When typical PD is performed, GDA is ligated and cut for complete resection of the lymph node.[2,3] However, for PD patients who have undergone gastric tube reconstruction, it is necessary to perform a special procedure to maintain blood flow to the gastric tube. Inoue et al[4] reported 3 different surgical approaches: (1) PD with GDA and RGEA preservation; (2) PD with divisions of both, GDA and RGEA/V, after microvascular reconstruction; or (3) PD with divisions of GDA and RGEA/V, removal of the gastric tube, and reconstruction with the small or large intestine. Gastroduodenal artery and RGEA-preserving PD can only be used for patients with no arterial invasion or lymph node metastasis in terms of curability. When PD with RGEA reconstruction is performed, the anastomosis method depends on the defect length. If the defect is short, RGEA is directly anastomosed to GDA. If the defect is too long to anastomose RGEA to GDA, the use of an interposition graft is needed. Pancreaticoduodenectomy with removal of the gastric tube enables complete resection of the lymph node; however, this approach is extremely invasive. It is necessary to choose the method while considering the length of the vascular defect and curability. In our case, RGEA was encased by the tumor and therefore needed to be resected for curability. In our case, the defect length was short, approximately 3 cm; therefore, RGEA and GDA were directly anastomosed. When performing PD after gastric tube reconstruction, it is crucial to assess the blood flow and plan surgery beforehand.[5]

Tissue perfusion can be evaluated by the HEMS. After indocyanine green is injected intravenously as a contrast agent, the imaging device emits near-infrared ray. Then, indocyanine green emits near-infrared fluorescence through the blood vessels, and the camera receives infrared fluorescence and immediately provides an image. Thus, with this system, blood flow can be assessed on the basis of the light intensity, and necrosis caused by tissue ischemia can be prevented. Pagkratis et al[6] used the SPY system, similar to HEMS, to evaluate blood flow of the gastric tube after PD. No complications were observed in their case. However, there is no standard method to evaluate blood flow of the gastric tube using HEMS. It is not possible to evaluate the blood flow at the tip of the gastric tube from the abdominal cavity. Thus, it is recommended that a clear evaluation method be established in the near future. If there is a system that can evaluate blood flow endoscopically during the surgery, it will be useful because it will not be overly invasive and will enable the evaluation of ischemia of the mucosa.

We described our experience of treating a patient with gastric tube–preserving PD with RGEA reconstruction. The HEMS could be used to evaluate blood flow of the gastric tube. It is necessary to plan a surgical procedure that includes revascularization on the basis of preoperative blood flow evaluation.

*The authors declare no conflict of interest. K.W. wrote the manuscript. All authors read and approved the final manuscript. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. All data generated during this report are included in this published article.*


## ACKNOWLEDGMENTS

*The authors thank Edanz Group (https://en-author-services.edanz.com/ac) for editing a draft of this manuscript.*



**Kenji Watanabe, MD**
Department of Surgery and Science
Graduate School of Medical Sciences
Kyushu University
Fukuoka, Japan
watanabe.kenji.512@m.kyushu-u.ac.jp

**Noboru Harada, MD, PhD**
**Tomonari Shimagaki, MD, PhD**
**Huanlin Wang, MD, PhD**
**Takeshi Kurihara, MD, PhD**
**Yoshihiro Nagao, MD, PhD**
**Takeo Toshima, MD, PhD**
**Shinji Itoh, MD, PhD**
**Tomoharu Yoshizumi, MD, PhD**
**Masaki Mori, MD, PhD**
Department of Surgery and Science
Graduate School of Medical Sciences
Kyushu University
Fukuoka, Japan


## REFERENCES


1. Uehara H, Kondo S, Hirano S, et al. Gastric tube–preserving pancreatoduodenectomy after esophagectomy and reconstruction using the gastric tube: report of a case. *Surg Today*. 2004; 34:623–625.
2. Okimoto S, Kobayashi T, Kuroda S, et al. Pancreaticoduodenectomy with preservation of gastric tube blood flow after esophagectomy: report of a case. *Int J Surg Case Rep*. 2014;5: 746–749.
3. Orii T, Yoshimura M, Kitahara H, et al. Pylorus-preserving pancreatoduodenectomy for pancreatic head cancer after surgery for esophageal cancer with gastric tube reconstruction in a long-term survivor: a case report. *Int J Surg Case Rep*. 2019;55:92–98.
4. Inoue A, Akita H, Eguchi H, et al. Gastric conduit-preserving, radical pancreaticoduodenectomy with microvascular reconstruction for pancreatic head cancer after esophagectomy: report of a case. *Surg Today*. 2014;44:786–791.
5. Fragulidis GP, Athanasopoulos PG, Melemeni A, et al. Pylorus-preserving pancreaticoduodenectomy after transhiatal esophagectomy sparing the right gastroepiploic vessels and gastric tube. *J Gastrointest Surg*. 2011;15:367–670.
6. Pagkratis S, Virvilis D, Phillips BT, et al. Creation of gastric conduit free-graft with intraoperative perfusion imaging during pancreaticoduodenectomy in a patient post esophagectomy. *Int J Surg Case Rep*. 2015;9:39–43.


# Isolated Intraductal Papillary Mucinous Tumor Arising in the Santorini's Duct With Malignant Transformation

***To the Editor:***

Intraductal papillary mucinous neoplasm of the pancreas (IPMNs) originates from the ductal epithelium and can progress to an invasive cancer, but not all IPMNs are premalignant and thus not all of them require surgical resection. Therefore, the development of a classification of the malignant risk and need for surgery is critical. Several guidelines have been designed to provide the best recommendation for nonoperative management in those with low risk for malignancy and to identify and recommend resection for those with overt or latent malignancy.[1,2] With the increase in the detection of pancreatic cysts, a larger number of patients are being studied. New radiographic and clinical features associated with high risk for malignancy are being described and incorporated in the guidelines since the Sendai criteria.[1] Here, we present a case of IPMN restricted to Santorini's duct (SD) with high-grade dysplasia and invasive carcinoma.

## CASE REPORT

A 33-year-old woman presented with epigastric pain after meals. She had given birth to a healthy baby 4 months before the symptoms. Upper endoscopy disclosed an extrinsic compression of the duodenum. Computed tomography showed a 4.3-cm solid cystic lesion in the head of the pancreas (Fig. 1A). Initial diagnosis was solid pseudopapillary neoplasm based on this radiological finding in a young female. A multidisciplinary team decided for upfront surgery. The patient underwent pancreaticoduodenectomy with uneventful recovery. Analysis of the surgical specimen revealed a solid cystic tumor (Fig. 1C). On histological evaluation, there was an invasive ductal adenocarcinoma

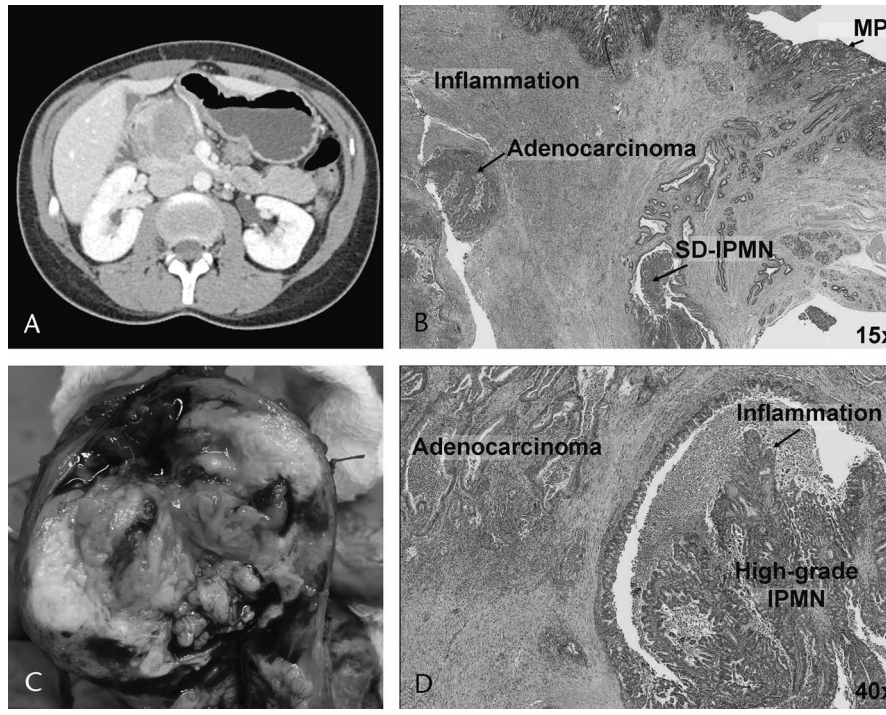


**FIGURE 1.** Santorini's duct IPMN. A, Computed tomography scan shows a large solid cystic mass in the head of the pancreas. B, Hematoxylin and eosin staining (15×). Invasive ductal adenocarcinoma measuring 1.6 cm occupying the center of the lesion, permeated by desmoplasia and moderate inflammation. C, Surgical specimen. D, Hematoxylin and eosin staining (40×). Well-defined high-grade intraductal mucinous neoplasm with minor invasive component and exuberant exudative/suppurative inflammatory process in organization surrounded by fibrosis. MP, minor papilla; SD-IPMN, IPMN arising in the SD.

measuring 1.6 cm occupying the center of the lesion (Fig. 1B). A well-defined intraductal mucinous neoplasm with minor invasive component (4.3 cm) was found (Fig. 1D). High-grade pancreatobiliary IPMN was restricted to the SD (Figs. 1B, D). There was no neoplastic involvement of the main pancreatic duct. Interestingly, there was an intense suppurative inflammatory process with duct rupture and mucin leakage. Surgical margins were free. There was no metastasis in any of 35 harvested lymph nodes. Final pathological staging was pT1cpN0.

## DISCUSSION

The pancreas has its embryological origin as 2 buds developing on the dorsal and the ventral side of the duodenum.[3] The ventral bud arises immediately adjacent to the hepatic diverticulum, and the dorsal bud arises on the opposite side of the gut tube. The ventral bud forms the posterior part of the head, or uncinate process, while the dorsal bud forms the remainder of the organ. The ventral duct fuses with the distal part of the dorsal duct to become the main pancreatic duct (Wirsung), and the proximal part of the dorsal duct becomes a small accessory duct, the duct of Santorini. The SD usually drains the anterior and superior portion of the head. In approximately 70% of individuals, it drains to the minor papilla, while in 30%, it persists as a branch of the main duct.[4]

Most branch-duct IPMN are benign or low-grade malignant lesions, compared with those developing in the main pancreatic duct, which presents a higher malignant potential. Branch-duct IPMNs have a lower rate of malignancy (20%–45%) while main-duct IPMNs are malignant in 75% to 100% of cases.[3,5] It raises an important question. Should IPMN that originates from the SD be considered as a branch-duct or main-duct type? If we consider the SD as a branch of the main pancreatic duct (as it occurs in 30% of patients), it may present a more benign course. However, in 70% of patients, SD is the main drainage system for a significant part of the head of the pancreas.

Santorini's duct IPMN has been considered as a branch-type lesion in the literature. However, a review found that 9 of 12 cases (75%) were malignant.[6] Since then, 3 cases were added to the literature, 2 of them malignant.[7–9] After a scrutiny of all articles reporting IPMN in the SD, we found a total of 21 cases, including ours. There were 12 women and 9 men, with mean age of 66 years (range, 33–78 years). Sixteen patients (76.2%) presented with malignant disease at diagnosis. All cases were from Eastern countries. The present case is the first case of isolated SD IPMN in a Western country and the youngest one.

Despite the pathological findings of inflammation, mass forming lesion (Fig. 1C), and duodenum compression, our patient had uncharacteristic symptoms. The main duct and the common bile duct were normal, and the lesion was restricted to the SD. Correct diagnosis of this lesion is difficult because in most cases, dilation of main duct could also be present, and the true origin of the tumor may not be correctly identified.[7] The diagnosis of SD IPMN can be suspected when a dilatation of the minor papilla orifice is observed in patients without pancreas divisum during routine upper endoscopy. In the present case, the SD was filled with tumor making the correct diagnosis impossible preoperatively. Another interesting feature was the rupture of the SD with the spilling of pancreatic mucin inside the parenchyma with an inflammatory reaction and a mass formation simulating a huge pancreatic tumor, mimicking solid pseudopapillary neoplasm. Rupture of pancreatic duct in patients with IPMN and peritoneal mucin spillage has been previously reported, but intrapancreatic rupture was not mentioned in the literature.[10]

In summary, this case report and literature review show that IPMN arising in the SD may have malignant behavior like the main pancreatic IPMN and should be considered as a high-risk criterion during management of IPMN.

*The authors declare no conflict of interest. The case report complies with the Declaration of Helsinki. The patient was contacted and gave oral and written informed consent.*

**Marcel C. Machado, MD, FACS**
**Emerson S. Abe, MD, FACS**
Department of Surgery
Sirio Libanes Hospital
São Paulo, Brazil

**Thales P. Silveira, MD**
Department of Pathology
Sirio Libanes Hospital
São Paulo, Brazil

**Fernanda C. Capareli, MD**
Department of Oncology
Sirio Libanes Hospital
São Paulo, Brazil

**Marcel Autran Machado, MD, FACS**
Department of Surgery
Sirio Libanes Hospital
São Paulo, Brazil
dr@drmarcel.com.br

## REFERENCES

1. Tanaka M, Chari S, Adsay V, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. *Pancreatology*. 2006;6:17–32.
2. Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatology*. 2017;17:738–753.
3. Yamaguchi K, Ogawa Y, Chijiiwa K, et al. Mucin-hypersecreting tumors of the pancreas: assessing the grade of malignancy preoperatively. *Am J Surg*. 1996;171:427–431.
4. Slack JM. Developmental biology of the pancreas. *Development*. 1995;121:1569–1580.
5. Kimura W, Sasahira N, Yoshikawa T, et al. Duct-ectatic type of mucin producing tumor of the pancreas—new concept of pancreatic neoplasia. *Hepatogastroenterology*. 1996;43:692–709.
6. Hirano S, Kondo S, Ambo Y, et al. Intraductal papillary-mucinous tumors arising in Santorini's duct: clinicopathologic features and the treatment of choice. *World J Surg*. 2005;29:208–211.
7. Kim SC, Kim SH, Myung SJ, et al. [A case of intraductal papillary mucinous neoplasm of the pancreas arising from pancreas divisum without ventral pancreatic duct of Wirsung]. [Article in Korean]. *Korean J Gastroenterol*. 2006;47:218–223.
8. Akashi S, Yamada Y, Sugimori S, et al. [A synchronous intraductal papillary-mucinous carcinoma arising in the accessory pancreatic duct and extrahepatic bile duct carcinoma]. [Article in Japanese]. *Jpn J Gastroenterol Surg*. 2016;49:1141–1149.
9. Komatsubara H, Kato H, Noguchi D, et al. Protruded duodenal tumor arising from Santorini's duct of the pancreas: a rare case of intraductal papillary mucinous neoplasm mimicking a duodenal polypoid tumor. *BMC Gastroenterol*. 2020;20:303.
10. Rosenberger LH, Stein LH, Witkiewicz AK, et al. Intraductal papillary mucinous neoplasm (IPMN) with extra-pancreatic mucin: a case series and review of the literature. *J Gastrointest Surg*. 2012;16:762–770.

# Menstruation-Associated Pancreatitis in a Perimenopausal Woman

***To the Editor:***

Hereditary pancreatitis (HP) is a rare genetic condition, which is characterized by recurrent episodes of pancreatic attacks. The mutations of *PRSS1* and *SPINK1* genes are suggested as the most common causes. Menstruation-associated pancreatitis is a rare type of HP, which is presented as recurrent acute pancreatitis (RAP) and appears in the first or second day of the menstrual cycle. The *PRSS1* gene mutations have been recognized as the main etiologies, and the mutations in the second, third, and tenth exons provide more evidence for the diagnosis. Menstruation-associated RAP has been reported in just 2 cases until now, and both of them were young. There is no report discussing menstruation-associated pancreatitis in perimenopausal women, and no therapy has been shown to be effective and safe.

A 46-year-old woman was referred to the emergency room for a sudden severe abdominal pain and mild vomiting in December 2016. She had no fever and jaundice during the course, she denied any history of alcoholic consumption and drug intake. The patient had experienced RAP 15 times from 2005 to 2016. It always occurred in the first 2 days of her menstrual cycle. Currently, the symptoms appeared on the first day of this menstrual cycle. The blood analyses showed that the neutrophilic granulocyte percentage was $15.81 \times 10^9$/L (reference range, $3.7–9.2 \times 10^9$/L), and the serum amylase level was 64.8 U/L (reference range, 0–95 U/L). The alanine aminotransferase, aspartate aminotransferase, bilirubin, and triglycerides were normal. The abdominal computed tomography scan showed pancreatic edema and peripancreatic fluid collection (Fig. 1A). Magnetic resonance cholangiopancreatography indicated no stone, tumor, malformation or anatomy variance in biliary system (Fig. 1B). The patient had no systemic inflammatory response syndrome and multiple organ failure in the onset of 24 hours and was diagnosed with mild acute pancreatitis. Somatostatin analogs, fluid resuscitation, and pain relief therapies were included.

To formulate an accurate diagnosis and provide adequate management for the RAP, the patient and her immediate relatives were suggested to sequence *PRSS1* and *SPINK1* genes, which are strongly associated with the HP. Unfortunately, both of her parents were unavailable to access our hospital, and the sequencing data of the patient and her 2 sisters were obtained. No difference was found in the *SPINK1* gene among them. However, five mutations in exon 2 of the *PRSS1* gene (L14V, A16V, N29T, N54S, and G62A) were revealed in the patient's sequencing, 2 of which (L14V and G62A) have never been discovered (Fig. 1C).[1,2] No mutation was found in her sisters' sequencing.

Contraceptives have been shown as an effective therapy for young cases with menstrual cycle associated RAP. Then, gynecological examination and pelvic ultrasound were performed, and no abnormalities were detected. Sex hormone analyses indicated lower levels of progesterone (0.2 ng/mL; reference range, 0.77–2.30 ng/mL) and luteinizing hormone (3 mIU/mL; reference range, 17–77 mIU/mL). Thus, contraceptives, which contains 2-mg dienogest and 0.03-mg ethinylestradiol in each dose, were recommended for daily oral administration.

Previous studies have identified several mutations in the second, third, and tenth exons of *PRSS1*, including R122H, N29I, Arg122, which play crucial roles in HP. Here, we presented a case of perimenopausal pancreatitis whose episodes of recurrence were strictly dependent on menstrual cycle. The *PRSS1* and *SPINK1* genes were sequenced, and 3 common mutations and 2 novel ones (L14V and G62A) were identified in the second exon of *PRSS1* gene. An oral contraceptive, which includes levonorgestrel and ethinylestradiol, has been suggested to reduce menstruation-associated pancreatitis recurrence.[3,4] However, there is no evidence of contraceptive preventing RAP in a perimenopausal woman. Estrogen could alter the response of the exocrine pancreas to physiologic and pathologic stimuli, which may explain the association between menstruation and RAP.[5] In addition, sex hormones are known to activate a series of genes during the menstrual cycle, which induce the activation of protease inhibitors and secretion of matrix metalloproteinases and cytokines.[6] With reference to the subject mentioned above, the patient was recommended to receive oral contraceptives. She has received 5 years of regular medication until now, and RAP has not recurred.