Case Report

Effect of Intra-Arterial Cisplatin on Multiple Liver Metastases from Rectal Cancer Associated with Ulcerative Colitis

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SHIBATA, C., JIN, X.-L., FUNAYAMA, Y., FUKUSHIMA, K., TAKAHASHI, K.-I., HASHIMOTO, A., NAGAO, M., HANEDA, S., WATANABE, K., MATSUNO, S., SASAKI, I. and NAITO, H. Effect of Intra-Arterial Cisplatin on Multiple Liver Metastases from Rectal Cancer Associated with Ulcerative Colitis. Tohoku J. Exp. Med., 2004, 202 (1), 57-61 —— We report a patient with synchronous multiple liver metastases from rectal cancer associated with ulcerative colitis. Because the liver tumors were unresectable, we performed total proctocolectomy and hepatic intra-arterial cisplatin infusion with systemic oral administration of fluorouracil. A complete response was obtained. The patient is alive without sign of recurrence 5 years postoperatively. Hepatic intra-arterial administration of cisplatin should be considered in the treatment of unresectable liver metastases from colorectal cancer. ——— cisplatin; colitic cancer; liver metastasis; ulcerative colitis
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Colorectal cancer associated with ulcerative colitis (UC) has been referred to as “colitic cancer.” Although treatment of patients with colitic cancer is similar to other patients with colon cancer (Hirai et al. 2002), the prognosis of patients with unresectable liver metastasis is poor. We report a patient with colitic cancer with multiple liver metastases in whom hepatic intra-arterial (IA) cisplatin achieved and maintained a long lasting complete response for greater than 5 years.

CASE REPORT

A 46-year-old man with a 16-year history of UC was referred with a 7cm distal rectal adenocarcinoma. Preoperative evaluation showed an increase in carcinoembryonic antigen (CEA) of 7.2 ng/ml (normal < 5 ng/ml) and in carbohydrate...
antigen (CA) 19-9 of 728 U/ml (normal <37 U/ml). Computed tomography (CT) showed multiple metastases (Fig. 1A) but no enlarged lymph nodes or ascites. Because the primary tumor was very close to the dentate line, a total proctocolectomy with end-ileostomy was performed (Fig. 2). Multiple small metastases were palpable in the liver during operation. Pathologic examination showed a T3 rectal cancer with metastatic perirectal lymph nodes (Fig. 3). His postoperative course
was uncomplicated.

He was treated with 5 courses of intravenous 5-fluorouracil (5-FU, 250 mg/day) and cisplatin (5 mg/day) postoperatively. CT showed stabilization of the liver metastases (Fig. 1B). He underwent percutaneous transarterial placement of a catheter for hepatic intra-arterial (IA) injection 3 months postoperatively. Hepatic IA cisplatin (5 mg over 2 hours) with oral 5-FU (300 mg/day) was performed weekly for 18 weeks and every other week for 48 weeks. At 5 months postoperatively, only 2 small lesions were evident (Fig. 1C), and at 13 months postoperatively, no lesions were apparent on the CT (Fig. 1D). Although mild liver dysfunction was evident during treatment (AST increased to 54 IU/liter), it did not require stopping the chemotherapy. The hepatic IA catheter was removed after 42 courses of IA chemotherapy. Currently at 68 months postoperatively, no metastatic lesions are evident, and serum CEA and CA 19-9 are within normal range.

**DISCUSSION**

The rectal cancer with flat elevation was found in this patient who had 16 year history as UC, and multiple liver metastases were simultaneously revealed with CT scan. Characteristic features of colitic cancers are, 1) the increase of cancer occurrence with time after the onset of UC (Gyde et al. 1988), 2) multiple cancers (Lennard-Jones et al. 1990), 3) frequent occurrence in the rectosigmoid region (Prior et al. 1982), 4) frequent occurrence in total colitis type (Langholz et al. 1992), 5) high risk in patients with UC who have family history of sporadic colorectal cancer and who complicate primary sclerosing cholangitis (Brentnall et al. 1996; Askling et al. 2001), and 6) high probability of mucosal dysplasia close to the cancer (Morson and Pang 1967). Our patient did not have family history of colorectal cancer, primary sclerosing cholangitis, and dysplasia around the cancer, and the cancer was not multiple. All other features of colitic cancer, however, met with our patient.

The contribution of hepatic IA cisplatin administration with systemic oral 5-FU was effective in our patient. Complete and partial responses were observed in about 46% of patients who underwent hepatic IA cisplatin and systemic intravenous 5-FU for unresectable colorectal metastases; three-year survival was 54% in patients who showed complete and partial responses but the authors did not mention five-year survival (Cortesi et al. 1994). Hepatic IA fluorodeoxyuridine produced complete and partial response in 50% of patients with liver metastases from
colorectal cancer, while objective tumor response occurred in 48% of patients receiving hepatic IA floxuridine infusion (Kemeny et al. 1987; Martin et al. 1990). These results suggest that hepatic IA cisplatin is as effective as other anti-cancer drugs and should be at least considered in the treatment of unresectable colorectal metastases. Although hepatic IA chemotherapy showed better anti-tumor effects than systemic intravenous therapy, the mean survival did not differ between these two treatments (Kemeny et al. 1987; Martin et al. 1990). The findings from our patient suggest the possibility that hepatic IA therapy might improve the mean survival.

Adverse effects for this treatment are drug-induced liver dysfunction, biliary stricture, ulcer disease, and nausea and vomiting (Kemeny et al. 1987; Hohn et al. 1989; Clavien et al. 2002). Only mild liver dysfunction was observed in our patient during hepatic IA treatment with cisplatin. We did not perform any surgical treatment for metastatic liver tumors because they disappeared 1 year after the operation. Surgical treatment including hepatic resection should be considered when the metastatic liver tumors are obvious.

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