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Case Report

A Liposomal Irinotecan and S-1 Combination is Shown to be Efficacious in the Treatment of Metastatic Pancreatic Acinar Cell Carcinoma: A Case Report

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Abstract

Pancreatic acinar cell carcinoma (PACC) represents a rare malignancy within the pancreatic tumor spectrum. Owing to its rarity, the establishment of a standardized chemotherapy regimen for patients presenting with either metastatic disease or recurrence after radical surgery remains elusive. Most previous studies and case reports have used gemcitabine-based and 5-fluorouracil-based regimens, however, no previous study has reported the use of liposomal irinotecan in combination with S-1. In this report, we present a patient with PACC who experienced disease progression with liver metastasis after radical tumor resection followed by chemoradiotherapy. The patient underwent second-line treatment with liposomal irinotecan in conjunction with S-1. Encouragingly, the patient has remained free of recurrence and progression during a follow-up period of 2 years and 3 months.

Keywords: Liposomal irinotecan, pancreatic acinar cell carcinoma, S-1

Introduction

Pancreatic acinar cell carcinoma (PACC) is a rare malignancy comprising only 1% of pancreatic neoplasms. It typically occurs around the age of 60.[1-3] Histopathologically, PACC exhibits high cellularity with a lobular architecture, minimal stroma, and positive immunohistochemical staining for exocrine enzymes such as trypsin and lipase.[1] Nearly half of patients (42%~54%) present with advanced disease during the initial diagnosis, often characterized by lymph node involvement or distant metastasis. The most common metastatic site is the liver.[3,4] Compared to pancreatic ductal carcinoma (PDAC), PACC typically presents with larger tumors, but fewer patients present with obstructive jaundice. Overall, the prognosis for PACC is better than for PDAC.[1]

There is currently no consensus regarding the optimal management for PACC due to a lack of prospective clinical

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trials. Surgical resection is the cornerstone of resectable disease treatment and represents the only potentially curative option.[1] Nevertheless, recurrence remains a significant concern postsurgery, affecting more than half of patients. For metastatic or recurrent disease, various chemotherapy regimens based on gemcitabine or 5-fluorouracil (5-FU) have been reported.[5] The lack of definitive evidence supporting the superiority of any particular treatment regimen for recurrent or metastatic disease highlights the challenges and complexities in clinical decision-making for these conditions.

In this report, we present a case of PACC located at the pancreatic head which recurred following pylorus-preserving pancreaticoduodenectomy and subsequent chemoradiotherapy. The disease was effectively controlled with treatment involving a liposomal irinotecan and S1 chemotherapy regimen.

Case Report

A 57-year-old male patient with Type II diabetes mellitus controlled with insulin presented with 10 kg weight loss over 3 months, poor appetite, and dull abdominal pain. Abdominal computed tomography (CT) revealed a pancreatic head tumor measuring 6.1 cm × 8.0 cm with encasement of the common hepatic artery, accompanied by regional lymph node enlargement. Notably, serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19–9 (CA-199) were within normal limits (CEA: 2.82 ng/mL [<0.5 ng/mL], CA-199: 9.47 unit/mL [<34.0 unit/mL]), and lipase and amylase levels were normal. Fine-needle aspiration performed through endoscopic ultrasound revealed poorly differentiated carcinoma. Comprehensive staging surveys using CT and liver magnetic resonance imaging did not reveal distant metastatic lesions. The clinical staging was T3N1M0.

Following the diagnosis, the patient underwent a pylorus-preserving pancreaticoduodenectomy. A pathological examination revealed a 6.2 cm acinar cell carcinoma. Immunohistochemical staining was positive for CK8/18 and trypsin, while SMAD4 and β-catenin were negative [Figure 1]. The tumor was found to have metastasized to the stomach, and metastatic lymphadenopathy (5 out of 7 lymph nodes, with metastatic periaortic lymph node) was observed. Encasement of the celiac trunk with tumor thrombosis was also identified. Peripancreatic soft-tissue involvement with tumor cells was noted, with a positive margin (R1 resection). The final pathological stage was pT4N2M1.

Disease progression with intra-abdominal lymphadenopathy was detected on a CT scan 1 month after tumor resection, and the patient underwent chemotherapy with nab-paclitaxel and gemcitabine. Upon completion of six cycles of chemotherapy, follow-up CT scans revealed stable disease. Consequently, the patient underwent concurrent chemoradiotherapy with gemcitabine (5000 cGy in 25 fractions). Subsequent imaging studies revealed multiple newly developed hypodense lesions in the liver, and a sonography-guided biopsy confirmed metastatic acinar cell carcinoma.

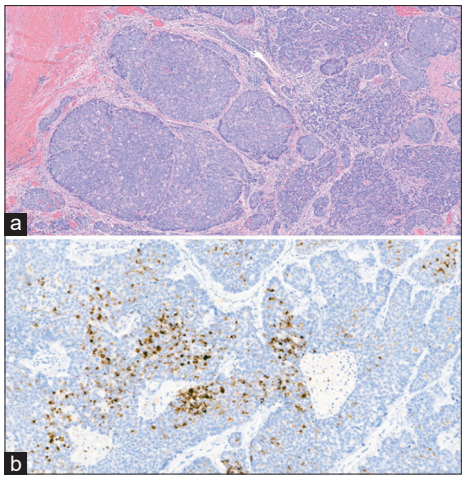

Figure 1: The pathology of the tumor. (a) H and E staining of the pathology reveals a solid to cribriform pattern of tumor cells, characterized by large nuclei and prominent nucleoli. The structure appears obscured compared to the surrounding acinar tissue, although small acinar structures are still discernible. Additionally, increased mitotic activity is evident. (b) The tumor cells showed positive staining with trypsin

One month after completing concurrent chemoradiotherapy, the patient initiated second-line chemotherapy consisting of liposomal irinotecan (70 mg/m^2) with 5-FU (2000 mg/m^2) and leucovorin (350 mg/m^2) administered every 2 weeks. Due to the inconvenience associated with the prolonged 46-h 5-FU infusion, the patient requested an alternative treatment option. Consequently, we switched from infusional 5-FU to oral S-1 (40 mg twice per day), administered in a 14-day cycle, comprising 10 days of medication and 4 days off. The combination of liposomal irinotecan and S1 effectively controlled the patient's metastatic acinar cell carcinoma. The adverse effects were tolerable, except for neutropenia, which eventually improved after granulocyte colony-stimulating factor treatment. A follow-up CT scan after 6 months of treatment revealed no metastatic liver lesions, consistent with a complete treatment response. After 2 years and 3 months of follow-up, subsequent imaging has revealed no disease recurrence [Figure 2].

Discussion

In this case report, we present a patient diagnosed with PACC whose disease was effectively controlled using a combination of liposomal irinotecan and S1. Notably, this is the first reported case of PACC to have demonstrated a favorable response to liposomal irinotecan treatment.

Our patient received gemcitabine and nab-paclitaxel treatment postoperatively, however, the disease progressed within 6 months. Previous studies have reported a high recurrence rate of 52%–64% following tumor resection in patients with PACC.[6,7] This suggests a propensity for micrometastasis to occur in these patients, underscoring the potential importance of adjuvant therapy. Nevertheless, evidence regarding the

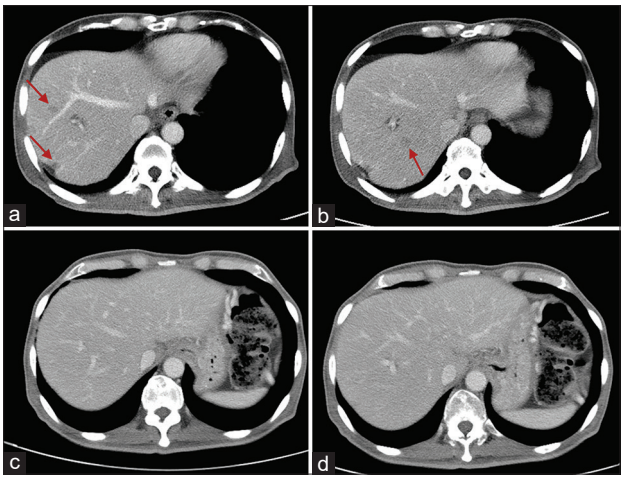

Figure 2: The computed tomography (CT) image before and after liposomal irinotecan and S-1 treatment. (a and b) Before treatment, the CT scan revealed multiple hypodense tumors in the liver. The red arrows in figure a and b show the multiple liver metastases. A sonography-guided biopsy confirmed the presence of metastatic acinar carcinoma. (c and d) Following treatment with irinotecan and S-1, a subsequent CT scan showed no evidence of metastatic liver tumors, consistent with a complete response

effectiveness of adjuvant chemotherapy for the treatment of PACC remains inconclusive due to conflicting data.[7,8]

The standard chemotherapy regimen for PACC also remains inconclusive. While a gemcitabine-based regimen has been established as the standard first-line therapy for pancreatic ductal adenocarcinoma, a previous study suggested that 5-FU-based chemotherapy may be preferable over gemcitabine for patients with PACC.[5] S1, also known as tegafur/gimeracil/oteracil, is an oral medication that undergoes metabolism to yield 5-FU. Yoshida *et al*. reported the case of a patient with PACC and multiple liver metastases who had a favorable and sustained response to S1 therapy.[9] However, due to limited evidence, the efficacy of S1 for treating PACC still requires further study.

The role of irinotecan in managing PACC has been discussed in small case series and reports. Takahashi *et al*. suggested a potential trend toward improved overall survival with irinotecan-containing regimens compared to nonirinotecan-containing regimens, although the difference did not reach statistical significance.[10] However, to the best of our knowledge, the present case is the first in the literature regarding the use of liposomal irinotecan specifically for PACC. Given the favorable response observed in our case and data supporting the use of irinotecan in the treatment of PACC, further investigations into the efficacy and safety of liposomal irinotecan in this setting are warranted.

As a result of shared genetic alterations, PACCs are chemosensitive to agents with activity against pancreatic adenocarcinomas.[1] According to the NAPOLI-3 study in 2023, NALIRIFOX, which includes liposomal irinotecan, has become a standard of care for patients with PDAC.[11] However, the NAPAN study (clinical trial ID: NCT03986294), a clinical trial investigating the combination of liposomal irinotecan and S-1 for PDAC, is still ongoing. Further research is necessary to evaluate the efficacy of irinotecan combined with S-1 for PACC.

In conclusion, this case report demonstrated a positive response to the combination of liposomal irinotecan with S-1 for metastatic PACC. Nonetheless, additional studies are necessary to establish solid evidence supporting the effectiveness of this treatment regimen for PACC.

Institutional review board statement

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Taichung Veterans General Hospital (protocol number: CE24145A, and date of approval: April 3, 2024).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Data availability statement

All data generated or analyzed during this study are included in this published article.

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Conflicts of interest

There are no conflicts of interest.

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