Ann. Cancer Res. Therap. Vol. 16, No. 1, pp. 21-22, 2008

Case Report

Advanced Pancreatic Cancer Successfully Treated with Biweekly Low-Dose Gemcitabine

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Abstract

A 74-year-old male was admitted to our hospital in August 2006 because of an exacerbation of the symptom of diabetes mellitus. Abdominal CT showed locally advanced cancer of the head of the pancreas with encasement of the superior mesenteric artery, suggesting that the lesion was unresectable. The patient was scheduled for treatment with gemcitabine at the standard dose of 1000 mg/m^2 once a week for 3 consecutive weeks followed by a one week rest, but on day 7 of cycle 1, grade 3 of hematological toxicity was diagnosed, and the schedule was changed to biweekly administration at a dose of 1000 mg/m^2. The biweekly low-dose gemcitabine regimen slightly reduced tumor size, and the regimen was continued for 12 months. This case suggests that this new biweekly regimen of gemcitabine can be used as a safe and effective first-line chemotherapy for patients with advanced pancreatic cancer who are unable to tolerate the standard regimen of gemcitabine.

Keywords: pancreatic cancer, gemcitabine, biweekly administration

(Received December 25, 2007; Accepted February 4, 2008)

Introduction

The incidence of pancreatic cancer has increased markedly in Japan over the past several decades, and in 2003, the total number of deaths from pancreatic cancer (PC) in the Japan was estimated to be 21,000, representing the fifth most common cause of cancer mortality[1)]. Because of the usually late onset of symptoms, only 10% –15% of patients present with resectable disease, and the majority of patients with pancreatic cancer are candidates for chemotherapy. Gemcitabine has recently come to be widely used as the standard first-line chemotherapy agent for unresectable pancreatic cancer[2)]. Although most gemcitabine toxicities are reversible and manageable, discontinuation of the standard regimen of gemcitabine is not rare, especially in elderly patients. We report a case of advanced PC that was successfully treated by a new low-dose biweekly gemcitabine regimen, and a survival time of 12 months was achieved. This case suggests the possibility that this new biweekly gemcitabine regimen will be effective in patients with unresectable pancreatic cancer who cannot tolerate the standard regimen of gemcitabine.

Case Report

A 74-year-old male was admitted to our hospital in August 2006 because of an exacerbation of diabetes mellitus. Because the patient complained of upper abdominal pain and weight loss, an abdominal CT scan was performed to rule out a gastrointestinal malignancy. The laboratory data on admission were within normal limits, except for an elevated glucose level of 240 mg/dl and carcinoembrionic antigen level (CEA) of 7.8 mg/dl. The CT scan showed locally advanced cancer of the head of the pancreas and encasement of the superior mesenteric artery, suggesting that the lesion was unresectable. The patinet was scheduled for treatment with gemcitabine at a dose of 1000 mg/m^2 once a week for 3 consecutive weeks followed by a one week rest. However, on day 7 of cycle 1, grade 3 hematological toxicity (neutropenia) was diagnosed, and the schedule was switched to biweekly administration at a dose of 1000 mg/m^2. The biweekly regimen slightly reduced tumor size ("stable disease" according to the WHO grading system), and the new regimen was continued for 12 months until tumor size was evaluated as "progressive disease"[3)]. The patient is now being treated with oral S-1 as second-line chemotherapy and has had good performance status for 15 months since the diagnosis.

Discussion

Gemcitabine (2',2'-difluorodeoxycytidine, dFdC) is widely used as the standard chemotherapy agent for advanced PC, and gemcitabine and erlotinib are currently the only agents approved by the US FDA for the treat-

ment of PC[4]. A multicenter, randomized trial by Burris et al. comparing gemcitabine with 5-FU as first-line therapy for patients with advanced PC showed a clinical benefit in the gemcitabine group[2]. Previous clinical trials have reported a median survival time of 5.1 to 6 months when treated with gemcitabine alone, and gemcitabine is the only agent that has shown significant efficacy in terms of prolongation of survival time and symptom relief in patients with advanced PC[2,5,6]. Gemcitabine improved disease-related symptoms in 70% of patients, and increased WHO performance status in 44%[7]. In many studies of gemcitabine for the treatment of PC, the dosage was 1000 mg/m^2 every 7 days for 3 consecutive weeks followed by a 1-week rest (mean dose intensity 500 mg/m^2)[5,7]. This schedule is currently approved in Japan for non-small-cell lung cancer, PC, and biliary tract cancer, and is considered a standard regimen worldwide[5,6,7,8]. Because the Phase II study by Anderson et al. showed little toxicity at the 800 mg/m^2 dose, the 1000 mg/m^2 was chosen as the standard dose thereafter[7]. Moreover, two disease-oriented Phase I trials of dose escalations from 1000 to 3500 mg/m^2/week in non-small-cell lung carcinoma, showed a clear trend toward higher responses at high dose levels (>2200 mg/m^2/week). As a result, the 1000~2200 mg/m^2 dose range has been approved for the treatment of PC[9,10]. The biweekly high-dose gemcitabine regimen (2200 mg/m^2), originally initiated by Ulrich et al. was concluded to have reduced the risk of toxicity of high-dose gemcitabine on the schedule of 3 consecutive weeks of treatment followed by a 1-week rest period[11,12]. Ulrich reported a 21% overall remission rate in 43 patients capable of being evaluated, and a median response duration of 6.5 months, suggesting that the biweekly high-dose gemcitabine regimen is effective palliative therapy for advanced PC. Although gemcitabine has a relatively safe profile compared to other chemotherapeutic agents, major toxicities include myelosuppression and flu-like symptoms, and some patients have not been able to tolerate it because of drug-induced toxicities[9]. In a phase II study of gemcitabine 9% of the patients were switched to reduced dose because of leukopenia and thrombocytopenia[7]. Okusaka et al. found that 27.5% of the biliary tract cancer patients in their series were unable to complete more than one cycle of the standard regimen of gemcitabine[8]. Here we report the possible usefulness of a biweekly low-dose regimen (biweekly dose 1000 mg/m^2, mean dose intensity 500 mg/m^2) for advanced PC and favorable toxicity profile even on the conventional gemcitabine treatment schedule. The most striking result of using this regimen in our patient was a long progression-free time (12 months) without no treatment-related clinical toxicities, including gastrointestinal symptoms. This finding suggests a possible advantage over the best supportive therapy in PC patients who are unable to tolerate the standard regimen of gemcitabine.

We concluded that chemotherapy with a biweekly regimen of low-dose gemcitabine may provide a favorable outcome in advanced PC. Clinicians should be aware of the usefulness of this safe and tolerable biweekly low-dose gemcitabine regimen when treatment with the standard regimen must be discontinued because of toxicity, especially in elderly patients with several complications or patients who present in poor general condition. A randomized controlled trial of a reduced dose of gemcitabine on the standard schedule (days 1, 8, 15) and this biweekly regimen at the standard dose (1000 mg/m^2) should be performed in patients who are unable to tolerate the standard regimen of gemcitabine.

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