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*Case Report*

# Malignant infiltrating intraductal papillary mucinous neoplasm with internal fistula: one case report and clinical practice

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**Abstract:** Background: Intraductal papillary mucinous neoplasm (IPMN) is a rare tumor that originates in the pancreatic duct. The diagnosis of benign, borderline or malignant to IPMN is significant in terms of making an appropriate treatment plan and prognosis. This article summarizes our clinical experience of a case report and discussion by literature review. Methods and case report: A 73 year old male patient was admitted for an occupying lesion of the pancreas. The magnetic resonance cholangiopancreatography (MRCP) scan considered IPMN, endoscopic retrograde cholangiopancreatography (ERCP) also confirmed diagnosis of IPMN. Both the biliary and pancreatic duct stents were replaced, but we did not obtain any evidence by cytological evaluation. One month later, ERCP and intraductal ultrasonography (IDUS) showed infiltrating growth of the tumor. Endoscopic ultrasonography guided fine-needle aspiration was performed at the same time, and pathological diagnosis was suggested as borderline IPMN. Results: In the absence of pathological support, the patient presented with the clinical diagnosis of infiltrating intraductal papillary mucinous adenocarcinoma (IPMC) and was recommended for surgery. However, the patient and his family refused surgery, and were discharged. Subsequently, the patient died 6.5 months (197 days) following first diagnosis. Conclusions: Currently, the definition and classification of IPMN is done by specification, although there remain some difficulties in diagnosing its subtypes. For diagnostic purposes, CT, MRCP, ERCP, IDUS, EUS and EUS-FNA can all be applied. Cytological negative pathology might not completely rule out malignancy, and would still require further examination and follow-up.

**Keywords:** Intraductal papillary mucinous neoplasm, magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography, endoscopic ultrasonography guided fine-needle aspiration, infiltrating intraductal papillary mucinous adenocarcinoma

## Introduction

Intraductal papillary mucinous neoplasm (IPMN) is a rare tumor that originates in the pancreatic duct. Since the 1990s, with the progression of several corresponding examinations including endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP), the incidence of IPMN has increased significantly [1]. The diagnosis of benign, borderline or malignant to IPMN is significant and enables the design of an appropriate treatment plan and in making an informative prognosis. In addition, computed tomography (CT), MRCP, ERCP, intraductal ultrasonography (IDUS), endoscopic ultrasonography (EUS) and endoscopic ultrasonography guided fine-needle aspiration (EUS-FNA) can all be applied in the diagnosis of IPMN, but they cannot be used to draw a final conclusion. One IPMN case, with details of the diagnosis and treatment option, with application of the above procedures is reported herein.

## Case presentation

A 73-year-old male was admitted for intermittent chills, and a high fever. Examination by ultrasound showed an occupying lesion of the pancreatic duct for more than one month, in September 2013. Past history included laparoscopic cholecystectomy (LC) in 1999 for gall-

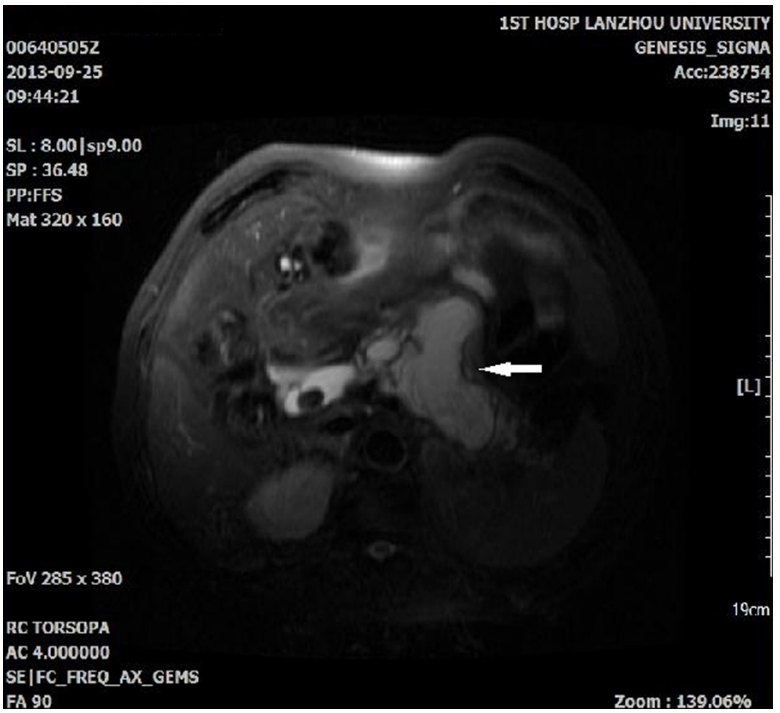


**Figure 1.** Image shows the main pancreatic duct dilation.

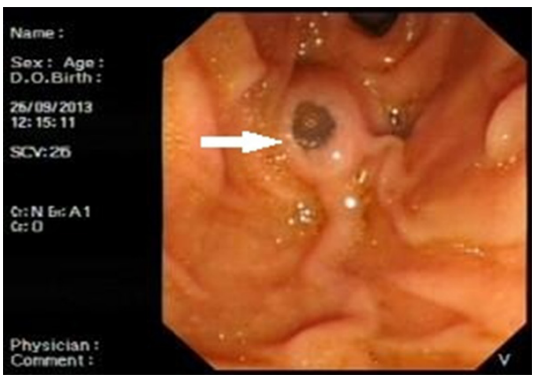


**Figure 2.** Showing major papilla dilation and jelly-like mucus, with a fish eye-like appearance.

stones, bilateral testicular castration in 2010 due to presentation of prostate cancer, a history of diabetes for 3-years that was well-controlled by regular insulin therapy. Physical exa minations showed skin and mucus without jaundice, and upper abdominal tenderness was positive. Laboratory tests showed carbohydrate antigen 199 (CA199) at 649.3 U/ml (<27.0 U/ml), alkaline phosphatase (ALP) at 541.0 U/L (20-125 U/L), gamma glutamyl transpeptidase (GGT) at 122.0 U/L (3-69 U/L). Magnetic Resonance Imaging (MRI, **Figure 1**) showed the following: 1. Pancreatic duct dilation, pancreatic tail with a mixed signal and with the branch duct connected, consider IPMN; 2. Post-cholecystectomy and stump inflammation; 3. Common bile duct distal stone and inter-extrahepatic bile duct dilation; 4. Several intrahepatic small abnormal signals, consider hemangioma and 5. Presence of retroperitoneal lymph nodes. Then, ERCP (**Figure 2**) under intravenous anesthesia showed major papilla dilation and jelly-like mucus, and angiography showed main pancreatic duct dilatation of approximately 1.2 cm, with a cyst of the pancreatic body evident (**Figure 3**), giving a diagnosis of IPMN. Procedurally, a 7.0 Fr 4 cm double pigtail plastic stent, and an 8.5Fr naso-pancreatic pipe was inserted into the main pancreatic duct, and a 8.5Fr 9 cm plastic biliary stent was inserted, to prepare the patient for cytology. However, the mucus was too sticky for cytology. Next, 48 hours after ERCP was reviewed, ALP levels were 401.0 U/L (20-125 U/L), and GGT levels were 86.0 U/L (3-69 U/L). One month later, the patient was readmitted to hospital for sustained abdominal pain without fever, and a secondary ERCP was done, at which point all stents were withdrawn. IDUS showed that the pancreatic duct was filled with a slightly higher echoes, the surrounding pancreatic tissue had widespread involvement, with suspected presence of a fistula with pylorus. In addition, EUS showed irregular pancreatic duct dilatation, which demonstrated a slightly papillary mass shadow, with ill-defined, and irregular morphology and lymph nodes present around the pancreas (**Figure 4**). Then EUS-FNA was reported that showed minimal tissue and mucus inspection, with thick papillary structures, a nipple axis of the fiber bundle veins, some areas that showed cellular hyperplasia with moderate dysplasia, also showing a high proliferation index. Immunohistochemistry results (**Figure 5**) showed the following: CKL (+), local Ki-67 (40%), P53 expression was locally weak (+), CEA expression present (++). Morphological and immunohistochemical analysis sup-

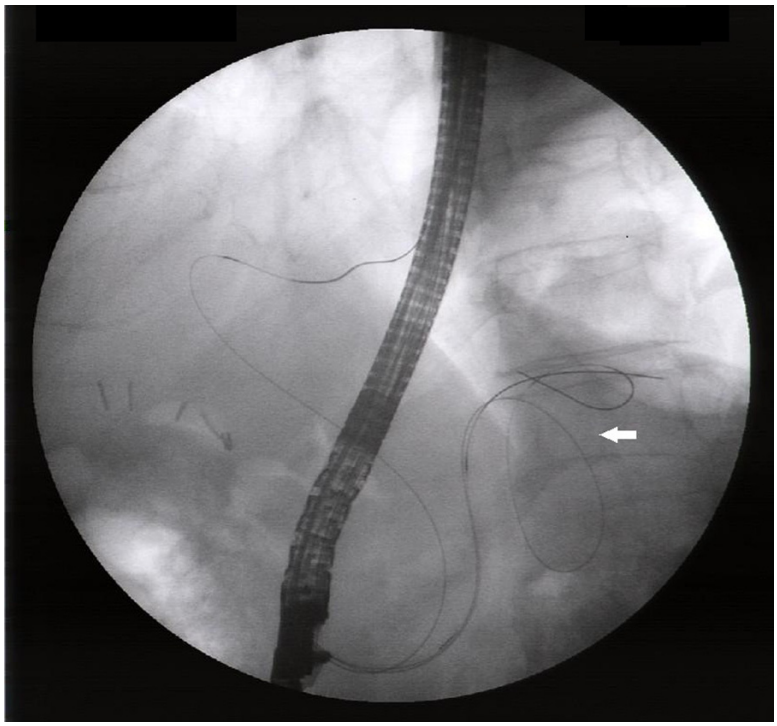

**Figure 3.** Image of the main pancreatic duct dilatation and presence of a sizeable cyst.

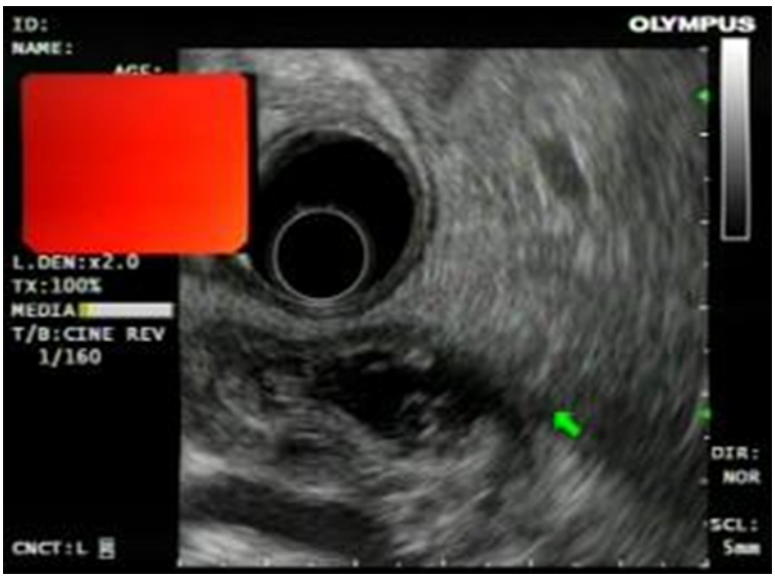


**Figure 4.** Showing irregular pancreatic duct dilatation, with slight papillary mass shadowing.

ported the assessment of the intraductal papillary mucinous borderline tumor, where the tissue was incomplete, and more serious disease could not be ruled out. In addition, pancreatic cancer cells were not found on liquid puncture smears, which contained few neutrophilic and lymphocytic infiltration.

Although lacking the support of pathology, the patient was given the clinical diagnosis of malignant infiltrating intraductal papillary mucinous neoplasm or intraductal papillary mucinous adenocarcinoma (IPMC) and was recommended for surgery; however, the patient and his family refused surgical intervention, and were discharged. With passing time, the patient was followed, and exhibited gradual weight loss, afternoon fever, mild nausea and vomiting, hypoglycemia as cachexia performance, and then died following the first visit 6.5 months (197 days) later.

## Discussion

Intraductal papillary mucinous neoplasms (IPMNs) are a class of rare tumors, but containing either benign or malignant pancreatic cystic tumors, and accounts for approximately 1% of exocrine pancreatic tumors [2]. IPMN was first reported by Ohhashi in 1982 [3]. Then in 2000, the World Health Organization (WHO) published the first definition of IPMNs [4]. By 2003, the JHH global pancreatic meeting defined IPMNs in greater detail [5].

IPMNs have no clear specific clinical features, but associate with the location and natural progression of the tumor itself. Abdominal pain, and weight loss are the most common symptoms, and are perhaps followed by obstructive jaundice, diabetes, pancreatitis, diarrhea, fatigue and anorexia, jaundice and diabetes, which is highly correlated with IPMN [6]. This patient had a diagnosis of IPMN by the MRCP and ERCP on his first visit, with the presence of abdominal pain

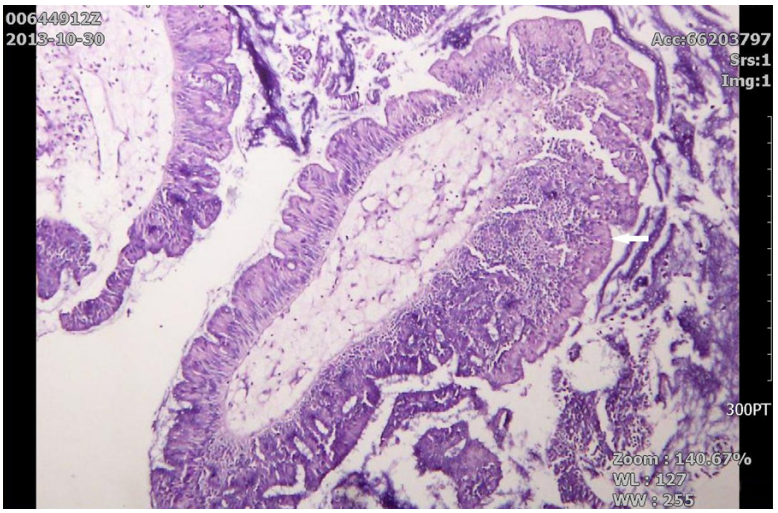


**Figure 5.** Showing that some areas display cellular hyperplasia with moderate dysplasia.

and diabetes at the same time. The patient had a common bile duct stone, chills and high fever, and cholangitis was being considered at that time. Thus, bile and pancreatic duct stents were inserted to relieve symptoms, and meanwhile an attempt was made to collect mucus for cytological observation, but this attempt failed. The secondary diagnosis was assisted by combined IDUS, EUS, and EUS-FNA. IDUS showed tumor-invasive growth, EUS detected positive lymph nodes around the pancreas, and thus the diagnosis turned to malignant infiltrating IPMN-IPMC, although by contrast, the results of EUS-FNA cytology and histology indicated borderline IPMN. The patient did not undergo surgery, but his natural progression until death was clinically confirmed as malignant infiltrating IPMN-intraductal papillary mucinous adenocarcinoma (IPMC).

Currently, the definition and classification of IPMNs is by specification, but there are still some difficulties in the diagnosis of its subtypes. Few related studies in the literature suggest the main duct type, weight loss, jaundice, mural nodule and its diameter being larger than 5 mm, with high levels of expression of CA199 and carcinoembryonic antigen (CEA) prompting IPMC [7, 8]. This case showed experience: 1. MRCP or CT combined with ERCP has a high positive rate in the diagnosis of IPMN. ERCP could show characteristic main duodenal papilla dilatation (i.e., fish-eye syndrome) and mucus secretion. In addition, the contrast injection also showed morphological distinction between the main pancreatic duct, branch duct and mixed type, and cytological brush slide examination is feasible. Some patients with obstructive jaundice and pancreatitis can be released by an insertion of biliary or pancreatic duct stent [9, 10]. 2. Cytologically negative results might not rule out malignancy completely, since there is still a need for further examination by EUS or IDUS to identify whether the tumor boundary is exhibiting infiltrative growth, or whether the tumor has invasive characteristics to any of the surrounding organs. However, in the current case it was highly suspected that the tumor had invaded and there was presence of a fistula with pylorus. Additionally, if necessary, EUS-FNA should be done to obtain both histological and pathological evidence [11, 12]. 3. IPMN has a high resection rate, so the patient that presents with the main pancreatic duct type of tumor, with invasive growth, combined with jaundice/diabetes/CA199 and significantly increased levels of CEA should accept surgical intervention in time. Whether surgery is elected or not, the IPMN patient should follow-up in a timely manner to detect nascent malignancy or tumor recurrence [13].

## Conclusion

Currently, the definition and classification of IPMNs is by specification, but there are still some difficulties in the accurate diagnosis of its subtypes. Moreover, CT, MRCP, ERCP, IDUS, EUS and EUS-FNA can all be applied to the diagnosis of this condition. Cytologically negative end-points might not rule out malignancy completely, since it still needs further examination and appropriate follow-up.

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## Disclosure of conflict of interest

None.

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