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A Case of Intracystic Papillary Neoplasm With an Associated Invasive Adenocarcinoma

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Intracystic papillary neoplasm (ICPN) is a preinvasive neoplasm of the gallbladder. Preoperative discrimination between ICPN and gallbladder cancer (GC) is difficult. The standard surgical strategy for ICPN has not yet been established. Herein, we report a case of ICPN with an associated invasive adenocarcinoma. A gallbladder tumor was detected by abdominal ultrasonography in an asymptomatic 69-year-old man, and he was referred to our hospital. Although computed tomography (CT), endoscopic ultrasonography, and magnetic resonance imaging findings in the present case were similar to those for GC, positron emission tomography-CT revealed that fluorodeoxyglucose (FDG) did not accumulate within the tumor. These imaging features suggested that patient was suspected to have GC with serosal invasion, and he underwent extended cholecystectomy and D2 lymph node dissection. He did not develop any postoperative complications, and he was discharged on postoperative day 7. There was no evidence of recurrence for 20 months after surgery. Histopathologic examination confirmed ICPN with an associated invasive adenocarcinoma. Because a previous study reported that almost half of ICPNs more than 1.0 cm in size often developed invasive cancer as our case, ICPNs more than 1.0 cm should be suspected of developing invasive carcinoma regardless of positive or negative accumulation of FDG.

Key words: Intracystic papillary neoplasm – Intraductal papillary neoplasm of the bile duct – Gallbladder cancer

The World Health Organization Classification of Tumours of the Digestive System (2010) has defined intracystic papillary neoplasm (ICPN) as a preinvasive neoplasm of the gallbladder.[1,2] The rate of ICPN among cholecystectomies is reportly very low (14/3265, 0.4%).[3] Preoperative diagnosis of ICPN is difficult, and almost half of ICPN cases are diagnosed radiologically as gallbladder cancer

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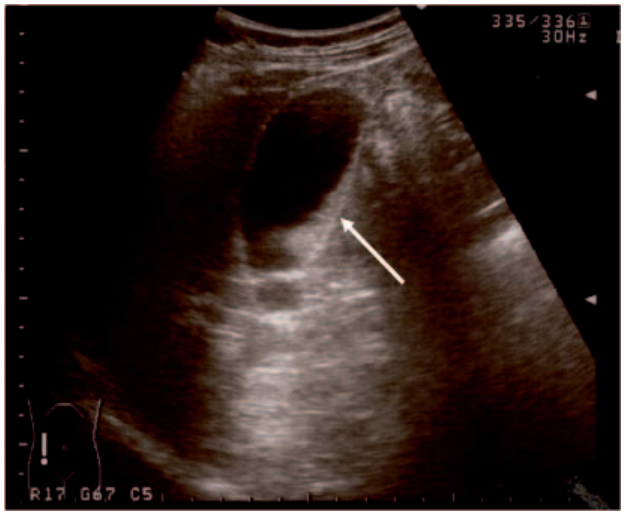

Fig. 1 Abdominal ultrasound revealed an irregular wall thickening in the gallbladder body (arrow).

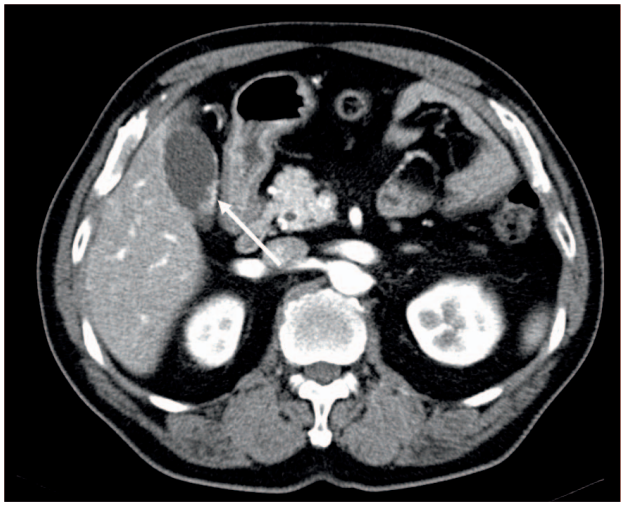

Fig. 2 Helical computed tomography revealed an irregular wall thickening in the gallbladder body that was enhanced in the arterial phase (arrow).

(GC).[3] Accordingly, the clinical imaging features of ICPN and optimum surgical strategy have not yet been established.

We encountered a case of ICPN with an associated invasive adenocarcinoma. Because ICPNs often develop an invasive cancer as in our case,[3] preoperative assessment and therapeutic strategy are important for treatment of ICPN. However, preoperative assessment and therapeutic strategy of ICPN are not established. Therefore, we report this case and discuss the clinical imaging features and treatment.

Case Report

A gallbladder tumor was detected in a 69-year-old man by abdominal ultrasonography, and he was referred to our hospital. He had shown no symptoms before detection of the tumor. He had a history of acute appendicitis, atrial septal defect, and inguinal hernia. The results of laboratory blood test and the levels of tumor markers such as carcinoembryonic antigen and carbohydrate antigen 19-9 were normal. Abdominal ultrasonography revealed irregular wall thickening in the body of the gallbladder (Fig. 1, arrow), which was enhanced in the arterial phase of helical computed tomography (CT) (Fig. 2, arrow). Magnetic resonance imaging (MRI) also revealed irregular wall thickening in the body of the gallbladder with slightly high intensity on diffusion-weighted imaging (DWI). Endoscopic ultrasonography (EUS) revealed a hyperechoic elevated lesion in the gallbladder body, and tumor infiltration was detected as a hypoechoic tumor invading the layers of the gallbladder wall (Fig. 3, arrow). Although positron emission tomography (PET)-CT showed no accumulation of fluorodeoxyglucose (FDG) in the wall of the gallbladder body, GC was suspected.

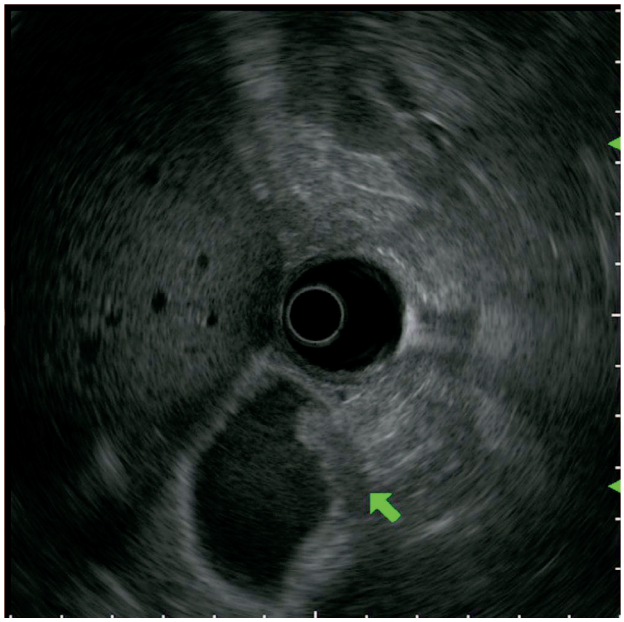

Fig. 3 Endoscopic ultrasonography revealed a high-echoic elevated lesion in the gallbladder neck and tumor infiltration as a hypoechoic tumor invading the layers of the gallbladder wall (arrow).

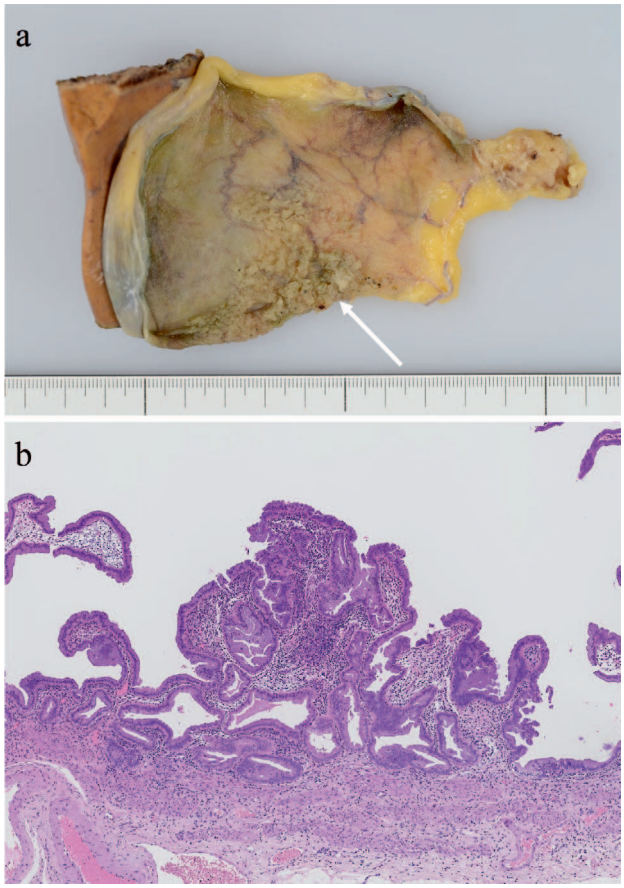

Fig. 4 Histopathologic examination revealed a 5.2- × 3.8-cm papillary tumor was in the (a) gallbladder body (arrow) and (b) tumor cells with irregular nuclei limited to the epithelium.

The patient underwent extended cholecystectomy and D2 lymph node dissection because of suspected GC with serosal invasion. As the stump of the cystic duct was negative for cancer, the common bile duct was not resected. He did not develop any postoperative complications, and he was discharged on postoperative day 7. There was no evidence of recurrence for 20 months after surgery.

Histopathologic examination revealed a 5.2- × 3.8-cm papillary tumor in the body of the gallbladder and irregular nuclei limited to the intraepithelial tumor cells (Fig. 4a and 4b, arrow). An associated adenocarcinoma, 4 mm in size, had invaded the proper muscular layer from low-grade dysplasia. There was no venous invasion, lymphatic vascular invasion, neuro invasion, liver invasion, or lymph node metastasis. Immunostaining revealed that the nuclei were diffusely positive for p53 (Fig. 5a), positive for MUC5AC and MUC6 (Fig. 5b and 5c),

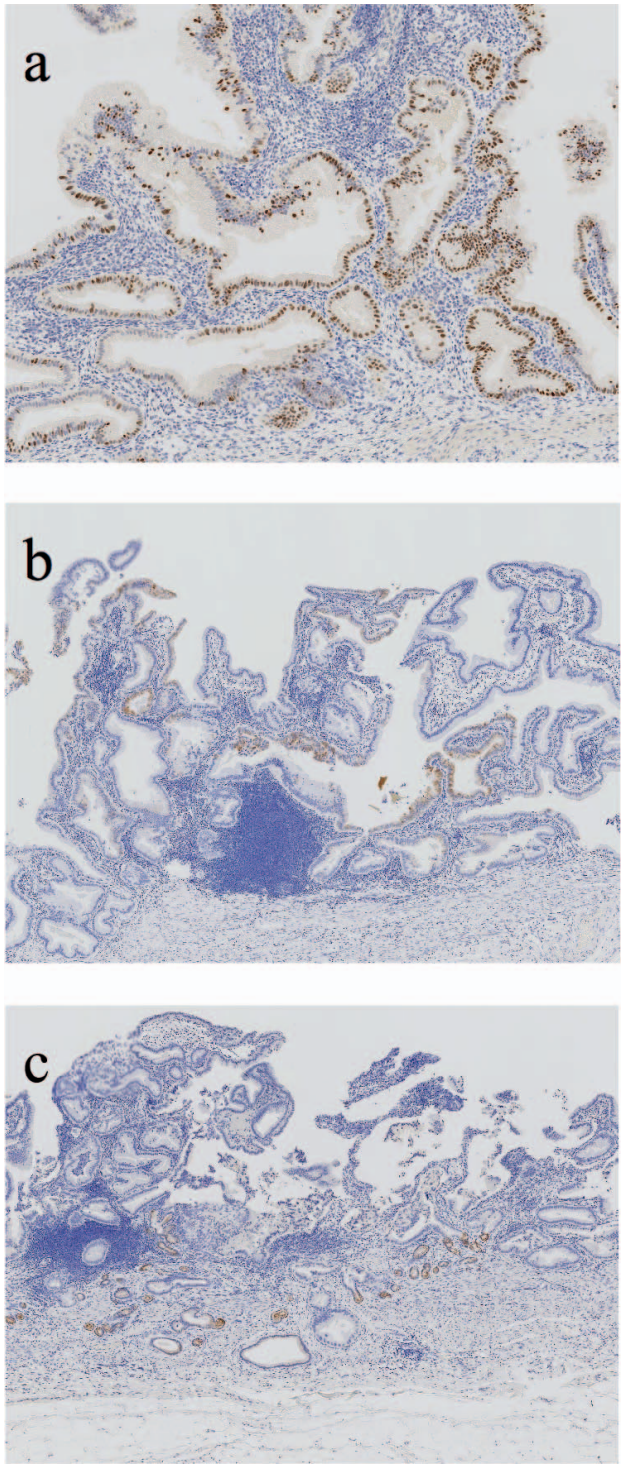

Fig. 5 p53 was diffusely positive in (a) the nuclei, and (b) MUC5AC and (c) MUC6 were also positive.

and negative for MUC2. Thus, the final diagnosis was gastric-type ICPN with an associated invasive adenocarcinoma.

Informed consent was obtained from the patient. The figures related to this article do not contain any information that could affect the patient's privacy in any way.

Discussion

Despite the presence of an associated invasive adenocarcinoma, the patient had no symptoms and abdominal ultrasound screening detected ICPN incidentally. Although CT, MRI, and EUS findings were similar to those of GC, PET-CT revealed no accumulation of FDG in the tumor of the present case.

The clinical imaging features of the present case were similar to those of GC. ICPN was visualized as an early enhanced lesion on helical CT, as a high intensity lesion on DWI, and as both a hyper- and hypoechoic lesion on EUS. These imaging features are similar to those of GC.[4–9] Other case reports have indicated that ICPN was visualized as a cystic tumor and a papillary tumor by enhanced CT.[10,11] Thus, the CT features of ICPN do not appear to be uniform, emphasizing the facts indicated that it is difficult to discriminate ICPN from GC by preoperative imaging modalities such as CT, MRI, and EUS. However, PET-CT in the present case showed no accumulation of FDG in the wall of the gallbladder body. PET-CT did not detect the tumor, because the associated invasive carcinoma was too small. There have been no reports on the use of PET-CT to visualize ICPN. At our institution, we have experienced 11 cases of intraductal papillary neoplasm of the bile duct (IPNB), which is a preinvasive neoplasm of the bile duct. PET-CT was performed for 7 of these cases. Although FDG was shown to be accumulated in 2 cases of IPNB with an associated carcinoma, no such accumulation was seen in 4 similar cases and a case of IPNB without malignancy. These facts suggest that FDG does not always accumulate in preinvasive neoplasm such as ICPN and IPNB. It will be necessary to determine whether PET-CT is useful for discriminating between ICPN and GC.

The optimum surgical strategy for ICPN have not yet been established. Because the present case was initially suspected to be GC with serosal invasion, extended cholecystectomy and D2 lymph node dissection were performed for radical resection according to the clinical practice guidelines for management of biliary tract cancers 2015, 2nd English edition.[12] An associated invasive adenocarcinoma had invaded the proper muscular layer, and we treated the patient successfully by radical resection. Almost half of ICPNs more than 1.0 cm in size develop an invasive cancer, and survival is lower than that for ICPN without invasive carcinoma.[3] Among GC patients with serosal invasion, those who underwent cholecystectomy alone had a 5-year survival rate of 0%.[13] Additionally, approximately half (40%–50%) in GC cases with serosal invasion develop lymph node metastasis.[14–16] In another case of ICPN with an associated invasive adenocarcinoma, extended cholecystectomy and lymph node dissection were performed, and the patient had no evidence of recurrence for 24 months after surgery.[10] Therefore, extended cholecystectomy and D2 lymph node dissection is recommended for cases of ICPN more than 1.0 cm in size and with suspected invasive cancer and serosa invasion. Further case reports or large population studies are required to determine the appropriate diagnostic and therapeutic strategies for ICPN.

The findings in the present case suggested that PET-CT might effectively discriminate between ICPN and GC. However, our case developed an invasive cancer despite no accumulation of FDG in tumor. Because previous study showed that ICPNs more than 1.0 cm in size often developed invasive cancer as our case,[3] ICPN more than 1.0 cm should be suspected of developing invasive carcinoma regardless of positive or negative accumulation of FDG. Therefore, radical surgery and surgical treatment for GC are appropriate for cases of ICPN more than 1.0 cm.

In conclusion, we reported a case of ICPN with an associated invasive adenocarcinoma that was treated successfully with extended cholecystectomy and D2 lymph node dissection.

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