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【 CASE REPORT 】

Dramatic Response to Carboplatin Plus Paclitaxel in Pancreatic Mucinous Cystadenocarcinoma with Liver Metastasis

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Abstract:

Mucinous cystic neoplasm (MCN) of the pancreas is a rare cystic tumor occurring in the pancreatic body and tail in young to middle-aged women that is pathologically characterized by an ovarian-like stroma. Chemotherapy for recurrent/advanced pancreatic MCN has been based on chemotherapy regimens for pancreatic ductal adenocarcinoma, but the prognosis is poor. We herein report a 37-year-old woman with pancreatic mucinous cystadenocarcinoma with liver metastasis that responded dramatically to carboplatin plus paclitaxel therapy (CBDCA+PTX). CBDCA+PTX may be a treatment option for recurrent/advanced pancreatic MCN with an ovarian-like stroma.

Key words: pancreas, mucinous cystadenocarcinoma, carboplatin, paclitaxel

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Introduction

Mucinous cystic neoplasm (MCN) of the pancreas is a rare cystic tumor occurring exclusively in the pancreatic body and tail of young to middle-aged women. MCN is pathologically characterized by an ovarian-like stroma (1). Surgical resection is recommended after the diagnosis of MCN because of the risk of malignancy (2, 3). Chemotherapy for recurrent/advanced pancreatic MCN has been based on chemotherapy regimens for pancreatic ductal adenocarcinoma, but the prognosis is poor (4, 5).

We herein report a 37-year-old woman with pancreatic mucinous cystadenocarcinoma (MCC) with liver metastasis that responded dramatically to carboplatin plus paclitaxel therapy (CBDCA+PTX).

Case Report

A 37-year-old woman was examined at another hospital with a complaint of a high fever. Abdominal ultrasonography showed a liver mass, and the patient was treated with antibacterial agents for a suspected liver abscess. However, the patient's condition did not improve, so she was referred to our hospital. The patient did not have any personal or family history of cancer. Laboratory tests revealed leukocytes, 36,430/μL (neutrophil, 89.5%; lymphocyte, 0.5%; monocyte, 5.5%; eosinophil, 0.5%; basophil, 0.5%; metamyelocyte, 3.0%; myelocyte, 0.5%; erythroblast, 1.0%); hemoglobin, 6.3 g/dL; platelets, 579,000/μL; prothrombin

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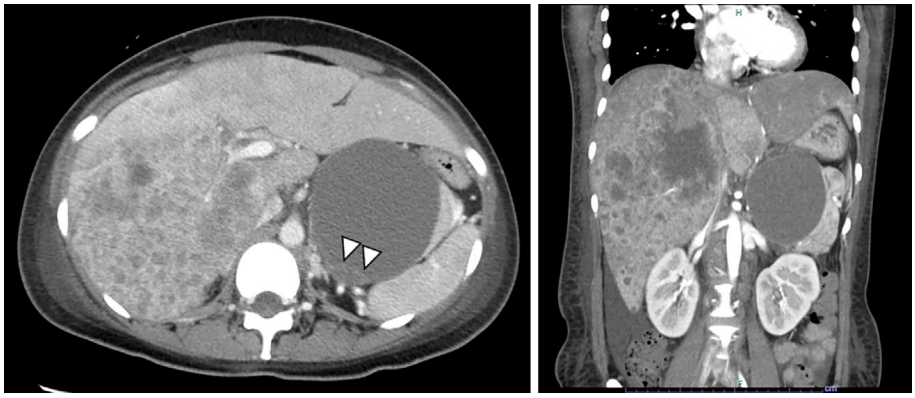

Figure 1. Abdominal computed tomography (A, B) showing a large mass with heterogeneous contrast enhancement occupying the right lobe of the liver and an 85-mm cyst with mural nodule (arrow heads, A) on the tail of the pancreas.

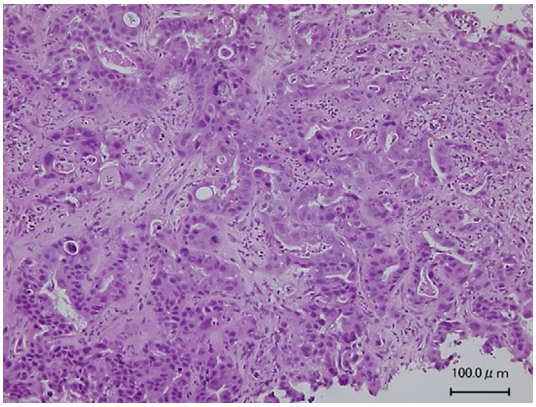

Figure 2. Hematoxylin and Eosin staining of the liver specimen obtained by a trans-venous needle biopsy showing adenocarcinoma with tubular and papillary growths.

time, 21.7 seconds; activated partial thromboplastin time, 31.2 seconds; fibrinogen, 1,257 mg/dL; fibrinogen/fibrin degradation products, 16.9 μg/mL; D-dimer, 8.7 μg/mL; HbA1c, 6.7%; serum aspartate aminotransferase, 63 U/L; alanine aminotransferase, 27 U/L; total bilirubin, 1.11 mg/dL; alkaline phosphatase, 1,031 U/L; lactate dehydrogenase, 443 U/L; amylase, 17 U/L; albumin 1.6 g/dL; C-reactive protein, 16.17 mg/dL; free triiodothyronine, 1.04 pg/mL; free thyroxine, 0.92 ng/dL; thyroid-stimulating hormone, 5.27 μIU/mL; carcinoembryonic antigen (CEA), 94.09 ng/mL; carbohydrate antigen (CA)19-9, 5.7 U/mL; CA125, 13,041 U/mL; and α-fetoprotein, 1.7 ng/mL. Hepatitis B and C were negative. Abdominal contrast-enhanced computed tomography (CT) showed a large mass with heterogeneous contrast enhancement occupying the right lobe of the liver, an 85-mm cyst with a mural nodule on the tail of the pancreas, para-aortic lymphadenopathies, and a large amount of ascites (Fig. 1). The hepatic inferior vena cava (IVC) was severely compressed by the liver tumor, and thrombosis was found in the left lower extremity. A trans-venous needle biopsy of the liver was performed, and adenocarcinoma with tubular and papillary growths was diagnosed (Fig. 2).

Her general condition worsened with the appearance of jaundice for several days (total bilirubin level increased to 4.37 mg/dL). Pelvic magnetic resonance imaging showed normal ovaries. Treatment with CBDCA+weekly PTX was started for the diagnosis of adenocarcinoma of an unknown primary site. After two courses of CBDCA+weekly PTX, the tumor gradually shrank (Fig. 3A, B) and her performance status (PS) improved from 3 to 1. Anemia due to inflammation and liver dysfunction associated with malignancy also improved after her response to chemotherapy (hemogrobin, 10.3 g/dL and total bilirubin, 0.51 mg/dL). The major grade ≥3 adverse events were grade 3 leukopenia, anemia, and thrombocytopenia and grade 4 neutropenia but not febrile neutropenia (Common Terminology Criteria for Adverse Events version 5.0). The thrombosis in her left lower extremity shrank following the administration of warfarin. Fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT after 3 courses of chemotherapy showed significantly reduced tumors in the right lobe of the liver (maximum standardized uptake value: 2.94) (Fig. 3D) and diminished para-aortic lymphadenopathies and ascites. FDG-PET/CT also revealed a high FDG uptake in the right lobe of the thyroid, suggestive of thyroid cancer (maximum standardized uptake value: 7.10). After 10 courses of chemotherapy, the serum CEA and CA125 levels were decreased to 6.3 ng/mL and 20.5 U/mL, respectively (Fig. 4); the liver tumor was reduced from a diameter of 125 to 23 mm; and the maximum response was considered to have been achieved (Fig. 3C); therefore, the patient underwent right hepatectomy with IVC resection and repair using artificial blood vessels, distal pancreatectomy, cholecystectomy, and splenectomy. Tubular and papillary invasive adenocarcinoma was identified from the columnar epithelium of the pancreatic cyst wall, and ovarian-like stroma was noted (Fig. 5A-C). The liver tumor had similar pathological findings (Fig. 5D). Finally, pancreatic MCC with liver metastasis was diagnosed.

After 3 courses of postoperative CBDCA+weekly PTX, the patient underwent right thyroidectomy and D1 lym-

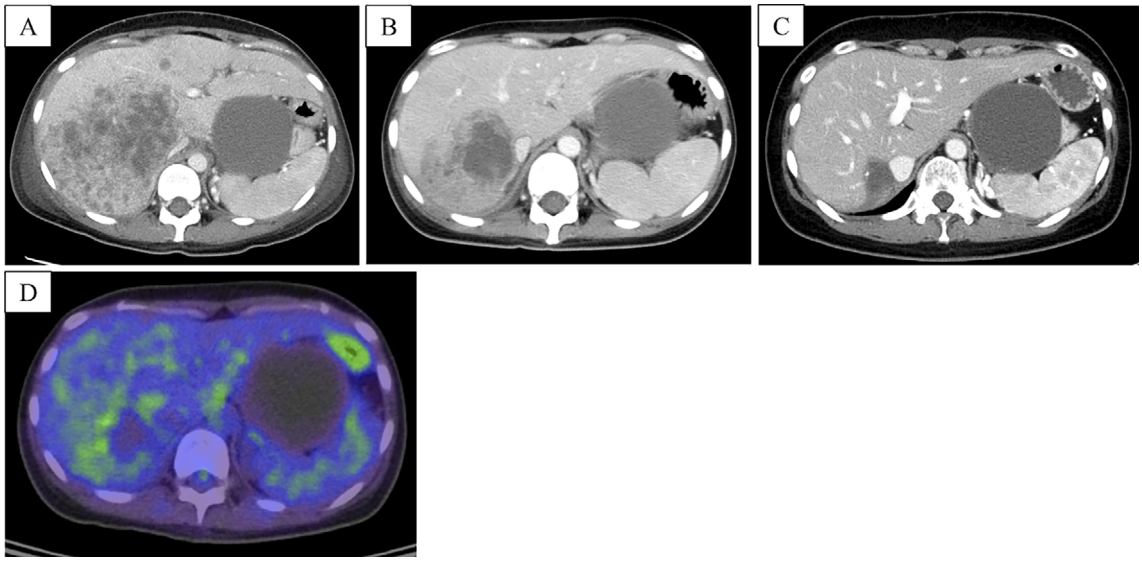

Figure 3. **Abdominal computed tomography before chemotherapy (A), after 2 courses of chemotherapy (B), and after 10 courses of chemotherapy (C). Fluorodeoxyglucose-positron emission tomography/computed tomography after 3 courses of chemotherapy (D) showing a significantly shrunken tumor in the right lobe of the liver (maximum standardized uptake value: 2.94).**

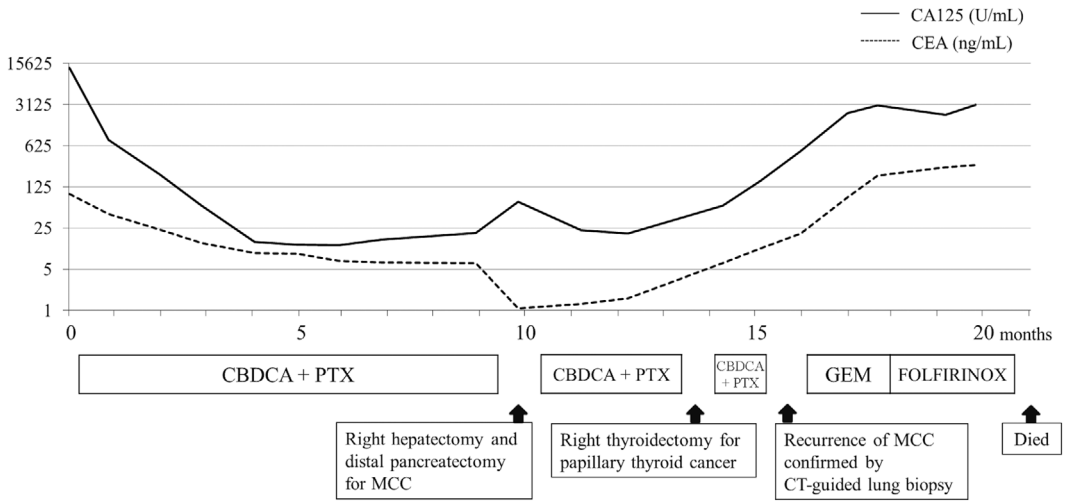

Figure 4. **Clinical course. CEA: carcinoembryonic antigen, CA125: carbohydrate antigen 125, CBDCA+PTX: carboplatin plus paclitaxel, GEM: gemcitabine, FOLFIRINOX: folinic acid plus 5-fluorouracil plus oxaliplatin plus irinotecan, MCC: mucinous cystadenocarcinoma, CT: computed tomography**

phadenectomy for papillary thyroid cancer. After one course of postoperative CBDCA+weekly PTX, the tumor relapsed, with lung metastasis confirmed by a CT-guided needle biopsy. The tumor did not respond to two courses of gemcitabine or six courses of folinic acid plus 5-fluorouracil plus oxaliplatin plusirinotecan (FOLFIRINOX), and she ultimately died of respiratory failure due to multiple lung metastases 21 months after CBDCA+weekly PTX was first started.

Discussion

MCN has a low prevalence of invasive carcinoma (<15% of resected cases), and MCN <4 cm in size without mural nodules tends to be benign (6, 7). Because of the relatively young age of most patients with MCN, the risk of progression to invasive carcinoma, and the common tumor locations of the pancreatic body and tail, surgical resection is recommended for all surgically fit patients (2). In this case, the MCN was large (85 mm in diameter) and had a mural nodule at the initial presentation, so there was a high probability of malignancy. Although the patient had a fairly progressive disease and poor PS, CBDCA+PTX rapidly improved her general condition, resulting in a dramatic therapeutic response. The diagnosis of liver metastasis of pancreatic MCC was ultimately made using surgical biopsies.

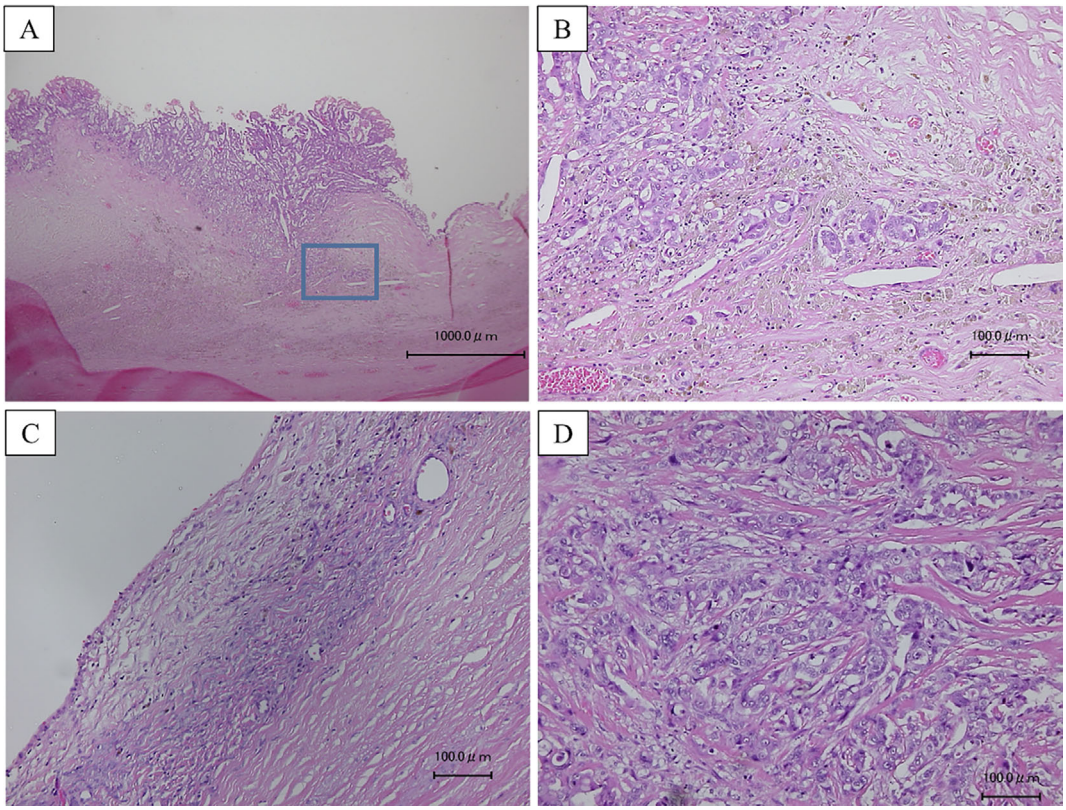

Figure 5. **Hematoxylin and Eosin (H&E) staining of the pancreatic tumor specimen showing tubular and papillary adenocarcinoma with stromal invasion from the columnar epithelium of the pancreatic cyst wall (A, B) and ovarian-like stroma (C). H&E staining of the liver tumor specimen showing tubular and papillary adenocarcinoma (D).**

The most appropriate chemotherapy for recurrent/advanced pancreatic MCN has not been investigated in clinical trials because of the rarity of the disease. In practice, regimens for pancreatic ductal carcinoma are often used. Brunetti et al. reported that 12 of 15 patients with pancreatic MCC were treated with chemotherapy including gemcitabine, and the remaining 3 were treated with FOLFIRINOX as the first-line therapy (4). Three of the 4 patients with an overall survival greater than 15 months received cisplatin plus gemcitabine as the first-line therapy: 1 had a partial response, and 2 had stable disease (SD). All three patients who received FOLFIRINOX as the first-line therapy had SD. The three patients who received gemcitabine plus nab-PTX as the first- or the second-line therapy responded insufficiently to this regimen: one had SD, and two had progressive disease. There have been other case reports of patients with pancreatic MCC who responded well to gemcitabine plus oxaliplatin and were able to undergo surgical resection (8, 9).

Considering the possibility of malignancy of ovarian origin rather than pancreatic/biliary origin in a young woman with high CA125 and normal CA19-9 levels, we chose CBDCA+PTX, which is the standard treatment for cancer of unknown primary site and also a standard treatment for ovarian cancer. Regarding the treatment choice at the time of recurrence, based on the final diagnosis of pancreatic MCC, we selected gemcitabine for the treatment of pancreatic cancer. It is interesting to note that CBDCA+PTX, the first-line therapy for ovarian cancer, worked well in this case of pancreatic MCC with an ovarian-like stroma, whereas the gemcitabine regimen was not successful. The left primitive gonad and dorsal pancreatic primordium are in close proximity at 4-5 weeks of embryonic development, providing evidence explaining the origin of MCN from an ectopic ovary (1). In a review of retroperitoneal MCC, this neoplasm was considered analogous to a primary ovarian tumor due to its similarity to ovarian mucinous adenocarcinoma (10, 11). These findings suggest that platinum-based regimens may be effective against pancreatic MCC.

A large retrospective study of surgically resected MCN cases in Japan recently reported that postoperative recurrences occurred in 2.2% of all MCNs and 19% of malignant MCNs (12). There were no cases of recurrence in benign MCN or minimally invasive carcinoma (T1a), and most recurrences occurred in invasive T3 carcinoma. Adjuvant therapy or neoadjuvant therapy for patients with MCN at high risk of recurrence (if an accurate preoperative diagnosis of the depth can be made) might improve the prognosis of patients with malignant MCN. The investigation of an appropriate chemotherapy regimen is warranted.

In conclusion, we believe this is the first reported patient with pancreatic MCC with liver metastasis to respond to

CBDCA+PTX. CBDCA+PTX may be a treatment option for recurrent/advanced pancreatic MCN with an ovarian-like stroma.

The authors state that they have no Conflict of Interest (COI).

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