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Case Report

Synchronous Intraductal Papillary Mucinous Neoplasms in the Ectopic and Orthotopic Pancreas: Two Case Reports with a Brief Review

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Abstract

Ectopic or heterotopic pancreases are normal pancreatic tissues located outside the pancreas. The ectopic pancreas has its own vascular and ductal systems and does not communicate with the normal pancreas. The prevalence of ectopic pancreas ranges from 0.6% to 15% among all autopsies. Many types of tumors, including intraductal papillary mucinous neoplasms (IPMNs), have been reported in the ectopic pancreas. However, little is known about the synchronous occurrence of IPMNs in both ectopic and orthotopic pancreas. In this study, we report, for the first time, two cases of concurrent IPMNs in an ectopic pancreas and an orthotopic pancreas. One patient had IPMNs both in the pancreas and in ectopic pancreatic tissue in the jejunum. Another patient had IPMNs in both the pancreas and ectopic pancreatic tissue in the duodenum. These cases may provide valuable insights into the etiological factors of IPMNs.

Introduction

Ectopic or heterotopic pancreases are normal pancreatic tissues located outside the pancreas. The ectopic pancreas has its own vascular and ductal systems and does not communicate with the normal pancreas. The prevalence of ectopic pancreas ranges from 0.6% to 15% among all autopsies.[1,2] Ectopic pancreatitis usually occurs in the gastrointestinal tract, including the stomach, duodenum, and jejunum.[3] Ectopic pancreas is also occasionally observed in extra-abdominal locations, such as the mediastinum.

Intraductal papillary mucinous neoplasms (IPMNs) are uncommon pancreatic lesions with malignant potential. Currently, little is known about the molecular mechanisms involved in the development of IPMNs. KRAS and GNAS mutations have been detected in resected IPMNs.[4] GNAS is also useful in distinguishing IPMNs from other pancreatic cystic neoplasms.[4] GNAS may be a key oncogene in IPMN.[5] It has been shown that 66% of 132 IPMNs had a GNAS mutation. A hotspot mutation of KLF4 has also been detected in low-grade dysplasia.[5]

The ectopic pancreas shares the same pathological conditions that can occur in the orthotopic pancreas.[3] Many types of tumors, such as adenocarcinoma, solid pseudopapillary neoplasms, and neuroendocrine neoplasms, have also been reported in patients with ectopic pancreas.[3] Cases of gastric IPMNs occurring in the ectopic pancreas have been reported.[2,3] However, little is known about the synchronous occurrence of IPMNs in both ectopic and orthotopic pancreas. In this study, we report for the first time two cases involving the concurrence of IPMNs in orthotopic pancreas and ectopic intestinal pancreatic tissue.

Case presentations

This study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine (2017NL-137-05), and it followed the Declaration of Helsinki.

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Patient one

A 59-year-old woman was admitted to our institution due to two years of abdominal pain. Her medical history and family history of cancer were unremarkable. Carcinoembryonic antigen and carbo-

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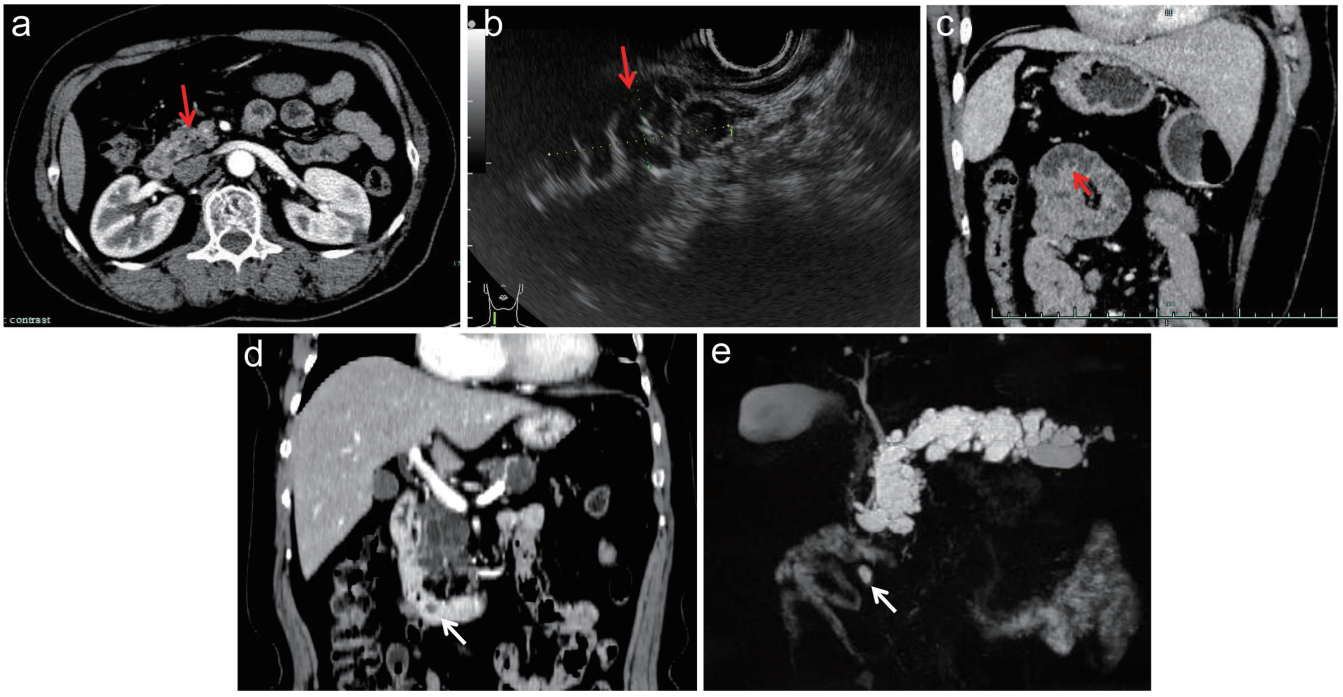

Fig. 1. Imaging findings of intraductal papillary mucinous neoplasms (IPMNs) in the orthotopic pancreas and ectopic pancreas in patients One (a-c) and Two (d, e). (a) Axial contrast-enhanced computed tomography (CT) revealed a 2.5 × 1.1 cm mild ring-enhanced lesion in the pancreatic uncinate (red arrow). (b) Endoscopic ultrasound image showing a 2.8 × 1.3 cm hypoechoic area in the pancreatic uncinate (red arrow). (c) Coronal contrast-enhanced CT revealed a 1.0 × 1.0 cm mass with ring enhancement in the proximal jejunum (red arrow). (d) Coronal contrast-enhanced CT revealed multiple low-density lesions in the pancreas and a 2.1 × 1.0 cm mass with ring enhancement in the horizontal part of the duodenum (white arrow). (e) Magnetic resonance cholangiopancreatography revealed multiple cysts in the pancreas and a small cyst in the horizontal part of the duodenum (white arrow).

hydrate antigen 19-9 levels were within the normal range (4.9 ng/ml and 33.3 U/ml, respectively). Computed tomography (CT) revealed a low-density lesion (2.5 × 1.1 cm) (Fig. 1a), and endoscopic ultrasound examination revealed a 2.8 × 1.3 cm multilocular cystic mass in the uncinate process of the pancreas (Fig. 1b). Magnetic resonance imaging (MRI) revealed a lesion with hypointensity on T1-weighted imaging and hyperintensity on T2-weighted imaging. Mild ring enhancement was observed via contrast-enhanced imaging. Dilatation of the pancreatic duct, common bile duct, and intrahepatic bile ducts was observed. Magnetic resonance cholangiopancreatography (MRCP) was not performed. All CT, endoscopic ultrasound, and magnetic resonance images revealed that the lesion communicated with the main pancreatic duct. The patient was referred for surgery for suspected IPMNs. Intraoperatively, one mass was found in the pancreatic uncinate process. The patient underwent pancreatoduodenectomy. Histopathologic examination of the orthotopic pancreas revealed IPMNs with low-grade dysplasia and irregular papillary or micropapillary structures lined by mucinous epithelium. Histochemical staining revealed MUC1(+), MUC2(−), MUC5AC(+), and a Ki-67 index of 3%. Unexpectedly, another mass (1.2 × 0.8 cm) was found in the adjacent jejunum. Ectopic pancreatic tissues, including numerous acini and a few ducts and islet cells, were observed in the walls of the jejunum (Fig. 2a). Interestingly, irregular papillary or micropapillary structures lined by mucinous epithelium were also found in the ectopic pancreas (Fig. 2b). Retrospectively, CT revealed a 1.0 × 1.0 cm mass with ring enhancement in the proximal jejunum (Fig. 1c). IPMNs with low-grade dysplasia were diagnosed. Twenty-four months after surgery, the patient was alive without recurrence.

Patient two

A 72-year-old woman was admitted to our institution due to the incidental detection of pancreatic lesions over two years. Her medical history was unremarkable, and no positive family history of cancer was reported. Carcinoembryonic antigen and carbohydrate antigen 19-9 levels were within the normal range. CT revealed multiple low-density lesions in the pancreas. MRI revealed that multiple lesions in the pancreas presented hypointensity on T1-weighted imaging and hyperintensity on T2-weighted imaging. No enhancement was observed in the pancreatic lesions during the CT and MRI examinations. Obvious dilatation of the pancreatic duct was observed on both CT and MRI. MRCP revealed multiple cysts in the pancreas. Both CT and MRI showed that the lesions communicated with the main pancreatic duct. Diffusely distributed IPMNs of the mixed type were diagnosed. The patient was referred for surgery for suspected IPMNs. Multiple cystic masses were found in the pancreas intraoperatively. Pancreatoduodenectomy and distal pancreatectomy were performed. Histopathologic examination of the resected mass in the pancreas revealed IPMNs with low-moderate-grade dysplasia. A cystic mass in the duodenum was incidentally found at 3.8 cm from the duodenal papilla. Histopathologic examination revealed that the lesion in the duodenum contained pancreatic tissues, such as a few ducts and islet cells (Fig. 2c). Moreover, mucin production and epithelial proliferation were also observed (Fig. 2d). Histochemical staining revealed MUC1(+), MUC2(+), MUC5AC(+), and a Ki-67 index of 5%. Retrospectively, CT revealed a 2.1 × 1.0 cm mass with ring enhancement in the horizontal part of the duodenum (Fig. 1d). MRCP also revealed a small cyst in the horizontal part of the duodenum (Fig. 1e). IPMNs

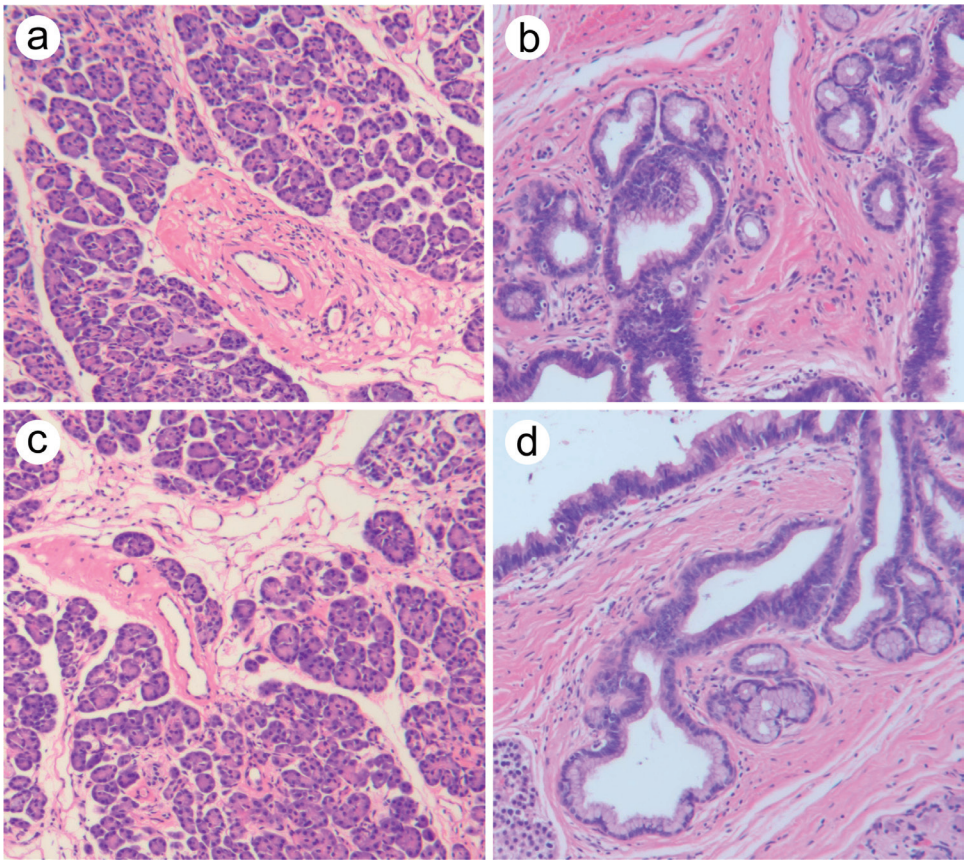

Fig. 2. Histologic examinations of the ectopic pancreas in Patient One (a, b) and Patient Two (c, d). Ectopic pancreatic tissues located in the walls of the jejunum, with numerous acini, few ducts, and islet cells (a), in which irregular papillary or micropapillary structures lined by mucinous epithelium were also observed (b). The lesion in the duodenum contained pancreatic tissues, a few ducts, and islet cells (c), as well as mucin production and epithelial proliferation (d). Magnification: 100×.

with low-grade dysplasia were diagnosed in the ectopic pancreas. The patients were followed up for 24 months, and no recurrence was observed.

Discussion

Malignant transformation of the ectopic pancreas has been reported.[3] Adenocarcinomas are the most common malignancy in ectopic pancreas. A few studies have also reported IPMNs arising in an ectopic pancreas.[1,6–8] However, little is known about whether IPMNs can co-occur in both the orthotopic and ectopic pancreas. Our case series is the first to report the unique characteristics of concurrent IPMNs in orthotopic pancreas and in ectopic intestinal pancreatic tissue. IPMNs may extend to adjacent organs,[9] such as the stomach and duodenum. Extension or metastasis can be excluded because normal pancreatic tissues, including developed acini and ductal structures, were observed in our patients. Interestingly, two case reports also revealed that IPMNs occurred in both the orthotopic pancreas and the gastric ectopic pancreas.[10,11]

The four cases of IPMNs reported in our study and previous studies provide a new perspective on the occurrence of IPMNs.[10,11] The ectopic pancreas develops during embryonic rotation and fusion of the dorsal and ventral pancreatic buds, where genes, rather than environmental factors, play crucial roles.[12] Both orthotopic and ectopic pancreas, similar to a pair of twins, are often used to investigate the genetic contributions of disease-related phenotypes.[13] The simultaneous existence of IPMNs in both orthotopic and ectopic pancreas may suggest an unidentified genetic predisposition for IPMNs. Genetic components may be involved in the pathogenesis of IPMNs.[14,15] Unfortunately, the results of genomic characterization for the four cases were inconclusive. Additionally, no family history of pancreatic cancer or tumors was reported. A recent study indicated that individuals with a higher inherent risk of pancreatic ductal adenocarcinoma (PDAC) did not have a higher risk of developing branch-duct IPMNs.[16] However, a genetic predisposition for IPMNs may still be associated with a higher risk of PDAC.[16] Do IPMNs have their own genetic predisposition independent of PDAC? Interestingly, Nambu *et al*.[17] reported that a patient with IPMN in the ectopic pancreas of the stomach had a *GNAS* mutation. However, *GNAS* mutations do not occur in PDAC.[18] The associations between genetic predispositions and cancer are complex.[16] Further studies are needed.

Our study has several limitations. First, intraoperative solid images or resected samples from the two patients were not collected. Second, these two patients were not followed up at our institution, so the long-term clinical outcomes are unknown. Both patients had low-grade dysplasia, and we speculated that their long-term outcomes were likely favorable. Third, we did not compare the clinical, imaging, and pathologic information of patients with IPMN in the ectopic and orthotopic pancreas with those who had IPMN in

the orthotopic pancreas only. Finally, the genetic information was not determined in our cases.

Conclusions

We reported two cases of patients with concurrent IPMNs in orthotopic and ectopic pancreas. Our study showed that tumors can occur in both orthotopic and ectopic pancreas. These unique cases may provide valuable insights into the etiological factors of IPMNs.

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Conflict of interest

XC has been an editorial board member of *Oncology Advances* since August 2023. The authors have no other conflicts of interest to declare.

Author contributions

Patient information collection (YZ, HZ, XW, CG), writing of the manuscript (YZ, HZ, XW, , CG, JW, XC), review of the pathologic and imaging findings, design and review of the manuscript (CG, XC). All authors have approved the final version and publication of the manuscript.

Ethical statement

This study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine (2017NL-137-05), and it followed the Declaration of Helsinki. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

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