

# Complicated intraductal papillary mucinous neoplasia requiring a two-stage operation

Vesselin Marinov<sup>1</sup>, Petko Karagyozev<sup>2</sup>, Konstantin Kostov<sup>3</sup>, Niya Emilova<sup>4</sup>, Stefka Ivanova<sup>5</sup>, Mariya Chaneva<sup>4</sup>, Ventseslava Petrova Atanasova<sup>6</sup>, Petar Atanasov<sup>4</sup>, Maria Vakrilova Becheva<sup>7</sup>

<sup>1</sup> Clinic of Hepato-Biliary, Pancreatic and General Surgery, Acibadem City Clinic University Hospital “Tokuda”, Sofia, Bulgaria

<sup>2</sup> Clinic of Gastroenterology, Acibadem City Clinic UMHAT “Tokuda”, Sofia, Bulgaria

<sup>3</sup> Department of General, Visceral and Emergency Surgery, University Emergency Medicine Hospital “N. Pirogov”, Sofia, Bulgaria

<sup>4</sup> Clinic of Internal Medicine, University Medicine Hospital “N. Pirogov”, Sofia, Bulgaria

<sup>5</sup> Bulgarian Pharmaceutical Science Society, Sofia, Bulgaria

<sup>6</sup> Bulgarian Pharmaceutical Union, Sofia, Bulgaria

<sup>7</sup> Medical University – Plovdiv, Medical College, Speciality “Rehabilitator”, Plovdiv, Bulgaria

Corresponding author: Stefka Ivanova ([ivanovastefka\\_pharm@yahoo.com](mailto:ivanovastefka_pharm@yahoo.com))

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## Abstract

**Introduction:** Intraductal papillary mucinous neoplasia (IPMN) is a benign cystic neoplasm that has the potential to transform into pancreatic cancer over time. These lesions are usually asymptomatic. A main pancreatic duct IPMN is usually symptomatic and may present as an emergency when occlusion of the common bile duct with thick mucinous secretion and jaundice develop. This complication is hard to manage pharmacotherapeutically or by endoscopic procedure and may require surgical treatment.

**Purpose:** This is a case report of a complicated main pancreatic duct IPMN that required an urgent, two-stage operation. A review of the literature on the topic was carried out.

**Case description:** A 67-year-old male patient with symptoms of jaundice was diagnosed with acute cholangitis, cholecystitis, and pancreatitis as complications of the mucinous obstruction of the main pancreatic duct and of the common bile duct (CBD) caused by IPMN. The condition was confirmed by cholangio-pancreatography and biopsy. Stenting of CBD was attempted, but the procedure turned out unsuccessful, and we proceeded to an emergency two-stage operation. The first operation consisted of the clearance of the bile ducts from infected mucinous secretion, cholecystectomy, and hepatico-jejunostomy. A Whipple procedure was performed as a second-stage operation.

**Discussion:** Cases of emergency are not common in patients with IPMN. However, obstructive jaundice by mucinous secretion due to the disease is hard to treat only by endoscopy because of the high risk of obstruction of the endoprosthesis. On the other hand, emergency pancreatic resections are associated with a high risk of perioperative complications.

**Conclusion:** Sometimes, the complicated main pancreatic duct IPMNs can pose a challenge for the interdisciplinary team of invasive gastroenterologists and surgeons, and the key to a successful outcome is surgical interventions in two- or three stages that include complications management as the first stage, followed by surgical resection as a second stage operation. Biliary drainage improvement is usually only temporarily successful with the insertion of biliary stents because of the rapid mucinous occlusion and the remaining risk of cholangitis and cholecystitis.

## Keywords

IPMN, complication, jaundice, pancreatic resection, mucinous secretion, pseudomyxoma peritonei

## Introduction

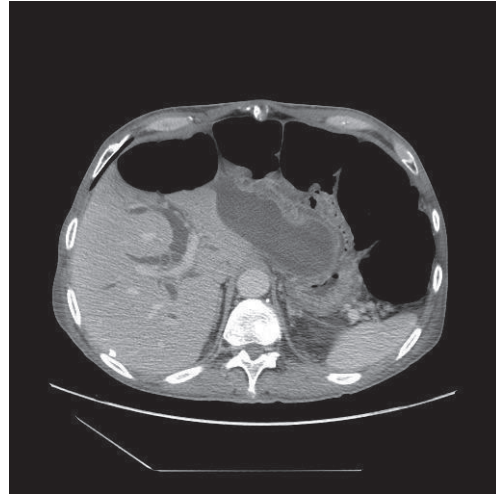
Substantial progress has been made in the knowledge of intraductal papillary mucinous neoplasia in the last two decades. This entity is now perceived as a heterogeneous disease based on the different involvement of ductal structures and the distinct cell type dysplasia and is believed to have a variable prognosis (Basturk et al. 2015). Each type of the main pancreatic duct IPMN, namely the main duct (MD), branch duct (BD), and mixed type (MT) IPMN, presents with different symptoms due to their characteristic localization.

The need for classification of the types of papillary changes according to the risk of potential complications and invasive carcinoma development, clinical presentation, and prognosis has led to efforts to establish standards in the description of the disease and follow-up. Sendai Classification 2004 (Tanaka et al. 2006), Fukuoka Consensus Guidelines 2012 (Tanaka et al. 2012), and the last revision of the guidelines dated from 2017 (Tanaka et al. 2017) clearly define therapeutic strategies in cases of IPMN. Almost half of all IPMN develops in the head of the pancreas. The disease is multifocal in nearly 41% of all cases. IPMN is an age-related disease, so it is most commonly encountered in the 6<sup>th</sup> and 7<sup>th</sup> decades. No difference can be seen regarding sex distribution (Tanaka et al. 2012). Jaundice is a complication that affects between 15% and 20% of all patients. It is often met in those suffering from main pancreatic duct IPMN (Pagliari et al. 2017). The latter type of complication is challenging for endoscopic management because the thick mucinous secretion of the tumor occludes endoscopic stents. Moreover, the endoscopic procedure may cause biliary infection, cholangitis, and acute cholecystitis. Usually, this complication requires an urgent operation.

## Case description

A 67-year-old male patient was admitted to our hospital with clinical signs of nausea, jaundice, and signs of large bowel dilatation. The patient has a history of body weight reduction of 20 kg and has reported complaints of chronic epigastric and back pain in the last 8 months. He was diagnosed with exocrine pancreas insufficiency for a similar period. The patient was admitted to the clinic of gastroenterology. A CT scan was performed. It showed a cystic tumor in the head of the pancreas, dilatation of the common pancreatic duct, common bile duct (CBD) with gall bladder distention, compression of the left side large bowel by peritoneal mass, and left side pleural effusion (Figs 1, 2).

The laboratory tests gave evidence of elevated serum bilirubin levels, liver function tests, and anemia. The endoscopic retrograde cholangiopancreatography (ERCP)



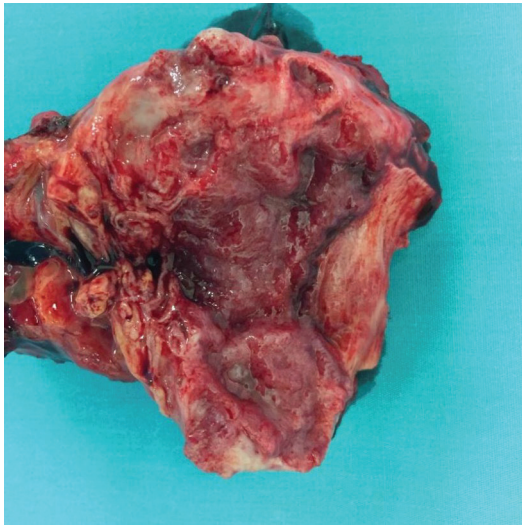
**Figure 1.** Dilatation of bile ducts. Large bowel distention.



**Figure 2.** Cystic mass in the head of the pancreas.

revealed a cystic dilatation of the head of the pancreas along with extensive papillary mass. The main pancreatic duct and CBD were full of thick mucinous secretions. A biopsy of the tumor was performed, and stents in the biliary and pancreatic ducts were placed. Two days after the procedure, the patient became persistently febrile, and other signs of infection supervened. Right upper abdominal pain recurred. Jaundice had no improvement, and the levels of serum bilirubin remained elevated. We suspected acute cholangitis and cholecystitis. The treatment with antibiotics has become ineffective. Sepsis has gradually developed and complicated the course of the disease.

The patient was urgently transferred to a clinic for hepato-biliary surgery. Because of the very high perioperative risk, duodeno-pancreatic resection was not attempted. During the operation, we found acute destructive inflammation of the gall bladder and acute cholangitis. The



**Figure 3.** Head of the pancreas. Main pancreatic dilatation, covered with papillary structures. Fibrosis of the pancreatic parenchyma.

diameter of the CBD was greater than 2 cm. The bile duct and the inserted biliary stent were obstructed by thick mucinous secretion. We performed a cholecystectomy and a hepatico-jejunostomy. A peritoneal mass under the left diaphragm (pseudomyxoma peritonei), which caused compression of the sigmoid bowel and large bowel obstruction, was also surgically removed. No complications occurred in the postoperative period. The patient's condition improved in the next 2 months. The repeated CT scan showed no pathologic abdominal fluid, a persistence of main pancreatic duct dilatation, but no new pancreatic head cysts.

Two months after the first operation, a planned duodeno-pancreatic resection was successfully carried out. We found a functionally preserved biliary anastomosis, but CBD was still filled with mucinous secretion distally. The remaining duct in the head of the pancreas was extremely dilated and invaded by papillae, forming neoplasm at gross appearance. Pancreatic parenchyma was fibrotic with signs of chronic inflammation. No residual peritoneal masses were found (Fig. 3).

The fibrosis of the pancreas parenchyma was visible. We performed a pancreatico-jejunostomy. The surgical intervention was not challenging due to the diameter of the main pancreatic duct, a fibrotic parenchyma of the pancreas, and a functioning hepatico-jejunostomy. The patient was discharged on the 9<sup>th</sup> postoperative day with no complications. The biopsy result revealed MD-IPMN intestinal type G2 with no invasive cancer in the complete resected specimen. In the follow-up period, the patient was diagnosed with diabetes mellitus, and the insulin regime was the treatment implemented. The pancreatic exocrine function was permanently impaired. Supplements containing pancreatic enzymes as well as vitamins and microelements were prescribed.

## Discussion

Whether BD IPMNs are usually asymptomatic and discovered incidentally on imaging studies (Grützmann et al.

2010), MD IPMNs are more likely to cause symptoms related to main pancreatic duct obstruction. Presenting symptoms are upper abdominal pain (50–70%), weight loss (20–40%), nausea and vomiting (11–21%), jaundice (15–20%), acute pancreatitis (15%), and back pain (10%) (Pagliari et al. 2017). Impaired exocrine pancreatic function results in weight loss and anorexia. The affected patients may stop eating because of recurrent pain. Anorexia may as well indicate a malignant transformation of IPMN. Furthermore, jaundice occurs as a result of obstruction of the common bile duct by increased mucinous secretion, mural nodules, or by its direct compression by the neoplasm itself. IPMNs are implicated in the formation of pathologic communications (fistulae) with the stomach, duodenum, CBD, pleura, and large and small bowels (Ravaud et al. 2015). These complications are rare and may be caused by high ductal pressure, autodigestion of pancreas parenchyma, or direct spread of invasive neoplasm (Machado et al. 2015).

The penetration into the biliary duct and the accumulation of mucinous secretion in the biliary duct are characteristic causes of failure of drainage by endoscopic stent placement in patients with IPMN. Thus, surgical drainage has proved to be far more effective (Tanaka 2004; Kurihara et al. 2000). Different approaches to the treatment of pancreatico-biliary IPMN fistulas are recommended in the literature. Kurihara K et al. reviewed two cases surgically resected after multiple unsuccessful attempts for endoscopic biliary drainage of CBD (Kurihara et al. 2000). A similar chance of endoscopic stent occlusion is reported in cases of percutaneous transhepatic biliary drainage (Kurihara et al. 2000). A working team has reported successful multiple biliary irrigation to achieve temporary drainage prior to pancreato-duodenal surgical resection (Chao Dai et al. 2016). Another approach is biliary by-pass construction for overcoming an obstruction of metal biliary prosthesis placed to relieve obstructive jaundice secondary to biliary mucinous secretion of non-resectable IPMN (Patel et al. 2005).

Currently, surgery is the mainstay of therapy for IPMN, as it is considered a premalignant condition. When facing an IPMN with a known invasive component, it is currently recommended that both medical and surgical treatment be carried out (Tanaka et al. 2017; European Study Group on Cystic Tumors of the Pancreas 2018). Adjuvant chemotherapy is a recommended strategy. It significantly reduces the risk of death (by 71%) and prolongs median survival (by 11.6 months) compared to surgery alone in node-positive invasive (I)-IPMNs, according to a recent meta-analysis of data (Chong et al. 2022). Gemcitabine-based adjuvant chemotherapy was used for 65.0% of patients in this meta-analysis, 5-fluorouracil (5-FU)-based for 33.6% of patients, and capecitabine alone for 0.7% of patients. Adjuvant radiotherapy in addition to chemotherapy was used in 61.2% of patients in this meta-analysis (Chong et al. 2022). Gemcitabine can mimic adenosine triphosphate and is incorporated into new deoxyribonucleic acid (DNA) strands being synthesized as the cell replicates, thus preventing DNA synthesis and cell division. Capecitabine is metabolized to 5-FU, which inhibits the

synthesis of the thymidine monophosphate required for the de novo synthesis of DNA. In turn, oxaliplatin forms both inter- and intra-strand cross links in DNA, which prevent DNA replication, causing cell death. Still, there is controversial evidence of a more favorable oncological outcome of IPMN after surgical resection when compared with de novo pancreatic ductal adenocarcinoma (PDAC). Thus, the optimal management of patients affected by an invasive IPMN (I-IPMN) is currently debated. A study published in 2024 shows that neoadjuvant therapy (given as a first step before surgery) resulted in a complete pathology response and a marked response in 4% and 19% of I-IPMN cases, respectively. Importantly, most patients included in this study were mildly diseased (ECOG score <1 for 2/3 patients) (Fogliati et al. 2022).

## Conclusion

Obstruction of CBD by the accumulation of thick mucinous secretion by penetrating IPMN is a rare complication of the disease. Insertion of metal or plastic biliary stents is not helpful because of rapid obstruction. The endoscopic procedure can cause an infection and acute cholangitis or cholecystitis due to partial biliary duct obstruction. As shown in the literature, percutaneous transhepatic stents are at the same risk of clogging as well. Surgical drainage remains the best option for this complication. Furthermore, pancreatic resection after biliary bypass is safe, easy to perform, and associated with very good perioperative results. Adjuvant chemotherapy is a recommended strategy for the treatment of I-IPMNs.

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