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CASE REPORT

Capecitabine in pretreated metastatic cholangiocarcinoma. A case report and review of the literature

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Summary

Cholangiocarcinoma is one of the most aggressive malignancies. Patients with advanced or metastatic disease have a particularly dismal prognosis. The role of chemotherapy remains a matter of debate. A number of recent trials have shown that capecitabine in combination with other agents seems to be active as first-line treatment in advanced biliary cancer. Clinical data regarding the activity of capecitabine in pretreated patients are limited. In this report we describe a patient with previously treated, metastatic cholangiocarcinoma who developed stabilization of the disease for 7 months following chemotherapy with capecitabine. The patient had previously received 2 lines of chemotherapy. Capecitabine was tolerated fairly well without serious adverse events. We consider this observation to be important given the absence of active, non-surgical treatments in unresectable tumors.

Key words: capecitabine, cholangiocarcinoma, metastatic, pretreated

Introduction

Cholangiocarcinoma is a relatively uncommon malignancy in Western countries. Surgical resection is considered the most effective treatment, although the vast majority of these patients are not eligible for surgery. Patients with advanced or metastatic disease have a dismal prognosis, and the majority of them will die within 6 to 12 months from diagnosis [1]. The impact of chemotherapy on patients' outcome remains controversial. To date, no standard chemotherapy regimen has been established for patients with unresectable disease [2].

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Case presentation

A 64-year-old man presented with multiple abdominal lymph nodes, mediastinal lymph nodes and pulmonary nodules in June 2003. Although bronchoscopy did not reveal endobronchial lesions, the cytology of the brushings was positive for adenocarcinoma. Carcinoembryonic antigen (CEA) was elevated (93.5 ng/ml, normal range 0.0-10), however endoscopic examination of the gastrointestinal tract did not yield abnormal findings. The patient was started on palliative chemotherapy with paclitaxel and carboplatin (7/2003-11/2003) as metastatic adenocarcinoma of unknown origin. Following the completion of 6 cycles of chemotherapy the patient developed jaundice. Repetition of imaging procedures (CT scan) and further evaluation by magnetic resonance cholangiopancreatography (MRCP) revealed dilatation of the common bile duct, the common hepatic and the intrahepatic biliary

ducts, findings consistent with a distal bile tract tumor. The diagnosis of cholangiocarcinoma was confirmed by endoscopic retrograde cholangiopancreatography (ERCP) and obstructive jaundice was relieved by placing a stent. Systemic chemotherapy consisting of gemcitabine started on February 2004 and continued until May 2004, when the patient developed cholangiitis simultaneously with an increase of CEA serum level (980 ng/ml). Progression of disease was documented by repeat ERCP. The stent was replaced endoscopically and the patient started oral capecitabine (1250 mg/m^2 twice a day for 14 days every 21 days) in June 2004. Capecitabine was tolerated fairly well without serious adverse events. Evaluation by CT scan demonstrated stabilization of the disease and CEA levels decreased to a minimum value of 170 ng/ml. The patient remained in good general condition, symptom-free without laboratory or radiographic evidence of disease progression for 7 months. In January 2005 the patient developed clinical deterioration with malaise and abdominal pain. Imaging procedures (1/2005) as well as CEA documented progression of the disease. Capecitabine was discontinued after 10 cycles and the patient started an oxaliplatin-based regimen. After 3 cycles of chemotherapy the patient developed further deterioration together with radiographic progression and died in June 2005.

Discussion

Cholangiocarcinoma is one of the most aggressive malignancies. The management of patients with inoperable disease remains a major challenge to medical oncologists. Although the results of a randomized study showed that 5-fluorouracil (5-FU)-based chemotherapy may improve survival and quality of life in patients with advanced biliary tract cancer [3], the role of chemotherapy remains a matter of debate. To date, no standard chemotherapy regimen that can clearly prolong survival has been established. The most extensively studied single agent has been 5-FU but responses have been poor (10-13%) [4,5]. Gebbia et al. have demonstrated improvement in response rates and median survival in biliary cancer with an infusional 5-FU-gemcitabine combination over gemcitabine alone [6].

A number of recent trials have been conducted in order to investigate the role of newer chemotherapeutic agents. Capecitabine in combination with agents such as gemcitabine, mitomycin or cisplatin seems to be active and well tolerated as first-line treatment in advanced biliary cancer with response rates ranging from 21-31% and overall disease control rates (response rate plus disease stabilization rate) ranging from 50-73% [7-9]. Moreover, in a randomised phase II trial in previously untreated patients with metastatic adenocarcinoma of the biliary tract the combination of capecitabine plus mitomycin was found to be superior in terms of response rate, progression-free survival and overall survival compared to gemcitabine plus mitomycin [8]. In another study using single-agent capecitabine in patients with hepatobiliary cancers the treatment was found to be safe, even to patients with cirrhosis, but the antitumor activity was most pronounced in patients with gallbladder carcinoma while it was poor in those with cholangiocarcinoma [10]. In another trial with capecitabine plus cisplatin, gallbladder cancer also appeared to respond more readily to chemotherapy [9] although other studies did not show different chemosensitivity according to primary sites [7]. Furthermore, clinical data regarding the activity of capecitabine in pretreated patients with advanced biliary tract cancer are limited. Stemmler et al. [11] reported 2 patients suffering from metastatic cholangiocarcinoma treated with capecitabine as second-line chemotherapy. In both cases, stabilization of the disease was achieved.

In our report, we also describe a pretreated patient with advanced cholangiocarcinoma who developed clinical and radiographic stabilization of the disease, together with response of CEA levels following chemotherapy with capecitabine. It is noteworthy that our patient had already received 2 lines of chemotherapy. It is also interesting that the stabilization lasted 7 months which is considered as a rather unusual long time, given the aggressiveness of this malignancy. Moreover, in our patient all cycles of chemotherapy were tolerated fairly well and we did not observe grade 3 and 4 toxicity. We consider this observation to be important given the limited options in pretreated, chemoresistant patients. Further studies are warranted to determine the chemosensitivity of this highly lethal malignancy to capecitabine.

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