CASE REPORT

A patient with unresectable advanced pancreatic cancer achieving long-term survival with Gemcitabine chemotherapy

Yoshiki Okamoto, Takashi Maeba, Keitarou Kakinoki, Keiichi Okano, Kunihiro Izuishi, Hisao Wakabayashi, Hisashi Usuki, Yasuyuki Suzuki

Yoshiki Okamoto, Keitarou Kakinoki, Keiichi Okano, Kunihiro Izuishi, Hisao Wakabayashi, Hisashi Usuki, Yasuyuki Suzuki, Department of Gastroenterological Surgery, Kagawa University, Kagawa 7610793, Japan

Takashi Maeba, Department of Surgery, Social Insurance Ritsurin Hospital, Kagawa 7610793, Japan

Correspondence to: Yoshiki Okamoto, MD, Department of Gastroenterological Surgery, Kagawa University, Miki-cho, Kita-gun, Kagawa 7610793, Japan. oyoshiki2001@yahoo.co.jp
Telephone: +81-87-8912438 Fax: +81-87-891-2439

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Abstract

A 68-year-old female visited a local clinic with epigastralgia. A routine laboratory test revealed jaundice and liver dysfunction. She was referred to this hospital. Abdominal computed tomography (CT) and endoscopic retrograde cholangio-pancreatography (ERCP) revealed that the density of the entire pancreas had decreased, and showed dilatation of the common bile duct (CBD) and the main pancreatic duct (MPD). Pancreatic cancer was diagnosed by cytological examination analyzing the pancreatic juice obtained by ERCP. When jaundice had decreased the tumor was observed *via* laparotomy. No ascites, liver metastasis, or peritoneal dissemination was observed. The entire pancreas was a hard mass, and a needle biopsy was obtained from the head, body and tail of the pancreas. These biopsies diagnosed a poorly differentiated adenocarcinoma. Hepaticojejunostomy was thus performed, and postoperative progress was good. Chemotherapy with 1000 mg/body per week of gemcitabine was administered beginning 15 d postoperatively. However, the patient suffered relatively severe side effects, and it was necessary to change the dosing schedule of gemcitabine. Abdominal CT revealed a complete response (CR) after 3 treatments. Therefore, weekly chemotherapy was stopped and was changed to monthly administration. To date, for 4 years after chemotherapy, the tumor has not reappeared.

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Key words: Gemcitabine; Long-term survival;

INTRODUCTION

Only 10%-20% of patients with pancreatic cancer present with localized or potentially resectable disease at the time of diagnosis, and the majority of patients are diagnosed at either an unresectable or metastatic stage^[1]. The prognosis of patients with advanced unresectable pancreatic cancer remains very poor. When pancreatic cancer is diagnosed, the disease progresses and curability remains unsatisfactory, especially in stage IVb pancreatic cancer^[2]. The Japanese Pancreatic Cancer Registry reported that the mean survival of patients with stage IVb pancreatic cancer is 6.2 mo^[3], and palliation for the relief of jaundice, duodenal obstruction, or pain is required for these patients. Recently, gemcitabine was developed for the treatment of advanced pancreatic cancer, and current studies have reported improvements in survival as well as clinical benefit in patients^[4]. Burris et al. reported that gemcitabine was more effective than 5-fluorouracil in the alleviation of some disease-related symptoms and improved survival was seen in patients with advanced pancreatic cancer^[5].

This report describes a case of advanced pancreatic cancer which was initially diagnosed during laparotomy as unresectable; however, the patient achieved long-term survival of over 4 years, following a treatment regimen of gemcitabine chemotherapy.

CASE REPORT

A 68-year-old female visited a local clinic complaining of epigastralgia. Routine laboratory tests revealed that she had jaundice (T. bil 6.5 mg/dL) and liver dysfunction

Figure 1 Cytological findings from pancreatic fluid. An adenocarcinoma was indicated.

Figure 2 Abdominal CT before surgery. A low density area was observed throughout the entire pancreas, the common bile duct and main pancreatic duct were dilated, the intra-hepatic biliary duct was not dilated. CT: Computed tomography.

(GOT 416 IU/L, GPT 489 IU/L, ALP 2055 IU/L and γ GTP 190 IU/L). Initial laboratory studies included

Figure 3 Needle biopsy performed during laparotomy. A: From the head; B: From the body; C: From the tail of the pancreas. All specimens were diagnosed as poorly differentiated adenocarcinoma.

a serum total bilirubin value of 2.6 mg/dL, serum glutamic-oxaloacetic transaminase (GOT) of 416 U/L, serum glutamic-pyruvic transaminase (GPT) of 489 IU/L, alkaline phosphatase (ALP) of 2055 IU/L, and γ -glutamyl transferase (γ GTP) of 190 IU/L. Her CA19-9 was not elevated (27.8 U/mL). She was referred to this hospital. She had a past history of rhabdomyosarcoma of the urinary bladder at the age of 56. On admission, abdominal computed tomography (CT) revealed that the density of the whole pancreas had decreased, and showed dilatation of the common bile duct (CBD) and the main pancreatic duct (MPD). In addition, stricture of the lower CBD was revealed on magnetic resonance cholangio-pancreatography (MRCP) (Figures 1 and 2). The MPD in the pancreas head appeared irregular on endoscopic retrograde cholangio-pancreatography (ERCP). The presence of pancreatic cancer or biliary duct cancer was suspected, because a cytological examination of the pancreatic juice obtained by ERCP

Figure 4 Abdominal CT. A: 12 mo after CTx; B: 16 mo after chemotherapy (CTx); C: 18 mo after CTx; D: 24 mo after CTx; E: preoperative; F: 1 mo after CTx; G: 2 mo after CTx; H: 6 mo after CTx; CT: Computed tomography; CTx: Chemotherapy.

detected adenocarcinoma cells. After amelioration of her jaundice by biliary drainage through percutaneous transhepatic gallbladder drainage (PTGBD), surgical treatment was selected based on a presumptive diagnosis of pancreatic cancer or biliary duct cancer. Laparotomy revealed no liver metastasis or peritoneal dissemination. The entire pancreas was hard, and a needle biopsy

was obtained from the head, body, and tail of the pancreas. Examination of frozen sections revealed a poorly differentiated adenocarcinoma in each specimen (Figure 3). We therefore considered total pancreatectomy, however, a radical resection was considered excessive. Hepaticojejunostomy was performed. The postoperative course was uneventful. On postoperative day 14,

administration of chemotherapy with 1000 mg/body per week of gemcitabine was initiated. However, because the patient experienced adverse effects, such as eyelid swelling, larynx swelling, grade 1 fever and grade 3 leucopenia and neutropenia, the chemotherapy schedule was thus changed to biweekly, with the additional of granulocyte colony stimulating factor (G-CSF) (Figure 4).

After 3 courses of chemotherapy, an abdominal CT scan revealed a complete response (CR), in which the decrease in density of the entire pancreas had disappeared, and dilatation of the MPD had improved. Therefore, weekly chemotherapy was stopped after 3 courses, and changed to monthly chemotherapy with hospitalization. To date, 4 years after the initial chemotherapy, the tumor has not reappeared.

DISCUSSION

The incidence of pancreatic cancer has recently increased worldwide, and the prognosis of patients with this disease remains very poor^[2,6]. Pancreatic cancer is a major cause of cancer-related mortality in Japan and remains one of the most aggressive diseases in the world. In fact, the National Registry of the Japan Pancreas Society reported that only 9.7% of these patients attained 5-year survival^[7]. Early-stage diagnosis of pancreatic cancer is difficult because of the lack of specific early symptoms, and surgery with a curative intent can be performed in only 5%-20% of patients^[2]. When the diagnosis is made, less than 10% of patients will survive for a year, and many require relief from jaundice and the symptoms of gastric outlet obstruction^[2,5,8,9]. The prognosis for unresectable pancreatic cancer thus remains extremely poor.

Gemcitabine was recently developed for the treatment of advanced pancreatic cancer, and current studies have reported an improved survival as well as clinical benefit in patients treated with this agent^[5,10]. Gemcitabine is a prodrug that requires initial intracellular phosphorylation by deoxycytidine kinase, ultimately undergoing phosphorylation to the active gemcitabine triphosphate, a cytotoxic agent that inhibits DNA synthesis.

Today an extensive pancreatic resection may not influence survival, although some studies have recommended an extensive resection for advanced pancreatic cancer^[11,12]. Gemcitabine has been reported to be a strong factor in influencing the survival of patients after resection of pancreatic cancer, and the resection techniques used may not influence a patient's survival when gemcitabine is administered^[9]. Although stage IVb pancreatic cancer without distant metastasis can technically be resected, it normally does not lead to a good recovery and a satisfactory QOL for the patient. As a result, gemcitabine may be the most effective clinically proven treatment for patients with stage IVb pancreatic cancer.

It is interesting that this case achieved a lengthy CR of 4 years after a gemcitabine dose of 800 mg/m² per month. The prognosis of pancreatic cancer is still

poor, despite the findings in this patient who achieved long-term survival following the administration of gemcitabine for progressive pancreatic carcinoma which could not be excised. In addition, such a high success is surprising. Recently, the receptivity of anti-cancer drugs in cancer therapy has been shown to be remarkable, and there may be a specific mechanism which results in the high receptivity of gemcitabine in pancreatic cancer. The publication of further studies on the use of gemcitabine is therefore necessary. In several phase III studies^[5,13-23], objective responses were observed in 4.4%-17.3% of patients treated with gemcitabine alone. Progression-free survival in patients treated with gemcitabine alone was 2-4 mo and median survival was 5.4-7.3 mo for gemcitabine alone. In these studies, patients received either 1000 mg/m² per week of gemcitabine for 3 wk out of every 4 or for 7 wk out of every 8.

Total pancreatectomy results in complete ablation of the exocrine and endocrine pancreatic functions. Despite the administration of insulin and pancreatic enzyme replacement, total pancreatectomy often results in uncontrollable diabetes, as well as persistent diarrhea and steatorrhea, which compromises patients' nutritional status.

In this case, long-term CR and long-term survival were achieved without excision, however, this is a very rare case. The development of gemcitabine has brought about a change in the treatment of pancreatic cancer, but the effect is less than 20%, and the drug has yet to demonstrate satisfactory results. Gemcitabine may be used as second line treatment in patients who have failed first line therapy. Early detection of pancreatic cancer is important for treatment selection, and gemcitabine has been shown to be effective in some pancreatic cancers, as it was in this case. When it is deemed that an aggressive operation would clearly be disadvantageous to a patient, then the patient may undergo conservative surgery followed by appropriate chemotherapy.

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