CASE REPORT

Concurrent Chemoradiation in a Patient with Unresectable Cholangiocarcinoma

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Cholangiocarcinoma is a catastrophic tumor with a high mortality rate, for which surgery is the most reliable treatment. However, these tumors progress insidiously and are difficult to diagnose early. Most patients lack the opportunity to receive surgery due to the advanced disease stage at the time of the diagnosis, at which point only few alternative treatments are available. There is a need for more effective therapy to improve the survival or quality of life of these patients. The present case was a 73-year-old male who presented with jaundice and fatigue underwent CT imaging, in which a 3.5×4.0-cm low-attenuation mass was found in hepatic segment 4. Cholangiocarcinoma was diagnosed by cytological examination of the bile juice. A combination of CyberKnife radiosurgery and S-1 oral chemotherapy was performed. The patient was alive at a 8-month follow-up, and serial CT scans revealed a markedly regressed tumor. Therefore, we suggest that concurrent chemoradiation with the CyberKnife and S-1 is a treatment option for advanced cholangiocarcinoma. (*Gut Liver* 2010;4:103-105)

Key Words: Cholangiocarcinoma; Radiotherapy; Chemotherapy

INTRODUCTION

Cholangiocarcinoma is a destructive cancer arising from biliary epithelia. The prevalence of this disease is approximately 10% to 15% of all hepatobiliary malignancies.¹ This tumor progresses insidiously and death may result in due to liver failure, biliary sepsis, malnutrition and cancer

cachexia. Clinically, treatment options for cholangiocarcinoma are limited. Hepatic resection and liver transplantation are the only curative options for cholangiocarcinoma. However, most patients often present with locally advanced, unresectable disease where extensive tumor spread exists beyond the gross tumor margins. Thus, many patients would not be suitable for surgery.² In patients with unresectable disease, palliative treatments using either or both the chemotherapy, and radiotherapy remain as treatment options. CyberKnife[®] is a newly introduced local approach that allows for accuracy and flexibility in targeting the tumor through the image-guided stereotactic body radiotherapy (SBRT) system.³ It can deliver higher dose of radiation to tumors for local control of tumor mass. We report a case with unresectable cholangiocarcinoma treated with combination of SBRT and S-1 chemotherapy. To our knowledge, this is the first case reporting a patient with advanced cholangiocarcinoma treatment with SBRT and oral chemotherapy.

CASE REPORT

A 73-year-old male was admitted due to jaundice, fatigue and darkening of urine starting two weeks ago. His past medical history revealed was no significantly noticeable disease apart from duodenal ulcer medically treated 6 months ago. No palpable mass was found on physical examination of the abdomen. Laboratory examination demonstrated red blood cells $4.25 \times 10^{12}/L$, hemoglobin 12.3 g/L, white blood cells $4.3 \times 10^9/L$, platelets $2.12 \times 10^{11}/L$, total bilirubin 5.1 mg/dL, direct bilirubin 2.2 mg/dL, as-

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partate aminotransferase 111 IU/L, alanine aminotransferase 201 IU/L, alkaline phosphatase 937 IU/L, γ -GTP 762 IU/L and carbohydrate antigen (CA) 19-9 was 222 U/mL. Hepatitis B surface antigen and hepatitis C virus antibody were negative. The history of alcohol abuse was denied by the patient. Abdominal computed tomography (CT) showed the 3.5×4.0 cm-sized low attenuated mass in hepatic segment 4, invading the bifurcation of intrahepatic duct (IHD) and common hepatic duct (Fig. 1). The cytological examination of bile juice revealed adenocarcinoma.

Palliative treatment was planned. Through the previously preformed bilateral percutaneous transhepatic routes, two biliary stents were inserted into the ob-

structive lesion of both IHD. For the purpose of concurrent chemoradiation, firstly the patient was put under the chemotherapy using S-1 (30 mg/B.S.A. twice a day

Fig. 1. Abdomen CT performed before treatment revealed a 3.5×4.0-cm low-attenuation mass in hepatic segment 4.

Fig. 2. Gold marker: The gold markers were successfully delivered into the liver parenchyme (arrow).

Fig. 3. Serial abdomen CT scans taken after treatment, showing that the tumor gradually became smaller. (A) CT scan taken after radiosurgery and three cycles of S-1 chemotherapy. (B) CT scan taken after six cycles of chemotherapy. (C) CT scan taken after nine cycles of chemotherapy.

for 14 days, 3 weeks/cycle), an oral 5-FU prodrug preparation and radiosensitizer. After 2 weeks, SBRT using synchrony motion tracking system (generation 4 CyberKnife®) was performed after insertion of gold fiducial markers into the liver (Fig. 2). A total 4,500 cGy was delivered in five fractions during 5 consecutive days. Nine cycles of S-1 monochemotherapy was maintained after SBRT.

After radiosurgery treatment, abdominal CT serially checked every 3 cycles showed significant reduction of the tumor volume (Fig. 3). Serum CA19-9 was normalized. The patient is still alive with good performance and there is no sign of tumor progression or distant metastasis 8 months after the treatment.

DISCUSSION

Surgery is the most suitable means for cure in patients with cholangiocarcinoma. With curative surgery, three-year survival rates have been reported to be approximately 40-60%.⁴ However the curative resection in patient with cholangiocarcinoma is often discouraged due to advanced stage at presentation. Patients with advanced unresectable cholangiocarcinoma have a dismal prognosis owing to complications induced by bile stasis. Therefore, palliative therapy is important in aspect of increasing quality of life as well as the survival rate.

Palliative therapy includes chemotherapy, radiotherapy and photodynamic therapy as well as biliary drainage, although the role of each treatment is limited. When treated with chemotherapy, the patients' median survival is approximately 5-9 months.⁵ Palliative external radiation therapy and percutaneous intraluminal iridium-192 for patients with unresectable locally advanced tumors failed to improve survival rate.⁶ In another study, for patients who were treated with external beam radiation therapy with doses of 45-50 Gy, combined with either additional intraluminal brachy therapy boost or chemotherapy, the median survival was only 9-12 months.⁷ Recent report on photodynamic therapy showed some promising results on improving palliation and survival in patients with unresectable hilar cholangiocarcinoma⁸ although further reports should verify its effects. In general the survival rate of cholangiocarcinoma showed no improvement.

CyberKnife® radiosurgery is a SBRT using real time respiratory-motion tracking system, and is known to exert minimal tissue injury around tumor. Therefore high dose of radiation treatment in a few fractions is possible to the targeted tumor mass.

S-1 is an oral type of 5-FU prodrug, and is known for its ability to maintain the therapeutic blood concentration of 5-FU. S-1 plays a role as a radiosensitizer and opti-

mizes the effect of a few fractions of SBRT. Therefore, the treatment of cholangiocarcinoma with SBRT in combination with S-1 chemotherapy is expected to have a meaningful result as palliative treatment. In cholangiocarcinoma where curative resection is not feasible, locally advanced tumors without distant metastasis are frequent. SBRT might have some roles in this kind of tumors although studies have not been carried out. The prospective study may need to be investigated in the future.

No serious complications occurred after SBRT in this particular patient. However, in a previous report where 162 patients with hepatocellular carcinoma were treated with proton beam therapy, late biliary toxicity was observed in two patients after 29 and 38 months following irradiation, respectively. In addition decline in liver function was observed in seven patients.⁹ It seems that SBRT has a potential for liver toxicity. Safety of radiation and appropriate dose should be investigated in a prospective study.

In conclusion, we experienced a case of a patient with advanced, unresectable cholangiocarcinoma treated with concurrent chemoradiation using SBRT and S-1. Although complete remission was not achieved, the tumor markedly reduced in size and did not regrow following SBRT. We suggest that this combined treatment might be a useful treatment option in advanced, unresectable cholangiocarcinoma.

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