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Successful Conversion Surgery of Common Hepatic Arterial and Portal Vein Resection Combined with Preoperative Chemotherapy and Coil Embolization for Locally Advanced Pancreatic Cancer: A Case Report

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ABSTRACT

The standard treatment for unresectable locally advanced pancreatic ductal adenocarcinoma (UR-LA PDAC) is chemotherapy or chemoradiotherapy except for surgery. Although conversion surgery (CS) for UR-LA PDAC has been useful strategy, owing to recent advances in the other treatment, the significance and safety of CS remains unclear. We described a case of successful conversion surgery of common hepatic arterial and portal vein resection combined with chemotherapy and preoperative coil embolization for locally advanced pancreatic cancer. A 65-year-old man was diagnosed with UR-LA PDAC which was in contact with common hepatic artery (CHA) -gastroduodenal artery (GDA)-proper hepatic artery (PHA), with invasion extending from the superior mesenteric vein (SMV) to portal vein (PV) without distant metastasis. After gemcitabine plus nab-paclitaxel, the primary tumor had decreased and tumor contacts with the CHA and invasion extending from the SMV to PV were still observed, indicating to the change of borderline resectable PDAC (BR-A). We performed preoperative CHA and GDA embolization to prevent postoperative ischemic complications. Five days after embolization, pancreaticoduodenectomy (PD) with common hepatic arterial resection and portal vein resection were performed, preserving right gastric artery (RGA). Arterial reconstruction was not performed as intraoperative ultrasonography confirmed RGA-PHA blood flow was sufficient to cover the bilateral lobes of the liver. Although liver enzymes levels were moderately increased, the patient was discharged on postoperative day 15 without any ischemic liver event. He had received adjuvant chemotherapy with S-1 for 12 months and alive at 36 months after initial treatment without any tumor recurrence.

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Abbreviations

UR-LA PDAC: Unresectable Locally Advanced Pancreatic Ductal Adenocarcinoma
CS: Conversion Surgery
CHA: Common Hepatic Artery
GDA: Gastroduodenal Artery
PHA: Proper Hepatic Artery
SMV: Superior Mesenteric Vein
PV: Portal Vein
RGA: Right Gastric Artery
CT: Computed Tomography
GNP: Gemcitabine Plus Nab-Paclitaxel
BR: Borderline Resectable
NCCN: National Comprehensive Cancer Network

Introduction

Conversion surgery for UR-LA PDAC may have some unresolved issues regarding to surgical safety and prognosis. In recent years, multidisciplinary treatment combining surgical resection and chemotherapy or chemoradiotherapy have been applied to improve prognosis for UR-LA PDAC. This report describes a case of successful conversion surgery after preoperative chemotherapy and arterial embolization for initially UR-LA PDAC.

Case Report

A 65-year-old man was admitted to our hospital because of abdominal discomfort and jaundice. He had no comorbidities, except for hypertension and no family history of pancreatic cancer or genetic disorders. He had smoked until 21 years old and drunk a moderate amount of alcohol. The initial serum level of pancreatic cancer tumor markers, CA19-9 was 113.7 U/mL high, but CEA was 2.6 ng/mL within normal range and enzymes of the hepatobiliary

system were elevated. Abdominal dynamic computed tomography (CT) revealed a hypovascular tumor measuring 28 mm in the head of the pancreas. The tumor was in contact with common hepatic artery (CHA) -gastroduodenal artery (GDA)-proper hepatic artery (PHA), with invasion extending from the SMV to PV (Figure 1a-b). Distant metastasis was not confirmed. Endoscopic biliary decompression was done (Figure 1c), and serum level of CA19-9 quickly normalized. The histological finding of endoscopic ultrasonography-guided fine needle aspiration biopsy was pancreatic adenocarcinoma. Based on these findings, the patient was diagnosed to have a T3N0M0 clinical stage IIA pancreatic cancer (PC) on the Japan Pancreatic Society classification, 7th edition or T2N0M0 clinical stage IB PDAC on the 8th edition of the UICC criteria and was categorized as unresectable locally advanced PC (UR-LA PDAC).

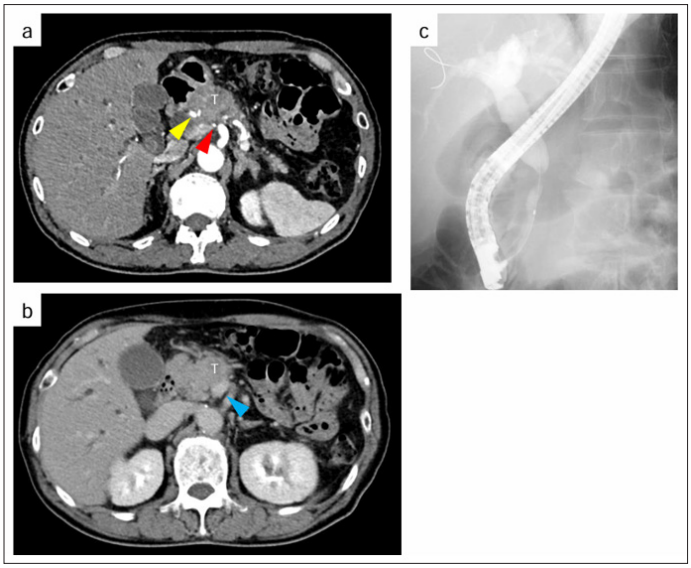

Figure 1: Dynamic computed tomography and endoscopic retrograde cholangiopancreatography at initial diagnosis. T: tumor; red arrowhead: CHA; yellow arrowhead: PHA; blue arrowhead: PV.

a,b: Dynamic computed tomography showed that a hypovascular tumor measuring 28 mm in the head of the pancreas. The tumor was in contact with CHA-GDA-PHA, with invasion extending from the SMV to PV

c: Endoscopic retrograde cholangiopancreatography showed common bile duct obstruction at the level of pancreas.
CHA common hepatic artery; PHA proper hepatic artery; PV portal vein; GDA gastroduodenal artery.

According to UR-LA PDAC, we performed systemic chemotherapy consisting of gemcitabine plus nab-paclitaxel (GnP) (gemcitabine 1000mg/m2 and nab-paclitaxel 125mg/ m2 on days 1,8, 15 every 4 weeks). The effect of chemotherapy was estimated by dynamic CT. After 8 courses of combination chemotherapy, CT imaging demonstrated an effective response to chemotherapy, so that the primary tumor had decreased to 18 mm in diameter, whereas tumor contacts with the CHA and invasion extending from the SMV to PV were still observed, indicating to the change of borderline resectable (BR-A) PDAC (Figure 2a-b). Distant metastasis and progression disease was not confirmed. We opted to perform preoperative CHA and GDA embolization to prevent postoperative ischemic complications. Angiography after CHA and GDA embolization confirmed CeA-LGA-RGA-PHA flow to the bilateral lobe liver. Five days after embolization (Figure 3), pancreaticoduodenectomy with common hepatic arterial resection and portal vein resection (portal vein-SMV direct end-to-end anastomosis) were performed, preserving RGA. Arterial reconstruction was not performed as intraoperative ultrasonography confirmed RGA-PHA blood flow was sufficient to cover the bilateral lobes of the liver. The margins of the bile duct and stump of the pancreas were negative for cancer on intraoperative pathological diagnosis of a frozen section.

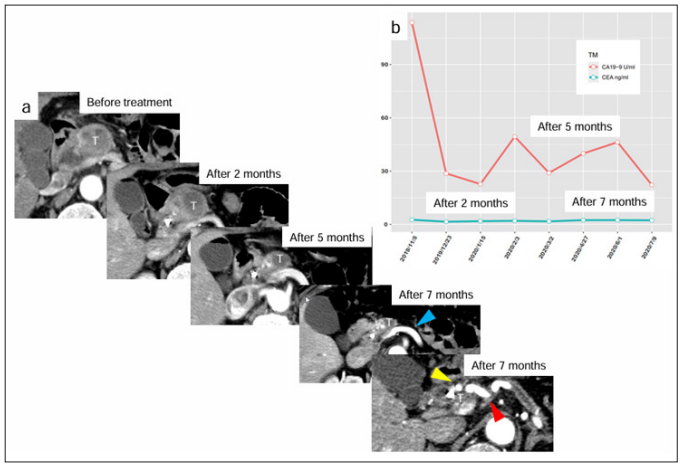

Figure 2: Clinical Change in Dynamic Computed Tomography and the Serum ca19-9 an CEA from Initial Diagnosis to 7 Months Preoperative Chemotherapy. T: Tumor; Red Arrowhead: CHA; Yellow Arrowhead: PHA; Blue Arrowhead: PV.
A. The tumor has shrunk, and tumor contact with PHA has disappeared, but contacts with the CHA and PV remained.
B. The elevation of CA19-9 was not shown in the clinical course other than their elevation before endoscopic biliary decompression. There was no elevation of CEA during the period.
CHA common hepatic artery; PHA proper hepatic artery; PV portal vein.

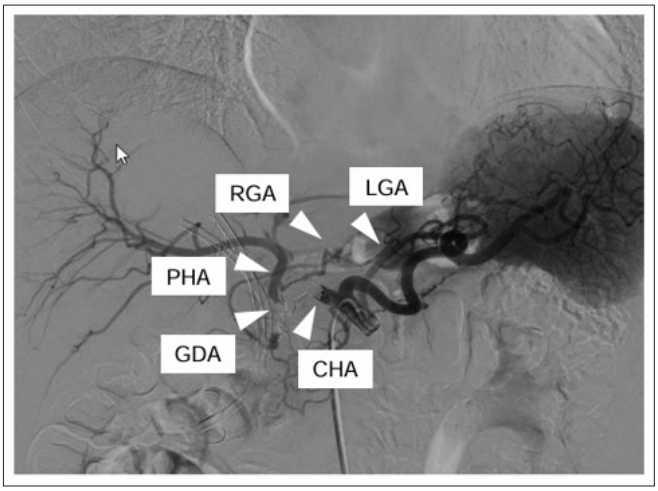

Figure 3: Preoperative Angiography and Embolization of the CHA and GDA
After embolization of the CHA and GDA by the coil, blood flow of the liver was supplied via RGA. CHA common hepatic artery; GDA gastroduodenal artery; RGA right gastric artery; PHA proper hepatic artery; LGA left gastric artery.

Histopathological examination revealed an invasive ductal carcinoma, por>mod, Ph, TS2 (23mm), infiltrative type, ypT3, INFγ, ly0, v0, mpd0, ypCH0, ypDU0, ypS0, ypRP1, ypPV0, ypA0, ypPL1, ypOO0, ypPCM0, ypBCM0, ypDPM0, ypN0 (0/30), ypM0, ypStage III according to the Japan Pancreatic Society classification, 7th edition.

According to the 8th edition of the UICC criteria, the tumor was diagnosed as T2N0M0, stage IB (Figure 4). Microscopic pathological examination showed R0 (no residual tumor) resection, and 10-50% of the tumor cells were replaced with fibrosis (Evans' criteria IIb). Histologic examination showed that the tumor was in contact with but did not invade to the CHA and PV, consisted of fibrotic tissues which had prominent hemosiderin deposits and foam cells partially with coagulation necrosis and had giant cell proliferation with atypical cells showing slight ductal formation.

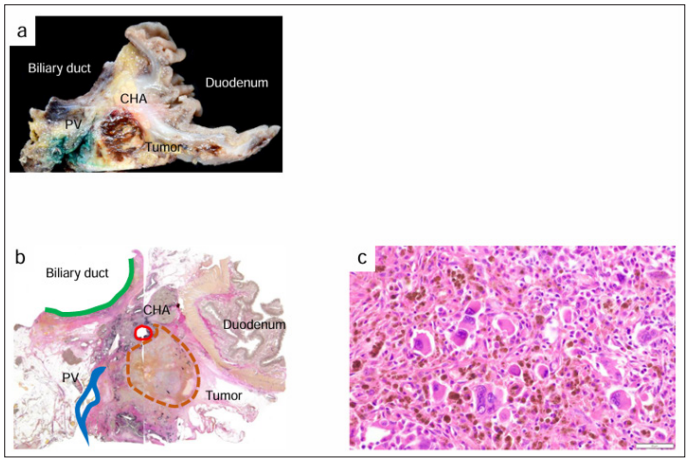

Figure 4: Images of Resected Tumor
a. Macroscopic finding of the resected specimen showed that the brown tumor was largely replaced by coagulation necrosis.
b. Elastica van Gieson stained photomicrograph (loupe image) showed that
the tumor was in contact with but did not invade to the CHA and PV.
c. HE stained photomicrograph (40×) showed that the tumor consisted of fibrotic tissues which had prominent hemosiderin deposits and foam cells partially with coagulation necrosis. The tumor had giant cell proliferation with atypical cells showing slight ductal formation. The scale bar represents 50 μm. CHA common hepatic artery; PV portal vein.

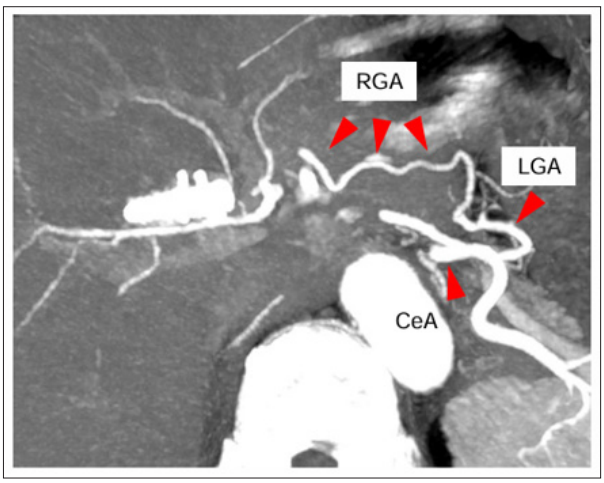

Figure 5: Postoperative Dynamic Computed Tomography
CT showed RGA had more enlarged than preoperative. RGA right gastric artery; LGA left gastric artery; CeA celiac axis.

Although liver enzymes levels were moderately increased, the patient was discharged on postoperative day 15 without any ischemic liver event. He had received adjuvant chemotherapy with S-1 (50mg, orally administered twice a day for 28 days followed by a 14 days rest, every 6 weeks [one cycle]) for 12 months. He is alive at 36 months after initial treatment without any tumor recurrence.

Case Discussion

Surgical resection is the only curative treatment for PDAC, but primary resectable cases account for only 15-20% of all patients [1]. This is due to a lack of specific symptoms and reliable screening tools resulting in tumor detection at early stage of disease[2, 3]. While UR-LA PDAC is generally defined by local tumor growth with involvement of the celiac axis or the superior mesenteric artery, according to the National Comprehensive Cancer Network (NCCN)[4], this present case diagnosed as UR-LA PDAC by the Japan Pancreatic Society classification, 7th edition (involvement of CHA and PHA).

Previous two randomized trials have provided contradict information on the survival benefit of chemoradiation versus chemotherapy alone for UR-LA PDAC [4-6].

Upfront systemic chemotherapy is generally recommended for patients with UR-LA PDAC to control or delay symptoms of tumor progression, prolong survival, and maintain quality of life. In patients with good performance status, the recommended first-line chemotherapy, equivalent to the Japanese guidelines for patients with UR-LA PDAC, is Gemcitabine alone, S-1 alone, FOLFIRINOX or gemcitabine plus nab-paclitaxel (GnP). Ueno et al. demonstrated that GnP (response rate: 69.2%) showed better efficacy than Gemcitabine or Gemcitabine +S-1 (response rate: 30%) in patients with UR-PDAC [7]. We adopted GnP, taking into account to conversion surgery as a recent review reported that new regimens such as FOLFIRINOX and GnP resulted in tumor shrinkage in a relatively short time [8].

The actual benefit of conversion surgery in UR-PDAC remains controversial. It may not be oncological reasonable because it is associated with high morbidity and mortality and prognosis is poor due to early local and systemic recurrence. On the other hand, the long-term prognosis of patients with UR-PDAC in whom conversion surgery was performed was significantly better than that of unresected patients who underwent chemotherapy [9, 10]. Moreover, surgical resection can be successfully achieved in selected patients with initially unresectable pancreatic cancer after a favorable response to chemotherapy. Although the patient's tumor was actually defined as unresectable as it had invaded the CHA, the proximal portion of the PHA, the GDA by initial dynamic CT, he had effective response to systemic chemotherapy consisting of GnP with the change of BR-PC and was decided to have operation.

It was necessary to pancreatoduodenectomy with common hepatic arterial and portal vein resection to achieve R0 surgery in this case. PV and SMV resection is generally performed for PDAC with infiltration to the PV/SMV to achieve R0 resection and is recommended in the clinical guideline [11]. Although the safety of arterial resection for pancreatic cancer remains unclear and is associated with significantly high morbidity and mortality rates long-term survival can be observed in highly select cases [9,10]. It has been reported that preoperative embolization strategy for the combined resection of replaced right hepatic artery in pancreaticoduodenectomy could be a feasible choice for surgical management [12]. In this case, we conducted preoperative coil embolization of CHA and GDA with compensation from the preserved RGA-PHA to omit the combined CHA reconstruction and postoperative complications, including loss of arterial blood flow into liver. Liver enzymes levels were moderately increased

after post-operative some days, but no other clinical problems were encountered. Recent studies demonstrated that most patients who received conversion surgery had no evidence of a response on imaging and no survival difference between responder and non-responder [13, 14]. In addition, cases with a marked decrease in the CA19-9 level after preoperative treatment was reported to correlate with better survival8, but this case was not consistent, according to the normalization of preoperative biliary decompression, so another useful indicators for conversion surgery are needed. Moreover, there are problems in terms of a complete resection that preservation of the RGA may result in inadequate lymphadenectomy.

Another problem is the prognostication of patients after preoperative chemotherapy and conversion surgery for UR-LA PDAC. These patients tend to have early recurrence or die within 12 months and might benefit from adjuvant chemotherapy if individual performance status and postoperative morbidity permit [14,15]. There is no evidence for a standard adjuvant therapy after preoperative chemotherapy and conversion surgery. In the present patient, we had chosen S-1 alone not gemcitabine which was effective preoperative chemotherapy, according to clinical guideline for resectable PDCA. It will be necessary to perform further study of adjuvant chemotherapy after CS for UR-LA PDAC.

Conclusions

We report a case with PD for pancreatic cancer with CHA and PV invasion, combined resection of CHA and PV after preoperative embolization of CHA and GDA with compensation from the preserved RGA-PHA. Even for CHA initially in contact with the tumor, CHA resection with preoperative arterial embolization is a safe and effective option when tumor contact disappears due to chemotherapy, preserving oncologically and anatomically arterial blood flow into liver including RGA. Further studies are necessary to evaluate and determine the optimal treatment regimen, duration and criteria for UR-LA PDAC.

Declarations

Acknowledgements

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Ethic Approval and Consent to Participate

The institutional ethics committee determined that approval was not necessary for a case report.

Competing Interests

The authors declare that they have no conflict of interest.

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