Liver metastasis surgery followed by radical treatment for pancreatic ductal adenocarcinoma: A case report

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Abstract. The prognosis of patients with pancreatic ductal adenocarcinoma (PDAC) with liver metastasis is poor; therefore, chemotherapy is often selected instead of surgical intervention. However, there are some reports of cases becoming resectable after multidisciplinary treatment. On the other hand, there have been a few cases of long-term survival in which liver metastases were resected first, followed by prolonged chemotherapy and subsequent resection of the primary tumor. The present study describes the case of a patient with PDAC in which a liver metastasis was resected first, followed by chemotherapy and subsequent resection of the primary tumor, resulting in long-term survival. Briefly, a 72-year-old man diagnosed with resectable PDAC was scheduled to undergo subtotal stomach-preserving pancreaticoduodenectomy after neoadjuvant chemotherapy. Intraoperatively, a liver metastasis was detected, and partial hepatectomy was performed. The patient received 13 cycles of modified 5-fluorouracil, leucovorin, irinotecan and oxaliplatin. A subtotal stomach-preserving pancreaticoduodenectomy was then performed when no new lesions were observed. The patient received S-1 as adjuvant chemotherapy for 1 year postoperatively. Currently, 5 years after diagnosis, and 4 years and 3 months after the last surgery, the patient has experienced no recurrence. In conclusion, even if curative surgery is not possible because of a liver metastasis at the time of the initial operation, some patients may achieve long-term survival through resection, and preoperative and postoperative chemotherapy.

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Abbreviations: α-SMA, α-smooth muscle actin; CA19-9, carbohydrate antigen 19-9; CT, computed tomography; EUS, endoscopic ultrasound; FNA, fine needle aspiration; mFOLFIRINOX, modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; H&E, hematoxylin and eosin; MSI, microsatellite instability; NAC, neoadjuvant chemotherapy; PDAC, pancreatic ductal adenocarcinoma; S, segment; SSPPD, stomach-preserving pancreaticoduodenectomy

Key words: PDAC, liver metastasis, surgery, chemotherapy

Introduction

The prognosis of patients with pancreatic ductal adenocarcinoma (PDAC) remains poor, with a 5-year survival rate less than 10% (1). Outcomes are even worse in PDAC cases with distant metastases, particularly in those with liver involvement (2). These cases are typically considered unresectable. Generally, patients with PDAC and liver metastases are treated with palliative chemotherapy rather than surgery, as systemic disease progression is common and surgical intervention has traditionally not been recommended.

However, recent advances in chemotherapy regimens, such as combination therapy with modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) and gemcitabine-based combinations, have led to improved response rates, raising the possibility of conversion surgery in selected cases (3). Such progress has sparked growing interest in expanding surgical indications and reevaluating treatment strategies for advanced PDAC.

Despite these encouraging findings, the clinical criteria for selecting candidates for such aggressive multimodal treatment remain unclear, and evidence is still limited. Furthermore, in most reported cases of successful treatment for liver metastases from PDAC, conversion surgery was performed following long-term chemotherapy (4-7). Reports describing an alternative approach, initial resection of liver metastases followed by chemotherapy and subsequent radical resection of the primary tumor, are extremely limited (8).

Here, we report a patient with PDAC in which the liver metastasis was resected first, followed by conversion surgery of the primary tumor, and who has remained disease-free for >4 years.

Case report

In May 2020, a 72-year-old man with a history of diabetes and hypertension presented to his physician with decreased

appetite and weight loss. Blood tests revealed liver dysfunction, and computed tomography (CT) showed a 2 cm tumor in the pancreatic head with poor contrast enhancement (Fig. 1). In July 2020, the patient was referred to the gastroenterology department of our hospital. His blood test results were as follows: carbohydrate antigen 19-9 (CA19-9), 26.7 U/ml (<37.0), and carcinoembryonic antigen, 2.7 ng/ml (<5.0). Endoscopic ultrasound (EUS) revealed a 20 mm tumor in the pancreatic head. Although imaging suggested possible pancreatic head cancer, we planned to administer neoadjuvant chemotherapy (NAC), and an EUS fine-needle aspiration (EUS-FNA) was performed to obtain a definitive pathological diagnosis. However, the results of EUS-FNA did not provide a definitive diagnosis of cancer (Fig. 2). The patient was diagnosed with resectable pancreatic head cancer. In August 2020, the patient was referred to the surgery department. The patient received NAC combination therapy with gemcitabine and S-1. He was scheduled to undergo subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) in October 2020. Intraoperatively, a 1.5 cm liver nodule was found on the surface of segment (S) 3 (Fig. 3). Peritoneal lavage cytology was performed and proved negative for malignant cells. No distant metastatic sites beyond S3 were observed during intraoperative inspection. To confirm the pathological diagnosis and allow for the small chance of complete resection in the future, partial hepatectomy of S3 was performed. Intraoperatively, the liver nodule was diagnosed as an adenocarcinoma, and the SSPPD was discontinued. Although the pathological diagnosis of the primary lesion was not confirmed, the patient was diagnosed with a hepatic metastasis from the pancreatic head cancer based on the clinical context. Although metastasis was not identified preoperatively, a retrospective examination revealed a small metastasis in S3 on the CT performed after NAC completion (Fig. 4). The absence of hepatic metastases prior to NAC, and the lack of elevated tumor markers led to the assumption that the likelihood of distant metastasis was low. These assumptions, along with the difficulty of identifying small lesions at the hepatic margin, contributed to the oversight of the hepatic metastatic lesions.

On postoperative day 19 after hepatic resection, the patient started a 6-month course of 13 cycles of modified FOLFIRINOX. Fluorouracil (2,400 mg/m^2), leucovorin (200 mg/m^2), irinotecan (150 mg/m^2), and oxaliplatin (85 mg/m^2) were administered in a 14-day cycle for PDAC liver metastasis. The primary tumor showed no changes and no new metastatic lesions were found on dynamic CT, positron emission tomography-CT, or gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging (MRI).

After obtaining informed consent, we decided to perform the SSPPD as a conversion surgery in May 2021. There was no evidence of metastatic lesions during the operation. Owing to surgical adhesions, the operation lasted 657 minutes, with a blood loss of 2,806 ml. The patient required 4 units of red blood cells and 4 units of fresh frozen plasma. A small intra-abdominal abscess and wound infection were observed; however, these improved with antibiotic treatment, and the patient was discharged on the 18th postoperative day.

Histopathological findings revealed that, according to the 8th edition of the Union for International Cancer Control guidelines, the diagnosis was T3N0M1 well-differentiated adenocarcinoma. The estimated residual cancer cell rate following chemotherapy is between 50 and 90%, corresponding to Evans grades IIa-IIb (9). Hematoxylin and eosin (H&E) staining of the pancreatic specimen revealed that atypical cells with enlarged round nuclei and strong staining proliferated invasively while forming large irregularly shaped glandular ducts (Fig. 5A). Immunohistochemical staining revealed positivity for both CK7 (Fig. 5B) and CK20 (Fig. 5C). H&E staining of the liver specimens from the initial procedure revealed similar findings (Fig. 5D), and immunohistochemical staining was positive for both CK7 (Fig. 5E) and CK20 (Fig. 5F). Based on the above findings, the liver tumor resected during the initial procedure was diagnosed as a PDAC liver metastasis.

Postoperatively, the possibility of readministering modified FOLFIRINOX, which had been administered preoperatively, was considered; however, considering the patient's tolerance, S-1 was selected instead. Approximately 1 year after the initiation of adjuvant chemotherapy, symptoms including muscle weakness and ptosis appeared, leading to the discontinuation of adjuvant chemotherapy. He was followed up at the outpatient clinic every 3 months. At the time of this case study, 5 years after the start of treatment and 4 years and 3 months after the last operation, the patient is still alive without any recurrence.

We investigated the favorable clinical course of this patient by examining the types of genetic mutations and characteristics of the immune microenvironment. The presence of specific genetic mutations has been linked to a more favorable prognosis in PDAC. For example, patients with tumors with high microsatellite instability (MSI) have been reported to achieve a 5-year survival rate of 77% (10). We requested MSI testing for this case from SRL Inc., and the result was negative. MSI testing was performed using formalin-fixed, paraffin-embedded tumor tissue. The specimen was fixed in 10% neutral buffered formalin for 60 h and sectioned at 5 μm thickness. Macrodissection was applied to enrich tumor areas and tumor cellularity was confirmed to be about 20%. DNA was extracted from unstained slides and subjected to multiplex PCR amplification targeting five mononucleotide repeat markers: BAT-25, BAT-26, NR-21, NR-24, and MONO-27. Fragment analysis was conducted via capillary electrophoresis, and peak profiles were analyzed using dedicated software provided by SRL Inc. MSI status was determined based on the presence of instability in multiple markers. Samples showing instability in two or more markers were classified as MSI-High, while those with no instability were considered microsatellite stable. The assay was performed under room temperature conditions.

High expression of α-smooth muscle actin (α-SMA) in PDAC has been reported to be associated with poor prognosis (11). In our patient, although α-SMA was diffusely expressed in the peritumoral stroma, no areas of strong staining were observed (Fig. 7A). Furthermore, although CD10-positive pancreatic stellate cells have been reported to promote PDAC progression (12), CD10-positive stromal cells were not detected (Fig. 7B). Although MSI was low, weak α-SMA positivity and negative CD10 expression suggest that the malignancy of the PDAC cells was low, which may be related to the favorable prognosis in this patient.

The histopathology techniques were as follows: Tissue samples were fixed in 10% neutral buffered formalin solution

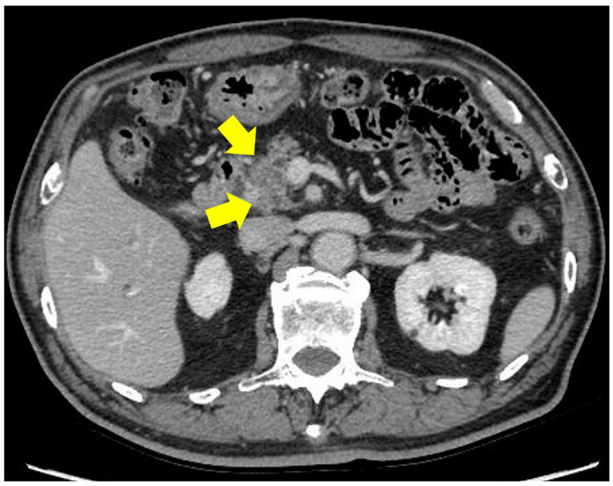

Figure 1. Image findings of contrast-enhanced dynamic-computed tomography before neoadjuvant chemotherapy. Image shows a hypovascular tumor of the pancreatic head (yellow arrow).

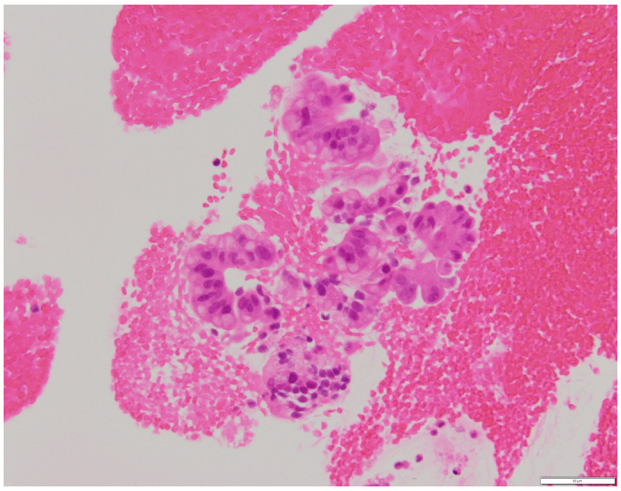

Figure 2. Hematoxylin and eosin staining of the endoscopic ultrasound-fine-needle aspiration specimen revealed focal nuclear enlargement and disorganized nuclear arrangement; however, atypical cells were scarce, and a definitive diagnosis of adenocarcinoma could not be established.

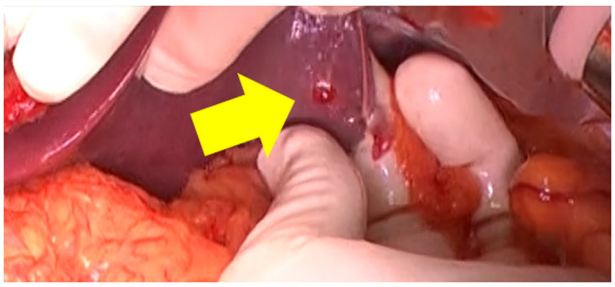

Figure 3. Intraoperative finding. A 1.5-cm nodule on the surface of liver segment 3 (S3) (yellow arrow).

at room temperature for 60 h, paraffin embedded, cut to 3 μm thick, and dewaxed as per standard procedures (13). H&E staining was performed at room temperature for 10 min for Hematoxylin and 4 min for Eosin. The microscope was an Olympus BX53 (light microscope). The following primary antibodies were used in immunohistochemical staining: smooth muscle actin (SMA) (1:4; clone1A4; Cat. No.: IR61161-2; Dako), and CD10 (Ready to use, clone 56C6; Cat. No.: 413261; Nichirei). CC1 buffer (Cat. No. : 950-124; Roche) was used for antigen retrieval. The antigen retrieval step was performed at 95˚C for 64 min. Primary antibody incubation was performed at 36˚C for 32 min. Secondary antibody (ultraView Universal DAB Detection Kit; Cat. No.; 951-124; Roche) incubation was performed at 36˚C for 20 min.

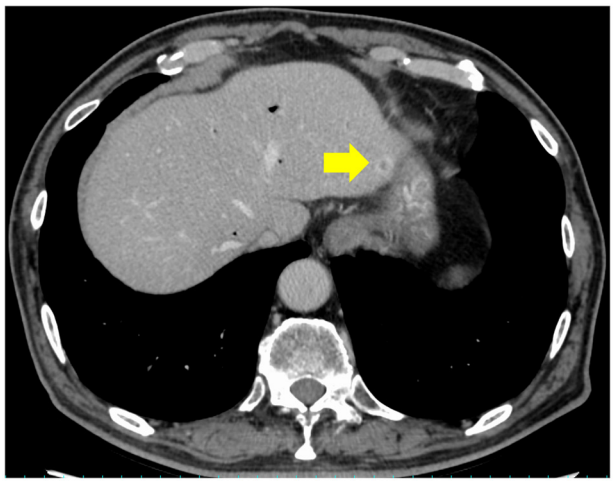

Figure 4. Image findings of the contrast-enhanced dynamic-computed tomography performed after NAC. Image shows an 8-mm ring-enhanced nodule in liver segment S3 (yellow arrow).

Discussion

Despite advances in multidisciplinary treatment options, the 5-year survival rate of patients with PDAC remains below 10% (1). In particular, for PDAC with distant metastasis or recurrence, surgical intervention is not recommended except in patients with remnant pancreatic recurrence (14,15). In recent years, even in select patients with lung metastasis, improved prognoses have been reported after surgical resection (16). Similarly, for other types of metastatic recurrence, there has been an increase in reports showing favorable outcomes for oligometastases treated using multidisciplinary approaches, including surgery. Although liver metastases from PDAC are associated with poor prognosis (2), some reports have demonstrated the utility of resection in such patients (3). Yamada *et al* (17) reported that achieving long-term survival through resection alone for liver metastases is difficult, emphasizing the importance of developing new treatment modalities. However, there are some reports of achieving long-term survival through metastatic lesion resection for PDAC liver metastasis with comprehensive treatment (18-20). Sakaguchi *et al* (4) reported that the median overall survival in patients with synchronous liver metastases who underwent conversion surgery following a favorable response to initial chemotherapy was 27 or 34 months. Frigerio *et al* (5) reported that local resectability, good nutritional status, and low inflammatory scores could be useful indicators for predicting the benefits of chemotherapy

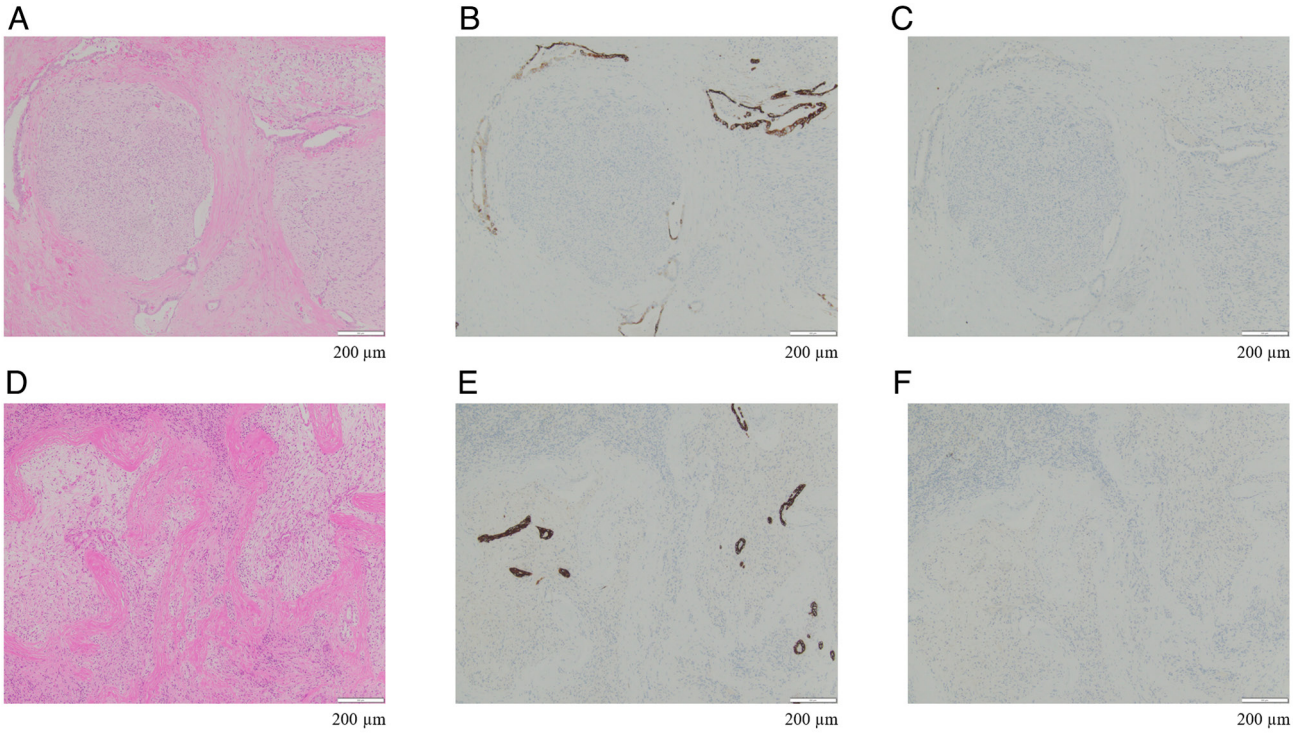

Figure 5. (A) H&E staining of the pancreatic specimens. Atypical cells with enlarged, round nuclei and strong staining proliferated invasively while forming large, irregularly shaped glandular ducts. Immunohistochemical staining of the pancreatic specimens; (B) CK7 and (C) CK20 were positive. (D) H&E staining of the hepatic specimen. It shows an appearance similar to that of the pancreatic specimen. Immunohistochemical staining of the hepatic specimens; (E) CK7 and (F) CK20 were positive. Scale bar, 200 μm. H&E, hematoxylin and eosin.

Figure 6. Clinical course of this patient. Throughout the course, the tumor markers consistently remained within the normal range. GS, combination therapy of gemcitabine and S-1; mFOLFIRINOX, modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen.

and surgical resection. Furthermore, Lu *et al* (6) recommended the resection of metastatic lesions only for patients where (I) R0 can be achieved, (II) the primary tumor has responded to neoadjuvant chemotherapy, (III) oligometastasis is resectable, and (IV) the patient is in good health with few comorbidities. Changes in CA19-9 levels and the RECIST criteria appear to be important considerations for conversion surgery.

A systematic review by Clements *et al* demonstrated the efficacy of surgical resection for PDAC with liver

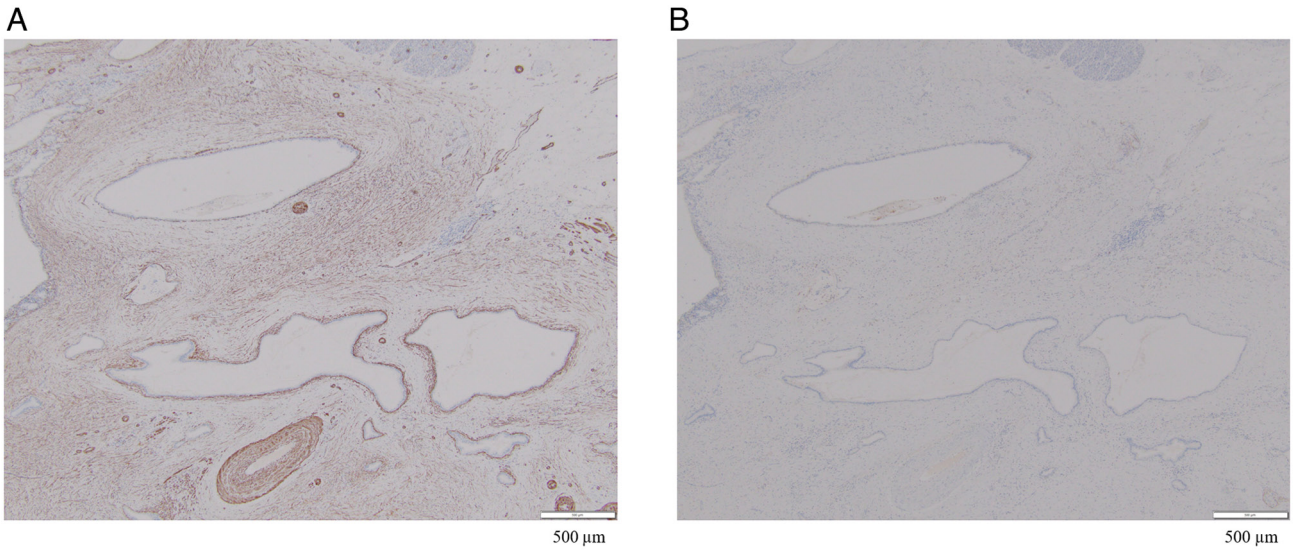

Figure 7. (A) In pancreatic specimens, immunohistochemical staining for α-SMA revealed diffuse staining of the stroma surrounding the carcinoma, but no areas showed particularly strong positivity. (B) Immunohistochemical staining of the pancreatic specimens. CD10 was negative in the stromal cells. α-SMA, α-smooth muscle actin. Scale bar, 500 μm.

metastases (7). They identified the following 3 factors as important: i) response to induction chemotherapy, ii) ability to achieve R0 resection, and iii) minimally invasive approaches, which remain critical for optimal patient selection.

In this case, the patient had no vascular invasion, was in good health, had good nutritional status, and had no findings suggestive of inflammation. The CA19-9 levels remained consistently within the normal range throughout the study period (Fig. 6). These findings suggested that the patient had a favorable long-term prognosis.

One characteristic of this patient was the sequential resection of only the metastatic liver lesion, followed by resection of the primary lesion. There is only one case report of PDAC with synchronous liver metastasis in which, after prolonged chemotherapy, the liver metastasis was resected and a pathological complete response was confirmed before proceeding to curative resection (8). All other reports either administered chemotherapy until the liver lesions disappeared and then performed pancreatectomy alone or carried out simultaneous resection of both the pancreatic primary and liver metastases.

By performing hepatectomy alone rather than radical resection upon identification of the oligometastasis in S3 of the liver, we were able not only to confirm the diagnosis but also to initiate intensive chemotherapy promptly postoperatively and fully observe its excellent chemosensitivity.

The implications of this case are as follows: If a liver metastasis that was not identified preoperatively is discovered incidentally intraoperatively, and it is determined that the lesion may be controllable, it should be resected for diagnosis and future curative treatment. Subsequently, chemotherapy should be administered while assessing the disease status through various modalities for PDAC with distant metastasis. Surgical intervention may be useful if the disease is controlled and deemed curable.

In conclusion, in patients with PDAC with liver metastases, chemotherapy is typically administered first, and resection is considered if disease control is satisfactory. However, as demonstrated in the present case, even when hepatic metastasis is initially resected, a favorable response to chemotherapy can permit subsequent curative resection, leading to an excellent prognosis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

TT contributed to the conception and design of the study, acquisition of data, and analysis and interpretation of the findings, in addition to drafting the manuscript. MT revised the manuscript. NM performed EUS and other diagnostic procedures, leading to the diagnosis of PDAC in the patient. MT, KF and YM performed the procedures. THi and THa were responsible for postoperative management of the patient and contributed to determining the postoperative treatment strategy. JA made the diagnosis based on imaging findings. HO determined the pathological diagnoses. TT and MT confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

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

Competing interests

The authors declare that they have no competing interests.

References

1. Siegel RL, Miller KD and Jemal A: Cancer statistics, 2016. CA Cancer J Clin 66: 7-30, 2016.
2. Kneuertz PJ, Cunningham SC, Cameron JL, Torrez S, Tapazoglou N, Herman JM, Makary MA, Eckhauser F, Wang J, Hirose K, *et al*: Palliative surgical management of patients with unresectable pancreatic adenocarcinoma: Trends and lessons learned from a large, single institution experience. J Gastrointest Surg 15: 1917-1927, 2011.
3. Wright GP, Poruk KE, Zenati MS, Steve J, Bahary N, Hogg ME, Zuriekat AH, Wolfgang CL, Zeh HJ III and Weiss MJ: Primary tumor resection following favorable response to systemic chemotherapy in stage IV pancreatic adenocarcinoma with synchronous metastases: A Bi-institutional analysis. J Gastrointest Surg 20: 1830-1835, 2016.
4. Sakaguchi T, Valente R, Tanaka K, Satoi S and Del Chiaro M: Surgical treatment of metastatic pancreatic ductal adenocarcinoma: A review of current literature. Pancreatology 19: 672-680, 2019.
5. Frigerio I, Malleo G, de Pastena M, Deiro G, Surci N, Scopelliti F, Esposito A, Regi P, Giardino A, Allegrini V, *et al*: Prognostic factors after pancreatectomy for pancreatic cancer initially metastatic to the liver. Ann Surg Oncol 29: 8503-8510, 2022.
6. Lu F, Poruk KE and Weiss MJ: Surgery for oligometastasis of pancreatic cancer. Chin J Cancer Res 27: 358-367, 2015.
7. Clements N, Gaskins J and Martin RCG II: Surgical outcomes in stage IV pancreatic cancer with liver metastasis current evidence and future directions: A systematic review and meta-analysis of surgical resection. Cancers (Basel) 17: 688, 2025.
8. Shimura M, Mizuma M, Hayashi H, Mori A, Tachibana T, Hata T, Iseki M, Takadate T, Ariake K, Maeda S, *et al*: A long-term survival case treated with conversion surgery following chemotherapy after diagnostic metastasectomy for pancreatic cancer with synchronous liver metastasis. Surg Case Rep 3: 132, 2017.
9. Evans DB, Rich TA, Byrd DR, Cleary KR, Connelly JH, Levin B, Charnsangavej C, Fenoglio CJ and Ames FC: Preoperative chemoradiation and pancreaticoduodenectomy for adenocarcinoma of the pancreas. Arch Surg 127: 1335-1339, 1992.
10. Eikenboom EL, Nasar N, Seier K, Gönen M, Spaander MCW, O'Reilly EM, Jarnagin WR, Drebin J, D'Angelica MI, Kingham TP, *et al*: Survival of patients with resected microsatellite instability-high, mismatch repair deficient, and lynch syndrome-associated pancreatic ductal adenocarcinomas. Ann Surg Oncol 32: 3568-3577, 2025.
11. Sinn M, Denkert C, Striefler JK, Pelzer U, Stieler JM, Bahra M, Lohneis P, Dörken B, Oettle H, Riess H and Sinn BV: α-Smooth muscle actin expression and desmoplastic stromal reaction in pancreatic cancer: Results from the CONKO-001 study. Br J Cancer 111: 1917-1923, 2014.
12. Ikenaga N, Ohuchida K, Mizumoto K, Cui L, Kayashima T, Morimatsu K, Moriyama T, Nakata K, Fujita H and Tanaka M: CD10+ pancreatic stellate cells enhance the progression of pancreatic cancer. Gastroenterology 139: 1041-1051, 2010.
13. Sato M, Kojima M, Nagatsuma AK, Nakamura Y, Saito N and Ochiai A: Optimal fixation for total preanalytic phase evaluation in pathology laboratories: A comprehensive study including immunohistochemistry, DNA, and mRNA assays. Pathol Int 64: 209-216, 2014.
14. Thomas RM, Truty MJ, Nogueras-Gonzalez GM, Fleming JB, Vauthey JN, Pisters PW, Lee JE, Rice DC, Hofstetter WL, Wolff RA, *et al*: Selective reoperation for locally recurrent or metastatic pancreatic ductal adenocarcinoma following primary pancreatic resection. J Gastrointest Surg 16: 1696-1704, 2012.
15. Miyazaki M, Yoshitomi H, Shimizu H, Ohtsuka M, Yoshidome H, Furukawa K, Takayasiki T, Kuboki S, Okamura D, Suzuki D and Nakajima M: Repeat pancreatectomy for pancreatic ductal cancer recurrence in the remnant pancreas after initial pancreatectomy: Is it worthwhile? Surgery 155: 58-66, 2014.
16. Groot VP, Blair AB, Gemenetzis G, Ding D, Burkhart RA, van Oosten AF, Molenaar IQ, Cameron JL, Weiss MJ, Yang SC, *et al*: Isolated pulmonary recurrence after resection of pancreatic cancer: The effect of patient factors and treatment modalities on survival. HPB (Oxford) 21: 998-1008, 2019.
17. Yamada H, Hirano S, Tanaka E, Shichinohe T and Kondo S: Surgical treatment of liver metastases from pancreatic cancer. HPB (Oxford) 8: 85-88, 2006.
18. Imai K, Margonis GA, Wang J, Wolfgang CL, Baba H and Weiss MJ: Liver metastases from pancreatic ductal adenocarcinoma: Is there a place for surgery in the modern era? J Pancreatol 3: 81-85, 2020.
19. Gu J, Xu Z, Ma Y, Chen H, Wang D, Deng X, Cheng D, Xie J, Jin J, Zhan X, *et al*: Surgical resection of metastatic pancreatic cancer: Is it worth it?-a 15-year experience at a single Chinese center. J Gastrointest Oncol 11: 319-328, 2020.
20. Klein F, Puhl G, Guckelberger O, Pelzer U, Pullankavumkal JR, Guel S, Neuhaus P and Bahra M: The impact of simultaneous liver resection for occult liver metastases of pancreatic adenocarcinoma. Gastroenterol Res Pract 2012: 939350, 2012.