

Received: 2021.04.05

Accepted: 2021.07.12

Available online: 2021.07.28

Published: 2021.09.02

# Pancreatic Ductal Adenocarcinoma Concomitant with Main Duct Type Intraductal Papillary Mucinous Neoplasm of the Pancreas: A Case Report

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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Literature Search F  
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**Conflict of interest:** None declared

**Patient:** Male, 67-year-old

**Final Diagnosis:** Pancreatic ductal adenocarcinoma concomitant with main duct type intraductal papillary mucinous neoplasm of the pancreas

**Symptoms:** Asymptomatic

**Medication:** —

**Clinical Procedure:** —

**Specialty:** Gastroenterology and Hepatology

**Objective:** Rare coexistence of disease or pathology

**Background:** Intraductal papillary mucinous neoplasm of the pancreas (IPMN) and pancreatic ductal adenocarcinoma (PDAC) often coexist in the same pancreas. Almost all IPMNs involving PDACs concomitant with IPMN have been shown to be branch duct type IPMNs (BD-IPMNs), and their histological subtypes are gastric type. Therefore, PDACs concomitant with main duct type IPMNs (MD-IPMNs) are considered to be rare. We herein report a rare case preoperatively diagnosed as being a PDAC concomitant with MD-IPMN on the basis of imaging findings and histological findings of pancreatic specimens endoscopically obtained from 2 lesions.

**Case Report:** A 67-year-old man was referred to our hospital due to an enlarged pancreas. Using imaging studies, a solid mass was found in the pancreatic head and intraductal papillary masses in the dilated main pancreatic duct of the body and tail with a fistula in the duodenum. On the basis of histological results using specimens endoscopically obtained from each of the 2 lesions, total pancreatectomy was planned due to suspected PDAC concomitant with an MD-IPMN. Finally, resected specimens were used to confirm the presence of a rare case of PDAC concomitant with MD-IPMN.

**Conclusions:** We encountered a rare case of a PDAC concomitant with an MD-IPMN which could be preoperatively diagnosed by using imaging studies and histological specimens endoscopically obtained. In addition to invasive cancers derived from IPMNs, PDACs concomitant with IPMNs can rarely develop in the pancreas involving MD-IPMNs.

**Keywords:** Carcinoma, Pancreatic Ductal • Endoscopy, Gastrointestinal • Pancreatectomy • Pancreatic Intraductal Neoplasms

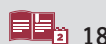
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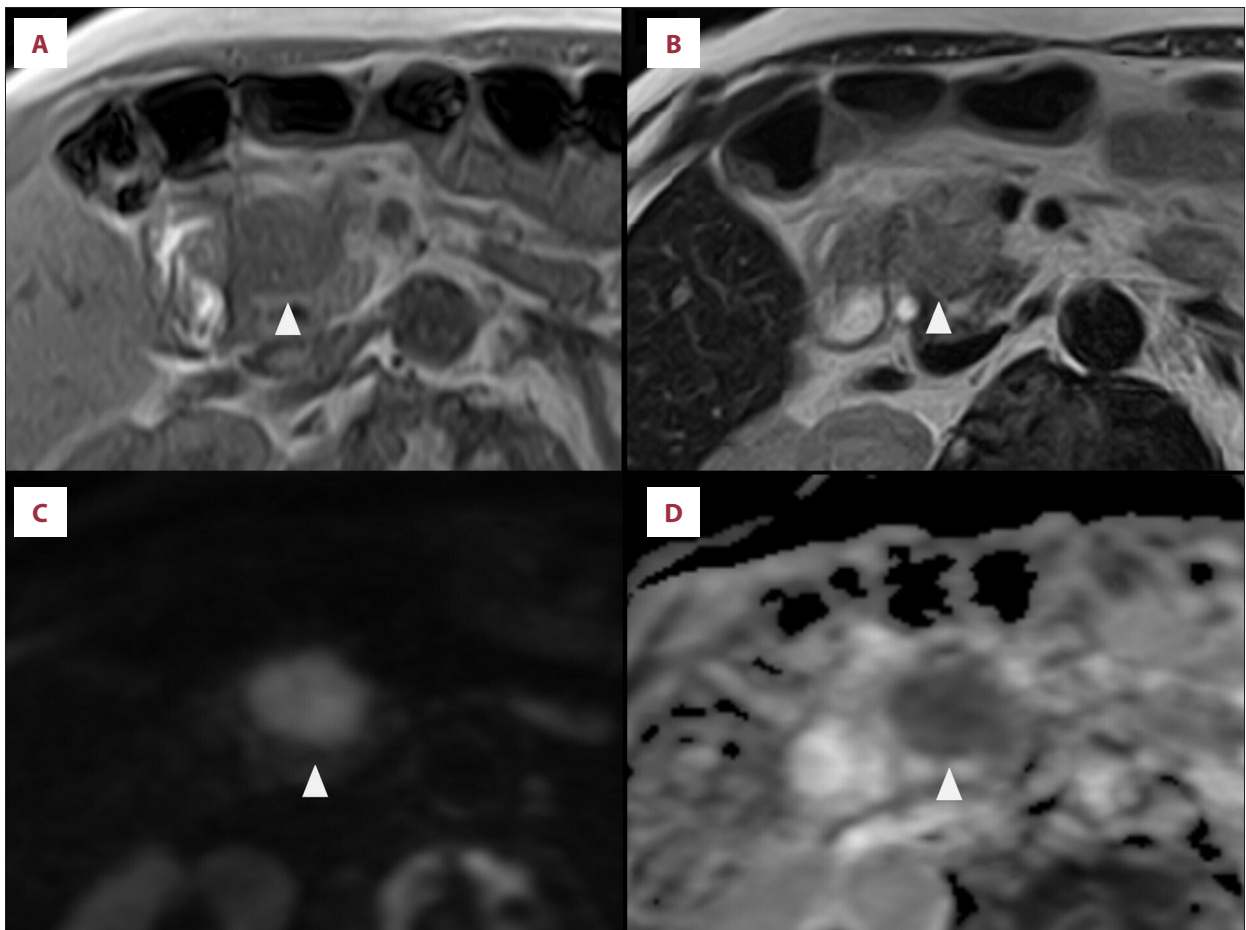


## Background

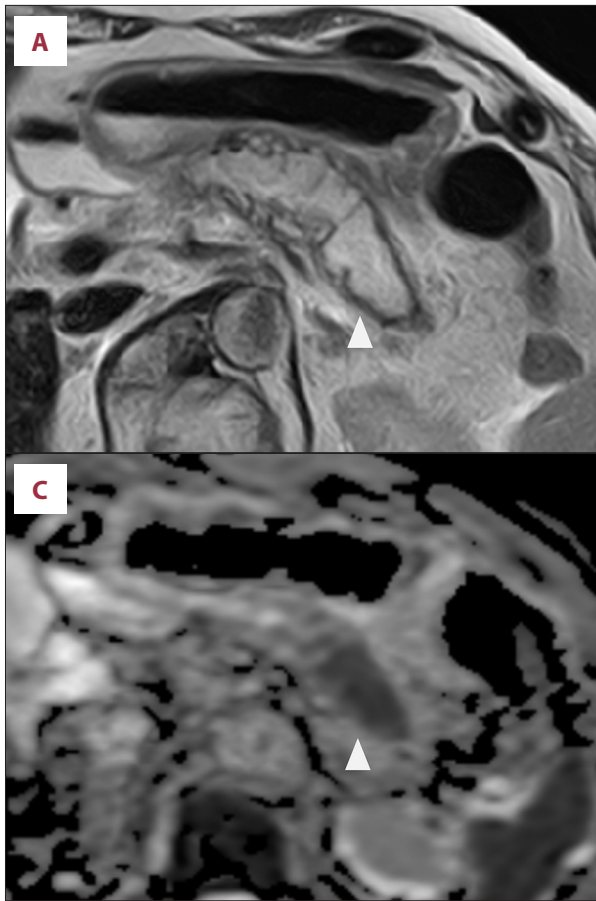
Intraductal papillary mucinous neoplasm of the pancreas (IPMN) and pancreatic ductal adenocarcinoma (PDAC) often coexist in the same pancreas. When these 2 pancreatic lesions can be separated by using imaging studies, histology, and genetic analyses, PDACs like this are defined as PDAC concomitant with IPMN [1]. On the other hand, when a PDAC is histologically or genetically proven to originate in an IPMN adjacent to the PDAC, this PDAC is defined to be derived from the IPMN [1]. From previous reports, almost all IPMNs involving PDACs concomitant with IPMN have been shown to be branch duct type IPMNs (BD-IPMNs), and their histological subtypes are gastric type [2-4]. Therefore, PDACs concomitant with main duct type IPMNs (MD-IPMNs) are considered to be rare. We herein report a rare case preoperatively diagnosed as being a PDAC concomitant with MD-IPMN on the basis of imaging findings and histological findings of pancreatic specimens endoscopically obtained from 2 lesions.

## Case Report

A 67-year-old asymptomatic man was referred to our medical center because his primary care physician detected the enlargement of the pancreas by using screening tests, including abdominal ultrasonography and computed tomography (CT). His past medical history included ulcerative colitis, atrial fibrillation and hypertension. He had a habit of smoking (a pack per day for 45 years) and drinking (pure alcohol of >72 g per day). He had no family history of pancreatic cancer. For laboratory data on admission, the serum levels of liver and pancreatic enzymes, except gamma glutamyl transpeptidase (64 IU/L), were within normal ranges. Serum carbohydrate antigen 19-9 and carcinoembryonic antigen levels were slightly elevated (54.8 and 5.4 IU/L, respectively). By using contrast-enhanced CT scan, a mass with a size of 30 mm in the pancreatic head was heterogeneously enhanced at the portal/late phases. In addition, a main pancreatic ductal (MPD) dilation with intraductal air bubbles was detected in the pancreatic body and tail, suggesting the formation of fistula in

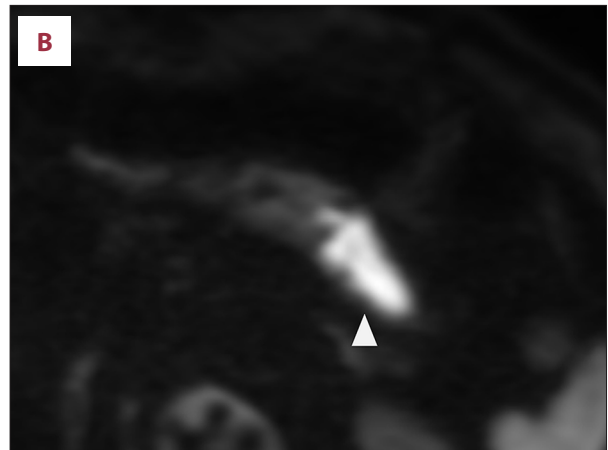


**Figure 1.** Magnetic resonance imaging (pancreatic head). A mass lesion in the pancreatic head showed low signal intensity on both T1- (A) and T2-weighted images (B) and a decrease in apparent diffusion coefficient values on diffusion-weighted image (C, D, arrowhead).



the third part of the duodenum. Magnetic resonance imaging (MRI) showed the signal intensity of the mass lesion in the pancreatic head was low in both T1- and T2-weighted images, and there was a decrease in the apparent diffusion coefficient values in diffusion-weighted images (Figure 1). On the other hand, we detected the main pancreatic duct dilation with a maximum diameter of 16 mm in the pancreatic body and tail on T2-weighted image and a decrease in apparent diffusion coefficient values on diffusion-weighted image (Figure 2). By using endoscopic ultrasonography (EUS), a 30-mm low-echoic mass with a heterogeneous internal echo was visualized in the head of the pancreas, whereas papillary protrusions with a maximum height of 10 mm filled in the dilated MPD of the pancreatic body and tail. Although the intraductal lesions in the pancreatic body and tail were considered to be an MD-IPMN penetrating into the duodenum by using the above-mentioned imaging findings, the mass lesion in the pancreatic head was suspected of being a PDAC that did not originate from the possible MD-IPMN lesion due to lack of the continuity between the 2 lesions shown by imaging studies.

To obtain histological evidence for these 2 lesions, EUS-guided fine-needle aspiration (EUS-FNA) for the mass lesion in the pancreatic head was performed by using a 22-G needle (EZ

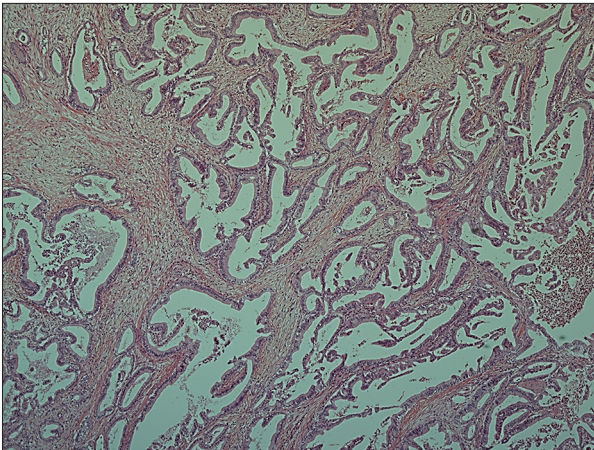


**Figure 2.** Magnetic resonance imaging (pancreatic body and tail). The main pancreatic duct (MPD) dilation with a maximum diameter of 16 mm in the pancreatic body and tail was detected on (A) T2-weighted image, and the inside of the dilated MPD in the pancreatic tail showed a decrease in apparent diffusion coefficient values on diffusion-weighted image (B, C, arrowhead).

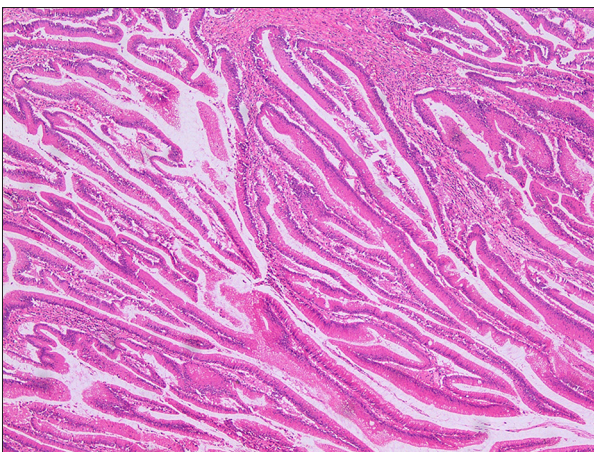
shot 3™: Olympus, Tokyo, Japan). The specimens collected by using EUS-FNA were processed using a cell-block method [5] and were subjected to hematoxylin and eosin (HE) staining and immunostaining. From histological diagnosis of the specimens, the lesions were suspected to be adenocarcinoma. In addition, we performed duodenoscopy by using a short single-balloon enteroscope (SIF-290: Olympus Co., Tokyo, Japan) to obtain specimens from the intraductal lesions in the pancreatic body and tail through the fistula in the third portion of the duodenum. Under duodenoscopy guidance, the fistula with mucus discharge was endoscopically detected in the 3<sup>rd</sup> portion of the duodenum, and the tip of the enteroscope could be directly inserted into the MPD via this fistula. We could endoscopically observe papillary protrusions filling the inside of the MPD and performed biopsies on these intraductal lesions. By using HE staining, the biopsy specimens were found to include atypical epithelial cell clusters with papillary structure, which were histologically determined to have IPMN with high-grade dysplasia of an intestinal type on the basis of the presence of cells, which were positive for MUC2 and CDX2 stainings and negative for MUC1 staining and had a high Ki-67 labeling index of 30%. Based on these findings, the patient underwent total pancreatectomy due to the diagnoses of a PDAC in the pancreatic head and an MD-IPMN in the pancreatic body and tail. At this time, the transverse colon was partially resected due to the adhesion to the pancreas caused by colonic diverticulitis.

In the cross-section of the resected specimens, a white mass with a size of 45 mm was macroscopically identified in the pancreatic head, whereas the dilated MPD of the pancreatic





**Figure 3.** Histological findings of the resected specimens (pancreatic head). A well-differentiated tubular adenocarcinoma occupied the pancreatic head (hematoxylin and eosin staining, orig. mag., ×40).



**Figure 4.** Histological findings of the resected specimens (pancreatic body and tail). The inside of the main pancreatic duct was packed with atypical papillary epithelium in the pancreatic body and tail (hematoxylin and eosin staining, orig. mag., ×40).

body and tail was filled with papillary masses. Macroscopically, these 2 lesions were separated. In addition, the pancreatoduodenal fistula covered by mucus was detected in the third part of the duodenum. From histological findings of the resected specimens, a well-differentiated tubular adenocarcinoma occupied the pancreatic head (Figure 3). On the other hand, in the pancreatic body and tail, the inside of the MPD was packed with atypical papillary epithelium (Figure 4). From immunostaining findings, the atypical papillary epithelium was shown to be positive for MUC2 and CDX2 stainings and to have a high Ki-67 labeling index of 30%, resulting in a histological diagnosis of an MD-IPMN with high-grade dysplasia and an intestinal histological subtype. No other IPMN lesions were observed in the resected pancreas. Since both malignant lesions

were found to be separated histologically, the patient was diagnosed as having a PDAC (fStage IIB) concomitant with a malignant MD-IPMN (fStage 0).

## Discussion

IPMNs have recently been shown to be a risk factor for PDACs in addition to malignant transformation of IPMN itself [6-8]. From a systematic review conducted by Choi et al, pancreatic malignancies, including PDACs, developed in almost 8% of the cases of low-risk IPMNs (those defined as being without MPD involvements or mural nodules) and in almost 25% of cases of high-risk IPMNs (those defined to have MPD involvement and/or mural nodules) within 10 years [9]. In other words, pancreatic malignancies can develop even in the pancreas involving IPMNs unlikely to develop malignant transformations of the IPMNs themselves. In 2009, Yamaguchi et al proposed the concept of “PDACs concomitant with IPMNs” by analyzing 765 patients who underwent surgery for IPMNs [10]. In that study, PDACs concomitant with IPMNs were defined as lacking histological transitions between PDAC and IPMN lesions and were discriminated from invasive cancers derived from IPMNs. In addition, the study indicated the following histological characteristics of PDACs concomitant with IPMNs by comparing those of invasive cancers derived from IPMNs: 30% of invasive cancers derived from IPMNs were colloid carcinomas, whereas all PDACs concomitant with IPMNs were tubular adenocarcinomas.

Based on the international consensus guidelines revised in 2017, IPMNs are morphologically classified into 3 types on the basis of imaging and/or histological findings: MD-IPMN, BD-IPMN, and mixed type IPMN [1]. MD-IPMNs can be determined from those 3 types when all the following imaging findings are met: 1) segmental or diffuse MPD dilation of  $\geq 5$  mm without being caused by other diseases, 2) branch duct dilation of  $< 5$  mm, and 3) the findings indicative of mucus production or the detection of mural nodules in the dilated pancreatic duct. With regard to the morphological type of IPMNs involving PDACs, Ingkakul et al reported that 22 of 236 patients who underwent surgery for their IPMNs could be histologically diagnosed with PDACs concomitant with IPMNs and that the morphological type of involved IPMNs was a BD-IPMN for all 22 patients [3]. This tendency applies to a case series related to PDACs concomitant with IPMNs reported by Mandai et al [4]. In addition, from the histological database of our medical center between January 1985 and December 2016, a total of 160 patients who underwent pancreatic surgery and were histologically found to have PDACs were identified. Although 47 of those patients were determined to have PDACs concomitant with IPMNs, all the coexisting IPMNs in the pancreas involving PDACs were branch duct type (unpublished date). In

contrast, Yamaguchi et al have reported that 50% of patients (61/122) with PDACs derived from IPMNs had MD-IPMNs [10]. In addition, some reports have described the relationship between pancreatic malignancies associated with IPMNs and histological subtypes of those IPMNs [2,11,12]. From a report by Ideno et al, 16 of 110 patients who underwent surgery for their IPMNs were PDAC concomitant with IPMN and the histological subtype of those IPMN were all gastric type [2], whereas Furukawa et al found that approximately 30% of invasive cancers derived from IPMNs developed in IPMNs with an intestinal type [11]. From the viewpoint of the morphological and histological types of background IPMNs involving pancreatic malignancies, those results may support that those 2 types of pancreatic malignancies are different in their pathogeneses.

Unlike the above-mentioned reports, a PDAC in the pancreatic head of this patient was histologically shown to develop apart from an MD-IPMN in the same pancreas. To the best of our knowledge, there are no case reports or clinical studies involving a case of PDAC concomitant with MD-IPMN. Although it may be rare that PDAC and MD-IPMN lesions separately develop in the same pancreas, it may be due to a very low frequency of developing MD-IPMNs compared with that of developing BD-IPMNs or mixed-type IPMNs. In any case, it is meaningful for clinical practice to recognize that PDACs concomitant with IPMNs can occasionally develop even in the pancreas involving MD-IPMNs. In other words, it may be necessary to investigate whether or not PDAC lesions are involved, even in the pancreas where MD-IPMNs develop before determining the surgical procedures for MD-IPMN lesions.

In addition, this case is meaningful because preoperative diagnoses of those 2 separate pancreatic diseases have been determined using imaging findings and specimens obtained endoscopically. When 2 or more pancreatic lesions, including pancreatic mass lesions and IPMNs, coexist in the same pancreas, preoperative evaluations for IPMNs may become important determinants for surgical procedures because IPMNs are sometimes difficult to determine to be suitable for surgery only by using imaging findings. In such cases, endoscopic approaches to obtain histocytological specimens for IPMNs may be effective for determining treatment plans for pancreatic diseases [13-17]. Although surgery is generally indicated when an MD-IPMN lesion has mural nodules on the basis of imaging findings, endoscopic approaches to obtain histocytological

specimens may be necessary for some patients having MD-IPMNs with mural nodules, like elderly patients and patients with several comorbidities, because approximately 40% of MD-IPMNs with mural nodules have been shown to be benign [15]; therefore, an MD-IPMN lesion with mural nodules may not be a prognostic factor for some patients with a high risk for surgery [18]. For this case, since total pancreatectomy, which was indicated for the patient on the basis of imaging findings, is a highly-invasive surgical procedure, endoscopic tissue acquisitions were performed at the 2 pancreatic lesions separately to determine whether or not total pancreatectomy should be performed.

## Conclusions

We encountered a rare case of a PDAC concomitant with an MD-IPMN which could be preoperatively diagnosed by using imaging studies and histological specimens endoscopically obtained. In addition to invasive cancers derived from IPMNs, PDACs concomitant with IPMNs can rarely develop in the pancreas involving MD-IPMNs.

## Acknowledgements

We greatly appreciate Fumiyoshi Fujishima, MD, PhD, Department of Pathology, Tohoku University School of Medicine and Miwa Uzuki, MD, PhD, Department of Nursing, Faculty of Medical Science and Welfare, Tohoku Bunka Gakuen University for histocytological evaluations by using cytological specimens and resected specimens from all subjects, and all staff in the Department of Pathology at Sendai City Medical Center for immunostaining all specimens of this case. In addition, we are very grateful to Dr. Brian Breedlove, Associate Professor, Tohoku University School of Science for English proofreading.

## Conflict of Interest

None declared.

## Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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