Clinical Case Report

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Resection of benign side-branch intraductal papillary mucinous neoplasm of the pancreas—is long term follow-up indicated?

A case report and review of the literature

Stefan Fritz, MD*, Regina Küper-Steffen, MD, Katharina Feilhauer, MD, Christoph M. Sommer, MD, Götz M. Richter, MD, René Hennig, MD, Jörg Köninger, MD

Abstract

Rationale: Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) are benign cystic tumors with a relevant risk of malignant transformation over time. Currently, follow-up after surgical resection of benign IPMNs remains controversial.

Patient concerns: This is a case report of a 68-year-old male who underwent pancreatic head resection for a multicystic side-branch IPMN with low-grade epithelial dysplasia in March 2009 at the Katharinenhospital Stuttgart, Germany.

Diagnoses: During postoperative follow-up, a new solid, slightly hypodense lesion in the tail of the pancreas measuring 2.4 cm in diameter was diagnosed in July 2016. Preoperative staging revealed no signs of distant metastasis.

Intervention: Subsequently, the patient underwent pancreatic tail resection including splenectomy. Histology revealed IPMN-associated adenocarcinoma of the pancreas pT3, pN1 (2/24), M0, R0.

Outcomes: Patients with IPMN bare a relatively high overall risk of developing pancreatic cancer. The 5-year incidence has been described to be as high as 6.9%. The current Consensus-Guidelines therefore recommend a structural life-time follow-up. In contrast, in 2015 the American Gastroenterological Association (AGA) explicitly states that follow-up is not recommended for resected benign IPMN. Currently, a general and international consensus is lacking.

Lessons: The presented case demonstrates that even more than 5 years following resection of benign IPMN, pancreatic cancer can occur in a separate location of the pancreatic gland. We believe that IPMNs can be considered as indicator lesions for pancreatic cancer. Patients with resected side-branch IPMN should therefore undergo long term follow-up.

Abbreviations: AGA = American Gastroenterological Association, CT = computed tomography, IPMN = intraductal papillary mucinous neoplasm, MRI = magnetic resonance imaging.

Keywords: branch-duct IPMN, cancer risk, intraductal papillary mucinous neoplasm, IPMN, natural history

1. Introduction

Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) are characterized by cystic dilation of the pancreatic duct system, intraductal papillary growth, and excessive mucin secretion.[1] Although IPMNs are primarily thought to be benign tumors, there is a relevant risk of malignant transformation over time.[2] According to their relationship to the pancreatic duct system, main duct-IPMNs have to be distinguished from side-branch IPMN.[3] Although surgical resection is generally warranted for main-duct IPMN due to a high malignancy rate of more than 60%,[4] the indication for surgical resection in side-branch IPMNs is more sophisticated because of a significantly lower risk of malignancy.[4] Overall, approximately 80% of resected side-branch IPMNs are benign without histopathological features of high-grade intraepithelial neoplasia or invasive tumor growth. To date, the follow-up after surgical resection of benign side-branch IPMNs remains controversial because little is known about the natural history of this disease.[5] As evidence-based guidelines are missing, all recommendations currently available are based on expert consensus.[6] This is a clinical case report with review of the current literature focusing on the follow-up management of resected benign side-branch IPMNs. Before publication, informed consent of the patient was received. For a case presentation without providing personal data, an ethical approval was not necessary.

2. Case presentation

A 68-year-old male was referred to our hospital for a multicystic tumor in the head of the pancreas in March 2009. Preoperative abdominal computed tomography (CT) revealed a large multicystic tumor in the head and uncinate process and of the pancreas.

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RH and JK contributed equally to this study.

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Department of General, Visceral, Thoracic and Transplantation Surgery, Katharinenhospital Stuttgart, Stuttgart, Germany.

** Correspondence: Stefan Fritz, Department of General, Visceral, Thoracic, and Transplantation Surgery, Katharinen Hospital Stuttgart, Kriegsbergstraße 60, D-70174 Stuttgart, Germany (e-mail: st.fritz@klinikum-stuttgart.de).*

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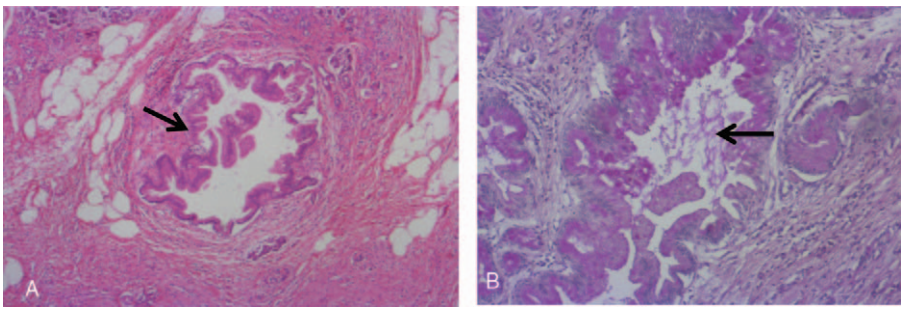

Figure 1. Branch-duct intraductal papillary mucinous neoplasm with low-grade intraepithelial dysplasia in March 2009. (A) Histopathology (hematoxylin-eosin staining). Histopathology of the pancreatic head following Whippl procedure in March 2009 reveals an intraductal papillary mucinous neoplasm with low-grade intraepithelial dysplasia characterized by papillary proliferation of an atypical mucus producing ciliated epithelium (arrow). (B) Histopathology using Periodic Acid Schiff staining. Intraductal papillary mucinous neoplasm with low-grade epithelial dysplasia and intraductal periodic acid schiff-positive mucus (arrow).

There were no signs of infiltrative tumor growth and no dilation of the pancreatic or biliary duct system. Moreover, the pancreatic body and tail were regularly configured. Except for a mild arterial hypertension, the patient revealed no relevant comorbidity. In March 2009, the patient underwent pylorus-preserving pancreatic head resection (Whipple procedure) at the Katharinenhospital Stuttgart, Germany. The postoperative hospital stay was uneventful except for a prolonged return to regular feeding habits due to a post-surgical ileus. Histopathology revealed a benign side-branch IPMN with low-grade epithelial dysplasia, formerly called IPMN adenoma (Fig. 1A and B).

Postoperative yearly follow-up by magnetic resonance imaging (MRI) was uneventful until May 2015 (Fig. 2A). In July 2016, a new solid, slightly hypodense lesion in the tail of the pancreatic measuring 2.4 cm in size was diagnosed (Fig. 2B). The first aspect of the tumor reminded on a neuroendocrine tumor. To rule out a multifocal neuroendocrine neoplasia, an DOTATOC-PET/CT examination was conducted which showed no signs of contrast enhancement and therefore no evidence for a Somatostatin receptor-positive tumor. At that time, the patient was 75 years' old and clinically asymptomatic without loss of weight, night sweats, or fevers. Preoperative staging revealed no signs of distant metastasis. Subsequently, the patient underwent pancreatic tail resection including splenectomy (Fig. 3A). On final histological diagnosis, an adenocarcinoma of the pancreas pT3, pN1 (2/14), M0, R0 was found (Fig. 3B). The tumor developed in direct association to an IPMN and therefore had to be considered as an IPMN-associated adenocarcinoma. Except for postoperative abscess formation in the place of the spleen, which was successfully treated by an interventional radiologic drainage, the postoperative clinical course was uneventful. Postoperatively, the patient had normal blood glucose levels without the need of insulin substitution. According to a tumor board decision, adjuvant chemotherapy was recommended. The patient therefore received 6 cycles of Gemcitabine. Starting from cycle number 3, the patient additionally was given Xeloda. The most recent follow-up CT took place in August 2017 and showed no signs for recurrent disease or distant metastasis. On clinical follow-up examinations, the patient presented in a good general condition with regular eating habits.

3. Discussion

To date little is known about the natural history of IPMNs.[5] It has been reported that disease progression occurs in 10% to 40% of patients during a 5-year period. Moreover, the calculated risk of developing pancreatic cancer during 10 years was described to be as high as 20%.[7,8] However, patients with IPMNs do not only reveal a risk of malignant transformation in the cystic lesion, they are also at a higher risk of developing concomitant sporadic pancreatic cancer in a location distinct from the lesion, either synchronously or metachronously.[9] In these cases, some authors assume that the cystic lesion visible on abdominal imaging displays only the tip of the iceberg of a genetic pancreatic field defect[10] that leads to neoplastic transformation over time.[11] The 5-year incidence has been described to be as high as 6.9%.[12] This is the reason why the current international Consensus-Guidelines recommend a structural life-time follow-up.[4] Likewise, the European Consensus guidelines 2013 suggest

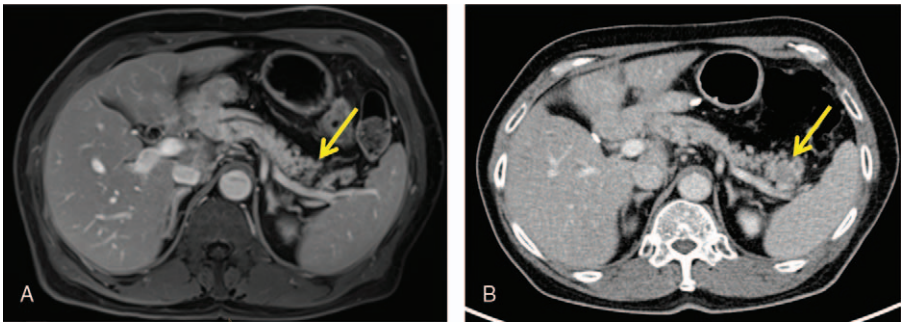

Figure 2. Thin-sliced abdominal follow-up imaging. (A) Follow-up magnetic resonance imaging (MRI) in May 2015. Unremarkable remnant of the pancreas after Whipple procedure 03/2009 (arrow). (B) Follow-up computed tomography scan in July 2016. Diagnosis of a novel hypodense lesion of 2.4-cm diameter in the pancreatic tail (arrow).

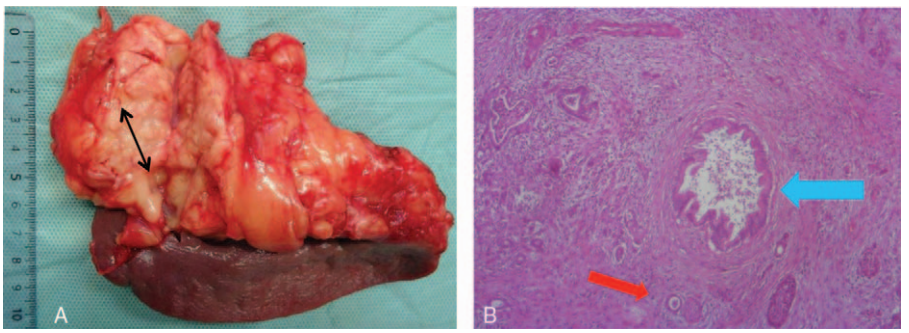

Figure 3. Distal pancreatectomy and splenectomy for adenocarcinoma in July 2016. (A) Surgical specimen including pancreatic tail and spleen. Solid white shining tumor of 2.5 cm in diameter (double-headed arrow). (B) Histopathology (hematoxylin-eosin staining). Intraductal papillary mucinous neoplasm (blue arrow) with associated adenocarcinoma (pT3, pN1 [2/14], M0, R0) including perineural invasion (red arrow).

yearly follow-up with preferably nonradiating imaging such as MRI or endoscopic ultrasound for surgically fit patients, who underwent a partial pancreatectomy for noninvasive IPMN.[13]

In contrast, in 2015, the American Gastroenterological Association (AGA) explicitly states that follow-up is not recommended for resected benign IPMN.[14] Currently, a general and international consensus concerning this issue is lacking.

As it is known that patients with IPMN show an increased risk of pancreatic malignancy in general, it has to be feared that resection of benign IPMN does not necessarily prevent the risk of developing pancreatic cancer at a later time point. In spite of a close follow-up program, the progression to pancreatic cancer can be missed. It has even been reported that patients developed unresectable or metastastic disease during close follow after IPMN resection.[7] In the case presented above, a developing pancreatic adenocarcinoma was identified early and surgical resection was performed before clinical symptoms or distant metastasis occurred. At least, by resecting benign IPMN with negative margins, the risk of malignant disease progression in the cystic lesion itself can be excluded.

The presented case demonstrates that even >5 years following resection of a benign side-branch IPMN, pancreatic cancer can occur in a separate location of the pancreatic gland. To date, reliable biomarkers are lacking that predict the risk of developing pancreatic cancer following resection of a benign IPMN. Thus, the only option for the patients is a close follow-up to detect a novel neoplasia before distant metastasis or local tumor progress occurs.

4. Conclusions

Patients with resected branch-duct IPMN reveal a higher risk of developing ductal adenocarcinoma over time compared to the general population. Side-branch IPMNs can be considered as indicator lesions for pancreatic cancer. Patients with resected side-branch IPMN should therefore undergo long-term follow-up.

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