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Case Report

Malignant intraductal oncocytic papillary neoplasm of the common bile duct

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Abstract: Recently, several cases of intraductal oncocytic papillary neoplasm (IOPN) of the liver and hepatic bile ducts have been reported. The author herein reports the first case of IOPN of the common bile duct (CBD). A 78-year-old man was admitted to our hospital because of jaundice. Imaging modalities including US, CT, MRI revealed an intraductal tumor of the middle CBD and biliary dilation distal to the tumor. A partial resection of the CBD was performed. Grossly, a papillary tumor measuring 20 x 15 mm was found within the CBD. Mucus is absent. Histologically, the papillary tumor was composed of atypical oncocytes. The atypia was enough to be diagnosed as adenocarcinoma. No invasive features were noted. Immunohistochemically, the tumor cells were positive for pancytokeratins (CK), CK 7, CK 18, CK19, EMA, CA19-9, CEA, mitochondria, p53 protein, C-erbB2, Ki-67 (labeling = 80%), MUC2, MUC5AC and MUC-6,. The tumor cells were negative for CK8, CK20, chromogranin, synaptophysin, neuron-specific enolase, S100 protein, CD56, MUC1, CD10 and CDX2. These immunohistochemical findings were compatible with IOPN. The patient died of other non-tumorous disease 7 year after the operation. In summary, the author presented the first case of IOPN of the CBD.

Keywords: Common bile duct, intraductal oncocytic papillary neoplasm, immunohistochemistry, histopathology

Introduction

Recently, several cases of intraductal oncocytic papillary neoplasms (IOPN), previously reported as biliary papillomatosis [1] have been reported in the intrahepatic bile ducts of the liver [2-7]. It is a liver counterpart of the well known IOPN of the pancreas [8]. The author herein reports a case of IOPN of the common bile duct (CBD). This is the first case of IOPN occurring in the CBD.

Case report

A 78-year-old man was admitted to our hospital because of jaundice. Imaging modalities including US, CT and MRI revealed an intraductal tumor of the CBD and biliary dilation distal to the tumor. A partial resection of the common bile duct was performed. Grossly, papillary tumor measuring 20 x 15 mm was found within the middle CBD (**Figure 1**). No mucus is present. Histologically, the papillary tumor consisted of atypical oncocytes (**Figures 2A** and **2B**). The atypia was enough to be diagnosed as adenocarcinoma (**Figure 2B**). No invasive features were noted (**Figure 2A**). Mucin stains revealed no mucus hypersecretion. The surgical margins

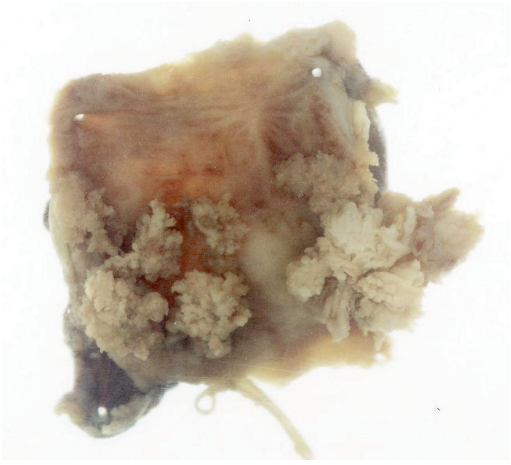

Figure 1. Gross features. The resected common bile duct shows papillary tumors measuring 20x15 mm. The common bile duct is dilated.

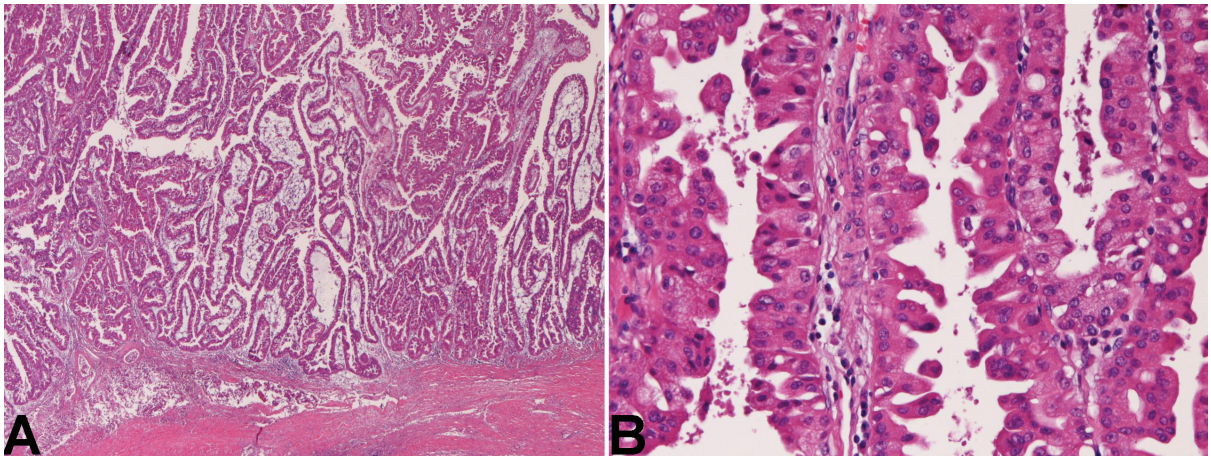

Figure 2. Microscopic picture. A: Low power view demonstrates papillary proliferation of tumor cells. HE, x40. B: High power view shows that the papillary tumor is composed only of atypical oncocytes, which are regarded as malignant cells in view of the structural and cytological atypia. HE, x200

were negative for tumor cells. An immunohistochemical study was performed by Dako's Envision method (Dako, Glostrup, Denmark), as previously described [9-17]. The evaluation of immunohistochemistry was categorized as follows: -, less than 1% positive; +, 2-33% positive; 2+, 33-67% positive; and 3+, 68-100% positive. The tumor cells were positive for pancytokeratins (CK), CK 7, CK 18, CK19, epithelial membrane antigen, carbohydrate antigen19-9 (CA19-9), carcinoembryonic antigen (CEA), mitochondria, p53 protein, C-erbB2, Ki-67 (labeling = 80%), epidermal growth factor receptor (**Figure 3A**), MUC2 (**Figure 3D**), MUC5AC (**Figure 3E**), and MUC (**Figure 3F**). The tumor cells were negative for CK8, CK20, chromogranin, synaptophysin, neuron-specific enolase, S100 protein, CD56, CD10, HER2/neu, MUC1, and CDX2. The patient died of other non-tumorous disease 7 year after the operation.

Discussion

The present tumor was located in the CBD and showed papillary proliferation of oncocytes. The oncocytes showed cellular and structural atypia regarded as adenocarcinoma. The oncocytes may be due to a large number of mitochondria, as suggested by the immunohistochemistry. The positive reactions for p53 protein, CA19-9 and CEA and high Ki-67 labeling (80%) highly suggest the malignant nature of the present tumor [18-20]. The positive C-erbB2 also suggests malignant nature of the present tumor [21]. Therefore, the present CBD tumor is a malignant IOPN of the CBD. This is the first report of IOPM occurring in the CBD.

In the past, the authors studied intraductal papillary mucinous neoplasms (IPMN) of the pancreas and intraductal tubular neoplasm (ITN) of the pancreas [22-27]. The present tumor is not IPMN or ITN because of the lack of mucin hypersecretion and of the lack of tubular structures.

Neuroendocrine differentiation may occur in some tumors. In the present tumor showed no reactions for CD56, chromogranin, synaptophysin, and neuron-specific enolase. The findings indicate that the present tumor is not neuroendocrine tumor or tumor with neuroendocrine differentiation.

Recently, IPMN of the liver has been reported [28, 29]. Pancreas and hepatobiliary organs share many phenotypes. Both arise from the common embryonic bud [30]. The similarity of the bile ducts and pancreatic ducts are evident. For example, the pancreas show pancreatic hepatocytes [31] and hepatobiliary organs show pancreatic acinar cells [32]. Both pancreatic ducts and bile ducts have been demonstrated to contain pancreatic digestive enzymes [33-40]. In addition, pancreatic acinar cells and bile ducts having pancreatic digestive enzymes have been observed in fetal organogenesis of bile ducts [41-47]. These findings highly suggest the common phenotypes and biologic characters between pancreatic ducts and bile ducts. Thus,

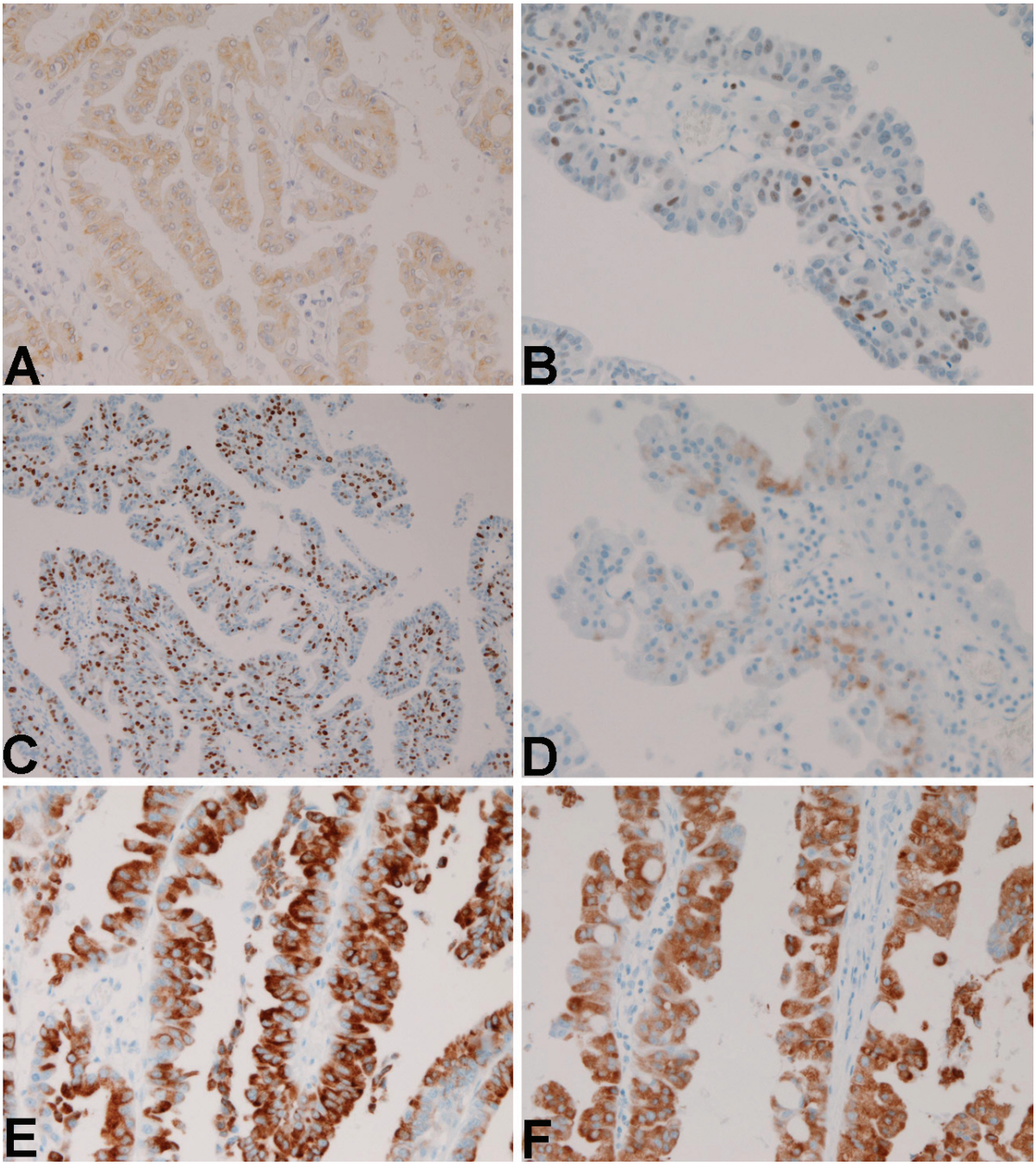

Figure 3. Immunohistochemical findings. A: The tumor cells are positive for cytokeratin. x 200. B: The tumor cells are positive for p53 protein. x 200. C: The tumor cells are positive for Ki-67 antigen. The labeling is 80%. x100. D: The tumor cells are positive for MUC2. x200. E: The tumor cells are positive for MUC5AC., x200. F: The tumor cells are positive for MUC6, x200.

it is not strange that IPMN and IOPM occur in the biliary tracts, as is well established in the pancreas. The present case also supports the above statements.

IPMN of the pancreas is classified by mucus type into gastric type, oncocytic type, pancreatobiliary type and intestinal type [48]. In the present study, MUC2, MUC5AC and MUC6 were

positive, being compatible with oncocytic type [48]. The negative immunostaining of CD10 and CDX2 suggest that the present tumor have no intestinal phenotypes.

The present tumor was characterized by a little or no cytoplasmic mucins and no mucus secretion. Since MUC apomucins were present in the tumor cell cytoplasm, it is possible that glycosylation is not operative in the cytoplasm. The negative mucus secretion may indicate that mucus secretory process is impaired in the present IOPN.

The CK profile of the normal pancreatic ducts and intrahepatic bile ducts is CK7 +, CK8 +, CK18 +, CK19 + [49, 50]. In the present IOPM, the CK profile was CK7 +, CK8 -, CK18 +, CK19 +. This suggests that the expression of CK8 diminishes and disappears during the tumorigenesis of IOPM in the present case.
In summary, the author presented the first case of IOPN of the CBD.

Interest of conflict

The author declares that he has no conflict of interest

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