CASE REPORT

Pancreatico-Gastric Fistula: A Rare Complication of Intraductal Papillary Mucinous Neoplasm

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ABSTRACT

Background Intraductal papillary mucinous neoplasms arise from the main pancreatic duct and/or branch ducts and are characterized by intraductal papillary proliferation of mucin-producing epithelial cells exhibiting various degrees of dysplasia. The intraductal papillary mucinous neoplasms of the pancreas rarely penetrates others organs. **Case presentation** We report an unusual case of intraductal papillary mucinous neoplasms fistulating into the stomach in a patient who previously underwent distal gastrectomy. Pancreatoduodenectomy was performed with resection of fistulisation site at the posterior gastric wall. The histopathological examination of the surgical specimen showed high-grade dysplasia with invasive carcinoma. **Conclusion** In treatment of intraductal papillary mucinous neoplasms with fistula, the fistula should be removed to avoid a possible malignant dissemination. The extent of resection depends on the extent of cancer invasion.

BACKGROUND

Intraductal papillary mucinous neoplasm (IPMN) is a distinct entity characterized by papillary proliferations of mucin-producing epithelial cells with excessive mucus production exhibiting various degrees of dysplasia, with cystic dilatation of the main pancreatic duct (MD-IPMN) and/or the branch ducts (BD-IPMN). The IPMN of the pancreas has been previously reported to occasionally fistulate into adjacent organs [1]. Kobayashi G *et al.* (2) reported a cases of IPMN that penetrated into other organs as follows: duodenum (64%), common bile duct (56%) and stomach (17%). IPMNs are generally considered slowly growing tumors with a good outcome after surgical resection, but invasive ones have been associated with a poorer prognosis. We report an unusual presentation history of IPMN in a patient who declined surgery and was therefore on regular follow-up. The patient provided written informed consent before the start of the study, which was approved by the Ethics Committee of Kyoto University in accordance with the Declaration of Helsinki of 1996.

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Keywords Fistula; Pancreas
Abbreviation ERP endoscopic retrograde pancreatography; IPMN intraductal papillary mucinous neoplasms; MRCP magnetic resonance cholangiopancreatography; MRI magnetic resonance imaging
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CASE REPORT

A Seventy-eighty-year-old Japanese man who was in internal medicine follow-up clinic in 2012 for DM, when they found that the serum amylase was always high. Further radiologhical investigations revealed dilated main pancreatic duct only. In 2014, CT Abdomen performed and revealed left renal pelvis carcinoma and pancreatic IPMN with dilated main pancreatic duct. After that, laparoscopic assisted left nephroureterectomy was performed. The patient declined surgery for IPMN, and he was on follow up by our clinic. His past medical history included distal gastrectomy 30 years ago for gastric ulcer. His physical examination in the last follow-up showed no abnormal findings other than a midline surgical scar on the upper abdomen. The blood chemistry analysis showed creatinine of 1.24 mg/dL and amylase of 77 U/L. Serum tumor markers of CA19-9 and CEA were 6.7 U/mL (<27.0 U/mL) and 0.7 ng/ml (<3 ng/mL), respectively.

His last follow-up CT and MRCP showed a fistula formation between the main pancreatic duct and stomach. Therefore, upper GI endoscopy was performed and demonstrated bulging duodenal papilla with specific high intraductal pressure due to the IPMN and white mucin discharging from the fistula foramen on the gastric wall side **(Figure 1)**. Biopsies were taken from the fistula orifice on the stomach side and revealed high-grade dysplasia. Endoscopic ultrasound (EUS) showed cystic dilatation of the main pancreatic duct with mural nodules and fistulous tract **(Figure 2)**. Computed tomography of the abdomen (CT) showed markedly dilated main pancreatic duct penetrating into the antrum of the stomach with fistula formation **(Figure 3)**.

Magnetic resonance cholangiopancreatography (MRCP) and magnetic resonance imaging (MRI) of the abdomen showed dilatation of the main pancreatic duct with filling defect and fistulous tract between the main pancreatic duct and the stomach **(Figure 4)**. Endoscopic retrograde pancreatography (ERP) revealed dilated pancreatic duct with contrast extravasation. Surgery was considered as the investigations revealed malignant cells on biopsy and fistula formation into the stomach in radiological imaging. Pancreaticoduodenectomy and partial gastrectomy were performed. Histopathological study revealed intraductal papillary mucinous neoplasia (high-grade dysplasia of intestinal type) with associated invasive carcinoma, gastric penetration by IPMN with high-grade dysplasia, and no lymph node metastases (0/38), to conclude pathological staging as pT3N0 **(Figure 5)**. On microscopic examination of the pancreatectomy specimen, it showed the main pancreatic duct obliterated with tumor and gastric wall invasion **(Figure 6)**. The postoperative course was uneventful and the patient discharged.

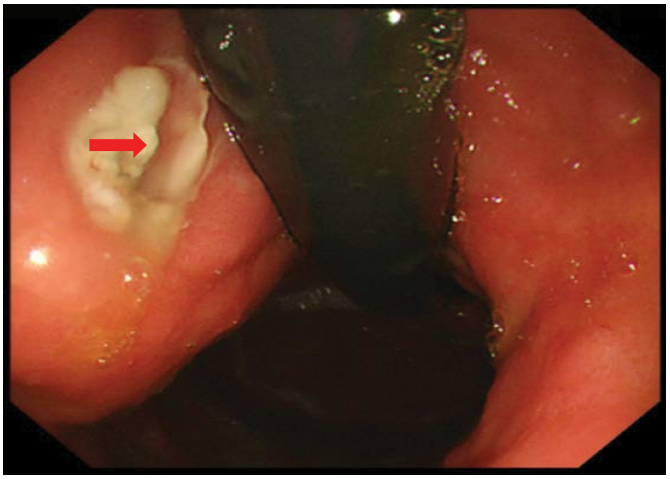

Figure 1. Esophagogastroduodenoscopy showing a fistula orifice producing a mucinous discharge into the body of the stomach (red arrow).

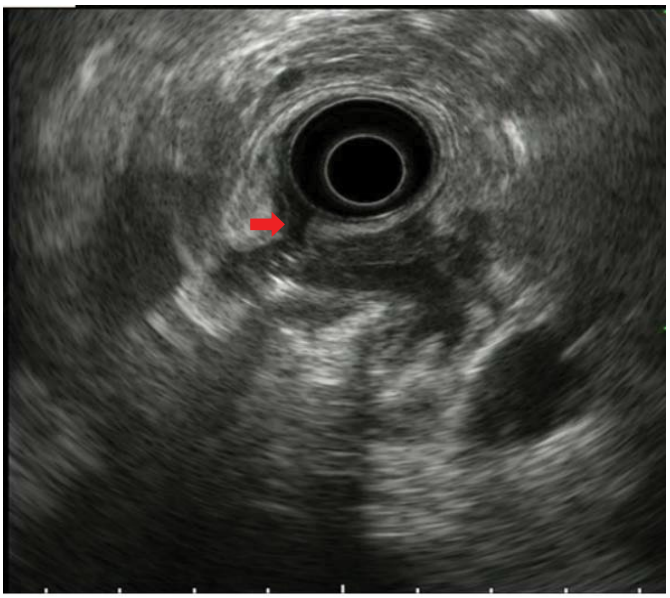

Figure 2. Endoscopic ultrasound showed cystic dilatation of the pancreatic duct with papillary projections- mural nodule, and fistula track to stomach (red arrow).

DISCUSSION

IPMNs account for 5% of all cystic pancreatic lesions and are predominantly observed in older male patients. Fistula formation with an IPMN was first reported by Ohhashi *et al.* in 1980 as a pancreaticobiliary fistula [1]. IPMN, whether benign or malignant, can become complicated in 6.6% cases forming a fistula into the adjacent organs [2]. The most common organ fistulized is the duodenum (64%), followed by the common bile duct (56%) and the stomach (17%) [3]. Kobayashi *et al.* reported two factors in the fistula pathogenesis: direct invasion of IPMN into adjacent organs (33%), and/or pancreatic perforation due to inflammatory stimulation and high pressure in the pancreatic ducts (67%). The first pattern is seen mostly in malignant tumors only, while the second pattern is seen mostly in benign IPMN, although a large malignant IPMN

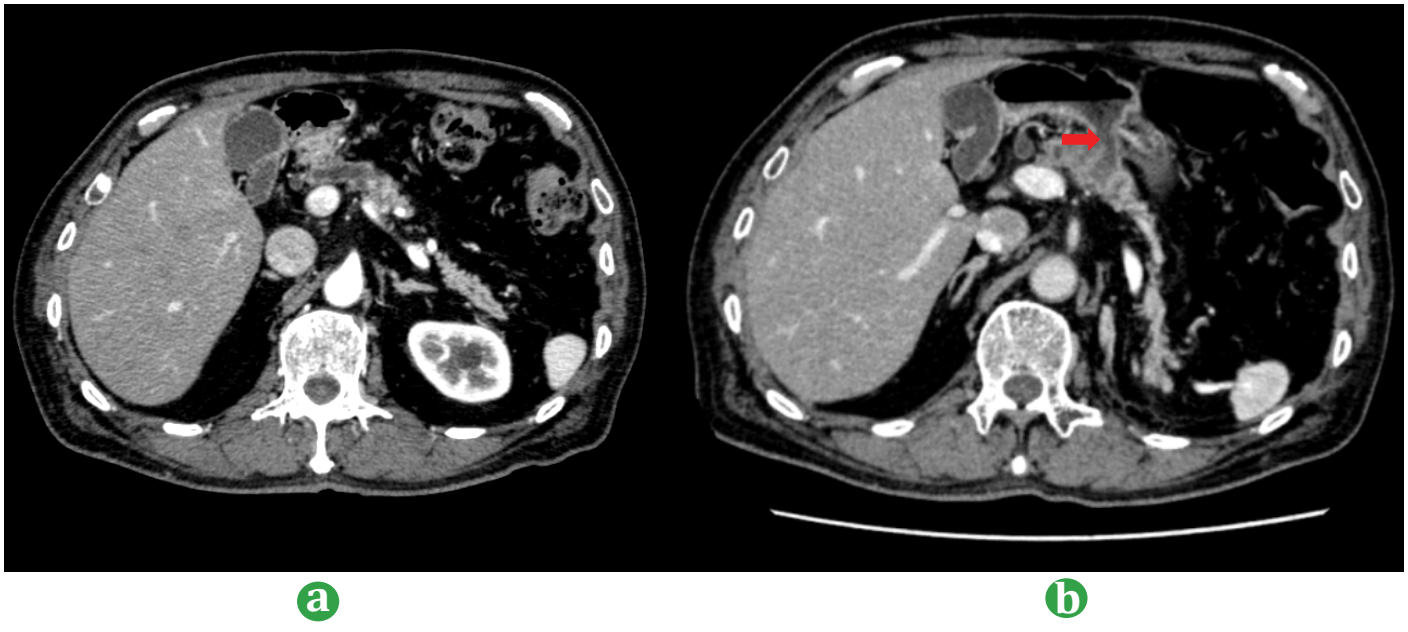

Figure 3. Computed tomography **(a).** 6 months before discovering the fistula, and the **(b).** last CT scan where the communication between the pancreatic duct and stomach is apparent.

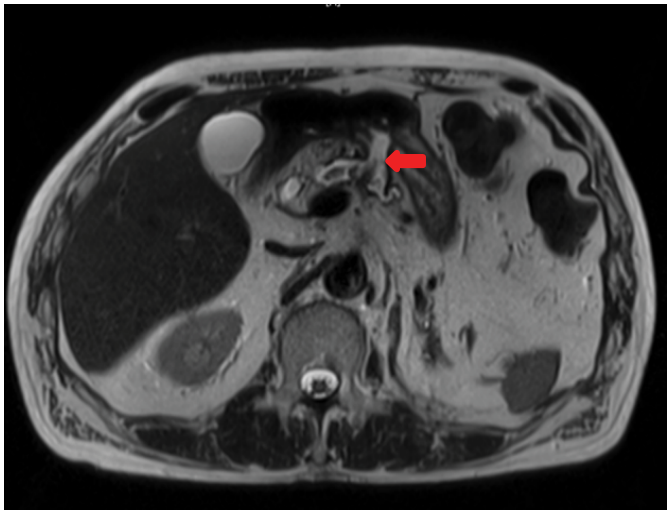

Figure 4. Magnetic resonance imaging abdomen showed a large irregular main pancreatic duct with filling defects, fistula track between main pancreatic duct and stomach.

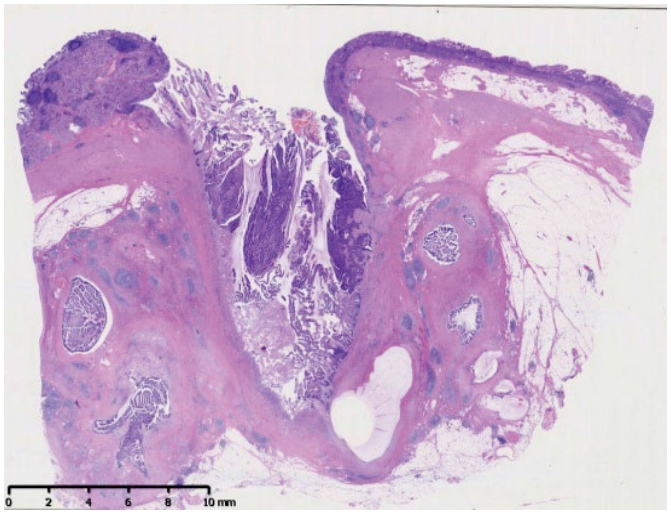

Figure 5. Intestinal-type IPMN. The tumor penetrated through the stomach with expansile invasion.

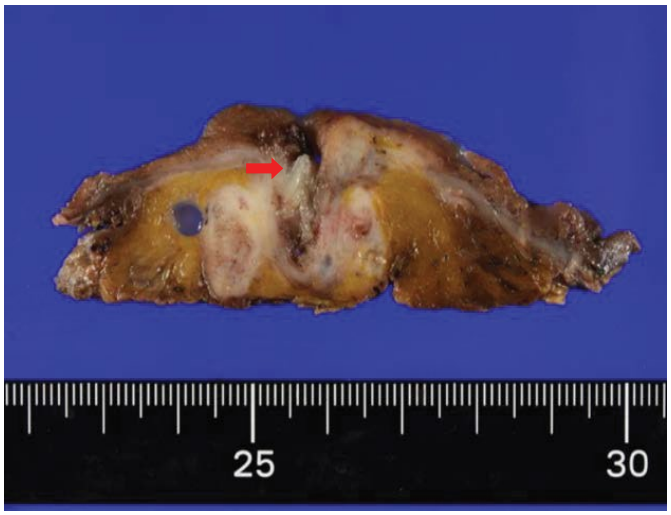

Figure 6. Pancreatectomy specimen showed fistulous orifice on the gastric antrum, tumor infiltration of pancreatic duct and gastric wall.

can also have this type of fistula [2]. In our patient, the IPMN was discovered 2 years ago, and at the same time the patient was diagnosed with renal cell carcinoma for which he underwent left nephrectomy. However, the cytology result was benign for IPMN, but because of a high risk for malignant transformation of the main duct IPMN, we suggested surgery. The patient declined surgery due to comorbidities and surgical risk. Patient surveillance was employed by a regular check every 6 months with enhanced abdominal CT, MRI, MRCP, and endoscopic ultrasound (EUS). There was no suspicious malignant transformation until a month before surgery. Latest biopsies taken from the fistula orifice revealed malignant cells. We performed pancreaticoduodenectomy with partial gastric resection.

In our case, biopsy from fistula site in the gastric wall also showed high-grade dysplasia. So, it was classified as an invasive/penetrating type with superadded fistula formation. The prognosis of IPMN invading other organs is usually poorer than those without any local invasion, because the malignant cells exist at the invasion site [4].

CONCLUSION

Surgery should be considered in the main duct IPMN due to the high risk of malignant transformation. Patients who decline surgery and want to follow-up, have to undergo close surveillance to early detect any pathological malignancies. The present case also reports, that IPMN could be complicated by a pancreaticogastric fistula.

In the treatment of IPMN with fistula, the fistula should be removed regardless to avoid possible malignant dissemination. As usual, the extent of resection depends on the extent of cancer invasion.

Conflict of Interest

The authors declare that they have no conflict of interest.

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