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Intraductal tubulopapillary neoplasm of the pancreas presenting as recurrent acute pancreatitis: A case report

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ABSTRACT

INTRODUCTION: The 2010 World Health Organization classification of intraductal neoplasms of the pancreas includes intraductal tubulopapillary neoplasms (ITPNs) and intraductal papillary mucinous neoplasms, the latter being a rare and new concept. ITPN sometimes cause acute pancreatitis; therefore, distinguishing ITPN from idiopathic acute pancreatitis is important but challenging.
PRESENTATION OF CASE: We present the case of a 72-year-old male who had recurrent pancreatitis for the past 2 years, his diagnosis was idiopathic acute pancreatitis. He was admitted to our hospital with severe acute pancreatitis and cholangitis due to intrapancreatic bile duct stenosis. After the treatment of cholangitis, contrast-enhanced computed tomography revealed a tumor at the pancreatic head. Endoscopic retrograde cholangiopancreatography (ERCP) showed stenosis of the main pancreatic duct and distal bile duct, and adenocarcinoma was detected using brush cytology of the bile duct stricture and pancreatic juice. The patient was diagnosed with invasive ductal carcinoma and pancreaticoduodenectomy was performed. Histopathological findings revealed dilation of the pancreatic duct, and proliferation of columnar cells and cuboid epithelial cells in the main pancreatic duct of the pancreatic head. Mucus production was poor, and immunostaining results revealed ITPN. The patient is alive and do not exhibit signs of recurrence for 12 months.
DISCUSSION: ITPNs can cause acute pancreatitis, which can be challenging to preoperatively diagnose. ITPNs presenting as acute pancreatitis are rare, with reported only 5 cases.
CONCLUSION: It is important to be keep in mind that there is a possibility of ITPN after diagnosis of idiopathic acute pancreatitis.

1. Introduction

Intraductal neoplasms of the pancreas can be classified as intraductal tubulopapillary neoplasms (ITPNs) and intraductal papillary mucinous neoplasms (IPMNs) according to the 2010 World Health Organization classification. ITPN is a rare malignant lesion and newly defined clinical presentation that sometimes lead to acute pancreatitis, and it is critical yet challenging to distinguish ITPN from idiopathic acute pancreatitis, which we illustrate in this case report.

2. Presentation of case

A 72-year-old male was admitted to our hospital with abdominal tenderness and rigidity in the epigastric region. He had been undergone treatment for recurrent acute pancreatitis three times during the last 2 years, and pancreatic pseudocysts were found following pancreatitis treatment. The cause of recurrent acute pancreatitis was determined as idiopathic acute pancreatitis with no malignant findings using multiple modalities including contrast-enhanced computed tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP). Laboratory findings at the time of admission were as follows: white blood cell count, 13710/μL with 93.1% neutrophils; aspartate aminotransferase, 323 U/L; alanine aminotransferase, 285 U/L; γ-GTP, 470 U/L; alkaline phosphatase, 566 U/L; amylase, 180 U/mL; C-reactive protein, 25.14 mg/dL; carcinoembryonic antigen, 1.3 ng/mL; CA19-9,

Abbreviations: ITPN, intraductal tubulopapillary neoplasm; IPMN, intraductal papillary mucinous neoplasm; IDC, invasive ductal carcinoma of pancreas; CT, computed tomography; MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; PD, pancreaticoduodenectomy; DP, distal pancreatomy.

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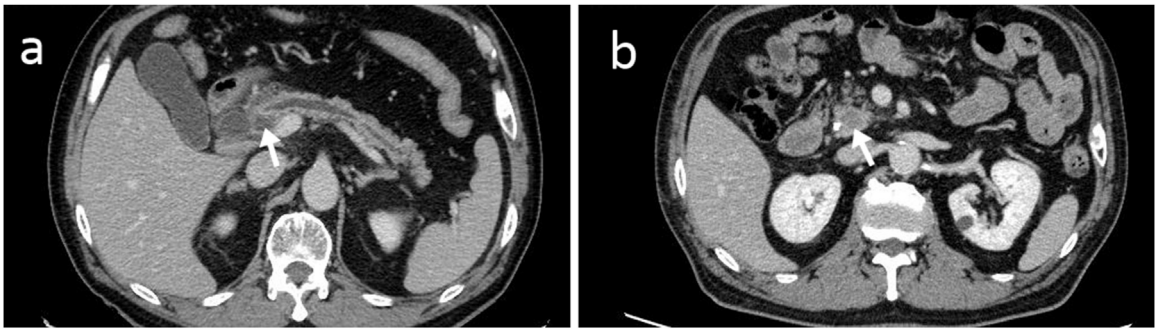

Fig. 1. (a) Contrast-enhanced computed tomography findings at the time of admission showing bile and pancreatic duct dilation and increased radiodensity around the pancreatic head. A pancreatic pseudocyst could also be observed (arrow). (b) Contrast-enhanced computed tomography after treatment for acute cholangitis and pancreatitis showing tumor (arrow) in the main pancreatic duct at the pancreatic head. The high-density structure in the bile duct was due to the endoscopic retrograde biliary drainage tube. Note the improvements in dilation of the bile and pancreatic ducts.

16.1 U/mL; and SPAN-1, 16.2/mL. Contrast-enhanced CT findings at the time of admission showed bile and pancreatic duct dilation and increasing radiodensity around the pancreatic head (Fig. 1a). The patient was diagnosed with severe acute cholangitis and acute pancreatitis. ERCP was performed, and a bile duct and pancreatic duct stents was placed with systemic management. Contrast-enhanced CT performed after treatment of cholangitis and pancreatitis revealed a tumor detail at the pancreatic head (Fig. 1b).

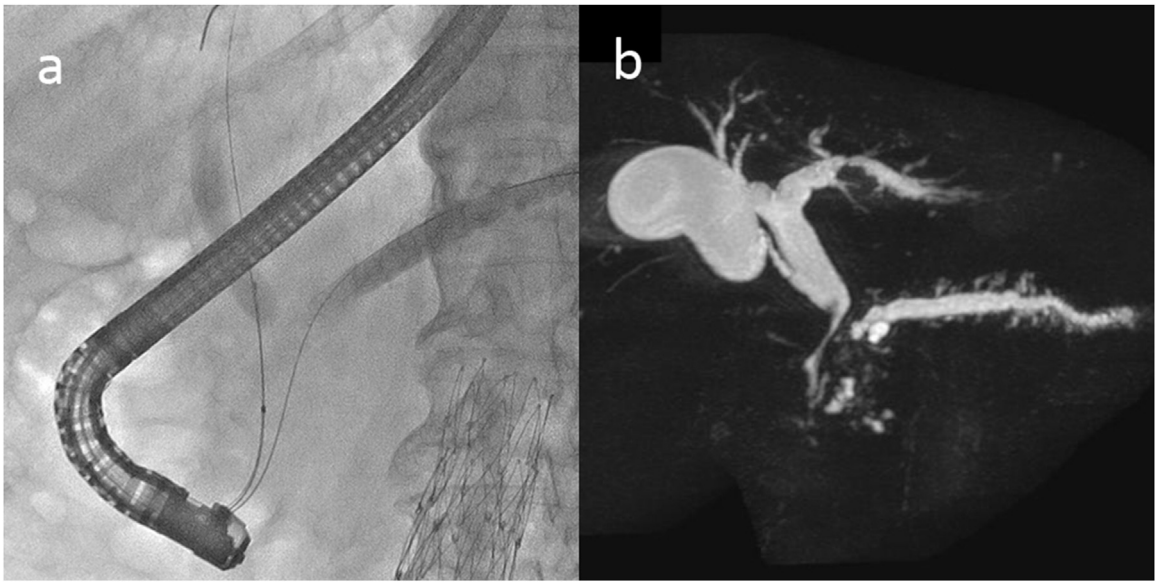

Fig. 2. Endoscopic retrograde cholangiopancreatography (a) and magnetic resonance cholangiopancreatography (b) showing stenosis of the common bile duct and main pancreatic duct.

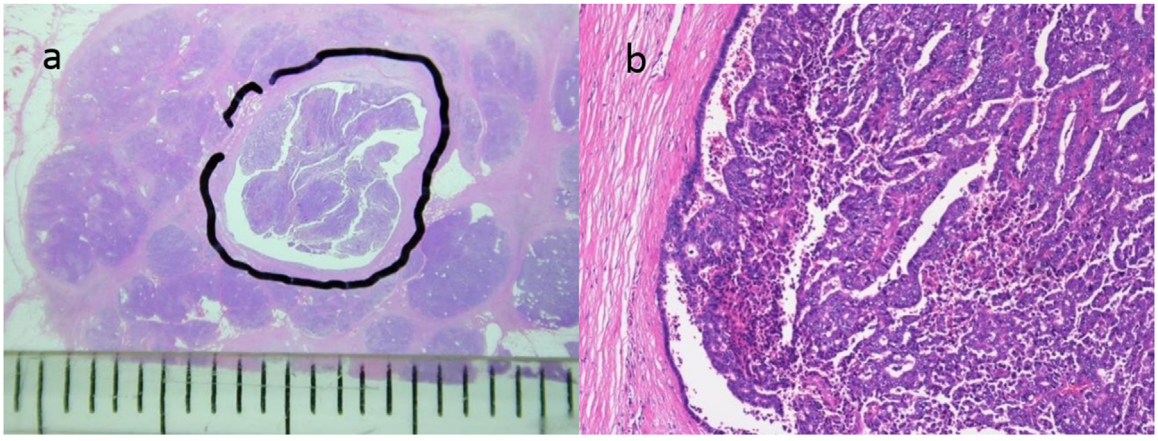

Fig. 3. Histopathological findings revealed dilation of the pancreatic duct, and proliferation of columnar cells and cuboid epithelial cells occupying the main pancreatic duct of the pancreatic head. (a) low-power field, (b) high-power field.

Table 1
Five reported cases of intraductal tubulopapillary neoplasm with acute pancreatitis.

Author	Age of patient	Sex	Causes of diagnosis	Period to diagnosis from symptoms	Preoperative diagnosis	Surgery	Postoperative prognosis
Muraki et al. [3]	74	M	Follow-up after pancreatitis	6 months	Intraductal neoplasm	PD	N/A
Ahls et al. [4]	43	F	Acute pancreatitis	short term	Intraductal neoplasm	PD	No recurrence for over 2 years
Mizuno et al. [5]	62	M	Acute pancreatitis	short term	Intraductal neoplasm or IDC	DP	No recurrence for 18 months
Shimizu et al. [6]	63	M	Acute pancreatitis	short term	Intraductal neoplasm or IDC	DP	Recurrence in remnant pancreas 40 months postoperatively. No recurrence for 32 months after the second surgery
Our case	72	M	Follow-up after pancreatitis	2 years	IDC	PD	No recurrence for 12 months

PD, pancreaticoduodenectomy; DP, distal pancreatomy; IDC, invasive ductal carcinoma of pancreas.

ERCP and magnetic resonance cholangiopancreatography (MRCP) showed stenosis of the distal bile and main pancreatic ducts (Fig. 2a and b). Therefore, he was diagnosed with invasive ductal carcinoma (IDC) with invasion to common the bile duct based on the presence of adenocarcinoma cells detected using brush cytology of the bile duct stricture and pancreatic juice; the patient underwent surgery. Subtotal stomach-preserving pancreaticoduodenectomy followed by modified Child's reconstruction was performed. Because of severe adhesion around the pancreatic head due to pancreatitis, tunneling between the pancreas and the portal vein could not be achieved. However, severe adhesion between the right wall of the portal vein and pancreatic parenchyma could be separated without combined resection of the portal vein. No malignant findings were observed in the adhesion sites by rapid intraoperative pathological evaluation. The postoperative course of the patient was uneventful, and no postoperative pancreatic fistulas occurred. The patient was discharged on postoperative day 17. Histopathological findings revealed dilation of the pancreatic duct, and proliferation of columnar cells and cuboid epithelial cells in the main pancreatic duct of the pancreatic head (Fig. 3). Mucus production was poor, and immunostaining results of the tumor specimen revealed MUC1-positive and MUC2-negative; therefore, the definitive diagnosis was ITPN. There were inflammatory changes in the bile duct, but there was no infiltration of malignant cells; thus, malignant findings by preoperative biliary brush cytology were considered to be false positive. After discharge, the patient received postoperative adjuvant therapy with tegafur, gimeracil, and oteracil and did not exhibit signs of recurrence for 12 months.

3. Discussion

ITPNs, first defined by Yamaguchi et al. in 2009, is particularly rare among pancreatic tumors and accounts for less than 0.9% of all pancreatic exocrine neoplasms [1]. Approximately 50% of ITPN occur in the pancreatic head, 35% grow diffusely, and 15% are located in the pancreatic tail [1]. ITPN has characteristic macroscopic features including solid nodules obstructing dilated ducts without visible secreted mucin and somewhat dilated ducts surrounding solid areas [1]. Clinical findings of ITPN are nonspecific and include abdominal pain, jaundice, and pancreatitis symptoms accompanied by obstruction of the pancreatic or bile duct. Therefore, imaging findings are critical for ITPN diagnosis. Distinctive ITPN signs are cork-of-wine-bottle and two-tone duct signs usually recognized by MRCP or ERCP. The cork-of-wine-bottle sign is caused by the tumor mass surrounded by pancreatic fluid in the dilated duct, whereas some tumors occupying the entire lumen of the dilated duct present as abrupt disruption in the continuity of the duct. The two-tone duct sign, defined as the distinct tones of the tumor and the dilated duct without the tumor, is used to indicative of an intraductal tumor [2]. However, these distinctive ITPN signs, which were not observed in our patient, might depend on lesion size and degree of progression. In the absence of these characteristic findings, preoperative diagnosis of ITPN and its differential diagnosis from IDC is challenging.

Obstructive chronic pancreatitis due to ITPN is thought to result from slow obstruction of the pancreatic duct, and typical ITPN histopathology shows obstructive chronic pancreatitis. Acinar atrophy, stromal fibrosis, and ductal dilatation in the pancreatic parenchyma distal to the tumor are suggestive of chronic obstructive pancreatitis [1]. However, acute pancreatitis due to ITPN can be difficult to distinguish from idiopathic acute pancreatitis in some cases.

Our PubMed search using "intraductal tubulopapillary neoplasm" and "acute pancreatitis" as keywords identified two cases [3,4]. A search of Japanese literature using the same keywords revealed two other cases report [5,6]. Five reported cases of ITPN presenting as acute pancreatitis, including the current case, are summarized in Table 1. Idiopathic acute pancreatitis was suspected at the initial presentation in two of the cases; detailed evaluation and follow-up led to the definitive diagnosis of pancreatic cancer or intraductal lesion including ITPN in these cases. These findings suggest the need to consider pancreatic duct lesions including ITPN even in patients diagnosed with idiopathic acute pancreatitis. There were only two reported cases that were diagnosed with intraductal neoplasms preoperatively, further highlighting the difficulty in the preoperative diagnosis of ITPN. Surgery was performed in all five reported cases, including pancreaticoduodenectomy and distal pancreatomy in three and two cases, respectively. Postoperative prognosis was relatively good in all cases. In the case reported by Mizuno et al., IDC was found in the remnant pancreas 40 months after the primary surgery, which was subsequently removed by total pancreatectomy. The authors reported no recurrence thereafter.

In a review of 37 ITPN cases, 1-, 3-, and 5-year survival rates postoperatively were 97.3%, 80.7%, and 80.7%, respectively. The 5-year survival rate of invasive ITPN after complete resection was 81.5%, whereas that of noninvasive ITPN was 77.8% [7]. The prognosis of ITPN appears to be better than that of IDC and IPMNs-associated pancreatic cancer [8], and early surgery might further improve ITPN survival rates. Therefore, preoperative differential diagnosis is important. Diagnosis may be difficult in patients with acute pancreatitis, as seen in the current case, and ITPN should be considered in the differential diagnosis of idiopathic acute pancreatitis. Even patients diagnosed with idiopathic acute pancreatitis should be followed up to rule out the possibility of ITPN with acute pancreatitis. We think that it is important to examine the cause of every acute

pancreatitis closely; the cause of pancreatitis should be considered not only ITPN but also other pancreatic disease such as IDC. Especially, if recurrent acute pancreatitis has been observed for several months to several years, pancreatic diseases such as ITPN that are not idiopathic acute pancreatitis should be considered.

4. Conclusion

ITPN is a rare presentation with a limited number of reported cases. As illustrated in the current case, preoperative diagnosis of ITPN with acute pancreatitis can be difficult and ITPN should be considered in idiopathic acute pancreatitis.

Conflicts of interest

The authors of this manuscript have no commercial associations or financial disclosures, such as consultancies, stock ownership, equity interests, patent licensing arrangements, and payments for conducting or publicizing a study that might pose or create a conflict of interest with information presented in this manuscript. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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Ethical approval

Our institution has exempted ethical approval.

Consent

This patient consented to the reporting of this case in a scientific publication.

Author contribution

SS, YT, YS, and KK were the physicians attending to the case. SS, YF and YT drafted the manuscript. All authors have read and approved the final manuscript.

Registration of research studies

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