary convergence which was clearly pathologic. Peroperative endoscopy confirm several papillary lesions on left and right biliary ducts. Specimen examination had described a mixed IPNM with high grade dysplasia on the pancreas and IPNB with high grade and low grade dysplasia particularly on the right duct and the upper biliary convergence. All the resected lymph nodes were normal. The post operative period was marked by gastroparesis and glycemic imbalance. Finally, the evolution was favourable.
After a few months of relatively good general status, the patient developed fever, jaundice, malnutrition and intra hepatic abcess (Fig. 3). His condition needed multiple hospitalisations for antibiotics and enteral nutrition with jejunostomy. In six months, he has developed a secondary biliary cirrhosis.

Decision was taken to register him on the french liver transplant waiting list with request of priority. Cadaveric donor was available in April 2022. The procedure was very difficult with multiple biliary abcess and important hemorrhage. Postoperative recovery was quite simple. Specimen analysis of the explant liver (Fig.4) described diffuse IPNB with numerous areas of high grade dysplasia and cholangiocarcinoma lesions on the upper biliary convergence, exactly on the site of the first bilio-enteric anastomosis.

**Discussion**

IPNB can be localized or diffuse. The diffuse form represents a real therapeutic challenge. Endoscopic biopsies can not evaluate correctly the importance of the disease because different evolutionary stages exist in different part of the biliary tree. Currently, the curative treatment of the diffuse form must be resection of all the biliary tree that's to say pancreatecoduodenectomy and liver transplantation. Previous cases of liver transplant have been reported in this disease 4,5. Some authors have proposed a first surgical procedure (Liver resection or pancreatecoduodenectomy) to stage at the best the disease and eliminate advanced cases with lymph nodes encasement 5,6. It was our strategy in the case report and we have been confronted to a quick evolution to cholangiocarcinoma. The pancreatic disease of the patient, it was a mixed form, spanning the entire pancreas, with high grade dysplasia and some similiar cases, combining IPNB and IPMN, have been reported 7–13. There are some common points between IPNB and IPMN. Four subtypes of epithelium have been described : biliary pancreatic, intestinal, gastric and oncocytic. In IPNB and IPMN, the subtype has an influence on prognosis 6. Thus, pancreatobiliary type is associated to more invasive lesions, lymph nodes encasement and postoperative recurrence. IPNB and IPMN have mucin secretion and risk of neoplastic transformation 2,3. Some what, IPNB is the biliary mirror of IPMN. However, there are differences : the type more frequent in IPNB is pancreatobiliary while it is the gastric type in IPMN 14. IPNB can have non secreting form. Finally, IPNB had a worse prognosis.

In our case, the patient was followed since two years for IgG 4 related disease. A posteriori, this diagnosis was wrong, images of notch on the kidneys would be infectious sequelae.

**Conclusion**

IPNB are very rare biliary tumors wich can be localised or diffuse with a high risk of neoplastic transformation. The treatment is the complete resection wich can conduct to liver transplantation. IPNB has been described as the « biliary equivalent » of IPMN but IPNB seems to be a more agressive disease.

**Reference**

8. Intraductal mucinous tumors occurring simultaneously in the


