## **Case Report**

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# Occurrence of second primary cancer after curative resection of cholangiocarcinoma: a report of 5 cases

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#### **ABSTRACT**

The second primary cancer, a new cancer subsequent to the initial cancer, usually occurs in a person who has a history of cancer or the patient treated with curative resection. Although the pathogenesis of second primary cancer is unclear, it is always found that occurrence of second primary cancer is related to the age and family history. In our 5 cases' reports, second primary cancer occurs after curative resection of cholangiocarcinoma. And most of the second primary cancers belong to well differentiated adenocarcinomas which grow slowly and never metastasize distally in early stage. Therefore, operative excision is the most effective treatment. At the same time, conventional examination after operation could improve early diagnosis and timely surgical treatment.

Keywords: Curative resection, Cholangiocarcinoma, Second primary cancer

#### INTRODUCTION

The definition of second primary cancer (SPC) is a new primary cancer subsequent to the initial cancer occurs in a new site or tissue of a person who has a history of cancer. The frequency and type of secondary cancers may vary depending on the initial diagnosis and genetic predisposition. Even some treatments for initial cancer, such as chemotherapy and radiation therapy, may increase the risk of development of another unrelated cancer in the future.

Over past 30 years, advances in the treatment for cancer have led to improvements in cancer cure rates and reduction of risk factors have increased longevity further. However, cancer survivors are not only at the risk of the recurrence of the primary cancer but also at the risk of the development of SPCs. SPC is more common now, so researches on it are required intensively.<sup>3</sup> SPCs may

occur in the same tissue or organ as with the first cancer or in another site of the body. For instance, some examples of SPCs occurring in the same organ would be new or unrelated cancers which occurs in another new lobe of liver after a successful surgical resection of initial cancer in a liver lobe.

Some other examples of SPCs occurring in another site or organ might be gallbladder carcinoma after gastrointestinal tumor or other cancers being treated for a few years.

Likewise, some patients have a successful treatment for lung cancer, but they may suffer breast cancer or prostate cancer months or years later. And the cancer cells of SPCs may have same or different differentiation with initial cancers. Medicine treatment may not be a perfect measure, but it could be good for the prognosis of SPCs after the surgical resection again.

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#### CASE REPORT

350 cases with bile duct carcinoma or carcinoma of the ampulla of Vater were analyzed retrospectively in our hospital from 1990 to 2010, and 295 cases had surgical operations. Among the 295 patients, 133 patients were given a curative resection. 118 out of the 133 cases.

(the follow-up rate is 88.7%) were analyzed through a long-term follow-up for 1-7 years. And 5 cases occurred second primary cancer, including 1 case with gastric carcinoma, 2 cases with duodenum carcinoma, and 2 cases with colorectal carcinoma (Table 1 and 2). So second surgical operation was necessary for the 5 cases.

Table 1: Cholangiocarcinoma as the initial cancer.

Age	Gender	Tumor site	Methods	Pathologic diagnosis
52	Female	Portal	Lobus quadratus resection, tumor excision, cholangioenterostomy	Moderately differentiated adenocarcinoma
58	male	Right hepatic duct	Right lobe liver resection	Well differentiation adenocarcinoma
54	male	Portal	Tumor excision, cholangioenterostomy	Well differentiation adenocarcinoma
58	male	Common hepatic duct	Tumor excision, Choledochojejunostomy	Well differentiation adenocarcinoma
65	male	Common hepatic duct	Pancreatoduodenectomy	Moderately differentiated adenocarcinoma

Table 2: The second primary cancer after curative resection of cholangiocarcinoma.

Tumor site	Since the first surgical time	methods	Diagnose methods	Pathologic diagnosis
Lesser curvature	51-months	Subtotal gastrectomy	Gastroscope	Moderately differentiated adenocarcinoma
Duodenum	38-months	Pancreatoduodenectomy	Duodenoscope	Well differentiation adenocarcinoma
Duodenum	88-months	Subtotal gastrectomy	Gastroscope	Well differentiation adenocarcinoma
Ascending colon	67-months	Right hemicolectomy	Barium meal	Moderately differentiated adenocarcinoma
Descending colon	69-months	Left hemicolectomy	Colonoscope	Well differentiation adenocarcinoma

### **DISCUSSION**

Cholangiocarcinoma, which occurs either in the liver or in the extrahepatic bile ducts, is a fatal cancer of the biliary epithelium. It's a devastating malignancy which late presentation, markedly difficult to diagnose and high mortality. Surgical curative resection could be the only way for cure and the results depend on careful technique. Liver transplantation treats both the tumour and the underlying liver disease (the main risk factor for the development of new tumours), so patients receiving transplants have the highest chance of cure among all other treatment.4 However, in most cases, The goal of surgery is to achieve a curative resection with negative resection margins leaving an adequate liver remnant volume.<sup>5</sup> De Oliveira et al reported the results of 44 patients with intrahepatic cholangiocarcinoma treated with a complete resection, the 5-year survival rate was

63% and the median survival was 80 months in patients who could achieve R0 resection.<sup>6</sup>

Li SQ et al reported that the diagnosis of cholangiocarcinoma involves in 136 patients, and 79 patients underwent resection. The tumor resectability was 58.1%. 65 of the 79 patients who had a total resection of tumors achieved negative resection margins defined as curative resection. The curative resectability of the whole group was 47.8%.<sup>7</sup>

As the development of diagnosis technique and surgical level, 5-year survival rate of massive patients with cholangiocarcinoma treated with curative resection was increasing. However, the problem of occurrence of second primary cancer after curative resection of cholangiocarcinoma is still becoming highly valued. Kim et al reported the result of their study, a rare case of combined hepatocellular-cholangiocarcinoma and second

primary colon adenocarcinoma in a 67-year-old male patient with liver cirrhosis is presented.<sup>8</sup> In Japan, autopsy records have been published annually by the Japan Society of Pathology. An analysis of 1573 cases with cholangiocarcinoma indicated that 212 cases suffered SPCs during 1987 to 1991, except 33 cases with multiple cancer occurring in three or more sites. In our study, 5 cases of SPCs were found in the group of 118 cases (4.2%) during a long-term follow-up for 1-7 years in our hospital.

SPCs in patients with cholangiocarcinoma curative resection could occur in various organs or major tissues of the whole body. According to the report of 212 cases with SPCs in Japan, including 49 cases with colorectal carcinoma (23.1%) and 14 cases with gastric carcinoma (19.3%). Besides, in 1996, 4 cases with SPCs reported by Nakamura took place in the site of colon or duodenum. Similarly, 5 cases of our group mainly occurred in site of gastrointestinal tract (Table 2). What's more, all of these belong to moderate or well differentiated adenocarcinoma which would grow slowly and have a fair prognosis after timely operative treatment.

Although the pathogenesis of SPCs is unclear, the following risk factors might be obviously related to this cancer. Age might be the most major factor in the development of SPCs. SPCs could be frequently found in patients older than 50 years cholangiocarcinoma curative resection. In view of Tables, the average age of patients with cholangiocarcinoma was 55 years old, and the average age of SPCs of patients with cholangiocarcinoma after curative resection was 62 years old, all of them are beyond 55 years old. The age over 70-years appearing SPCs could achieve peak of the rates in Japan.

Observing the result of research about relationship between multiple cancer and genetic factors, we can infer that family history might also play a major role in the occurrence of SPCs and multiple cancer.<sup>9</sup>

Besides that, enhancing accurate preoperative diagnosis (such as the type and invasiveness of initial cancer), assessing the benefit of surgery, chemotherapy, radiation therapy, monitoring preoperative or postoperative dosage of chemotherapy and the field and dosage of radiotherapy, inspecting physical states regularly in hospital and avoiding other exposures of risk (such as bad dietary habit and internal environment disorders), all these might reduce the occurrence rate of SPCs.

Because SPCs occur frequently in alimentary canal, the patients with cholangiocarcinoma should do periodical examination of gastrointestinal tract after curative resection, such as inspection of upper gastrointestinal endoscopy, barium meal, inspection of barium enema in

lower gastrointestinal and proctocolonoscopy. In addition, alimentary canal tumor marker also should be detected, especially CEA and CA. 9-19 In our experience, 5 cases of SPCs were conformed early by gastrointestinal fiberscope and barium meal during the follow-up period, which would be helpful for surgical resection to cure the SPCs. Most of SPCs performed as well differentiated adenocarcinomas which grow slowly and never metastasize distally in early stage. Therefore, operative excision is the most effective treatment with favourable prognosis. Once finding tumor in gastrointestinal or in other site after operation of cholangiocarcinoma with curative resection, we should consider it's SPC.

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