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CASE REPORT

Long-term survival after distal pancreatectomy with celiac axis resection and hepatic artery reconstruction in the setting of locally advanced unresectable pancreatic cancer

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Abstract

The long-term survival of patients with locally advanced, unresectable pancreatic cancer is extremely poor. We present our experience with a 67-year-old woman who had a 40-mm mass in the body of the pancreas. Tumor infiltration reached the gastroduodenal artery, celiac artery, common hepatic artery, and splenic artery. After 10 courses of FOLFIRINOX, 2 courses of gemcitabine plus nab-paclitaxel, and 6 courses of gemcitabine alone, we performed distal pancreatectomy with celiac axis resection and hepatic artery reconstruction. The bifurcation of the gastroduodenal artery and the proper hepatic artery had to be resected, after which we created 2 anastomoses: proper hepatic-to-middle colic artery, and second jejunal-to-right gastroepiploic artery. Histopathologic examination revealed an Evans grade IIb histologic response to prior treatment and verified the R0 resection status. The patient was discharged on postoperative day 30 after treatment of a grade B pancreatic fistula and is still alive, without recurrence, more than 5 years after initiation of treatment. This patient with locally advanced, unresectable pancreatic cancer achieved long-term survival through perioperative multidisciplinary treatment, including distal pancreatectomy with celiac axis resection and hepatic artery reconstruction. This aggressive procedure could be a treatment option for patients with locally advanced, unresectable pancreatic cancer.

Keywords Locally advanced pancreas cancer · Conversion surgery · Distal pancreatectomy with celiac axis resection · Hepatic artery resection · Long-term survival

Abbreviations

URLA	Unresectable, locally advanced
PC	Pancreatic cancer
DP-CAR	Distal pancreatectomy with celiac axis resection
DUPAN-2	Duke pancreatic monoclonal antigen type 2
SPAN-1	S-pancreas antigen-1
CEA	Carcinoembryonic antigen
CA19-9	Carbohydrate antigen 19-9
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
RECIST	Response Evaluation Criteria in Solid Tumors
FFX	FOLFIRINOX
GnP	Gemcitabine plus nab-paclitaxel
Gem	Gemcitabine

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Introduction

Despite the development of new options for chemotherapy and chemoradiotherapy, the prognosis for patients with unresectable, locally advanced (URLA) pancreatic cancer (PC) is still unsatisfactory [1–3]. To increase the number of patients with URLA PC who can achieve long-term survival, efforts are being made to perform conversion surgery

when the preceding treatment has been significantly effective. However, a standard strategy for conversion surgery—including its indications, optimal interval between diagnosis and surgery, and ideal surgical procedure—has not yet been established. We present herein our experience with a patient who had URLA PC and achieved long-term survival of more than 5 years by undergoing multidisciplinary treatment, including conversion surgery consisting of distal pancreatectomy with celiac axis resection (DP-CAR) accompanied by hepatic artery reconstruction and right gastroepiploic artery reconstruction.

Case report

A 67-year-old woman was referred to our hospital for further evaluation of a dilated main pancreatic duct that was detected by abdominal ultrasonography performed by her primary care doctor. She had a history of hypertension and dyslipidemia. Laboratory testing showed elevated tumor markers, including duke pancreatic monoclonal antigen type 2 (DUPAN-2; 12,000 U/mL) and s-pancreas antigen-1 (SPAN-1; 180 U/mL), although her carcinoembryonic antigen (CEA; 4.1 ng/mL) and carbohydrate antigen 19-9 (CA19-9; 12 U/mL) levels were within normal limits. Initial multidetector computed tomography (CT) revealed a 40-mm, irregular, low-density mass in the body of the pancreas. The tumor contacted the celiac artery, common hepatic artery, and splenic artery (Fig. 1a). In addition, CT revealed irregularity of the gastroduodenal artery due to tumor infiltration (Fig. 1b). There were no visible distant metastases.

Endoscopic retrograde cholangiopancreatography revealed an area of stenosis approximately 22 mm in length in the main pancreatic duct, at the pancreatic neck; the part of the duct distal to the stenotic area was dilated (Fig. 2). Endoscopic ultrasonography revealed an irregular, 31 × 21 mm mass at the pancreatic neck. Cytologic examination of pancreatic fluid obtained from nasal drainage of the pancreatic duct was suspicious for adenocarcinoma (class IV). We performed endoscopic ultrasound-guided fine needle aspiration for pancreatic tumor, but histological examination showed no malignant findings (class II).

The patient was diagnosed with URLA PC based on the National Comprehensive Cancer Network guidelines for pancreatic adenocarcinoma, version 1.2021 [4]. She decided to undergo systemic chemotherapy. As first-line treatment, we administered FOLFIRINOX (5-fluorouracil, 2400 mg/m^2; leucovorin, 200 mg/m^2; irinotecan, 180 mg/m^2; and oxaliplatin, 85 mg/m^2) [5]. After 10 courses, we changed the chemotherapeutic regimen to gemcitabine (1000 mg/m^2) plus nab-paclitaxel (125 mg/m^2) [6] as a second-line regimen, owing to the grade 3 nausea and vomiting resulting

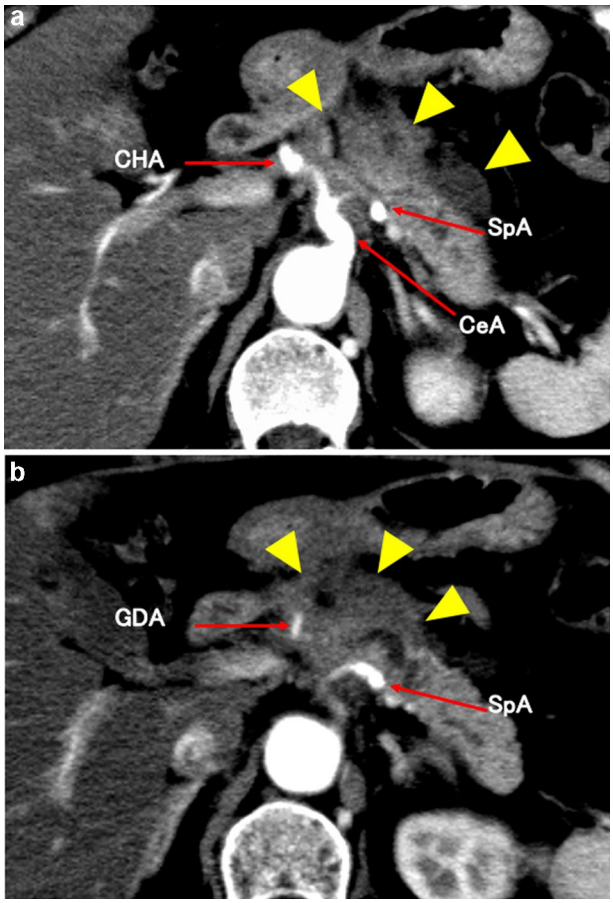

Fig. 1 Initial multidetector computed tomography (CT). **a** A 40-mm irregular low-density mass is present in the body of the pancreas (yellow arrow). The tumor contacts the celiac artery, common hepatic artery, and splenic artery. **b** There is irregularity of the gastroduodenal artery due to tumor infiltration

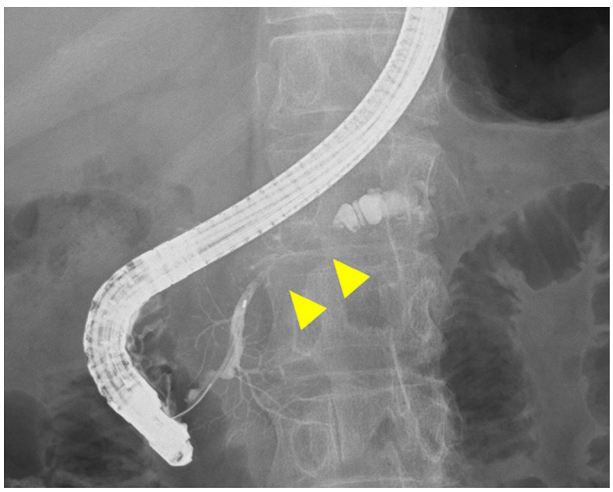

Fig. 2 Endoscopic retrograde cholangiopancreatography reveals stenosis of the main pancreatic duct at the pancreatic neck, approximately 22 mm in length, with dilation on the distal side

from FOLFIRINOX (based on the Common Terminology Criteria for Adverse Events [CTCAE], version 4.0) [7]. However, this regimen was terminated only after 2 courses because of grade 3 peripheral neuropathy. Although the tumor shrunk to 35 mm at this time, tumor response was still stable disease and we considered that the duration of chemotherapy seemed to be insufficient for conversion surgery. Subsequently, gemcitabine alone was administered for 6 courses as the third-line regimen. After completion of systemic chemotherapy, the tumor was reevaluated to assess its resectability and response to treatment. According to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [8], the tumor exhibited a partial response, as assessed by multidetector enhanced CT (maximum tumor size, 27 mm). Although her DUPAN-2 and SPAN-1 levels decreased to 1200 U/mL and 62 U/mL, respectively, during chemotherapy (Fig. 3), the tumor still contacted the celiac artery, common hepatic artery, and splenic artery (Fig. 4a), and irregularity of the gastroduodenal artery was still present (Fig. 4b). Although the diagnosis remained URLA PC, we judged that radical resection was possible using DP-CAR accompanied by resection of the gastroduodenal artery and reconstruction of the hepatic artery. We offered this to the patient as conversion surgery (Fig. 4c). Because of the no findings suggestive of distant metastasis in preoperative CT, positron emission tomography–CT, gadolinium ethoxybenzyl diethylenetriaminepentaacetic acid enhanced liver magnetic resonance imaging and staging laparoscopy were not performed according to the institutional policy at that time.

Preoperative abdominal angiography revealed that the left hepatic artery diverged from the left gastric artery and confirmed the irregularity of the gastroduodenal artery, although there was no irregularity or stenosis noted in the common hepatic artery or splenic artery (Fig. 5a). The common hepatic artery and left gastric artery were embolized for blood-flow modification, then the right hepatic artery and middle hepatic artery were visualized through the pancreatic head arcade by angiography from the superior mesenteric artery. In addition, blood flow of the left hepatic artery was observed; this was a retrograde supply from the right hepatic artery through the hilar plate (Fig. 5b).

Surgery was performed 1 week after arterial embolization. Intraoperative observation showed that the tumor was located mainly in the pancreatic body. As expected from her preoperative imaging, the tumor reached the bifurcation of the gastroduodenal artery and proper hepatic artery, and we decided to resect the gastroduodenal artery and reconstruct the proper hepatic artery. The right- and middle hepatic arteries were without tumor contact; we exposed the middle colic artery and constructed a middle colic-to-proper hepatic artery anastomosis (Fig. 6a, b). We also performed a second anastomosis of the jejunal artery to the right gastroepiploic artery, because the retrograde arterial blood flow from the left hepatic artery to the stomach, via the left gastric artery, appeared to be insufficient based on intraoperative observation (Fig. 6c, d). The operative time was 601 min and the estimated blood loss was 1989 ml.

Histopathologic examination of the resected specimen revealed a moderately differentiated tubular adenocarcinoma measuring 25 × 20 mm (Fig. 7a). There was no tumor invasion into the celiac artery, common hepatic artery, splenic artery, or gastroduodenal artery, but cancer cells were found

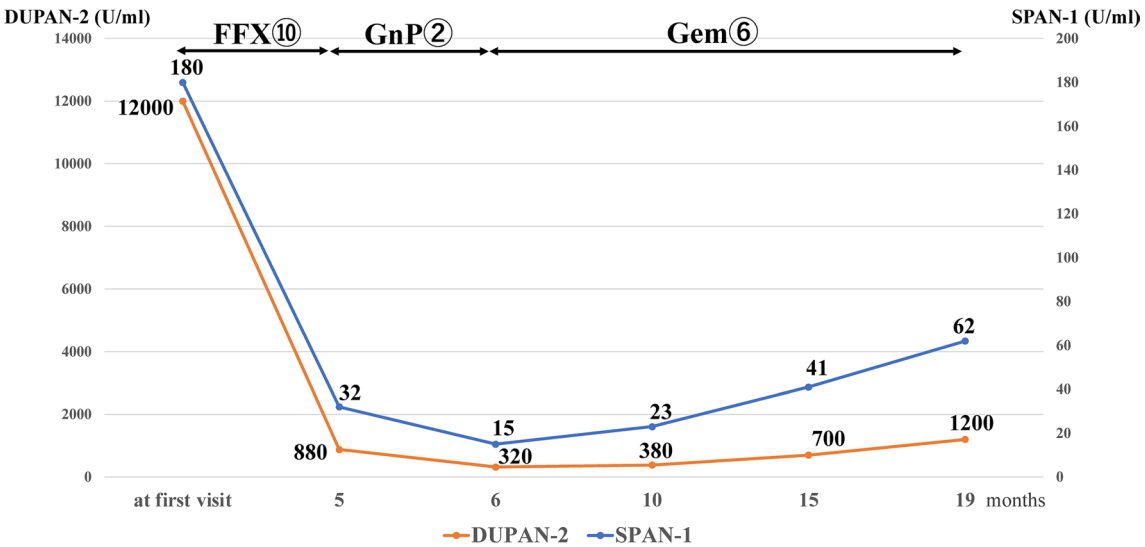

Fig. 3 The change of DUPAN-2 and SPAN-1 showed that DUPAN-2 and SPAN-1 levels decreased 12,000 to 1200 U/mL and 180 to 62 U/mL, respectively, during chemotherapy. CEA and CA19-9 were all time within normal limits. *DUPAN-2* duke pancreatic monoclonal antigen type 2, *SPAN-1* s-pancreas antigen-1, *CEA* carcinoembryonic antigen, *CA19-9* carbohydrate antigen 19-9, *FFX* FOLFIRINOX, *GnP* gemcitabine plus nab-paclitaxel, *Gem* gemcitabine

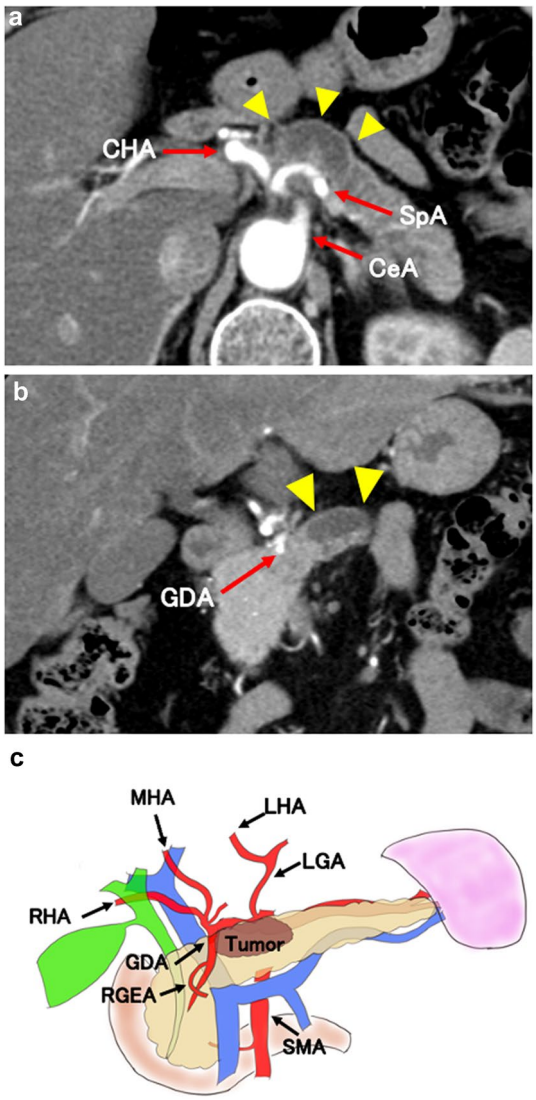

Fig. 4 Abdominal CT after chemotherapy. **a** The tumor now measures 27 mm in maximum diameter (yellow arrow). The tumor still contacts the celiac artery, common hepatic artery, and splenic artery. **b** There is persistent irregularity of the gastroduodenal artery. **c** Schematic of the anatomy before surgery. The tumor is still contacting the celiac artery, common hepatic artery, and splenic artery, with tumor infiltration extending to the gastroduodenal artery

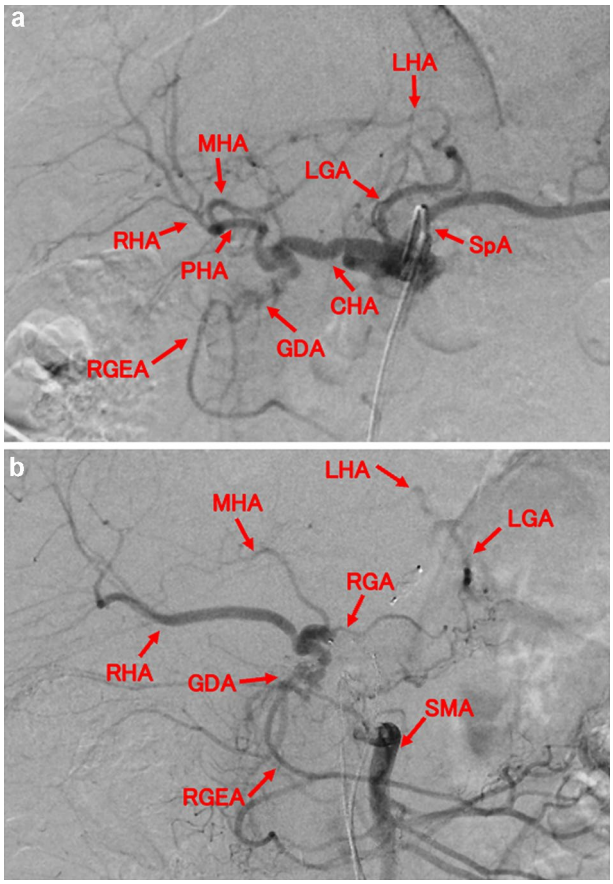

Fig. 5 Preoperative abdominal angiography. **a** The left hepatic artery diverges from the left gastric artery. There is irregularity of the gastroduodenal artery due to tumor infiltration but no irregularity or stenosis in the common hepatic artery or splenic artery. **b** After blood-flow modification, the right and middle hepatic artery are visualized through the pancreatic head arcade by angiography from the superior mesenteric artery. Blood flow is observed in the left hepatic artery, representing a retrograde supply from the right hepatic artery through the hilar plate

in the celiac artery plexus (Fig. 7b). Only stromal cells, not cancer cells, were observed in the plexus around the gastroduodenal artery. Approximately 70% of the cancer cells were degenerated and fibrotic, presumably due to the preoperative systemic chemotherapy. The Evans classification of tumor response was IIb [9] (Fig. 7c).

No cancer cells were found at the surgical margins, classifying this as an R0 resection. No lymph node metastases were found. The pathologic diagnosis was T2N0M0, stage Ib, based on the eighth edition of the Union for International Cancer Control tumor-node-metastasis classification. Postoperative CT showed good arterial blood flow to the liver and stomach.

The patient was discharged on postoperative day 30 after treatment of a grade B pancreatic fistula. She received 14 courses of adjuvant gemcitabine (700 mg/m^2) plus S-1 (tegafur/gimeracil/oteracil; 100 mg/ body) [10], which was administered as the standard adjuvant regimen in our institution at this time, and is still alive without recurrence more than 5 years after the initiation of treatment.

Discussion

In this report, we describe our experience with a patient who had a rare experience with URLA PC. She achieved more than 5 years of progression-free survival by undergoing

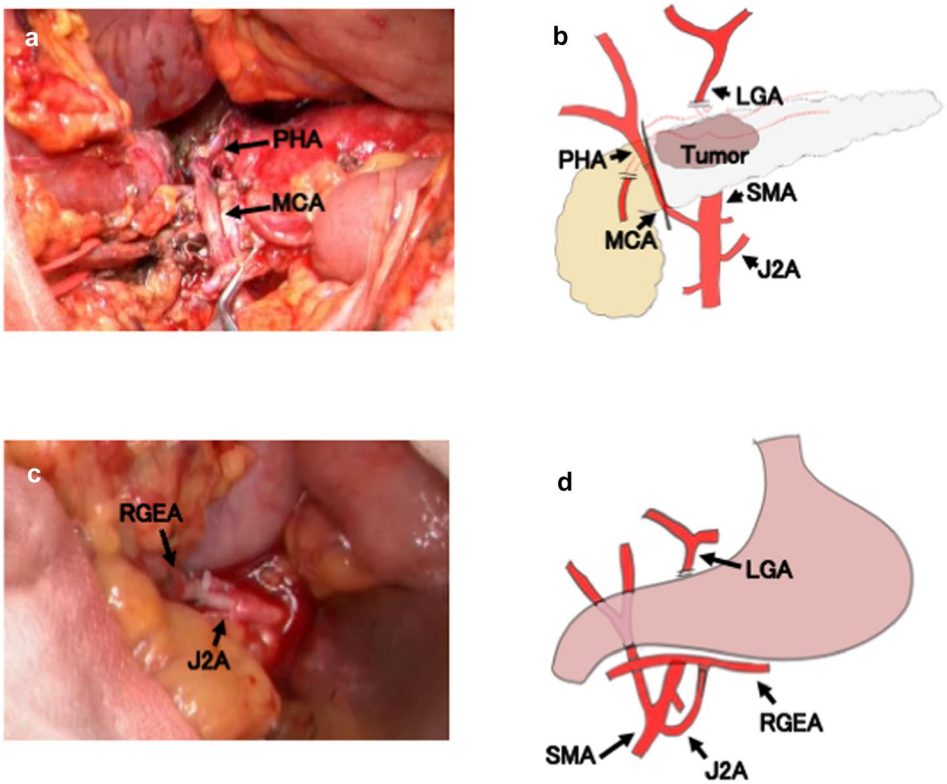

Fig. 6 Intraoperative findings. **a** Middle colic artery-to-proper hepatic artery anastomosis. **b** Schematic of the middle colic artery-to-proper hepatic artery anastomosis. **c** Jejunal artery-to-right gastroepiploic artery anastomosis. **d** Schematic of the jejunal artery-to-right gastroepiploic artery anastomosis

conversion surgery after 19 months of systemic chemotherapy. We performed DP-CAR accompanied by reconstruction of the hepatic artery and right gastroepiploic artery.

Approximately 30–35% of patients with PC are initially diagnosed with URLA PC [11], for which systemic chemotherapy and radiotherapy are commonly selected. Some patients with URLA PC experience significant improvement with such treatment, including tumor shrinkage and significant reductions in tumor markers, thanks to the development of new chemotherapy- and chemoradiotherapy regimens [5, 6, 12, 13]. Interest in conversion surgery for these patients has been increasing in recent years, with the expectation that this will further improve the prognosis for patients with URLA PC. Bickenbach et al. report that the postoperative survival time of patients with unresectable PC who undergo conversion surgery is similar to that of patients with resectable PC [14]. The median survival time of patients with URLA PC treated with conversion surgery is reportedly 14.4–39.7 months [15–18]. Thus, conversion surgery may contribute to the improved prognosis in selected patients with URLA PC, although this has not been proven by a randomized controlled trial.

Standard criteria for conversion surgery have not yet been established. We performed DP-CAR for our patient, combined with reconstruction of the hepatic artery and the right gastroepiploic artery. This procedure is seldom used for conversion surgery; DP-CAR is typically performed when the pancreatic head arterial arcade is free of cancer infiltration and can be preserved to maintain hepatic blood flow [19]. However, the treatment course of our patient appeared to be suitable for conversion surgery: she received chemotherapy for a total of 19 months while maintaining good health, her primary tumor shrank, and her tumor markers were significantly reduced. A recent large cohort study found that preoperative CA19-9 levels are a prognostic factor for survival after conversion surgery for unresectable pancreatic cancer [20]. Satoi et al. report that overall survival is extended when patients undergo chemotherapy or chemoradiotherapy for 8 months or longer before surgery in the setting of unresectable pancreatic cancer [15]. In addition, some prior reports of conversion surgery demonstrate favorable outcomes for radical pancreatectomy with arterial resection [21, 22]. On the other hand, additional radiotherapy was not selected for this patient based on the institutional policy, because it was difficult to find the superiority of additional radio therapy for URLA PC before conversion surgery in previous reports [23–25]. In addition, further prolongation of chemotherapy could cause tumor re-progression, considering that progression-free survival of gemcitabine plus nab paclitaxel and gemcitabine alone in the previous randomized controlled trial was 5.5 and 3.7 months, respectively [6].

Based on our patient's favorable conditions for conversion surgery, we decided to perform DP-CAR with hepatic artery reconstruction. We believe that the results of conversion surgery in this patient justify our decision, since she achieved an R0 resection and benefited from long-term

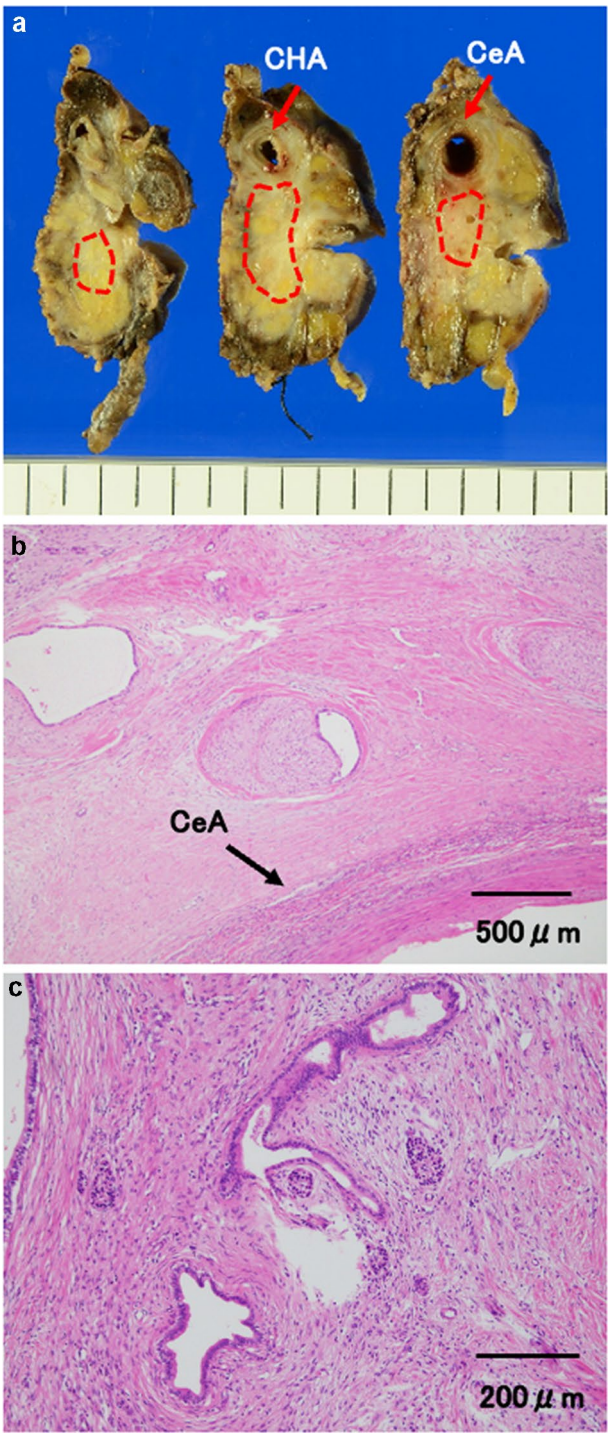

Fig. 7 **a** Histopathologic examination of the resected specimen reveals a tumor measuring 25 × 20 mm. **b** Cancer cells are present in the celiac artery plexus. **c** Approximately 70% of the cancer cells are degenerated and fibrotic, with a class IIb Evans classification

progression-free survival. To the best of our knowledge, this is the first report of a patient with URLA-PC undergoing DP-CAR with hepatic artery reconstruction and experiencing more than 5 years of progression-free survival. There is a single prior report of DP-CAR with hepatic artery reconstruction, but the long-term outcomes are not reported [26]. Based on our experience with this patient, we emphasize that one must always consider whether conversion surgery can be performed using arterial resection and reconstruction, even in patients with URLA-PC. It will be important to establish, through large-scale prospective studies, standard indications for conversion surgery in patients with URLA-PC, including the optimal preoperative treatment regimen, the most favorable interval between diagnosis and surgery, and the most useful markers to predict appropriate surgical timing.

Conclusions

Our patient with URLA PC achieved long-term survival by undergoing DP-CAR with reconstruction of the hepatic artery and right gastroepiploic artery. Since the number of patients who will benefit from long-term survival through aggressive surgery may gradually increase, given recent developments in chemotherapy and chemoradiotherapy, it is urgent to establish a standard treatment strategy for conversion surgery for patients with URLA-PC.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Human/animal rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from the patients included in this case report.

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