

World Journal of *Clinical Cases*

World J Clin Cases 2022 September 26; 10(27): 9550-9969



OPINION REVIEW

- 9550 Psychiatric disorders and pain: The recurrence of a comorbidity
Vyshka G

REVIEW

- 9556 Cardiovascular disease and COVID-19, a deadly combination: A review about direct and indirect impact of a pandemic
Vidal-Perez R, Brandão M, Pazdernik M, Kresoja KP, Carpenito M, Maeda S, Casado-Arroyo R, Muscoli S, Pöss J, Fontes-Carvalho R, Vazquez-Rodriguez JM
- 9573 Molecular factors, diagnosis and management of gastrointestinal tract neuroendocrine tumors: An update
Pavlidis ET, Pavlidis TE

MINIREVIEWS

- 9588 Human-induced pluripotent stem cell-atrial-specific cardiomyocytes and atrial fibrillation
Leowattana W, Leowattana T, Leowattana P
- 9602 COVID-19 and the cardiovascular system-current knowledge and future perspectives
Chatzis DG, Magounaki K, Pantazopoulos I, Bhaskar SMM

ORIGINAL ARTICLE**Case Control Study**

- 9611 PDCA nursing in improving quality management efficacy in endoscopic submucosal dissection
He YH, Wang F

Retrospective Study

- 9619 Impact of COVID-19 pandemic on the ocular surface
Marta A, Marques JH, Almeida D, José D, Sousa P, Barbosa I
- 9628 Anatomy and clinical application of suprascapular nerve to accessory nerve transfer
Wang JW, Zhang WB, Li F, Fang X, Yi ZQ, Xu XL, Peng X, Zhang WG
- 9641 Therapeutic effect of two methods on avulsion fracture of tibial insertion of anterior cruciate ligament
Niu HM, Wang QC, Sun RZ
- 9650 Efficacy of transcatheter arterial chemoembolization using pirarubicin-loaded microspheres combined with lobaplatin for primary liver cancer
Zhang C, Dai YH, Lian SF, Liu L, Zhao T, Wen JY

- 9657** Prognostic significance of sex determining region Y-box 2, E-cadherin, and vimentin in esophageal squamous cell carcinoma

Li C, Ma YQ

- 9670** Clinical characteristics and prognosis of orbital solitary fibrous tumor in patients from a Chinese tertiary eye hospital

Ren MY, Li J, Wu YX, Li RM, Zhang C, Liu LM, Wang JJ, Gao Y

Observational Study

- 9680** Altered heart rate variability and pulse-wave velocity after spinal cord injury

Tsou HK, Shih KC, Lin YC, Li YM, Chen HY

- 9693** Intra and extra pelvic multidisciplinary surgical approach of retroperitoneal sarcoma: Case series report

Song H, Ahn JH, Jung Y, Woo JY, Cha J, Chung YG, Lee KH

META-ANALYSIS

- 9703** Meta-analysis of gemcitabine plus nab-paclitaxel combined with targeted agents in the treatment of metastatic pancreatic cancer

Li ZH, Ma YJ, Jia ZH, Weng YY, Zhang P, Zhu SJ, Wang F

- 9714** Clinical efficacy analysis of mesenchymal stem cell therapy in patients with COVID-19: A systematic review

Cao JX, You J, Wu LH, Luo K, Wang ZX

CASE REPORT

- 9727** Treatment of gastric cancer with dermatomyositis as the initial symptom: Two case reports and review of literature

Sun XF, Gao XD, Shen KT

- 9734** Gallbladder hemorrhage—An uncommon surgical emergency: A case report

Valenti MR, Cavallaro A, Di Vita M, Zanghi A, Longo Trischitta G, Cappellani A

- 9743** Successful treatment of stage IIIB intrahepatic cholangiocarcinoma using neoadjuvant therapy with the PD-1 inhibitor camrelizumab: A case report

Zhu SG, Li HB, Dai TX, Li H, Wang GY

- 9750** Myocarditis as an extraintestinal manifestation of ulcerative colitis: A case report and review of the literature

Wang YY, Shi W, Wang J, Li Y, Tian Z, Jiao Y

- 9760** Endovascular treatment of traumatic renal artery pseudoaneurysm with a Stanford type A intramural haematoma: A case report

Kim Y, Lee JY, Lee JS, Ye JB, Kim SH, Sul YH, Yoon SY, Choi JH, Choi H

- 9768** Histiocytoid giant cellulitis-like Sweet syndrome at the site of sternal aspiration: A case report and review of literature

Zhao DW, Ni J, Sun XL

- 9776** Rare giant corneal keloid presenting 26 years after trauma: A case report
Li S, Lei J, Wang YH, Xu XL, Yang K, Jie Y
- 9783** Efficacy evaluation of True Lift®, a nonsurgical facial ligament retightening injection technique: Two case reports
Huang P, Li CW, Yan YQ
- 9790** Synchronous primary duodenal papillary adenocarcinoma and gallbladder carcinoma: A case report and review of literature
Chen J, Zhu MY, Huang YH, Zhou ZC, Shen YY, Zhou Q, Fei MJ, Kong FC
- 9798** Solitary fibrous tumor of the renal pelvis: A case report
Liu M, Zheng C, Wang J, Wang JX, He L
- 9805** Gastric metastasis presenting as submucosa tumors from renal cell carcinoma: A case report
Chen WG, Shan GD, Zhu HT, Chen LH, Xu GQ
- 9814** Laparoscopic correction of hydronephrosis caused by left paraduodenal hernia in a child with cryptorchism: A case report
Wang X, Wu Y, Guan Y
- 9821** Diagnosed corrected transposition of great arteries after cesarean section: A case report
Ichii N, Kakinuma T, Fujikawa A, Takeda M, Ohta T, Kagimoto M, Kaneko A, Izumi R, Kakinuma K, Saito K, Maeyama A, Yanagida K, Takeshima N, Ohwada M
- 9828** Misdiagnosis of an elevated lesion in the esophagus: A case report
Ma XB, Ma HY, Jia XF, Wen FF, Liu CX
- 9834** Diagnostic features and therapeutic strategies for malignant paraganglioma in a patient: A case report
Gan L, Shen XD, Ren Y, Cui HX, Zhuang ZX
- 9845** Infant with reverse-transcription polymerase chain reaction confirmed COVID-19 and normal chest computed tomography: A case report
Ji GH, Li B, Wu ZC, Wang W, Xiong H
- 9851** Pulmonary hypertension secondary to seronegative rheumatoid arthritis overlapping antisynthetase syndrome: A case report
Huang CY, Lu MJ, Tian JH, Liu DS, Wu CY
- 9859** Monitored anesthesia care for craniotomy in a patient with Eisenmenger syndrome: A case report
Ri HS, Jeon Y
- 9865** Emergency treatment and anesthesia management of internal carotid artery injury during neurosurgery: Four case reports
Wang J, Peng YM

- 9873** Resolution of herpes zoster-induced small bowel pseudo-obstruction by epidural nerve block: A case report
Lin YC, Cui XG, Wu LZ, Zhou DQ, Zhou Q
- 9879** Accidental venous port placement *via* the persistent left superior vena cava: Two case reports
Zhou RN, Ma XB, Wang L, Kang HF
- 9886** Application of digital positioning guide plates for the surgical extraction of multiple impacted supernumerary teeth: A case report and review of literature
Wang Z, Zhao SY, He WS, Yu F, Shi SJ, Xia XL, Luo XX, Xiao YH
- 9897** Iatrogenic aortic dissection during right transradial intervention in a patient with aberrant right subclavian artery: A case report
Ha K, Jang AY, Shin YH, Lee J, Seo J, Lee SI, Kang WC, Suh SY
- 9904** Pneumomediastinum and subcutaneous emphysema secondary to dental extraction: Two case reports
Ye LY, Wang LF, Gao JX
- 9911** Hemorrhagic shock due to submucosal esophageal hematoma along with mallory-weiss syndrome: A case report
Oba J, Usuda D, Tsuge S, Sakurai R, Kawai K, Matsubara S, Tanaka R, Suzuki M, Takano H, Shimozawa S, Hotchi Y, Usami K, Tokunaga S, Osugi I, Katou R, Ito S, Mishima K, Kondo A, Mizuno K, Takami H, Komatsu T, Nomura T, Sugita M
- 9921** Concurrent severe hepatotoxicity and agranulocytosis induced by *Polygonum multiflorum*: A case report
Shao YL, Ma CM, Wu JM, Guo FC, Zhang SC
- 9929** Transient ischemic attack after mRNA-based COVID-19 vaccination during pregnancy: A case report
Chang CH, Kao SP, Ding DC
- 9936** Drug-induced lung injury caused by acetaminophen in a Japanese woman: A case report
Fujii M, Kenzaka T
- 9945** Familial mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episode syndrome: Three case reports
Yang X, Fu LJ
- 9954** Renal pseudoaneurysm after rigid ureteroscopic lithotripsy: A case report
Li YH, Lin YS, Hsu CY, Ou YC, Tung MC

LETTER TO THE EDITOR

- 9961** Role of traditional Chinese medicine in the initiative practice for health
Li Y, Li SY, Zhong Y
- 9964** Impact of the COVID-19 pandemic on healthcare workers' families
Helou M, El Osta N, Husni R

- 9967** Transition beyond the acute phase of the COVID-19 pandemic: Need to address the long-term health impacts of COVID-19

Tsioutis C, Tofarides A, Spernovasilis N

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RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

September 26, 2022

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Synchronous primary duodenal papillary adenocarcinoma and gallbladder carcinoma: A case report and review of literature

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Specialty type: Gastroenterology and hepatology

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Hasan A, Egypt; Rakić M, Croatia

Received: April 14, 2022

Peer-review started: April 14, 2022

First decision: June 7, 2022

Revised: June 20, 2022

Accepted: August 16, 2022

Article in press: August 16, 2022

Published online: September 26, 2022



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Abstract

BACKGROUND

Synchronous primary cancers (SPCs) have become increasingly frequent over the past decade. However, the coexistence of duodenal papillary and gallbladder cancers is rare, and such cases have not been previously reported in the English literature. Here, we describe an SPC case with duodenal papilla and gallbladder cancers and its diagnosis and successful management.

CASE SUMMARY

A 68-year-old Chinese man was admitted to our hospital with the chief complaint of dyspepsia for the past month. Contrast-enhanced computed tomography of the abdomen performed at the local hospital revealed dilatation of the bile and pancreatic ducts and a space-occupying lesion in the duodenal papilla. Endoscopy revealed a tumor protruding from the duodenal papilla. Pathological findings for the biopsied tissue revealed tubular villous growth with moderate heterogeneous hyperplasia. Surgical treatment was selected. Macroscopic examination of this surgical specimen revealed a 2-cm papillary tumor and another tumor protruding by 0.5 cm in the gallbladder neck duct. Intraoperative rapid pathology identified adenocarcinoma in the gallbladder neck duct and tubular villous adenoma with high-grade intraepithelial neoplasia and local canceration in the duodenal papilla. After an uneventful postoperative recovery, the patient was discharged without complications.

CONCLUSION

It is essential for clinicians and pathologists to maintain a high degree of suspicion while evaluating such synchronous cancers.

Key Words: Synchronous primary cancers; Gallbladder carcinoma; Duodenal papillary adenocarcinoma; Surgical treatment; Case report

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Core Tip: Synchronous primary cancers (SPCs) of the duodenal papilla and gallbladder are rarely reported. Here, we report such a case. The lesion in the duodenal papilla was discovered by imaging examination of a 68-year-old man. Endoscopic biopsy was performed, and the pathological findings revealed moderate heterogeneous hyperplasia. The patient underwent pancreaticoduodenectomy, and intraoperative rapid histopathological examination surprisingly revealed adenocarcinoma in the papillary region and another adenocarcinoma in the gallbladder neck duct. SPC involving both the gallbladder and duodenal papilla is regarded as a rare occurrence. It is essential for the clinician and pathologist to maintain a high degree of suspicion while evaluating such lesions.

Citation: Chen J, Zhu MY, Huang YH, Zhou ZC, Shen YY, Zhou Q, Fei MJ, Kong FC. Synchronous primary duodenal papillary adenocarcinoma and gallbladder carcinoma: A case report and review of literature. *World J Clin Cases* 2022; 10(27): 9790-9797

URL: <https://www.wjgnet.com/2307-8960/full/v10/i27/9790.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i27.9790>

INTRODUCTION

With the widespread improvement in early diagnosis and regular medical check-ups, the occurrence of synchronous primary cancers (SPCs) has become increasingly frequent over the past decade[1]. However, it is very rare for duodenal papillary and gallbladder cancers to coexist, and no cases have been reported in the English literature. Here, we describe a case of SPC of the duodenal papilla and gallbladder and its diagnosis and successful management.

CASE PRESENTATION

Chief complaints

A 68-year-old Chinese man was admitted to a local hospital with the chief complaint of dyspepsia.

History of present illness

The patient's symptoms started a month prior to dyspepsia.

History of past illness

The patient had a history of distal gastric resection with Billroth II anastomosis for a bleeding marginal ulcer 30 years ago.

Personal and family history

The patient denied any family history.

Physical examination

After hospitalization, the patient's temperature was 37°C, heart rate was 88 beats per minute, respiratory rate was 19 breaths per minute, blood pressure was 127/79 mmHg and oxygen saturation in room air was 100%. The clinical examination showed no pathological signs.

Laboratory examinations

Blood tests, including tumor markers, showed that levels were completely normal except for glutamyl transpeptidase (GGT; 379 U/L, normal: 10-60 U/L) and alkaline phosphatase (ALP; 174 U/L, normal: 45-125 U/L).

Imaging examinations

Contrast-enhanced computed tomography of the upper abdomen performed at the local hospital revealed dilatation of the intrahepatic bile duct, common bile duct and pancreatic duct and a space-

occupying lesion in the duodenal papilla (Figure 1).

Endoscopic biopsy was performed because of the unclear nature of this occupancy. Endoscopy showed a tumor protruding from the duodenal papilla (Figure 2), and the pathological findings revealed that the biopsy tissue presented tubular villous growth with moderate heterogeneous hyperplasia (Figure 3).

FINAL DIAGNOSIS

Based on the above physical examination features and imaging data, a provisional diagnosis of space-occupying lesion in the duodenal papilla was made. After surgical resection, the final diagnoses were gall bladder adenocarcinoma and duodenal papilla adenocarcinoma.

TREATMENT

Since malignancy of the space-occupying lesion in the duodenal papilla could not be ruled out, surgical treatment was selected after communication with the patient and his family members. The patient was informed of the possible risks involved in this surgery before consent for the operation was obtained. Based on a careful preoperative evaluation and no obvious findings of contraindications of the surgery, the patient underwent a pancreaticoduodenectomy (Whipple's procedure) on July 11, 2019. Macroscopic examination of this surgical specimen revealed a 2-cm papillary tumor and another tumor with a 0.5-cm protrusion in the gallbladder neck duct (Figure 4). Intraoperative rapid pathology revealed adenocarcinoma without basement membrane breakthrough in the gallbladder neck duct and tubular villous adenoma with high-grade intraepithelial neoplasia and local canceration in the duodenal papilla. The examination also showed that no metastases were found in the resected lymph nodes. The cooccurrence of duodenal papillary and gallbladder cancers is very rare. The two tumors were independent of each other, and there was no relationship with metastasis.

OUTCOME AND FOLLOW-UP

The final pathological tumor stage was pT1bN0M0 for adenocarcinoma of the gall bladder and pT1N0M0 for adenocarcinoma of the duodenal papilla, and the patient was not provided adjuvant therapy. After an uneventful recovery, the patient was discharged without complications on postoperative Day 20. After one year, he was followed up by us, and there was no evidence of tumor recurrence.

DISCUSSION

The most common synchronous cancers are colorectum (37.2%), lung (18.6%), esophagus (16.8%), liver (9.7%), kidney (4.4%) and stomach (3.4%)[2]. The simultaneous occurrence of multiple cancers in the papilla of Vater and ampulla of Vater is rare, with approximately 7 cases and 14 cases, respectively, reported thus far in the English-language medical literature[3-21] (Table 1). However, this report is the first to detail the SPC of the duodenal papilla and gallbladder. The incidence of SPC from the biliary tree has been reported to vary from 5.0 to 7.4% [22], and it is important to distinguish between SPC and secondary deposits. The following diagnostic criteria have been adopted by most clinicians to differentiate synchronous primaries from malignant deposits: (1) Lack of anatomical continuity between two tumors; (2) a growth pattern typical of a primary tumor; and (3) clear histological differences between two tumors[23,24]. According to the above criteria, this case was determined to be SPC. Ultimately, both the gallbladder and duodenal papilla were labeled as primary adenocarcinomas by the pathologist as they had histological differences and a growth pattern typical of a primary tumor.

To date, the pathogenesis of SPC has not been elucidated. Several factors are involved, including genetic factors, environmental carcinogens, hormones, dietary factors, previous therapy, infective agents, smoking and alcohol use[25,26]. First, gallbladder cancer may be caused by infectious agents or gallstones due to chronic inflammation and recurrent trauma[27,28]. A reasonable assumption indicates that chronic irritation of the mucosa leads to dysplasia and causes malignant changes[29]. Additionally, 62.5% of SPCs of the biliary tract have been reported to be associated with abnormal pancreaticobiliary junction (APBJ) caused by persistent reflux of pancreatic juice with subsequent biliary inflammation[30-32]. In our case, the cystic duct was too long and had low confluence with the common bile duct. An excessively long cystic duct is adverse to bile outflow, and the duct can be easily blocked and infected by gram-negative bacilli. Eventually, these factors may lead to tumorigenesis. Second, duodenal

Table 1 Literature review of synchronous primary cancers occurring in the papilla/ampulla of Vater and other organs

Cases	Age (yr)/Sex	Tumor location	Treatment	Prognosis (mo)
Ueno <i>et al</i> [3]	58/M	Common bile duct, gallbladder, papilla of Vater (severe dysplasia)	Surgical resection	30/Disease-free survival
Seo <i>et al</i> [4]	42/F	Major and minor duodenal papilla of Vater	Endoscopic papillectomy	16/Disease-free survival
Parthasarathy <i>et al</i> [5]	60/F	Major and minor duodenal papilla of Vater	Surgical resection	8/Disease-free survival
Matheus <i>et al</i> [6]	50/F	Major and minor duodenal papilla of Vater	Surgical resection	24/Disease-free survival
Tamura <i>et al</i> [7]	78/M	Lung, papilla of Vater	Surgical resection	60/Disease-free survival
Takahashi <i>et al</i> [8]	66/M	Erythroleukemia, stomach, papilla of Vater	Jejunocolicostomy	N/A
Nishihara <i>et al</i> [9]	53/M	common bile duct, pancreas, papilla of Vater	Surgical resection	N/A
de Garcia de la Vega <i>et al</i> [10]	77/M	Esophagus, ampulla of Vater	Surgical resection	24/Recurrence due to liver metastasis
Sastry <i>et al</i> [11]	81/M	Pancreas, ampulla of Vater	Surgical resection	10/Die of liver metastasis
Cokmert <i>et al</i> [12]	63/F	sigmoid colon, ampulla of Vater	Surgical resection	N/A
Fukaya <i>et al</i> [13]	69/M	esophagus, stomach, ampulla of Vater	Surgical resection	12/Die of progressive disease
Wohlauer <i>et al</i> [14]	76/M	common bile duct, ampulla of Vater	Surgical resection	N/A
Rajalingam <i>et al</i> [15]	72/M	right colon, ampulla of Vater	Surgical resection	8/Disease-free survival
Aurello <i>et al</i> [16]	33/F	Duodenum, ampulla of Vater	Surgical resection	24/Disease-free survival
Athanasopoulos <i>et al</i> [17]	43/M	common bile duct, ampulla of Vater	Surgical resection	18/Disease-free survival
Eriguchi <i>et al</i> [18]	83/M	Stomach, ampulla of Vater	Surgical resection	3/Disease-free survival
Eriguchi <i>et al</i> [18]	74/M	Colon, ampulla of Vater	Surgical resection	24/ Die of liver metastasis
Eriguchi <i>et al</i> [18]	68/M	Renal pelvis, ampulla of Vater	Surgical resection	14/ Die of progressive disease
Mafune <i>et al</i> [19]	64/M	Esophagus, ampulla of Vater	Surgical resection	13/Disease-free survival
González Sánchez <i>et al</i> [20]	50/F	Colon, ampulla of Vater	Surgical resection	N/A
Yoshida <i>et al</i> [21]	58/M	Sigmoid colon, ampulla of Vater	Surgical resection	N/A

N/A: Not applicable.

papillary adenocarcinoma is a relatively uncommon malignant tumor that accounts for less than 1% of all gastrointestinal cancers[33]. Smoking is an important risk factor, and chronic infection and heredity are considered important susceptibility factors[18]. In the process of canceration, mutations in genes such as K-ras, p53 and p21/Waf1 play an important role[34,35].

Preoperative diagnosis of duodenal papilla occupancy is useful for making therapeutic decisions. Endoscopic biopsy has become a popular diagnostic tool and is used in a diverse range of digestive tract diseases. Histopathology from biopsy remains the gold standard for diagnosis. The positive rate of endoscopic biopsy is low, although the diagnostic value of the endoscopic appearance seems to be superior to that of endoscopic biopsy[36]. In the study case, endoscopy revealed a tumor protruding from the duodenal papilla, and endoscopic biopsy did not diagnose a malignant tumor. These findings demonstrated the importance of the endoscopic description of duodenal papilla. In addition, we were unable to diagnose this gallbladder carcinoma preoperatively. The presence of SPC was a histological surprise.

Few reports have focused on the treatment of patients with this rare disease, which remains a key challenge[37]. Curative resection, if possible, is the most effective method of prolonging patient survival. It is also important to note that surgical procedures may not necessarily lead to better prognosis in patients with SPC. Hepatopancreatoduodenectomy is indicated in locally advanced GBC patients with extensive retropancreatic lymphadenopathy that cannot be cleared without pancreatoduodenectomy. Moreover, HPD is associated with significant morbidity, with an overall major complication rate of approximately 50%. Thus, avoiding extensive hepatectomy has reduced morbidity after HPD[38,39].

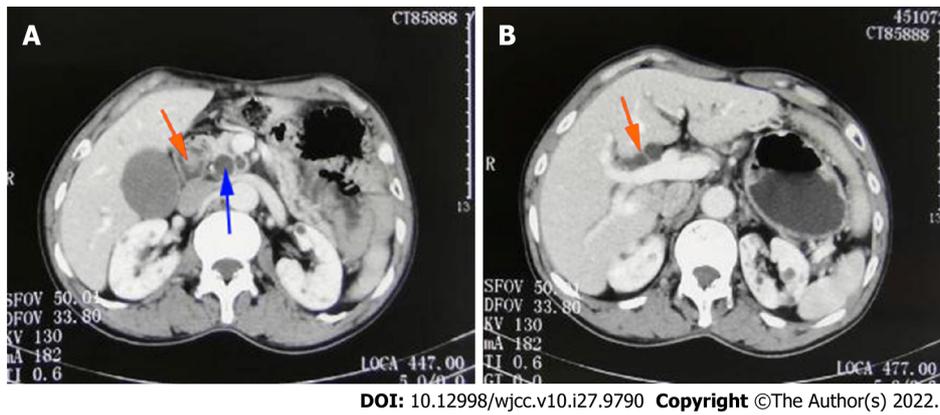


Figure 1 Contrast-enhanced computed tomography of the abdomen. A: Space-occupying lesion in the duodenal papilla (orange arrowheads) and dilatation of the common bile duct (blue arrowheads); B: dilatation of extrahepatic bile duct (orange arrowheads).

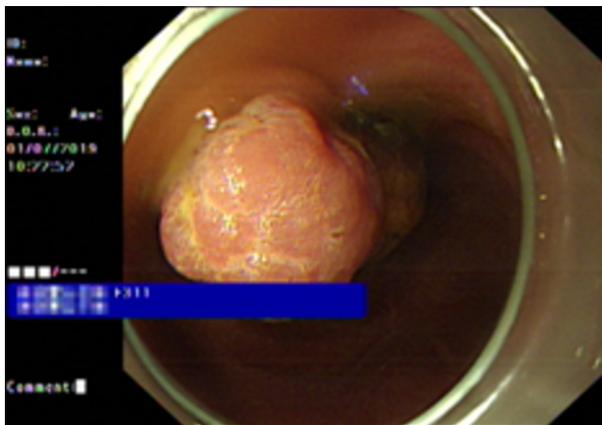


Figure 2 Endoscopic biopsy. Tumor protruding from the duodenal papilla.

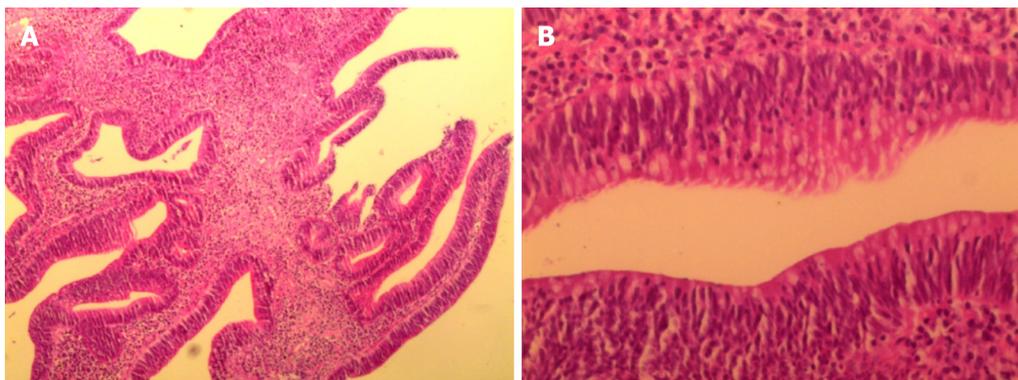


Figure 3 Histopathological findings of endoscopic biopsy. A: Tubular villous growth. B: Moderate heterogeneous hyperplasia.

In this case, a malignant tumor of the duodenal papilla could not be excluded, and the patient successfully underwent pancreaticoduodenectomy. To our surprise, adenocarcinoma of the gallbladder neck duct and involvement in the muscularis were discovered. Because the cystic duct presents low confluency with the common bile duct and the tumor was located on the gallbladder neck duct, no further treatment was needed, and an R0 resection was achieved with the classical Whipple's procedure. After an uneventful postoperative recovery, the patient was discharged without complications. The follow-up data 1 year after the operation were collected, and no tumor recurrence or metastasis was found.



DOI: 10.12998/wjcc.v10.i27.9790 Copyright ©The Author(s) 2022.

Figure 4 Macroscopic appearance of the surgical specimen. Papillary tumor (red circle) and gallbladder neck duct tumor (yellow circle) were present in the specimen.

CONCLUSION

SPC involving both the gallbladder and duodenal papilla is regarded as a rare occurrence but is becoming increasingly common during hepatobiliary surgery. It is essential for clinicians and pathologists to maintain a high degree of suspicion while evaluating these lesions and to look for the existence of APBJ. At the same time, it is necessary to develop a more accurate diagnostic tool and implement more refined treatment strategies to correctly diagnose SPC.

FOOTNOTES

Author contributions: Chen J and Zhu MY were the patient's surgeons, reviewed the literature and contributed to drafting the manuscript; Huang YH and Zhou ZC reviewed the literature and contributed to drafting the manuscript; Zhou Q and Fei MJ performed the pathological analyses and interpretation; and Shen YY and Kong FC revised the manuscript for important intellectual content. All authors issued final approval for the submitted version.

Supported by the Jiaying Science and Technology Plan Project (Civil Science and Technology Innovation Project), No. 2019AY32028.

Informed consent statement: Written informed consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: All authors declare that they have no conflicts of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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S-Editor: Liu JH

L-Editor: A

P-Editor: Liu JH

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