CASE REPORT

Nab-Paclitaxel Plus Gemcitabine Therapy after Novel Cell-Free and Concentrated Ascites Reinfusion Therapy for Refractory Ascites Associated with Pancreatic Adenocarcinoma: A Case Report

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ABSTRACT

Context Peritoneal dissemination is an important prognostic factor for patients with metastatic pancreatic adenocarcinoma. For an improved prognosis and quality of life, more effective treatment for ascites is necessary. **Case report** We describe a seventy-one-year-old Japanese man with pancreatic adenocarcinoma with malignant ascites who had responded to treatment with Nab-paclitaxel plus gemcitabine after novel cell-free and concentrated ascites reinfusion therapy. For ascites control, KM-CART was performed twice. After that, systemic chemotherapy was initiated. His performance status improved since KM-CART could control the refractory ascites, which allowed chemotherapy to be administered. As a result, the patient survived for 11 months and was able to live without hospitalization for most of this time. **Conclusion** KM-CART may be an effective treatment for refractory ascites associated with cancerous peritonitis of pancreatic adenocarcinoma.

INTRODUCTION

Peritoneal dissemination is an important prognostic factor for patients with metastatic pancreatic adenocarcinoma [1]. Progression of peritoneal dissemination causes accumulation of ascites, resulting in a marked decrease in the patient's quality of life. The prognosis for pancreatic cancer patients with peritoneal carcinomatosis is poor [2]. Some patients may experience an improved prognosis with chemotherapy. However, patients with peritoneal dissemination and a poor performance status only receive best supportive care, and have a corresponding poor prognosis [2]. For an improved prognosis and quality of life, more effective treatment for ascites is necessary.

Cell-free and concentrated ascites reinfusion therapy (CART) is one type of treatment for refractory ascites. In recent years, a novel form of CART, developed by Keisuke Matsusaki (KM-CART), has been introduced as an improvement on conventional CART, with a better therapeutic effect [3]. KM-CART is a novel form of CART with the ability to clean the filtration membrane. Herein, we present a case of pancreatic adenocarcinoma with malignant ascites that had responded to treatment with Nab-paclitaxel (PTX) plus gemcitabine (GEM) therapy after KM-CART.

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CASE REPORT

A Seventy-one-year-old man was admitted to our hospital because of abdominal bloating for 2 weeks. The patient had anorexia and body weight loss of approximately 5 kg within 2 months. A contrast-enhanced computed tomography (CT) scan showed a 3.2cm, delayed enhancing, low-density mass in the pancreatic tail **(Figure 1a)**. According to the CT image, the mass had infiltrated the splenic hilum, splenic artery, splenic vein, and left adrenal gland. In addition, a large amount of ascites was observed, with associated diffuse thickening of the peritoneum of the pelvis **(Figure 1b)**. Since pain presented with abdominal distension, the ascites was punctured and 2320 mL of fluid was drained. The results of cytology indicated class V ascites with adenocarcinoma. Over the next 3 days, the ascites increased markedly and drainage of 2000 mL was necessary. The clinical course is shown in **Figure 2**. Since control of the ascites was the primary medical concern, the patient was transferred to a certified institute of the Japanese CART Study Group on the 12th day after the initial visit, and KM-CART was performed. An ascites puncture

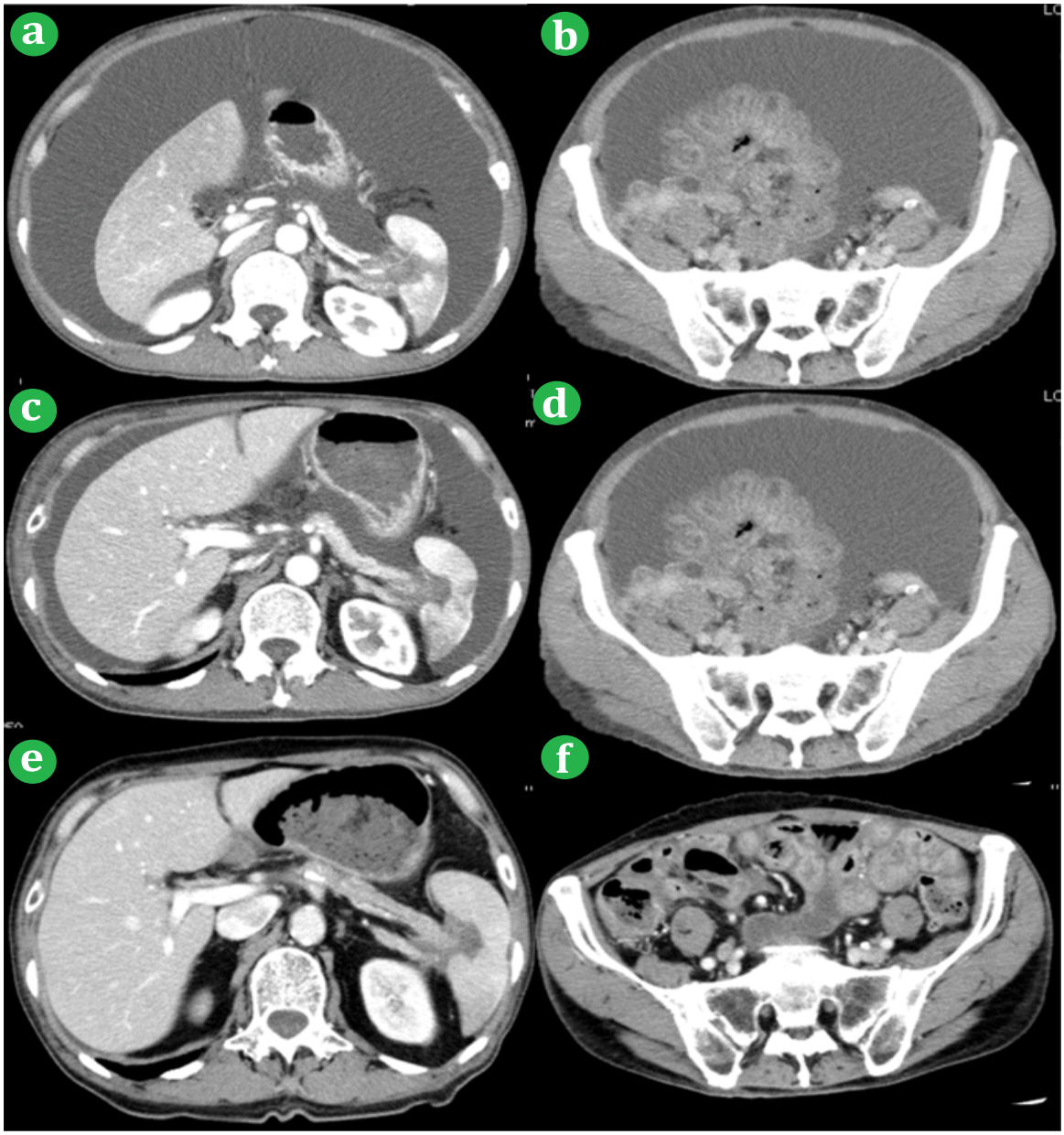

Figure 1. Imaging results of patient's findings.

(a). An initial computed tomography (CT) scan showed a 3.2-cm, delayed enhancing, low-density mass in the pancreatic tail. **(b).** An initial CT scan showed a large amount of ascites, with diffuse thickening of the peritoneum of the pelvis. **(c, d).** According to CT imaging after 3 courses of chemotherapy, the tumor had reduced in size with an associated decrease in the ascites. **(e, f).**According to CT imaging after 6 courses of chemotherapy, the ascites further decreased, with only a minimal amount present in the pelvis.

was performed and 8010 g of chyle ascites was collected. Cellular components, including blood cells and bacteria, were removed from the ascitic fluid using an ascitic fluid filter. Excess water was then removed using an ascitic fluid concentrator. A 1130 g concentrated protein solution was prepared and administered to the patient using intravenous injection, after which the abdominal distention markedly improved. Correspondingly, the patient's appetite recovered and his dietary caloric intake increased, with postural change and improved breathing. As the abdominal distension increased from the 20th day after the initial KM-CART, a second KM-CART was performed 1 week later. A total of 9060 g of ascitic fluid was collected, and 1130 g of concentrated protein solution was administered intravenously. After the second KM-CART, the symptoms subsided and systemic chemotherapy was initiated with PTX plus GEM 41 days after the initial visit. Chemotherapy was administered on days 1, 8, and 15 of a 28-day cycle and included Nab-PTX at 125 mg/m^2 and GEM at 1000 mg/m^2. There were no major adverse events after the start of chemotherapy. For treatment of the ascites, furosemide at 40 mg/day was started on the 48th day after the initial visit, with therapy changed to 20 mg furosemide and 25 mg spironolactone 55 days after the initial visit. Control of the ascites was sufficient with diuretics, with adequate dietary intake and no sign of abdominal distension. After 3 courses of chemotherapy, a CT scan revealed tumor size reduction, as well as a decrease in ascites **(Figures 1c, d)**. After 6 courses of chemotherapy, ascites was further decreased, with only a minimal amount present in the pelvis **(Figures 1e, f)**. The Nab-PTX dose was reduced to 80% because of the development of peripheral neuropathy during the 8th

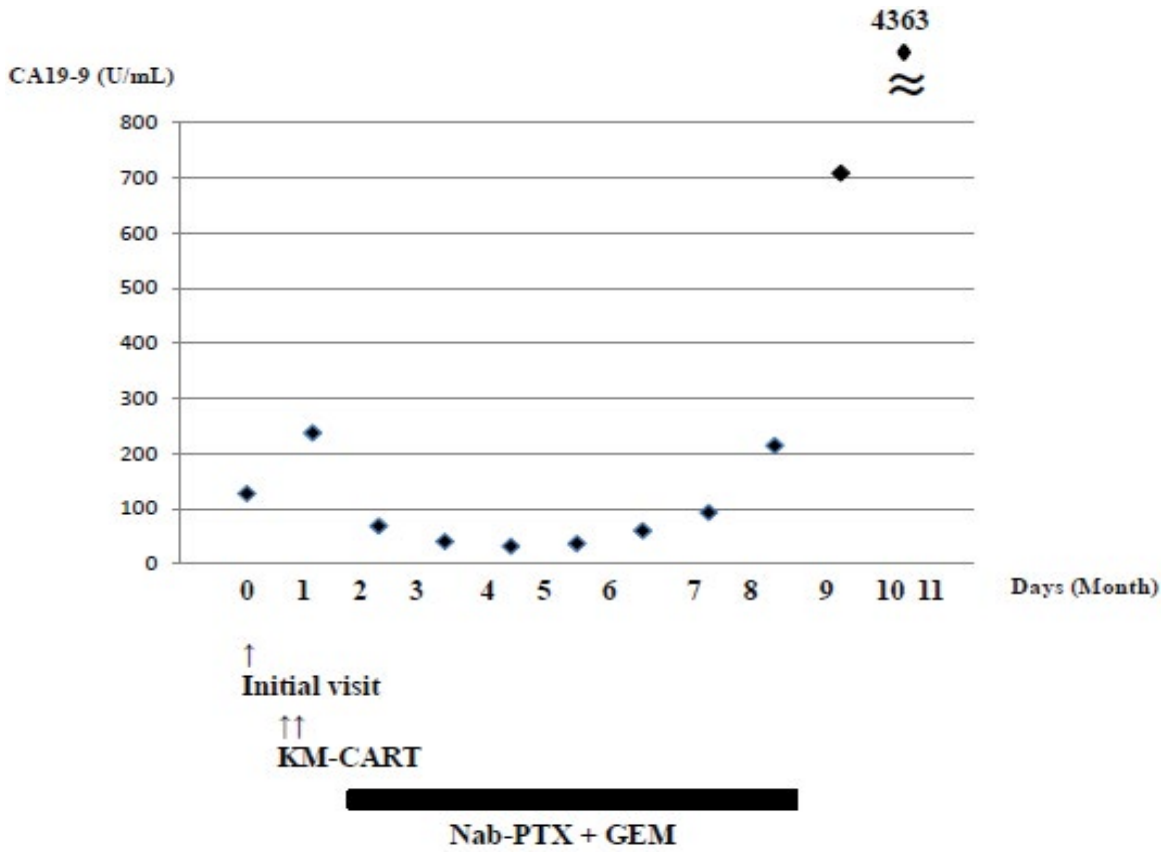

Figure 2. Clinical course of the patient.

course, and chemotherapy was continued up to a total of courses. Cancer antigen 19-9 (CA 19-9) levels increased from the end of the 9 courses **(Figure 2)**, and both the primary and disseminated foci were enlarged on CT imaging. After 10 months, ascites increased markedly and supportive therapy was administered. After 11 months, the patient died following deterioration of his general condition.

DISCUSSION

The prognosis of pancreatic cancer is poor, especially when it is accompanied by peritoneal dissemination. Takahara *et al*. reported that malignant ascites caused by peritoneal carcinomatosis developed in 15% of patients with advanced pancreatic cancer, with a median survival of 47 days [2]. In addition, their study reported that all patients with a performance status of 3 or 4 received best supportive care and had extremely poor prognoses with a median overall survival of 15 days [2]. In recent years, various chemotherapeutic drug combinations for the treatment of pancreatic cancer have become available [4]; Nab-PTX plus GEM therapy is one such treatment option [5]. However, patients benefiting from chemotherapy typically have an optimal performance status. Therefore, patients with malignant ascites require more effective treatment.

CART is the traditional treatment for malignant ascites, with Britton [6] reporting its application in a case of liver cirrhosis-derived ascites in 1961. However, cancerous ascites includes many cellular components, as well as mucus, and purification is a challenging process. Therefore, CART disappeared from the field of cancer treatment in the 1990s [3, 7]. To solve the problems associated with CART, Matsusaki *et al*. constructed the KM-CART system in 2008; it has a simpler circuit and employs an external pressure system with a membrane cleaning function [3]. The method significantly reduces the risk of membrane clogging, which allows a large amount of cancerous ascites to be quickly filtered and concentrated [3]. Clinically, KM-CART has been reported to be an effective treatment for cancerous ascites associated with ovarian cancer, gastric cancer, gallbladder cancer, colon cancer, and pancreatic cancer [3, 7].

CONCLUSION

In this case, the patient's performance status improved since KM-CART could control the refractory ascites, which allowed chemotherapy to be administered. As a result, the patient survived for 11 months and was able to live without hospitalization for most of this time. KM-CART may be an effective treatment for refractory ascites associated with cancerous peritonitis of pancreatic adenocarcinoma.

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Conflict of Interest

The authors have declared that no competing interests exist.

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