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Curative resection of carcinoma of the ampulla of Vater with lymph node metastases around the abdominal aorta after chemotherapy: A case report



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ABSTRACT

INTRODUCTION: For carcinoma of the ampulla of Vater, lymph node metastasis around the abdominal aorta is an inoperable factor equivalent to distant metastasis, such as hepatic metastasis or peritoneal carcinomatosis, making the cancer unresectable.

PRESENTATION OF CASE: A 53-year-old man was referred to our hospital and was diagnosed as having carcinoma of the ampulla of Vater with lymph node metastases around the abdominal aorta. Although only chemotherapy was initially scheduled, the chemotherapy was effective, and the metastases were dramatically reduced after 4 cycles of chemotherapy. Curative surgical resection was performed.

DISCUSSION: There were only eight case reports describing curative resections of initially unresectable biliary tract carcinomas excluding intrahepatic cholangiocellular carcinoma after chemotherapy.

CONCLUSION: Curative surgical resection after chemotherapy may be a feasible treatment plan in patients with unresectable biliary tract cancer.

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1. Introduction

For carcinoma of the ampulla of Vater, lymph node metastasis around the abdominal aorta is an inoperable factor equivalent to distant metastasis, such as hepatic metastasis or peritoneal carcinomatosis, making the cancer unresectable [1]. Here, we report a case of carcinoma of the ampulla of Vater with lymph node metastases around the abdominal aorta. The patient was able to undergo a curative operation after completing chemotherapy with gemcitabine and cisplatin and has not shown any signs of recurrence for 36 months.

2. Case report

A 53-year-old man complaining of itching and yellow skin visited a local hospital. He was suspected of having obstructive jaundice and was referred and admitted to our hospital for a thorough examination.

Upon examination, the abdomen was soft and flat, with no mass, tenderness, or rebound. Laboratory data at the time of admission showed serum total bilirubin and direct bilirubin levels of 17.7 mg/dL and 13.0 mg/dL, respectively. The aspartate aminotransferase level was 122 IU/L, the alanine aminotransferase level

was 205 IU/L, the alkali phosphatase level was 1647 IU/L, the γ -glutamyl transpeptidase level was 1146 IU/L, and the lactate dehydrogenase level was 270 IU/L. The carcinoembryonic antigen (CEA) and DU-PAN-II levels were 7.5 ng/dL and 687 U/dL, but the carcinoma 19-9 level was not elevated. The other test results were normal. A computed tomography (CT) scan revealed a dappled enhanced tumor 30 mm in size in the ampulla of Vater (Fig. 1a) with invasion to the duodenum and pancreas. Regional lymph nodes along the common hepatic artery (#8a) and in the hepatoduodenal ligament (#12b) had swollen to 21 mm and 33 mm in size, respectively (Fig. 1b, c); moreover, several distant lymph nodes around the abdominal aorta were also swollen, with one located between the upper border of the celiac artery and the lower border of the left renal vein (#16a2) swollen to 21 mm (Fig. 2a) and others located between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery (#16b1) swollen to 19 mm and 20 mm (Fig. 2b, c). An upper gastrointestinal endoscopy showed an exposed protruded tumor in the ampulla of Vater (Fig. 3a). Endoscopic retrograde cholangiopancreatography (ERCP) showed bile duct dilatation, and an endoscopic retrograde biliary drainage (ERBD) tube was placed to alleviate the obstructive jaundice (Fig. 3b). A pathological examination of the tumor revealed a poorly differentiated adenocarcinoma.

The clinical diagnosis at the time was carcinoma of the ampulla of Vater, exposed protruded type, T3b (Du2, Panc2), N1, H0, P0, M1 (LYN), c-Stage IV in the classification of biliary tract cancers established by the Japanese Society of Hepato-Biliary-Pancreatic

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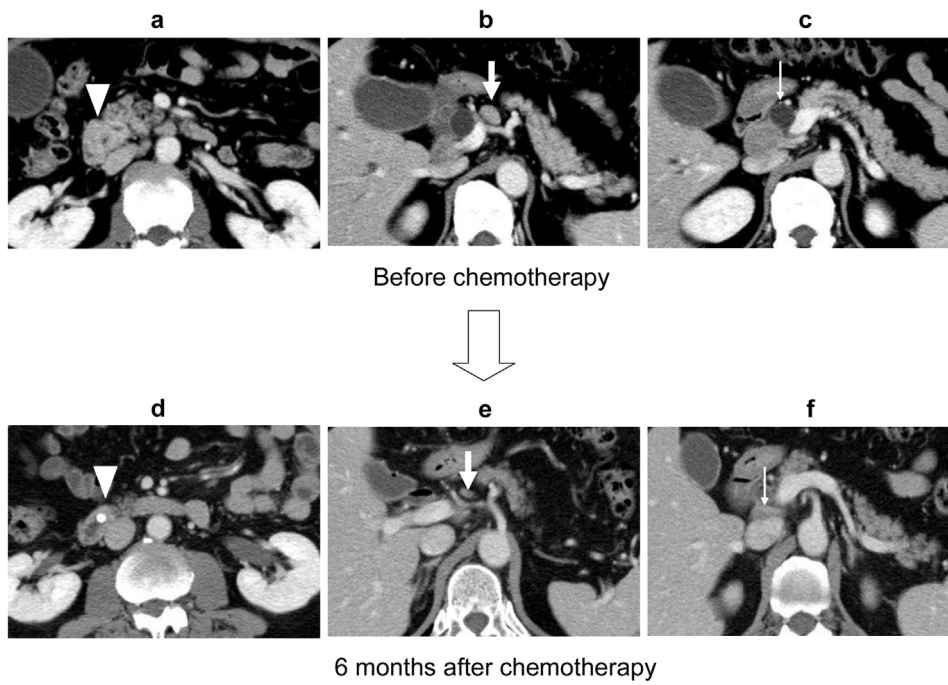


Fig. 1. CT scans show reduction of tumor (arrow heads) in the ampulla Vater (a,d), lymphnodes #8a (arrows) (b,e) and #12b (thick arrows) (c,f).

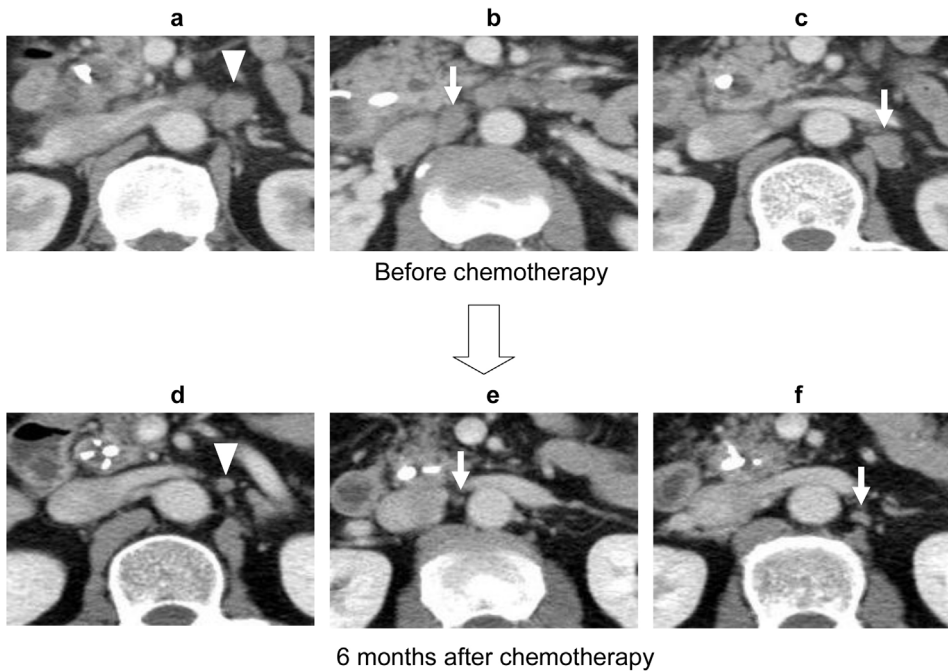


Fig. 2. CT scans show reduction of lymph nodes #16a2 (arrow heads) (a,d) and #16b1 (arrows) (b,c,e,f).

Surgery: 3rd English edition [1]. Because of lymph node metastases around the abdominal aorta, chemotherapy with gemcitabine and cisplatin was performed at dosages of 1000 mg/m² and 25 mg/m² weekly for 2 weeks, followed by a week rest. Four cycles later, the cancer markers CEA and DU-PAN-2 had decreased and were within the normal ranges (Fig. 4). A follow-up CT scan showed the shrinkage of the tumor in the ampulla of Vater (Fig. 1d), the disappearance of the lymph nodes at #8a (Fig. 1e), and the shrinkage of the lymph nodes at #12b (Fig. 1f) to 11 mm and 20 mm, respectively. Moreover, the lymph node at #16a2 (Fig. 2d) had shrunk to 7 mm and the lymph nodes at #16b1 (Fig. 2e, f) had shrunk to 5 mm and 7 mm.

Consequently, the chemotherapy with gemcitabine and cisplatin was judged to have induced a partial anticancer response. Because of the acceptable chemotherapy response, surgical resection was performed after obtaining informed consent. The operation consisted of a subtotal stomach-preserving pancreaticoduodenectomy with lymph node dissection of the regional lymph nodes and distant lymph nodes around the abdominal aorta as well as a IIA-3 reconstruction. The operation time was 578 min, and the blood loss was 2830 mL.

The tumor in the ampulla of Vater was an exposed, protruded-type mass, and the tumor specimen had decreased to a diameter of

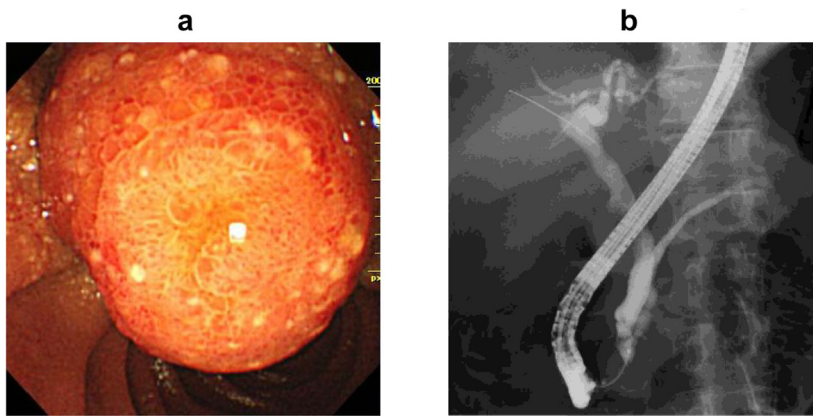


Fig. 3. ERCP revealed exposed protruded mass in the ampulla of Vater (a), and obstruction in bile duct (b).

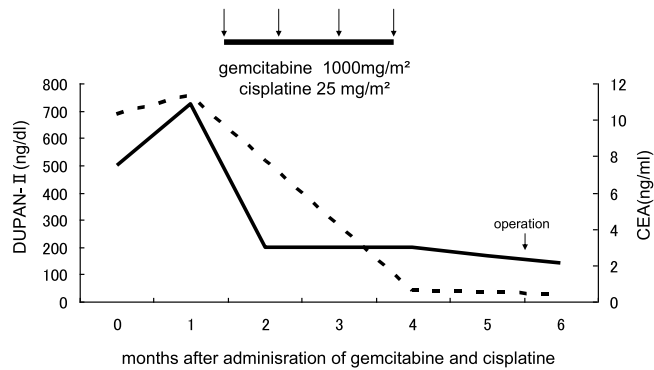


Fig. 4. Clinical course and changes in DUPAN-II and CEA.

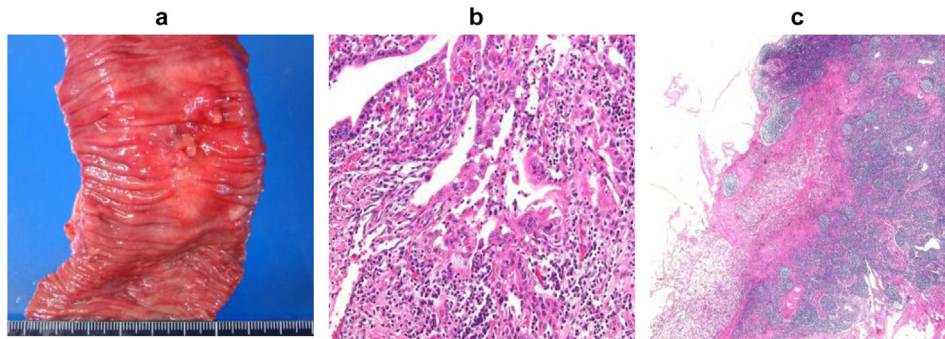


Fig. 5. A macrophotograph of tumor (a) in the ampulla Vater, and microphotographs of HE staining of tumor ($\times 20$) (b) and lymph node around the aorta ($\times 1.25$) (c).

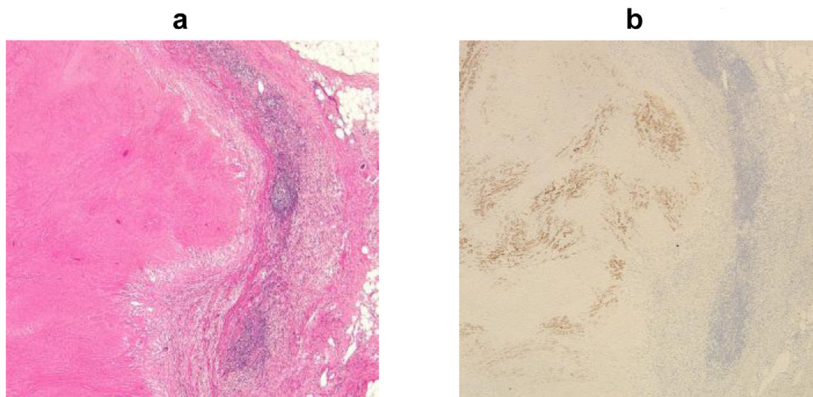


Fig. 6. pathological findings of lymph node in the hepatoduodenal ligament, showing the results of HE staining ($\times 1.25$) (a) and immunostaining with CK AE1/3 ($\times 1.25$) (b).

Table 1
Cases of R0 resection of biliary tract carcinoma.

author	location	year	age	Inoperable reason	chemo	effect	Stage	f/u(mo)	recurrence
Shirabe	GB	2008	75	Lymph node metastasis around the abd. Ao	GEM/CDDP/5FU	improvement	IV	25	none
Kitajima	GB	2008	53	Peritoneal dissemination	S-1	disappearance	I	–	–
Morimoto	GB	2008	69	Liver metastasis Lymph node metastasis around the abd. Ao	GEM	disappearance	IV	20	none
Hasegawa	GB	2010	64	Lymph node metastasis around the abd. Ao	S-1	disappearance	IV	13	none
Takita	GB	2011	57	Lymph node metastasis around the abd. Ao	GEM/S-1	disappearance	II	12	none
Rama	GB	2013	74	Lymph node metastasis around the abd. Ao	GEM/CDDP	disappearance	IV	16	None
Tanemura	BD	2008	78	Liver metastasis	GEM/rad	disappearance		–	–
Oono	ampulla	2009	53	Liver metastasis	GEM/S-1	disappearance	III	14	None
Our case	ampulla	2014	53	Lymph node metastasis around the abd. Ao	GEM/CDDP	disappearance	IV	36	None

15 mm (Fig. 5a). A pathological examination of the specimen using hematoxylin and eosin (HE) staining showed necrotic tissue and epithelia with dysplasia that was thought to be a remnant of adenocarcinoma (Fig. 5b). The invasion of inflammatory cells and fibrosis with follicular histiocytes under the mucosa were observed near the ampulla of Vater. The presence of histiocytes and fibrosis in the resected lymph nodes suggested inflammation (Fig. 5c). Especially, the immunostaining of lymph node #12b was positive for cytokeratin (CK) AE1/3 and was strongly suspected to have been a metastasis originating from the ampulla of Vater carcinoma (Fig. 6a, b). However, the immunostaining of lymph nodes from around the abdominal aorta was not positive for this factor, and only follicular histiocytes and fibrosis were observed, suggesting that these scar tissues might have been metastases originating from the carcinoma. The pathological diagnosis was carcinoma of the ampulla of Vater, exposed protruded type, pT1(Du0, Panc0) ly0, v0, ne0, pN0, pHM0, pPM0, pEM0, pPV0, pAO, R0, p-Stage I. [1]

The patient was discharged on the 41st postoperative day after recovering from a pancreatic fistula (grade II). Adjuvant chemotherapy was not performed, and no evidence of recurrence or metastases has been seen for 36 months since the operation.

3. Discussion

According to in the Biliary Tract Cancer Statistics Registry in Japan, the 5-year survival rates after surgical resection are about 40% for whole biliary tract cancer, 33.1% for bile duct cancer, 41.6% for gallbladder cancer, and 52.8% for ampulla of Vater cancer, while those of unresectable disease are 1% for bile duct cancer, 2% for gallbladder cancer, and 8% for ampulla of Vater cancer [2]. Ampulla of Vater cancer accounts for 14.0% of biliary tract cancers and has a high resectability rate of 89.4% and a curative resection rate of 93.0% [2]. For these reasons, ampulla of Vater cancer has a relatively better prognosis, and surgery tends to be more effective, compared with similar surgical procedures for other biliary tract cancers. However, invasion of the pancreas and (peri)neuroplexus and metastasis to lymph nodes worsens the prognosis considerably, even for ampulla of Vater carcinoma [3,4]. Generally, in patients with biliary tract cancer, long-term survival depends critically on complete tumor resection, and patients with distant metastasis to the liver, lungs, bone, or peritoneum are not eligible for surgery and instead are candidates for palliative chemotherapy [5–7]. Also, regional lymphadenectomy and lymphadenectomy near the abdominal aorta does not provide a survival benefit to patients with abdominal aortic disease, which has an influence on the prognosis equivalent to that of distant metastasis [5,7]. Chemotherapy with gemcitabine and cisplatin is the current stan-

dard for unresectable biliary tract cancer based on the results of the ABC-02 trial, but this combination results in an antitumor activity with an objective response rate of only 26.1% and a median survival of 11.7 months [5,8,9].

We searched the PubMed MEDLINE interface and the database of the Japan Medical Abstracts Society for reports published between 1983 and 2014. The search strategy was designed to be inclusive using the intersection of the following medical subject and keyword headings: *biliary tract carcinoma*, *carcinoma of ampulla*, *cholangiocellular carcinoma*, *chemotherapy*, and *resection*. Accordingly, we found eight case reports describing curative resections of initially unresectable biliary tract carcinomas excluding intrahepatic cholangiocellular carcinoma after chemotherapy, and all of these cases had favorable outcomes [10–17]. Six reports described gallbladder cancers and one report each described bile duct cancer and ampulla of Vater cancer. Of these nine reports included our case, many of them used different chemotherapy regimens. Two reports used a combination of gemcitabine and S-1, two used a combination of gemcitabine and cisplatin, and two used S-1 alone. One report used gemcitabine alone, one used gemcitabine and radiation, and one used gemcitabine, cisplatin and 5-FU. Inoperable factors were described as not only liver and lymph node metastases around the abdominal aorta, but also peritoneal dissemination (Table 1).

To our knowledge, only Oono et al. [10] has reported the curative resection of an ampulla of Vater carcinoma after chemotherapy. In their report, a 53-year-old patient had an ampulla of Vater carcinoma with liver metastasis and underwent surgery after completing 3 cycles of chemotherapy with gemcitabine and S-1. Liver resection was not performed because no evidence of liver metastasis was seen during an intraoperative echography.

Some clinical problems exist for cases with initially unresectable biliary tract cancer that becomes resectable after chemotherapy because of the lack of evidence supporting this strategy. First, the timing of such surgery remains uncertain. Some authors decided to perform surgery once a complete or partial anticancer response had been achieved, and one case report described the progression of a liver metastasis despite continuous chemotherapy. Second, the need for adjuvant chemotherapy also remains uncertain. Murakami et al. [18] reported that adjuvant chemotherapy with gemcitabine and S-1 may be a promising strategy for patients with advanced biliary tract cancer after curative resection. A randomized phase III study is expected to show that adjuvant chemotherapy is effective and well tolerated.

However, comparative studies are difficult to conduct, since few cases with conversions in treatment strategy exist. The further accumulation of reports is awaited to confirm the optimal timing

of surgery and the indications for adjuvant chemotherapy in cases with conversions in treatment strategies.

4. Conclusion

We performed the curative resection of an ampulla of Vater cancer in a patient with lymph node metastases around the aorta after the completion of 4 cycles of gemcitabine and cisplatin chemotherapy. Curative surgical resection after chemotherapy may be a feasible treatment plan in patients with unresectable biliary tract cancer.

Conflict of interest

None.

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Ethical approval

Kameda medical center ethics committee 16-039.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author's contributions

As 1st author, Wataru Fujii contributes to case report writing, data collection and discussion writing. All authors read and approved the final manuscript.

Registration of research studies

This paper is not a research study.

Guarantor

Wataru Fujii.

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