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CASE REPORT

# Reoperation for heterochronic intraductal papillary mucinous neoplasm of the pancreas after bile duct neoplasm resection: A case report

Gang Xiao, Tao Xia, Yi-Ping Mou, Yu-Cheng Zhou

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# **Abstract**

# BACKGROUND

Intraductal papillary neoplasm of the bile duct (IPNB) and intraductal papillary mucinous neoplasm (IPMN) of the pancreas have similar pathological manifestations. However, they often develop separately and it is rare for both to occur together. Patients presenting with heterochronic IPMN after IPNB are prone to be misdiagnosed with tumor recurrence.

#### CASE SUMMARY

A 67-year-old male patient was admitted 8.5 years after IPNB carcinoma and 4 years after the discovery of a pancreatic tumor. A left hepatic bile duct tumor with distal bile duct dilatation was found 8.5 years ago by the computed tomography; therefore, a left hepatectomy was performed. The postoperative pathological diagnosis was malignant IPNB with negative cutting edge and pathological stage T1N0M0. Magnetic resonance imaging 4 years ago showed cystic lesions in the pancreatic head with pancreatic duct dilatation, and carcinoembryonic antigen continued to increase. Positron emission tomography showed a maximum standard uptake value of 11.8 in the soft tissue mass in the pancreatic head, and a malignant tumor was considered. Radical pancreatoduodenectomy was performed. Postoperative pathological diagnosis was pancreatic head IPMN with negative cutting edge, pancreaticobiliary type, stage T3N0M0. He was discharged 15 d after the operation. Follow-up for 6 mo showed no tumor recurrence, and

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quality of life was good.

#### **CONCLUSION**

IPNB and IPMN are precancerous lesions with similar pathological characteristics and require active surgery and long-term follow-up.

Key Words: Intraductal papillary neoplasm of the bile duct; Intraductal papillary mucinous neoplasm of the pancreas; Pancreatoduodenectomy; Heterochronous tumor; Reoperation; Case report

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Core Tip: We report a rare case of heterochronous onset of malignant intraductal papillary neoplasm of the bile duct (IPNB) and malignant intraductal papillary mucinous neoplasm of the pancreas (IPMN). The time difference between the onset of the two diseases was 4.5 years. Left hepatectomy and radical pancreaticoduodenectomy were performed with excellent results. This case suggests that IPNB and IPMN are precancerous lesions of low-grade malignancy that require aggressive surgery and long-term postoperative follow-up.

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# INTRODUCTION

Intraductal papillary mucinous neoplasm of the pancreas (IPMN) is a mucus-producing tumor involving the main or branch pancreatic ducts that lacks the characteristic ovarian-like interstitium of mucinous cystic neoplasm. IPMN is characterized by intraductal papillary growth with excessive mucus secretion, resulting in cystic dilatation of the pancreas' primary and/or branch ducts[1]. Intraductal papillary neoplasm of the bile duct (IPNB) is a rare disease entity with a previously reported prevalence of 4% to 15% among bile duct tumors[2]. It was classified as a distinct pathological type by the World Health Organization in 2010[3]. IPNB is a slow-growing biliary tumor with intraductal papillae but can eventually progress to bile duct cancer. IPNB has a similar pathological presentation to IPMN, with excessive mucin secretion but with different histological subtypes and growth patterns. Cases of concurrent IPMN and IPNB are rare[4], with only 11 reported in the literature to our knowledge [5-15] (Table 1), and the heterochronic onset of IPNB with IPMN is even rarer.

We report a case of heterochronic onset of IPNB with IPMN at an interval of 4.5 years, and this is the first case reported in the literature. We performed aggressive reoperation on this patient, which had been diagnosed as recurrent tumor metastasis several times in different hospitals, and confirmed as heterochronous IPMN (Figure 1).

# **CASE PRESENTATION**

# Chief complaints

A 67-year-old Chinese man presented to our Department of Gastrointestinal and Pancreatic Surgery 8.5 years after diagnosis of IPNB and 4 years after diagnosis of pancreatic tumor.

# History of present illness

The patient had a 10-year history of primary hypertension and a 15-year history of asthma.

# History of past illness

The patient had no past illness.

# Personal and family history

The patient had no family history.

# Physical examination

The patient's vital signs on physical examination were stable, with a body temperature of 37.0 °C on admission. No jaundice or superficial lymphadenopathy was observed. No apparent abnormalities were observed upon pulmonary and cardiac examination. An old surgical scar about 30 cm in length was visible under the right costal margin, and a nodule



Table 1 Reported intraductal papillary neoplasms in the biliary and pancreatic duct

Ref.	Sex	Age	IPNB		IPMN		Heterochronic	Pancreaticobiliary
			Location	Pathology	Location	Pathology	occurrence	maljunction
Joo et al[5], 2000	Male	60	Left IHD	LGD	Branch duct	LGD	No	No
Ishida <i>et al</i> [6], 2002	Male	67	B1	Without dysplasia	Branch duct	Without dysplasia	No	No
Yamaguchi et al [7], 2005	Male	69	Left IHD	IC	Branch duct	MIC	No	No
Zalinski <i>et al</i> [8], 2007	Female	65	Bilateral IHD	IC	Main duct	HGD	No	No
Park <i>et al</i> [9], 2010	Male	67	Left IHD	LGD	Mixed duct	LGD	No	No
Valente <i>et al</i> [10], 2012	Male	76	Right IHD	IC	Branch duct	LGD	No	No
Xu et al[11], 2012	Female	68	Left IHD	LGD	Branch duct	Without dysplasia	No	No
Moon <i>et al</i> [12], 2014	Female	66	Left IHD	HGD	Main duct	HGD	No	No
Bansal <i>et al</i> [13], 2016	Male	70	Right IHD	IC	Main duct	IC	No	No
Kitahama <i>et al</i> [14], 2021	Male	52	CBD	MIC	Main duct	LGD	No	No
Aslam <i>et al</i> [15], 2020	Male	73	Left IHD	LGD	Main duct	HGD	No	No
Our case	Male	67	Left IHD	IC	Main duct	IC	Yes	Yes

IHD: Intrahepatic duct; LGD: Low-grade dysplasia; HGD: High-grade dysplasia; B1: Caudate lobe bile duct; IC: Invasive carcinoma; MIC: Microinvasive carcinoma; CBD: Common bile duct; IPNB: Intraductal papillary neoplasm of the bile duct; IPMN: Intraductal papillary mucinous neoplasm.

about 1 cm in size was palpable, with no abdominal pressure or rebound pain.

# Laboratory examinations

Serum tumor markers showed a significant increase in carcinoembryonic antigen of 20.7 mg/L, but carbohydrate antigen 19-9 was normal. Blood biochemistry showed that transaminases, total bilirubin, serum amylase, and blood glucose were within normal ranges.

# Imaging examinations

Computed tomography (CT) showed a mass in the pancreatic head with atrophy of the pancreatic tail and dilated pancreatic ducts. The intra- and extrahepatic bile ducts and common bile ducts were significantly dilated. A nodule in the anterior abdominal wall was considered to be a metastatic tumor. Positron emission tomography-CT showed a soft tissue mass in the pancreatic head (5.1 cm × 4.6 cm × 5.6 cm) with a maximum standard uptake value (SUVmax) of 11.8 and dilated pancreatic ducts. The anterior abdominal wall mass measured 1.0 cm × 0.9 cm × 0.8 cm, with SUVmax 2.6 (Figure 2).

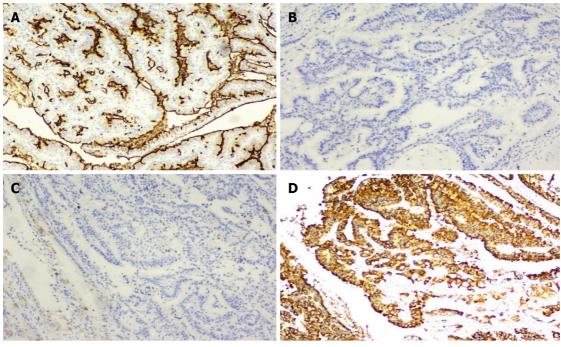
# FINAL DIAGNOSIS

Heterochronous malignant IPNB and malignant IPMN associated with abnormal pancreaticobiliary collaterals.

# **TREATMENT**

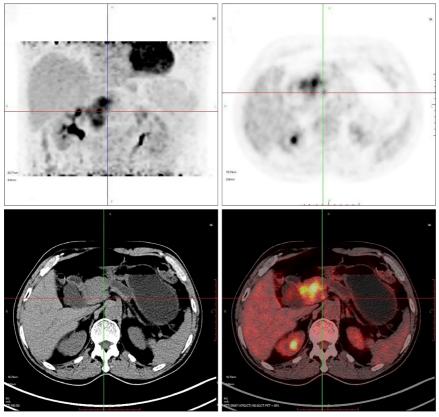
Radical pancreaticoduodenectomy was performed.

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Figure 1 Immunohistochemical examination of the resected specimen. A-D: Immunohistochemical staining for Muc-1 (A), Muc-2 (B), Muc-5AC (C), and Muc-6 (D), × 200.



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Figure 2 Positron emission tomography showed a mass in the head of the pancreas. Maximum standard uptake value: 11.8.

# **OUTCOME AND FOLLOW-UP**

The patient was successfully treated with surgery and had a good prognosis. During 6 mo postoperative follow-up, the

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patient gained weight without clinical symptoms or pancreaticobiliary duct dilatation.

# DISCUSSION

IPNB and IPMN both oversecrete mucin that eventually clogs the pancreaticobiliary duct and causes progressive dilation of the upstream ducts. Ultrasound, CT, and magnetic resonance cholangiopancreatography (MRCP) can easily detect these abnormalities, but it is not easy to distinguish between masses, wall nodules, and mucin in the ducts. Many cases are often diagnosed and treated as stones, which can easily be misdiagnosed and even affect the patient's prognosis because of delayed diagnosis leading to tumor progression. MRCP, in this case, clearly showed a filling defect at the beginning of the left hepatic duct and dilatation of the upstream bile duct (Figure 3), and an experienced radiologist made a definitive diagnosis[15]. IPNB and IPMN tend to grow longitudinally along the lumen, so pancreatic cholangiopancreatoscopy is a recommended method that can clearly visualize a large amount of mucin being expelled from the duodenal papilla. If available, we recommend the use of SpyGlass, which provides a clearer view of the interior of the bile or pancreatic ducts[4].

In this case, the patient developed IPNB first and then IPMN after an interval of 4.5 years with similar pathological types, which raised the possibility of a common tumor origin. MRCP and gross specimen analysis suggested abnormal pancreaticobiliary coarctation (Figures 3B and 4). Pancreaticobiliary fistulae leading to simultaneous malignant IPNB and benign IPMN have been reported[11]. Therefore, we believe that IPNB developed first and led to the development of IPMN after the tumor cells were shed and implanted into the pancreatic duct during disease progression. The bile duct is anatomically higher than the pancreatic duct, and tumor cells originating from the bile duct may be shed and excreted with bile to the abnormal pancreaticobiliary commissure, leading to implantation and metastasis. However, heterochronic IPNB and IPMN are very rare. IPMN in the present case occurred in the pancreatic neck, where the pancreatic duct forms a slight distortion, and tumor cells shed into the pancreatic duct tend to be deposited there, eventually leading to IPMN. Therefore, we consider IPNB and IPMN to be a single disease caused by diffuse involvement of the pancreaticobiliary tree and recommend that the bile and pancreatic ducts should be examined in patients with papillary tumors, regardless of whether the tumor is initially found in the pancreatic or biliary system[8]. Our case corroborated this view. During the long-term follow-up of our case, we were surprised to find that the patient developed IPMN 4.5 years after surgery because we performed the operation in time to achieve long-term survival.

We were concerned that the pathological findings were all suggestive of malignancy, yet all the lymph nodes examined were negative, indicating that IPNB and IPMN, although often benign, can become malignant over time. Lymphatic clearance is not mandatory because tumors in the regional lymph nodes are less likely to metastasize. We performed mass resection while obtaining negative margins, improving the patient's prognosis. This view is consistent with that of the known literature[16,17]. In our case, IPMN of the pancreatic head was positive for 0/16 regional lymph nodes despite malignancy, while intraoperative rapid cytopathology suggested negative resection margins, allowing preservation of the distal pancreas.

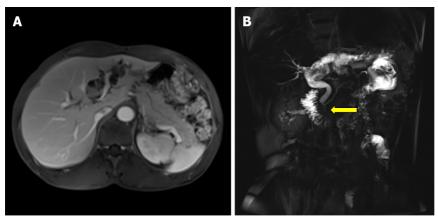
Most cases of IPNB (Table 1) have occurred in the left hepatic duct (7/12). Does this mean that the embryogenesis of the left hepatic duct and pancreatic duct is homologous or that the specific microenvironment of the left hepatic duct predisposes the development of IPNB? This requires further detailed clinical and molecular studies.

In our case, the patient was wrongly treated for distant metastasis, and chemotherapy was chosen after incisional implant metastasis was detected. However, the incisional implant metastasis was resectable along with the tumor, and the patient was able to achieve a longer survival time than chemotherapy. After receiving the patient, we developed an individualized treatment plan after careful preoperative examination, detailed multidisciplinary team discussions, and excluding contraindications to surgery. According to the European guidelines on pancreatic cystic neoplasms[18], we performed radical pancreaticoduodenectomy with resection of the incisional implant metastatic tumor. The patient recovered well after surgery and there was no tumor recurrence or metastasis detected at 6 mo follow-up. Therefore, we believe that junctional tumors similar to IPNB still require reoperation even if incisional implantation metastases have occurred. With the assurance of negative incisional margins, patients are able to achieve more prolonged overall survival.

There are reports in the literature on the effectiveness of radiotherapy in similar cases, and this may be a good therapeutic option[10]. However, surgical treatment was chosen in 10 of 11 cases of IPNB and IPMN (Table 1), and we opted for surgical treatment. After radical pancreaticoduodenectomy, the patient was cured and discharged from hospital. There was no recurrence or metastasis at 6 mo follow-ups. However, there are reports of postoperative pancreatic tumor recurrence and reoperation[14]. Therefore, the follow-up of this patient will be long-term.

# **CONCLUSION**

We recommend CT, MRCP, and endoscopic retrograde cholangiopancreatography to diagnose IPNB and IPMN, and a SpyGlass examination can be performed if possible. IPNB and IPMN both tend to grow locally and rarely metastasize to lymph nodes. Intraoperative frozen pathology can guide the extent of resection, and negative surgical margins can significantly improve the patient's prognosis. Long-term follow-up is warranted after IPNB or IPMN is first resected because of the potential for heterochronic morbidity.



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Figure 3 Preoperative imaging findings for the initial surgery. A: Magnetic resonance cholangiopancreatography showed a left hepatobiliary mass with dilatation of the upstream bile duct; B: Magnetic resonance cholangiopancreatography indicated pancreaticobiliary maljunction (indicated by arrow). The junction of the pancreatic and the bile duct was outside the duodenal wall with a long common channel.



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Figure 4 Gross specimens showed pancreaticobiliary maljunction (indicated by arrow). The pancreatic duct and bile duct shared a long common channel. The intraductal papillary mucinous neoplasm was located in the neck of the pancreas.

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# **FOOTNOTES**

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