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*Case Report*

# Metachronous pancreatic head ductal carcinoma three years after resection of gallbladder cancer

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**Abstract:** We report a rare case of female patient with metachronous gallbladder cancer and pancreatic head ductal carcinoma. At the age of 53 years, the patient underwent a cholecystectomy and resection of the liver bed for gallbladder cancer. The post-operation diagnosis was a well-differentiated adenocarcinoma with serosa involvement (T3N0M0, stage IIA). Three years later, an irregular and enhanced 2.4 cm mass in the pancreatic head with obviously pancreatic duct dilated was found by abdominal imaging. We considered it as pancreatic head cancer and performed pancreaticoduodenectomy. The histological diagnosis was a pancreatic ductal carcinoma (T2N0M0, stage I). No recurrence was found after thirty-three months follow up.

**Keywords:** Metachronous, multiple primary cancers, gallbladder cancer, pancreatic cancer

## Introduction

Gallbladder cancer has been considered as a highly lethal disease, mainly because of early recurrence and hepatic metastasis [1-4]. The co-occurrence of another new primary malignant tumor in patients with a gallbladder cancer is uncommon. Multiple primary cancers are defined as either synchronous tumors or metachronous tumors, according to whether the diagnostic intervals of the lesions are shorter or longer than six months, respectively [5]. We report the case of a 56-year-old woman with metachronous gallbladder cancer and pancreatic head ductal carcinoma.

## Case presentation

A 56-year-old woman was admitted for further evaluation of the pancreatic head mass. At the age of 53 years, she had undergone a cholecystectomy and resection of her liver bed for gallbladder cancer. The pathologic specimen revealed a well-differentiated adenocarcinoma with serosa invasion (**Figure 1**), no hepatic invasion, and with negative resection margins (T3N0M0, stage IIA). She did not receive adjuvant therapy and has been followed up periodically without evidence of tumor recurrence. However, three years later, abdominal ultrasound, computed tomography (CT) (**Figure 2**), magnetic resonance (MR) and ultrasound gastroscopy showed an irregular and enhanced 2.4 cm mass in the pancreatic head with obviously pancreatic duct dilated.

On admission, the patient presented no obviously symptoms and physical examination revealed no abnormalities. Laboratory test results showed WBC 6.7 × $10^3$/ul, hemoglobin 12.7 g/dl, hematocrit 42.3%, Plt 146 × $10^3$/ul, AST 33 IU/L, ALT 23 IU/L, total bilirubin 20.0 umol/L, alkaline phosphatase 87 IU/L, ferritin 312.20 ug/L, CEA and CA19-9: normal range. Combined with the abdominal CT and MR examination, there was no evidence of peritoneal metastasis or enlarged lymph nodes. The patient underwent curative pancreaticoduodenectomy (**Figure 3**). Pathologic specimens revealed a pancreatic ductal carcinoma (**Figure 4**), with negative lymph nodes metastasis (0/13) (T2N0M0, stage I). After the second operation and receiving prophylactic continuous hepatic arterial chemoinfusion therapy, now the patient is doing well with no evidence of recurrence for thirty-three months. These

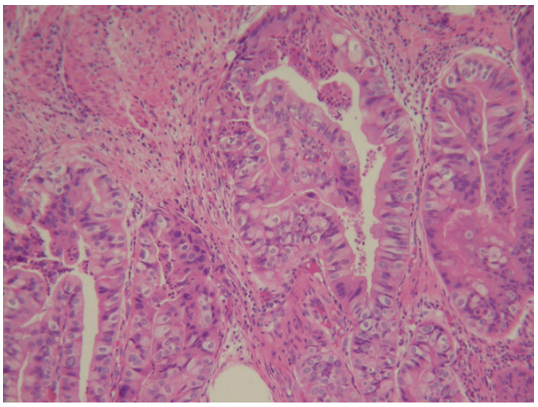

**Figure 1.** (He × 100): Histopathological finding of gallbladder cancer.

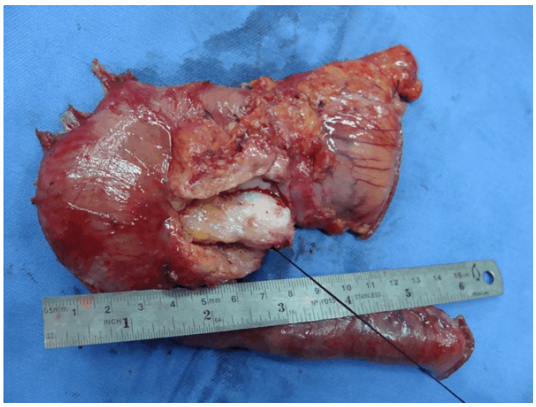

**Figure 3.** Gross specimen of pancreaticoduodenectomy.

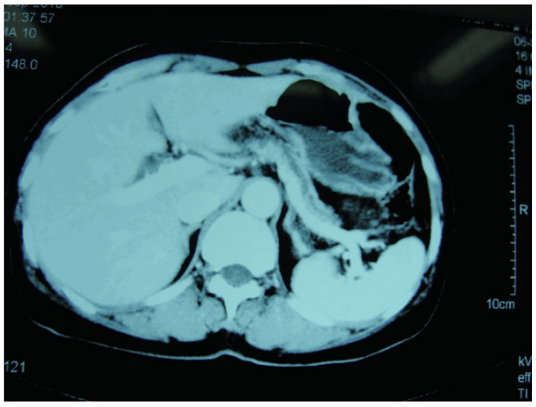

**Figure 2.** Abdominal CT: low-density mass in the pancreatic head.

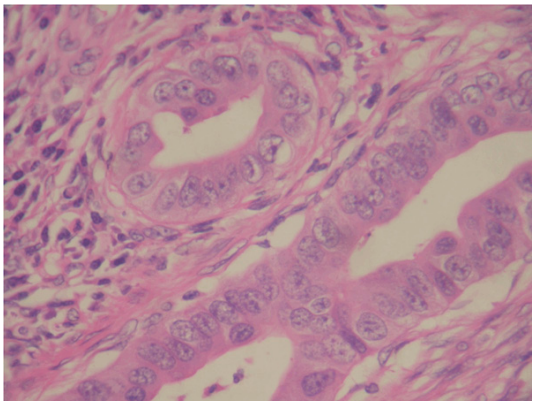

**Figure 4.** (He × 200): Histopathological finding of pancreatic head ductal carcinoma.

two cancers apparently occurred independently and each surgical treatment was successful.

## Discussion

Multiple primary cancers are classified into synchronous and metachronous multiple primary cancers. The former is referred to the occurrences of two primary cancers within six months; the latter is referred to another primary cancer occurred more than six months after the diagnosis of first cancer. In 1932, Warren and Gates proposed the three still generally accepted criteria that had to be met in order to consider malignant tumors as multiple primary tumors rather than recurrences: first, each of the tumors must present a definite picture of malignancy; second, each tumor must have a different histological appearance; third, the possibility that one might be a metastatic lesion from a former lesion must be excluded [6]. When multiple cancers are identified, sometimes it is easy to distinguish that they are multiple primary cancer, but sometimes the distinction between multi-centric primary cancers and cancer metastases is often clinically difficult. Tang et al [7] reported that analysis of microsatellite instability (MSI), loss of heterozygosity (LOH) may play an important role in diagnosing the second cancer as primary or metastatic tumors. Miranda et al [8] pointed out that the analysis of genetic and epigenetic changes can provide to detect some molecular differences between primary metastatic and nonmetastatic colorectal cancer. Therefore, in order to clearly diagnose double cancer, new diagnostic technology, such as genetic and epigenetic analysis, sometimes may be needed.

This case was diagnosed as metachronous pancreatic head ductal carcinoma, which devel-

oped three years after resection for gallbladder cancer, and was cured surgically. This case shows evidence to support a diagnosis of double primary cancers. First, both the gallbladder cancer and the pancreatic head cancer were malignant; Second, pathologic diagnosis of gallbladder cancer was well-differentiated adenocarcinoma, but the pathologic diagnosis of pancreatic cancer was ductal carcinoma, they were not the same histological differentiation; Third, the pancreatic head ductal carcinoma resembled a primary tumor from evidence of dysplastic changes near the main mass which would not be found in metastatic cancer.

After reviewing English literatures in the MEDLINE, we found only two reports about the metachronous primary cancer of the gallbladder and pancreas. Minami [9] in 2008 summarized seven cases and Lahmar [10] in 2010 reported one case of metachronous cancer of the gallbladder and pancreas associated with pancreaticobiliary maljunction with or without cystic dilatation of common bile duct. For our case, this patient had slightly dilatation of common bile duct and obviously dilatation of the pancreatic duct. However, no pancreaticobiliary maljunction was found in this patient. Therefore, the pancreaticobiliary maljunction may increase the possibility to develop of the metachronous primary cancer of the gallbladder and pancreas, but it is not the unique reason for this phenomenon. The true and comprehensive causes for this need further investigations.

As we know, the gallbladder cancer and the pancreas head ductal carcinoma are both considered as highly malignant tumors with bad biological behavior and poor prognosis. With regard to our case, after receiving two curative surgery resection apart 3 years and receiving prophylactic continuous hepatic arterial chemoinfusion therapy, the patient has been doing well with no evidence of recurrence for thirty-three months. Accordingly, for those patients with the metachronous multiple primary cancers, we should have an active and positive attitude and provide effective treatment to prolong the survival as long as cancer metastasis could be excluded.

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## Disclosure of conflict of interest

None.

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