

—Report on Experiments and Clinical Cases—

Resection of Liver Metastases from an α -fetoprotein-producing Gastric Cancer

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Abstract

We describe successful resection of rapidly enlarging liver metastases from an α -fetoprotein-producing gastric cancer, as these usually carry a dismal prognosis.

A 68-year-old woman underwent distal gastrectomy for an α -fetoprotein-producing gastric cancer without liver metastasis. The tumor was a moderately differentiated tubular adenocarcinoma with invasion of the muscularis propria. Venous and lymphatic invasion were noted, as was metastasis to lymph nodes along the greater curvature. Serum α -fetoprotein was 331 ng/mL before gastrectomy, decreasing to 18.6 ng/mL by postoperative day 28. At 2 months after operation, computed tomography detected no metastasis, but at 4 months α -fetoprotein increased to 2,190 ng/mL, and at 5 months liver tumors were detected by ultrasonography and computed tomography. Serum α -fetoprotein increased to 5,673 ng/mL, and serum PIVKA2 concentration was 18 mAU/ml just before operation. Extended left hepatectomy was performed. The resected specimen of segment 4 contained two well-defined tumors, measuring 5×4 cm and 2×2 cm, while that of segment 5 contained a similar-appearing tumor measuring 2×2 cm. The resected tumors had the same histologic appearance as the previously removed gastric cancer. The tumor cells were immunohistochemically reactive for α -fetoprotein. The postoperative course was uneventful, and the patient was discharged on postoperative day 15. Serum α -fetoprotein decreased to 20 ng/mL by postoperative day 15, and to 5 ng/mL by 2 months after operation. For 5 months since operation, no recurrence has become evident, and serum α -fetoprotein has remained within the normal range.

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Key words: gastric carcinoma, α -fetoprotein, metastatic liver tumor, hepatectomy

Introduction

Although α -fetoprotein (AFP) is a well-known marker for hepatocellular cancer and yolk sac

tumor, serum AFP concentrations sometimes also are high in patients with primary gastric cancer¹. AFP-producing gastric cancer generally produces multiple liver metastases and carries an extremely poor prognosis².

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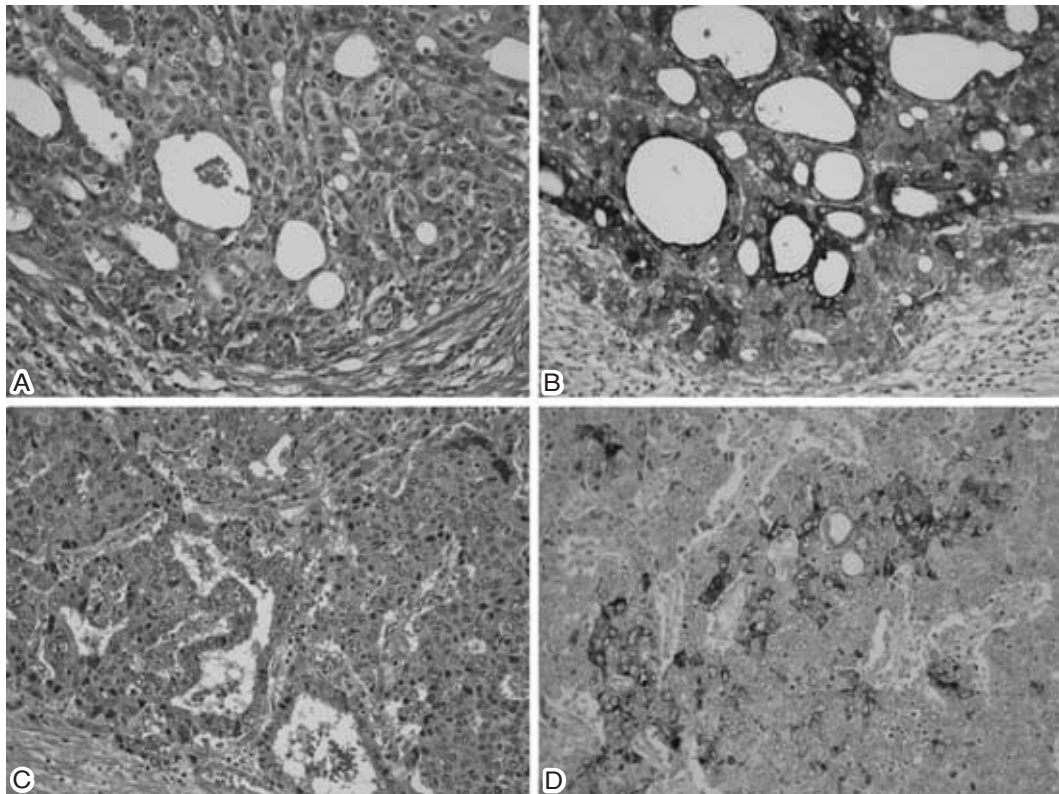


Fig. 1 Histologic appearance of gastric tumor with hematoxylin and eosin staining (A) and also immunostaining for α -fetoprotein (B). The tumor was a moderately differentiated tubular adenocarcinoma with depth of tumor invasion limited to the muscularis propria, and shows positive staining for α -fetoprotein. Histologic findings in liver tumors were compatible with metastasis of the gastric carcinoma with hematoxylin and eosin staining (C) and also immunostaining for α -fetoprotein (D) (20 \times).

We describe a patient with rapidly enlarging liver metastases from an AFP-producing gastric cancer treated successfully by hepatic resection.

Case Report

A 68-year-old woman underwent distal gastrectomy for an AFP-producing gastric cancer in the First Department of Surgery at Nippon Medical School in June, 2003. At that time, no liver metastasis could be detected by preoperative computed tomography (CT), or ultrasonography, or by intraoperative exploration. Microscopically, the tumor was a moderately differentiated tubular adenocarcinoma with depth of tumor invasion limited to the muscularis propria, and showed positive staining for α -fetoprotein (Fig. 1A, B). Venous and lymphatic invasion were evident. Metastasis had occurred to lymph nodes along the

greater curvature (T2, N1, M0, Stage 2). The serum AFP concentration was 331 ng/mL (normal, <20 ng/mL) prior to gastrectomy, but decreased to 18.6 ng/mL by postoperative day 28. CT performed 2 months after operation revealed no evidence of liver metastasis (Fig. 2A, B), but 4 months after operation serum AFP increased to 2,190 ng/mL. At 5 months after operation, liver tumors were detected in segments 4 and 5 by CT (Fig. 2C, D) and ultrasonography (Fig. 3). No serologic evidence of hepatitis B or C virus infections was found, and a diagnosis of liver metastasis from the AFP-producing gastric cancer was made. The patient was readmitted to our hospital. Arteriography revealed a radial pattern of tumor staining (Fig. 4). Serum AFP increased to 5,673 ng/mL and the serum PIVKA2 concentration was 18 mAU/mL (normal, <40 mAU/mL) just before operation. Extended left hepatectomy was performed. The resected specimen

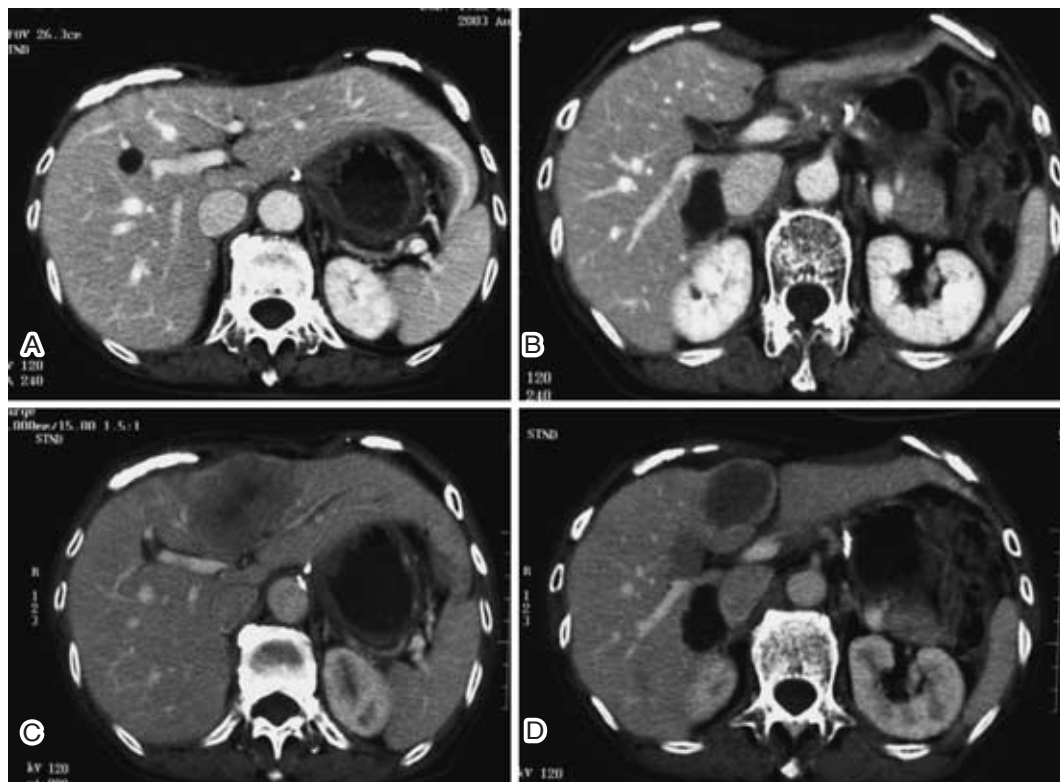


Fig. 2 At 2 months after gastrectomy, abdominal computed tomography (CT) disclosed no evidence of liver metastasis (A, B). However, at 5 months after operation, liver tumors were demonstrated in segments 4 and 5 by CT (C, D).



Fig. 3 Abdominal ultrasonography revealed hypoechoic mass in segment 4.

of segment 4 contained two well-defined tumors, measuring 5×4 cm and 2×2 cm (Fig. 5), while that of segment 5 contained a similar-appearing tumor

measuring 2×2 cm. The resected tumors had the same histologic appearance as the previously removed gastric cancer. The tumor cells were immunohistochemically reactive for AFP (Fig. 1C, D). The postoperative course was uneventful, and the patient was discharged on postoperative day 15. Serum AFP decreased to 20 ng/mL by postoperative day 15, and to 5 ng/mL by 2 months after operation. For 5 months since operation, no recurrence has become evident, and serum AFP has remained within the normal range.

Discussion

Among gastric cancers, 2% to 6% are reported to produce AFP³. Preoperative serum AFP is not ordinarily measured. In a study where AFP was elevated in only 2% of patients⁴, the authors concluded that routine measurement of AFP was of no value in staging or management of patients with gastric cancer.

AFP-producing cancers have been associated with

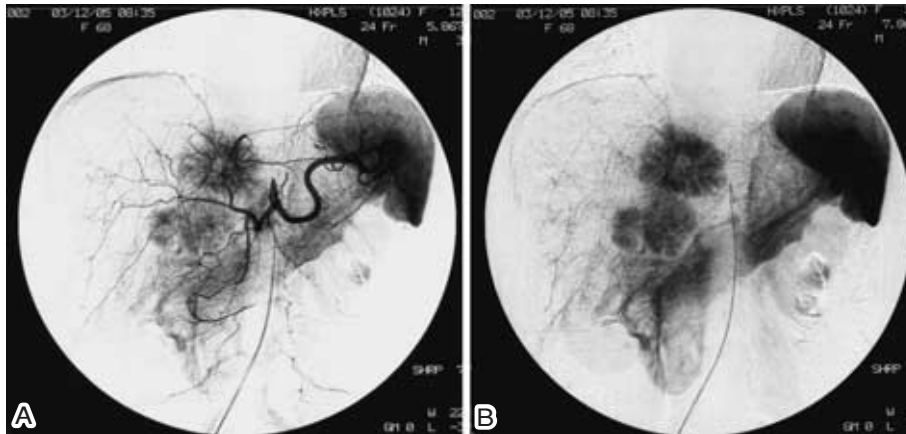


Fig. 4 Arteriography revealed a radial pattern of staining in liver tumors (early phase A, delay phase B).

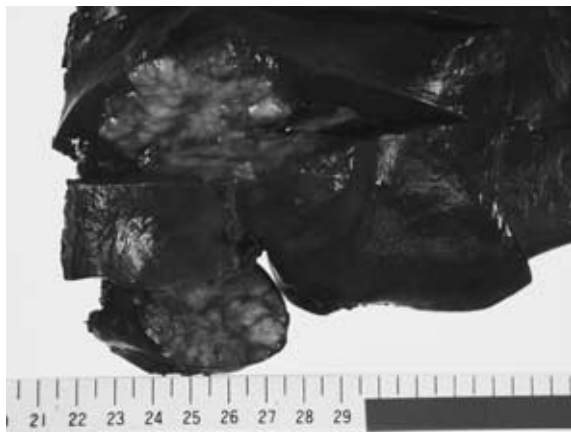


Fig. 5 The resected specimen of segment 4 contained two well-defined tumors, measuring 5×4 cm and 2×2 cm.

a higher incidence of concomitant lymph node metastasis, lymphatic and venous invasion of the gastric wall, liver metastasis, lower radical resectability rates, and a poorer prognosis than ordinary Borrmann type 2 and 3 gastric cancers at an advanced stage. Liver metastasis has been reported to occur in as many as 70% to 80% of cases. Approximately half of these are metachronous, with abnormal elevation of serum AFP usually developing before lesion detection by imaging^{5,6}.

Motoyama et al.⁷ proposed that AFP-producing gastric cancer should be divided into three subtypes, namely hepatoid type, yolk sac tumor-like type, and fetal gastrointestinal type. The first 2 respectively were suggested to be derived from hepatocellular metaplasia and yolk sac cell metaplasia within an

ordinary poorly differentiated medullary gastric adenocarcinoma. In contrast, the fetal gastrointestinal type appears to develop as recapitulation of fetal gastrointestinal epithelium in a tubular adenocarcinoma. The hepatoid type is the most common; unfortunately, most of these are highly malignant^{7,8}. This case was the hepatoid type. AFP-producing gastric cancer has a higher malignant potential (higher proliferative activity, less apoptosis, and richer neovascularization) than AFP-negative gastric cancer. These biologic characteristics of AFP-producing gastric cancers result in aggressive behavior and a poor prognosis⁹. Increased expression of c-Met also might explain the poor prognosis associated with AFP-producing gastric cancer². Takahashi et al.⁵ reported that 86.7% of AFP-producing gastric cancers had a medullary pattern with little stroma which might contribute to the frequency of liver metastasis.

The mainstay of systemic treatment for patients with metastatic gastric cancer remains 5-fluorouracil. However, a phase II study assessing efficacy and feasibility of combination chemotherapy with cisplatin and irinotecan hydrochloride in patients with metastatic gastric cancer demonstrated the regimen to be active and well tolerated¹⁰. Shimada et al.¹¹ reported achieving complete remission of metastatic liver tumors using irinotecan plus low-dose cisplatin was in a patient with AFP-producing gastric cancer. Unfortunately, diarrhea and leukopenia are serious dose-limiting toxicities of

irinotecan¹².

Metastatic liver tumors from AFP-producing gastric cancer usually are unresectable, given multiplicity metastases. In fact, only 3 liver resections for synchronous or metachronous metastases have been reported previously^{6,13,14}. The synchronous case reported by Tsurumachi et al.⁶ showed no sign of recurrence for 1 year after hepatectomy, while in the metachronous case reported by Chang et al.¹³, 2 hepatectomies were performed at different times. Tumor recurrence developed within 3 months after hepatic resection, accompanied by elevation of serum AFP; the patient died 23.5 months after the initial gastrectomy. Sato et al.¹⁴ performed partial resection of liver metastasis, noting no sign of recurrence at 1 year after this operation.

In conclusion, we experienced a case where rapidly enlarging liver metastases from an AFP-producing gastric carcinoma were successfully treated with hepatic resection. Examination of the serum AFP is important to detect recurrence of the AFP-producing gastric carcinoma.

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