

Case Report

**Intraductal Papillary Growth of Liver Metastasis Originating from Colon
Carcinoma in the Bile Duct: Report of a Case**

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ABSTRACT

Morphologically, liver metastases from colorectal carcinoma usually form as nodular tumor masses, whereas intra-ductal papillary growth in the bile duct is rare. A 65-year-old man underwent right hemi-colectomy for advanced colon carcinoma and histology of the primary carcinoma confirmed moderately differentiated adenocarcinoma with subserosal invasion, no vascular infiltration, and no lymph node metastasis. A liver tumor was found in the right paramedian Glisson's pedicle and intra-ductal growth of cholangiocarcinoma was seen on imaging. We performed right hepatectomy and macroscopically, the resected specimen contained a growth in the bile duct lumen similar to cholangiocarcinoma.

Histological examination revealed intraductal papillary proliferation of well-differentiated adenocarcinoma without vascular infiltration or lymph node metastasis in the hepatic hilum. Immunohistochemical staining revealed that the tumor cells were negative for cytokeratin 7 and positive for cytokeratin 20. Based on these findings, liver metastasis from colon carcinoma was diagnosed. Liver metastasis from colorectal carcinoma rarely arises as intraductal papillary growth in the bile duct, but the possibility of liver metastases with unusual morphology must be borne in mind in patients with a history of carcinoma in the digestive tract.

Key Words: Intraductal papillary growth, Bile duct, Liver metastasis, Colorectal carcinoma, Hepatectomy

Introduction

Liver metastasis is common after colorectal carcinoma resection.¹ The gross appearance of metastases is usually of a regular or irregular round mass.² Intrahepatic growth of liver metastasis originating from a colorectal carcinoma is a rare manifestation of metastatic liver carcinoma.³⁻⁷ This type of tumor usually shows biliary invasion of the main mass lesion and sometimes resembles intrahepatic cholangiocarcinoma with intraductal growth.⁵⁻⁹ Immunohistochemical examination is necessary to differentiate between metastatic liver carcinoma and cholangiocarcinoma.^{7,9,10} We report a case of liver metastasis resembling intra-hepatic cholangiocarcinoma.

Case Report

A 65-year old man underwent right hemi-colectomy for pathological stage II colon carcinoma. Histological examination of the primary tumor revealed a moderately differentiated adenocarcinoma with subserosal invasion, but no lymphatic or vascular infiltration or node metastasis. About 15 months postoperatively, his serum carcinoembryonic antigen (CEA) levels were found to be elevated slightly, at 5.2 ng/ml (normal range, < 5.0 ng/ml), although his CA19-9 (13.5 U/ml) and alpha-fetoprotein (1.1 ng/ml) levels were normal. Otherwise, the Laboratory data showed normal liver function, but slightly elevated levels of alkaline phosphatase (542 IU/ml). Computed tomography (CT) showed intrahepatic biliary dilatation in the right paramedian and lateral sectors. Enhanced multi-detector CT showed an irregular hypovascular lesion, 3 cm in diameter, along the right paramedian and lateral Glisson's pedicles with peripheral bile duct dilatation (Fig. 1a). Magnetic resonance cholangiography showed a deficit of cholangiogram in the confluent of the right paramedian and lateral bile ducts in the liver (Fig. 1b). Endoscopic retrograde cholangiography and intraductal biopsy were unsuccessful. As his liver function was well preserved, we performed a right hepatectomy following portal vein embolization. The initial preoperative diagnosis was intrahepatic cholangiocarcinoma, although colonic liver metastasis was differentially diagnosed. Therefore, right hepatectomy with lymph node dissection in the hepatoduodenal ligament surrounding the common hepatic artery and in the para-aortic lesion was added.

The resected specimen contained a solid tumor lesion along the right paramedian and lateral bile ducts, spread within 3.5 cm, with peripheral bile duct dilatation (Fig. 2). The macroscopic findings resembled intra-hepatic cholangiocarcinoma. Histological examination revealed papillary adenocarcinoma in the intra-luminal side of the bile duct

(Fig. 3), extending to the epithelium of the intrahepatic duct. Perineural infiltration was observed, but no portal or vascular infiltration or lymph node metastases were identified. At this stage, we suspected intraductal papillary bile duct carcinoma because of the differences in pathological differentiation from the primary colon carcinoma. However, after pathological consultation, immunohistochemical analysis showed positive expression of cytokeratin (CK)20 and negative expression of CK7 (intestinal type) (Fig. 4). Neighboring biliary epithelium was CK7-positive and CK20-negative (pancreatobiliary type). Based on the results of immunohistochemistry, the tumor was diagnosed as metastatic liver carcinoma arising from colonic carcinoma. Fig. 5 shows moderately differentiated adenocarcinoma in a primary colonic carcinoma, in which the papillary carcinoma component is similar to that in the liver tumor.

Discussion

We described the intraductal papillary growth of liver metastasis originating from a colon carcinoma, which is a rare phenomenon.³⁻⁷ The morphology of this tumor resembled a rare biliary carcinoma termed “intraductal papillary neoplasm of the bile duct” (IPNB) by Nakanuma and Chen *et al.*^{8, 11, 12} As in IPNB, the tumor in the present report showed marked dilatation of the bile duct without jaundice was observed with or without mucin secretion.^{11, 12} The histological findings of intraductal papillary growth of liver metastasis were also similar to IPNB as a papillary proliferation of carcinoma in the epithelium.^{3, 5, 6, 8} Because histological differentiation was different in the metastatic lesion and the primary carcinoma, we believed that the present tumor represented primary carcinoma in the bile duct. We have previously treated cases of IPNB similar to the present case, and several of these cases showed in situ carcinomas with or without adenoma that superficially extended along the biliary epithelium.^{13, 14} Compared with the usual histological findings of cholangiocarcinoma, the histological characteristics of IPNB were papillary growth different from the common cholangiocarcinoma, with deep ductal infiltration. Only HE staining cannot show the differential diagnosis between this type of cholangiocarcinoma and liver metastasis. immunohistochemical staining is necessary to confirm the diagnosis of IPNB.^{7, 9, 10} As the patient had undergone prior surgery for colon carcinoma, CK staining resulted in the present diagnosis. CK or mucin staining is very important, particularly in patients with a history of other intestinal cancers.

Previous reports have noted that a main metastatic tumor forming an irregular mass often infiltrates neighboring bile ducts.^{3, 5, 6, 8, 15} Tumor growth confined to the bile duct, as in the present case, has rarely been described.^{3, 5, 16} Itatsu *et al.*³ and Blumgart *et al.*¹⁶

provided summaries of a small number of cases. The gross appearance, primary location or stage and other demographics were not consistent in those reports.^{3-8, 15, 16} In some reports, biliary involvement of liver metastasis frequently showed intraductal growth connected with the intra-parenchymal main tumor but not a ductal stricture like invasive cholangiocarcinomas. This information would be useful for predicting this type of invasion of liver metastasis;^{3-9, 16, 17} however, the precise prediction of biliary infiltration of liver metastasis from only the gross appearance would be difficult because of the possibility of special types of cholangiocarcinoma, as described above.^{8, 11, 12}

Most patients underwent surgery, because of the diagnostic development on imaging.¹⁵ CT might be the most powerful imaging modality, although the usefulness of percutaneous transhepatic cholangiography was reported by Hiramatsu *et al.*¹⁷ Advanced imaging modalities can identify dilation and cystic changes in the biliary duct in the early stage. The tumor in the present case was limited to the liver and had not extended into the extrahepatic bile duct or surrounding vessels or lymph nodes. Thus, complete resection by right hepatectomy was feasible. Complete resection may improve the prognosis even for metastatic liver carcinoma from colorectal carcinoma.¹⁸⁻²⁰ In intrahepatic cholangiocarcinomas, extended hemihepatectomy with wide surgical margins has been recommended for curative treatment.²¹ For liver metastases in the bile duct, the same strategy may be better because of the wide spread of carcinoma along the biliary lumen and infiltration to microvessels or lymph nodes, although limited resection is acceptable for usual metastatic liver tumor.^{4, 5, 7, 22} This type of liver metastasis, like intrahepatic cholangiocarcinoma, would be a good indication for extended surgical resection to achieve complete resection, resulting in a better prognosis.²⁰ No definitive chemotherapeutic regimens for intra-biliary liver metastasis have been reported; however,

we gave our patient adjuvant chemotherapy consisting of 5-fluorouracil plus leucovorin after hepatectomy to prevent tumor recurrence.²³

In conclusion, we reported a rare case of intra-ductal papillary growth of liver metastasis from colonic carcinoma without vascular invasion or node metastasis, which we treated successfully with right hepatectomy and adjuvant therapy. The tumor resembled intra-ductal cholangiocarcinoma, but immunohistochemical staining for CK7/20 revealed liver metastasis. Thus, careful examination is needed to diagnose a liver tumor with atypical morphological appearance. Complete surgical resection may be the best therapeutic option for intra-biliary growth of liver metastasis to obtain a good prognosis.

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FIGURE LEGENDS

Fig. 1. (a) Computed tomography (CT) showed a low-density, hypovascular tumor lesion extending along the intra-hepatic Glisson's pedicle in the right paramedian and lateral sectors (arrow). The peripheral bile duct was mildly dilated. (b) Magnetic resonance cholangiography showed a deficit of cholangiogram in the right paramedian and lateral intrahepatic bile ducts (arrow).

Fig. 2. Resected specimen showing a growing tumor lesion in the lumen of the bile duct in the right paramedian and lateral bile ducts limited to within 3.5 cm with peripheral bile duct dilatation (arrow).

Fig. 3. Papillary adenocarcinoma in the intra-luminal side of the bile duct, resembling intra-ductal cholangiocarcinoma ($\times 40$).

Fig. 4. Magnification of the encircled area in Fig. 3 ($\times 200$). (A) Hematoxylin and eosin stain. Immunohistochemical analysis shows positive expression of CK20 (B) and negative expression of CK7 (C) ($\times 200$). The neighboring normal biliary epithelium was CK20-negative and CK7-positive (arrow).

Fig. 5. The primary colonic carcinoma showed moderately differentiated tubular adenocarcinoma (arrow). A papillary adenocarcinoma component (dotted arrow), similar to that in the biliary carcinoma, was observed.

Figure 1
(a)

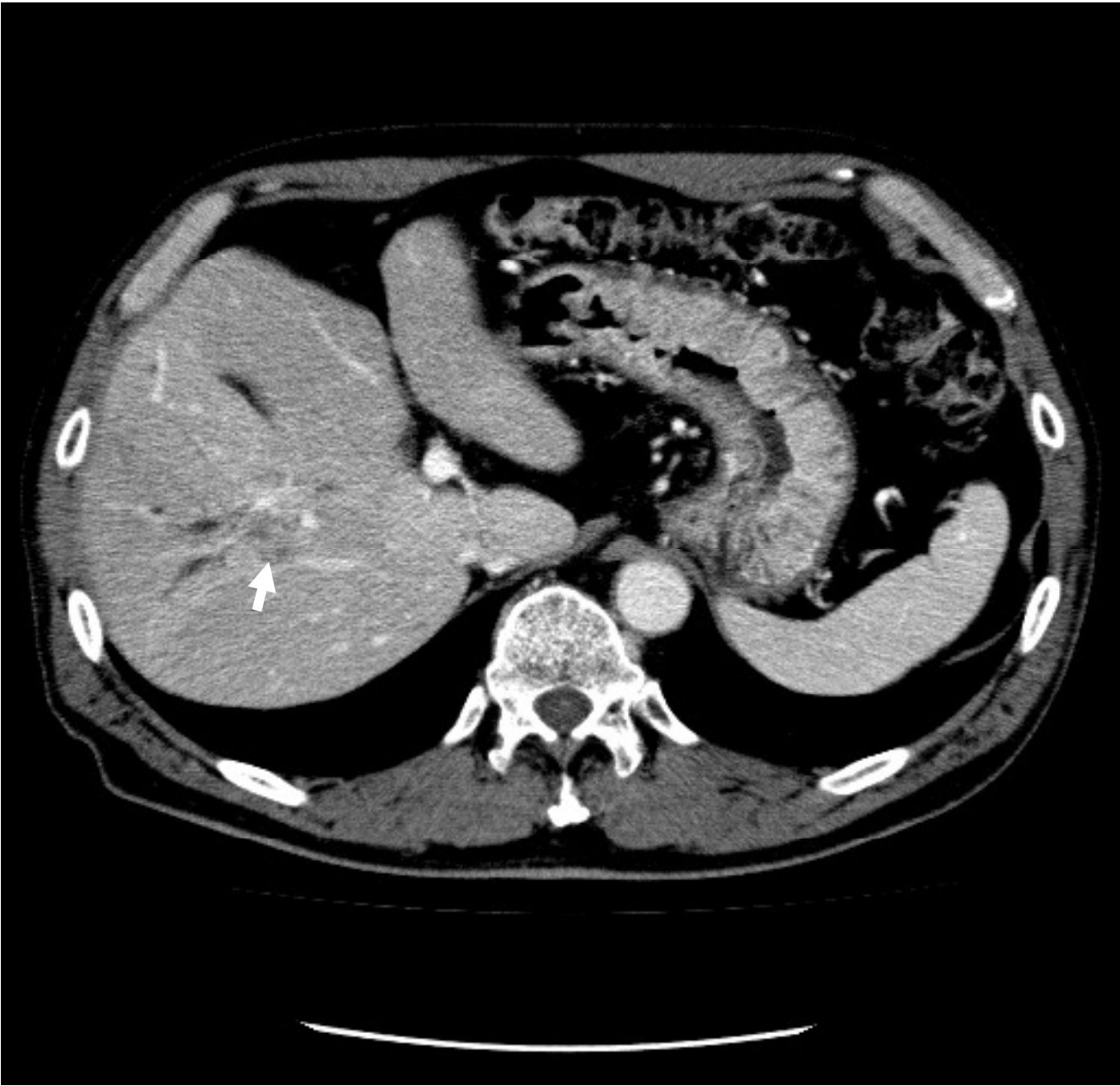


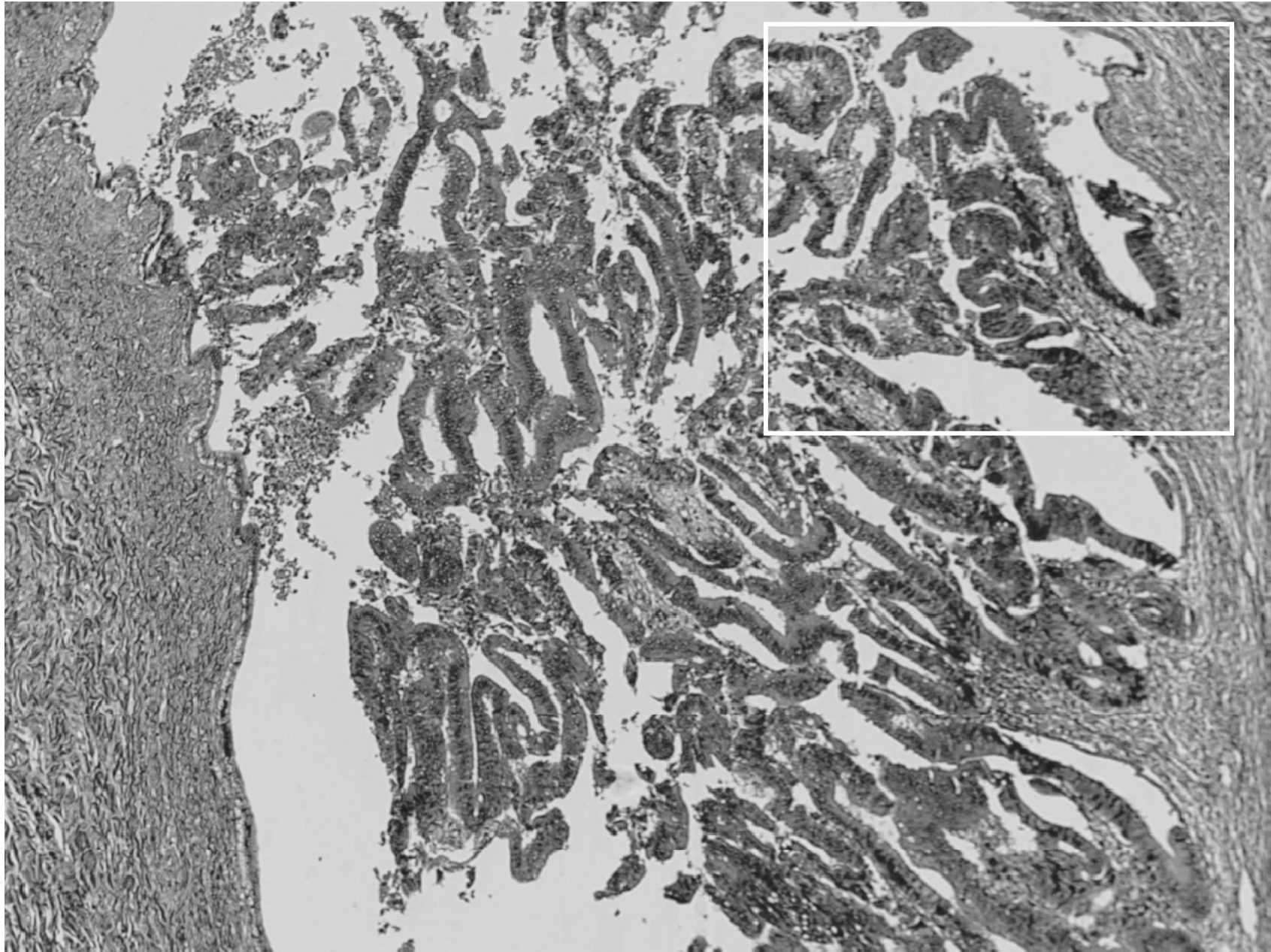
Figure 1
(b)



Figure 2



Figure 3



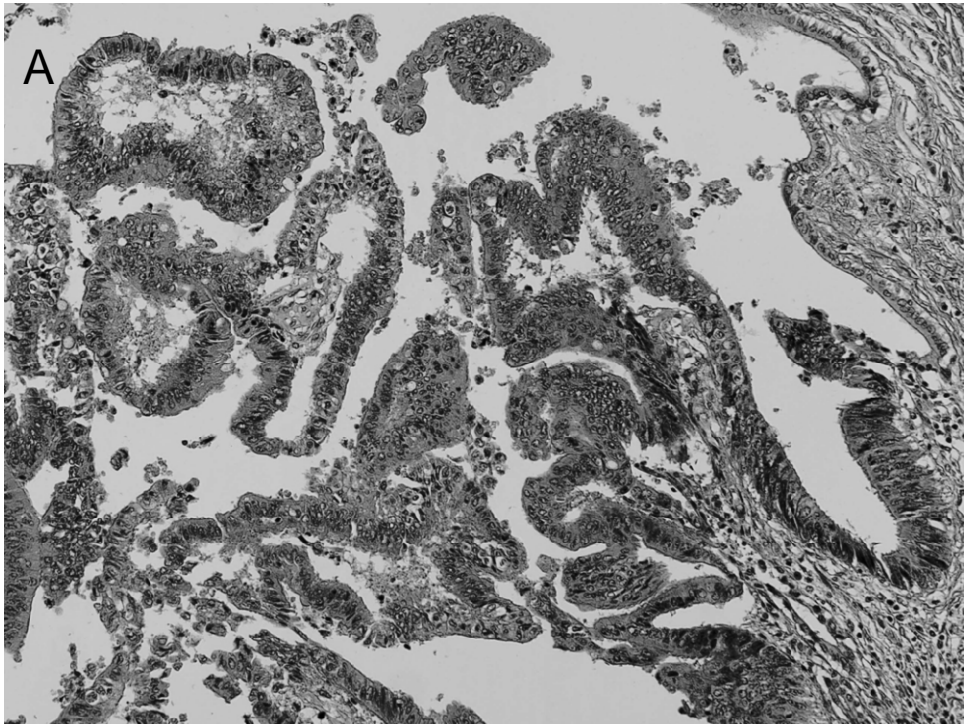


Figure 4

HE

CK20

CK7

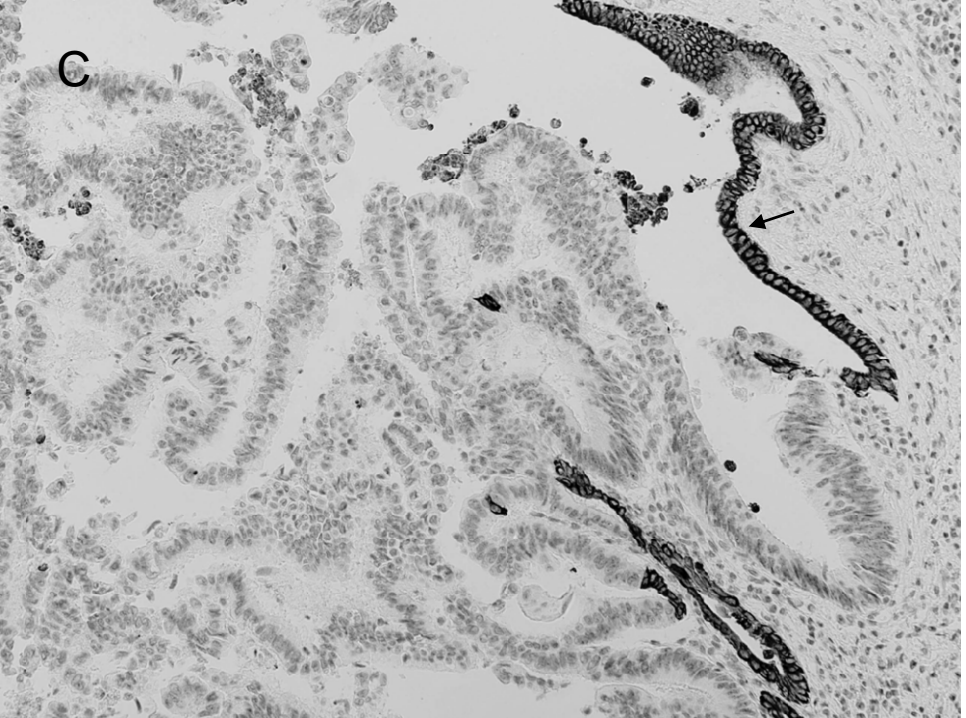
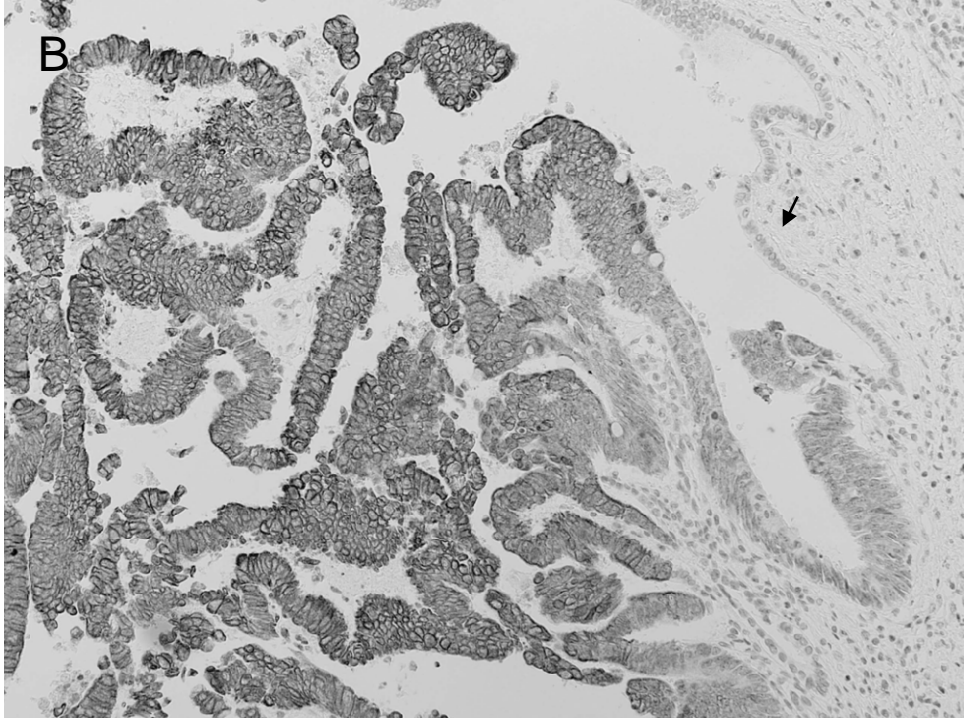


Figure 5

