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**Synchronous primary duodenal papillary adenocarcinoma and gallbladder carcinoma: an unusual case report**

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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 cancer 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 and its diagnosis and successful management.

**CASE SUMMARY**

<sup>3</sup> A 68-year-old man was admitted to our hospital with the chief complaint of dyspepsia for the past month. Contrast-enhanced computed tomography (CECT) of the abdomen performed at the local hospital revealed dilatation of the bile duct and pancreatic duct 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 heterosexual hyperplasia. Surgical treatment was selected. <sup>2</sup> Macroscopic examination of this surgical specimen revealed a 2 cm tumor at the papillary region 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 complication.

## CONCLUSION

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

## 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 <sup>[1]</sup>. However, it is very rare for duodenal papillary and gallbladder cancer 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*

<sup>3</sup> 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 with 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.

<sup>4</sup>

### *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 investigations, including tumor markers, 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*

A contrast-enhanced computed tomography (CECT) scan of the 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 heterosexual hyperplasia (Figure 3).

### **FINAL DIAGNOSIS**

Based on the above physical examination features and imaging data, a provisional diagnosis of space-occupying lesion in duodenal papilla was made. After surgical resection, the final diagnosis 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. <sup>1</sup> The patient was informed of the 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. <sup>2</sup> Macroscopic examination of this surgical specimen revealed a 2 cm tumor at the papillary region and another tumor and 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 cancer 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. <sup>2</sup> After an uneventful postoperative recovery, the patient was discharged without complications on postoperative Day 20. After one year, he was followed by us, and there were no evidences 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 detailing SPC of 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) <sup>1</sup> 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 gall bladder and duodenal papilla <sup>1</sup> 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 papillary adenocarcinoma <sup>2</sup> is a relatively uncommon 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. <sup>2</sup> 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 described 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 gall bladder 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 which 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].

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 complication. The follow-up data of 1 year after operation were collected and no tumor recurrence or metastasis was found.

## CONCLUSION

SPC involving both 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 such

lesions and to look for the presence of APBJ. At the same time, <sup>1</sup> it is necessary to develop more accurate diagnostic techniques and implement more refined treatment strategies to correctly diagnose SPC.



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