

Curative Resection After Gemcitabine, Cisplatin and S-1 Chemotherapy for Initially Unresectable Biliary Duct Cancer: A Case Report

KENEI FURUKAWA¹, TADASHI UWAGAWA¹, TARO SAKAMOTO¹,
HIROAKI SHIBA¹, JUN TSUTSUMI^{1,2} and KATSUHIKO YANAGA¹

¹Department of Surgery, Jikei University School of Medicine, Tokyo, Japan;

²Department of Surgery, Mashiko Hospital, Saitama, Japan

Abstract. A 68-year-old woman was diagnosed with unresectable upper bile duct cancer with suspected invasion of the right hepatic artery and para-aortic lymph node metastasis (T4N3M0, stage IVb). She underwent plastic stent placement for obstructive jaundice and enrolled in our phase I study for unresectable biliary tract cancer consisting of cisplatin (25 mg/m² i.v. for 120 min) followed by gemcitabine (1,000 mg/m² i.v. for 30 min) on days 1 and 8, and oral S-1 on alternate days. After 8 courses of neoadjuvant chemotherapy without adverse effects, computed tomography showed near-complete disappearance of the tumor of the upper bile duct and of swollen lymph nodes. She then underwent sub-total stomach-preserving pancreaticoduodenectomy and lymph node dissection. The pathological stage was pT1N0M0, stage I. The patient made a satisfactory recovery, was discharged 29 days after operation, and remains free of disease at 3 months after the operation under adjuvant chemotherapy using S-1.

Surgical resection is the only potentially curative treatment for biliary tract cancer. However, most cases are discovered at an advanced stage and curative resection is limited to a small number of cases, which exhibit poor prognosis (1, 2). We report a case of curative resection after combined neoadjuvant chemotherapy using gemcitabine, cisplatin and S-1 for initially unresectable biliary duct cancer.

Case Report

The patient was a 68-year-old female and was admitted to a local hospital with hepatopathy, complaining of back and

epigastric pain. Laboratory data were as follows: total bilirubin 1.4 mg/dl, aspartate aminotransferase 68 IU/l, alanine aminotransferase 125 IU/l, γ -glutamyl transpeptidase 954 IU/l, carcinoembryonic antigen 17.1 ng/ml and carbohydrate antigen 19-9 624.0 U/ml. Abdominal computed tomography (CT) showed wall thickening enhanced by contrast in the upper bile duct which was suspected to have invaded the right hepatic artery (Figure 1), and remarkably swollen lymph nodes, including those of the para-aortic region (Figure 2). The patient was diagnosed with unresectable locally advanced biliary tract cancer with para-aortic lymph node metastases (T4N3M0, stage IVb) and underwent plastic stent placement for obstructive jaundice. She was referred from the local hospital to our hospital for chemotherapy. The patient received combined neoadjuvant chemotherapy using cisplatin (25 mg/m² i.v. for 120 min) followed by gemcitabine (1,000 mg/m² i.v. for 30 min) on days 1 and 8, and oral S-1 (80 mg) on alternate days without adverse effect, which is now an ongoing phase I clinical trial for patients with unresectable or postoperative recurrent biliary tract cancer at our hospital (3). After neoadjuvant chemotherapy, CT showed near-complete disappearance of the upper bile duct tumor and of the swollen lymph nodes (Figure 3). Four weeks after completion of the neoadjuvant chemotherapy, surgery was performed. Intraoperatively, the proximal bile duct stump was free of cancer cells by intraoperative frozen section. She underwent sub-total stomach-preserving pancreaticoduodenectomy and lymph node dissection including the para-aortic region. Pathologically, tumor cells were only detected in the mucosa of the bile duct. According to the sixth edition of the Japanese general rules for clinical and pathological studies on cancer of the biliary tract in 2013, the pathological classification of the tumor was pT1N0M0, stage I (4). The patient made a satisfactory recovery without postoperative complications, and was discharged on postoperative day 29 in good condition. At 3 months after the operation, the patient is free of disease on adjuvant chemotherapy using S-1.

Correspondence to: Kenei Furukawa, Jikei University School of Medicine, 3-25-8, Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan. Tel: +81 334331111 ext.2345, Fax: +81 334331230, e-mail: k-furukawa@jikei.ac.jp

Key Words: Biliary duct cancer, neoadjuvant chemotherapy, case report.

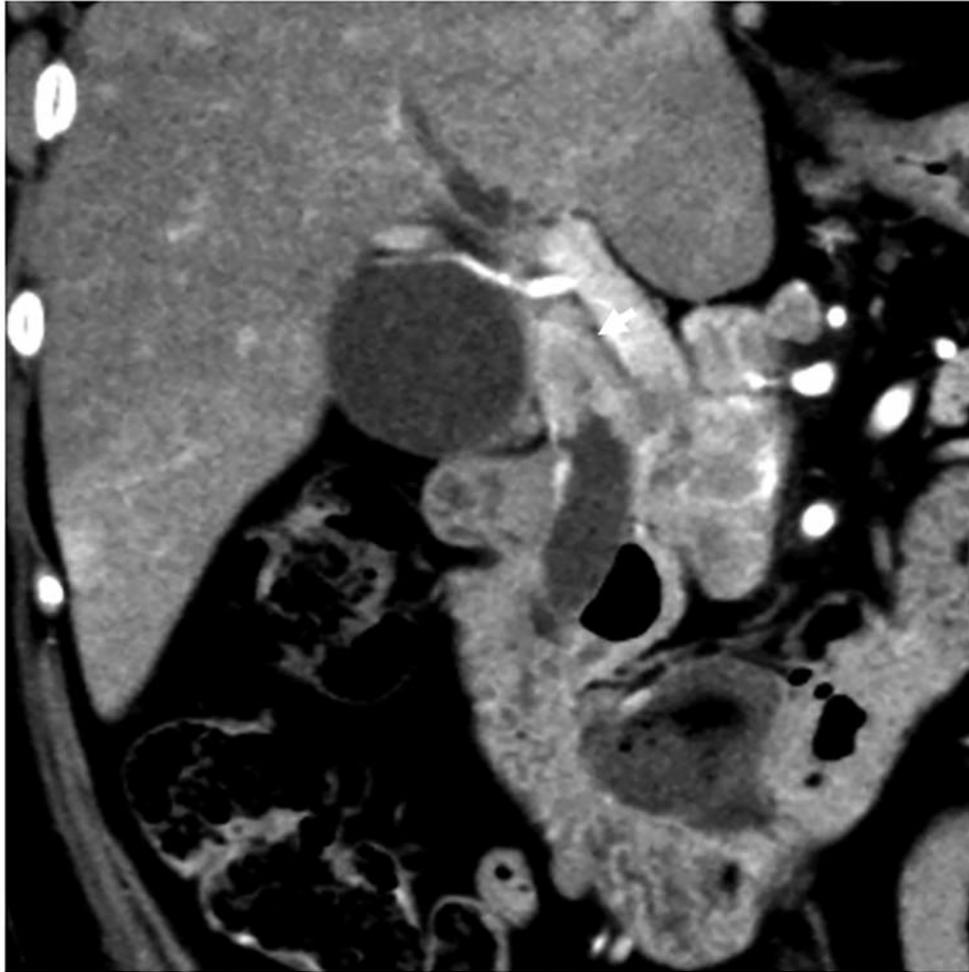


Figure 1. Computed tomography demonstrated wall thickening enhanced by contrast in the upper bile duct, which was suspected to have invaded the right hepatic artery (arrow).

Discussion

Although no effective chemotherapy existed for unresectable advanced biliary tract cancer, the UK ABC-02 study defined the standard treatment (5). In such a study, Valle *et al.* reported that cisplatin with gemcitabine (GEMC) was associated with a significant survival advantage compared to gemcitabine alone, with the median overall survival of 11.7 months compared to 8.1 months, respectively (5). However, this outcome is not satisfactory.

S-1 is an oral fluoropyrimidine, approved in Japan as a chemotherapeutic agent for biliary cancer (6). Therefore, we started combination chemotherapy using cisplatin, gemcitabine and S-1 for initially unresectable biliary cancer and recurrent biliary cancer after radical resection (3).

For colorectal and pancreatic cancer several authors recently reported the clinical advantage of neoadjuvant chemotherapy.

Adam *et al.* reported on radical hepatic resection after neoadjuvant chemotherapy for initially unresectable colorectal cancer liver metastases with 5-year survival rate of 33% in patients with major response (7). Morganti *et al.* reported that resection rates for initially unresectable pancreatic cancer after neoadjuvant chemotherapy ranged between 8.3 and 64.2% (8). On the other hand, the feasibility of neoadjuvant chemotherapy for biliary tract cancer has not been determined. In 2013, Kato *et al.* reported that eight patients with initially unresectable advanced biliary tract cancer who underwent neoadjuvant chemotherapy (gemcitabine) had significantly longer survival than 14 patients who were unable to undergo surgery (2-year overall survival rate of 45.0% and 19.0%, respectively) (9).

To our knowledge, only several such cases have been reported in the literature, and almost all patients received gemcitabine alone for neoadjuvant chemotherapy (10). The



Figure 2. Computed tomography showed remarkably swollen lymph nodes, including those in the para-aortic region (arrow).



Figure 3. The swollen para-aortic lymph nodes had almost disappeared after neoadjuvant chemotherapy, and were histologically cancer-free by postoperative pathological examination (arrow).

current case is the first report of curative resection after combined neoadjuvant chemotherapy using cisplatin, gemcitabine and S-1 for initially unresectable biliary duct cancer.

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Received April 11, 2015

Revised May 7, 2015

Accepted May 8, 2015