—**Report on Experiments and Clinical Cases**—

Ruptured Metastatic Liver Tumor from an α-fetoprotein-producing Gastric Cancer

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Abstract

We describe a patient with a ruptured and rapidly enlarging secondary tumor of the liver metastasized from an α-fetoprotein (AFP)-producing gastric cancer. The ruptured liver metastasis was successfully treated by transarterial embolization (TAE) followed by hepatic resection. A 65-year-old woman was admitted to our hospital with residual gastric cancer. No liver metastasis was detected by preoperative computed tomography (CT), or ultrasonography, and total gastrectomy was performed. Microscopically, the tumor was a poorly differentiated adenocarcinoma invading no deeper than the subserosa, with positive staining for AFP and positive staining for Ki67 in approximately 80% of the tumor cells. Severe venous and lymphatic involvements were evident. The serum AFP level was 100 ng/m*l* at 3 weeks after the total gastrectomy, but decreased to 16 ng/m*l* by the end of postoperative month 3. At 6 months, the patient was referred and readmitted to our hospital with sudden severe pain in the upper abdomen. She was admitted in a state of shock with laboratory findings of anemia. A liver tumor surrounded by effusion was detected in segment 8 and diagnosed as a ruptured liver metastasis. Emergency arteriography revealed a large hypervascular tumor, and a TAE performed promptly thereafter was successful in improving the blood pressure. A second TAE was performed 2 months after first TAE due to a dramatic elevation of serum AFP to 180,000 ng/m*l*. The second TAE decreased the patient's serum AFP to 2,200 ng/m*l*, but the level remained in the abnormal range. A right hepatectomy was performed after confirming the absence of other detectable metastatic tumors. The resected specimen contained a well-defined tumor, measuring 6×6 cm that appeared almost necrotic under microscope. Over the 6 years since the hepatectomy, no recurrence has appeared and serum AFP has remained within the normal range.
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Key words: gastric carcinoma, α-fetoprotein, metastatic liver tumor, hepatectomy, rupture

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Introduction

Hepatic tumors often rupture spontaneously in patients with hepatocellular carcinoma (HCC), but rarely in those with hepatic metastasis. The spontaneous rupture of a hepatic tumor is a potentially life-threatening condition[1], that urgently requires accurate diagnosis and adequate management, such as transarterial embolization (TAE) or an operation. Even when emergency hepatectomy is performed for the treatment of ruptured hepatic tumors, the operative mortality rates are very high (28.5～54.5%)[2-4]. We reported that TAE followed by elective hepatectomy was an effective treatment in patients with ruptured HCCs[4].

Although α-fetoprotein (AFP) is best known as marker for HCC and yolk sac tumor, serum AFP levels are sometimes elevated in patients with primary gastric cancers, as well[5]. Gastric cancers that produce AFP generally metastasize to multiple sites in the liver and have an extremely poor prognosis[6]. In this paper we describe the successful use of TAE followed by hepatic resection to treat a patient with a rapidly enlarging and ruptured liver metastasis from an AFP-producing gastric cancer.

Case Report

A 65-year-old woman with residual gastric cancer (**Fig. 1A**) was admitted to the First Department of Surgery at Nippon Medical School in November 1997. The patient had received a distal gastrectomy for a gastric ulcer many years earlier at the age of 35. No liver metastasis was detected by preoperative computed tomography (CT) (**Fig. 2A**), or ultrasonography, and total gastrectomy was performed (**Fig. 1B**). Microscopically, the tumor was a poorly differentiated adenocarcinoma invading no deeper than the subserosa, with positive staining for AFP and positive staining for the cell proliferation marker Ki67 in approximately 80% of the tumor cells. Severe venous and lymphatic involvements were evident (**Fig. 3A, B, C**). The tumor cells had metastasized to the lymph nodes along the greater curvature. The serum AFP level was 100 ng/m*l* (normal, <20 ng/m*l*) at 3 weeks after the total gastrectomy, but decreased to 16 ng/m*l* by the end of postoperative month 3. CT performed 3 months after the total gastrectomy, revealed no evidence of liver metastasis. At 6 months after the surgery, the patients was referred and readmitted to our hospital with sudden severe pain in the upper abdomen. Her blood pressure and pulse on admission were 86/46 mmHg, and 130/min. Routine laboratory tests showed anemia: red blood cell count $264 \times 10^4/\mu l$, hemoglobin 9.1 g/d*l*, and hematocrit 27.2%. No serologic evidence of hepatitis B or C virus infection was found. CT (**Fig. 2B**) and ultrasonography (**Fig. 4**) detected a liver tumor surrounded by effusion in

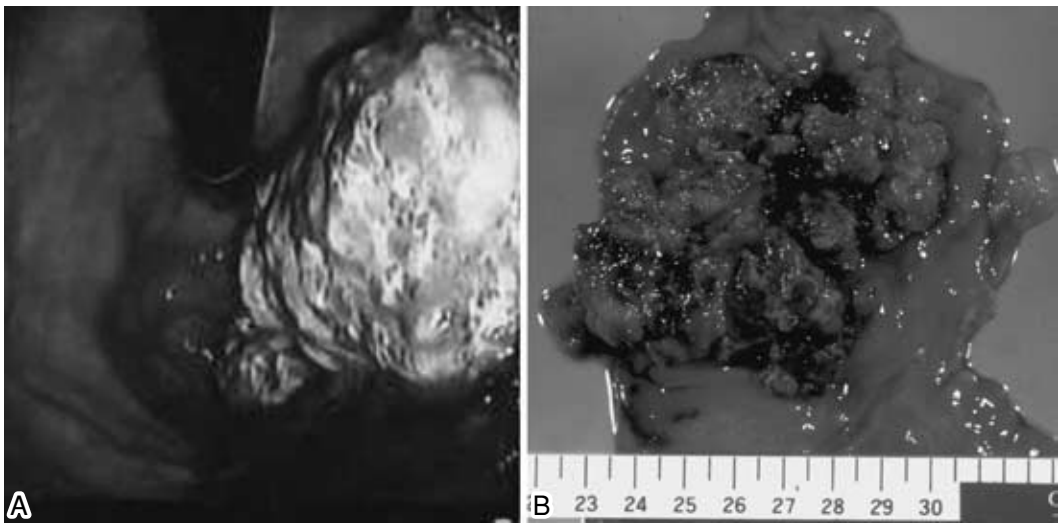

Fig. 1 Endoscopic examination (A) and resected specimen (B) revealed residual gastric cancer.

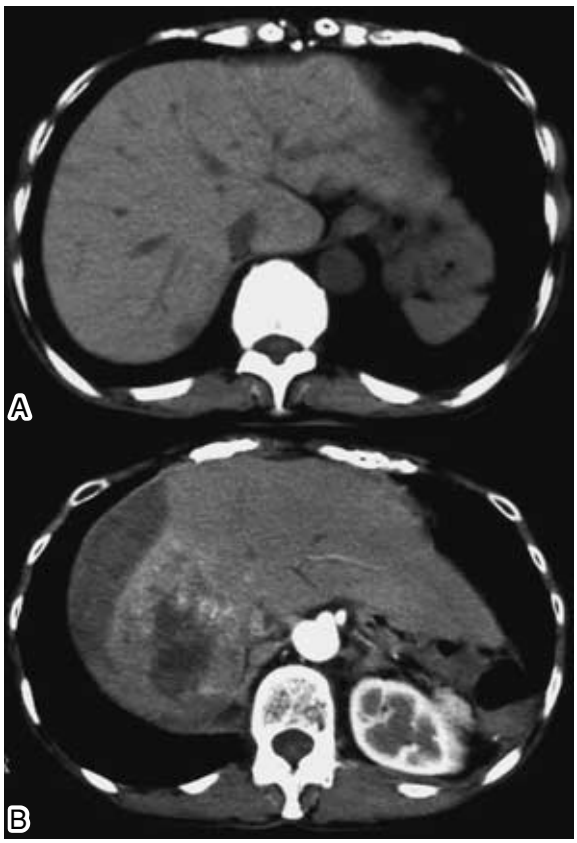

Fig. 2 No liver metastasis could be detected by preoperative computed tomography (A). A liver tumor surrounded by effusion was detected in segment 8 at 6 months after the total gastrectomy (B).

segment 8, and the case was diagnosed as a ruptured liver metastasis. Emergency arteriography revealed a large hypervascular tumor in segment 8 (**Fig. 5A**), and a TAE performed promptly thereafter was successful in improving the blood pressure. Upper abdominal pain and general condition were improved gradually, but the serum AFP level jumped sharply from 68,710 ng/m*l* before the TAE to 180,000 ng/m*l* 2 months after the procedure. An angiography performed 2 months after the TAE, detected a residual hypervascular area in the liver tumor, prompting us to perform a second TAE (**Fig. 5B**). The serum AFP was reduced to 2,200 ng/m*l* after the second TAE, but it remained in the abnormal range. A right hepatectomy was performed after confirming the absence of other detectable metastatic tumors. The specimen resected from segment 8 included a well-defined tumor, measuring 6×6 cm that appeared almost necrotic under microscope (**Fig. 6**). The postoperative course was uneventful, and the patient was discharged on postoperative day 15. Serum AFP decreased to 220 ng/m*l* by postoperative day 15, and to 7 ng/m*l* by the end of postoperative month 2. Over the 6 years since the hepatectomy, no recurrence has appeared and serum AFP has remained within the normal range (**Fig. 7**).

Discussion

While spontaneous ruptures are a comparatively common presentation of HCC, the mechanisms that lead to them remain obscure. Factors such as central necrosis in a rapidly growing HCCs, hemorrhage and venous congestion inside the tumors coagulopathy due to underlying cirrhosis, and even minor traumas can cause sudden increases in pressure within the tumors, facilitating their ruptures in the peritoneum[7–11].

Ruptures of metastatic liver tumors are uncommon. Among the published reports on spontaneous ruptures of hepatic metastasis, this is first report to describe a ruptured metastatic liver tumor metastasized from an AFP-producing gastric cancer.

Hemostat is the foremost concern when a liver tumor spontaneously reptures. Some reports have recommended, selective hepatic artery ligation[2] or emergency hepatectomy[12] as the treatments of choice in patients with limited tumors[2] and preserved liver function, followed by TAE as the next best alternative[12]. TAE has several advantages over the other methods, however the procedure has been effective in controlling 70～100% of bleeding HCCs and has an in-hospital mortality rate in the range of 0 to 29.4%[3,4,12–15]. Emergency hepatectomy (28.5～54.5%)[2–4] has had a higher operative mortality than elective hepatectomy (0%)[4,11,16]. According to Shimada et al.[17], patients with ruptured HCCs who undergo TAE alone have a lower median survival than patients treated by TAE followed by hepatic resection.

Among gastric cancers, 2% to 6% are reported to produce AFP[18]. AFP is generally not measured before the corrective surgeries. In 1 study showing

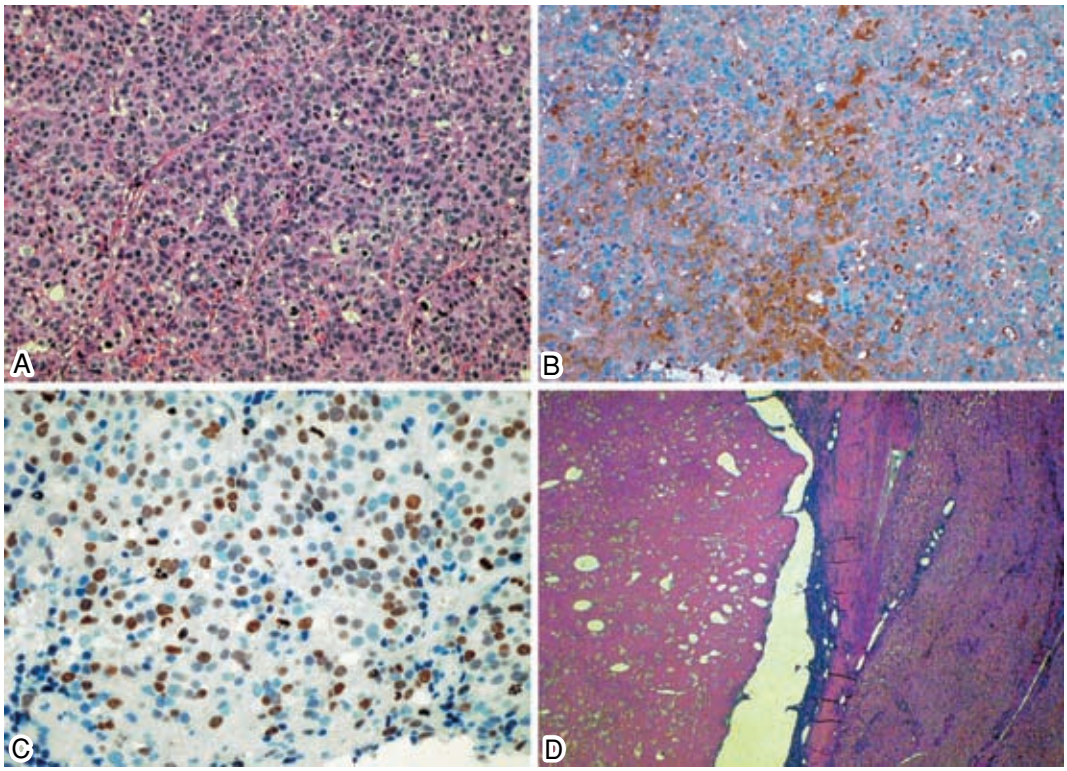

Fig. 3 Microscopically, the resected gastric tumor was a poorly differentiated adenocarcinoma that invaded no further than the subserosa (H.E. ×20) (A). Positive staining for AFP (×20) (B) and positive staining for Ki67 in approximately 80% of the tumor cells (×40) (C) are shown. The resected liver tumor was almost necrotic (H.E. ×2) (D).

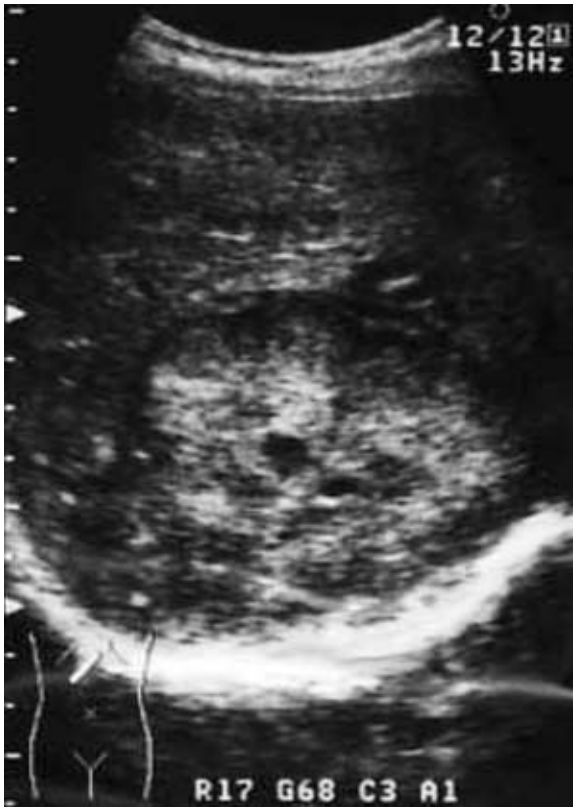

Fig. 4 Abdominal ultrasonography revealed a hyperechoic mass in segment 8.

an elevation of AFP in only 2% of patients[19], the authors concluded that routine measurement of AFP was of no value in staging or managing patients with gastric cancer.

AFP-producing gastric cancer has a higher malignant potential (higher proliferative activity, less apoptosis, and richer neovascularization) than AFP-negative gastric cancer. The present case showed positive Ki-67 staining in about 80% of the tumor cells, a finding suggestive of aggressive growth tumor. AFP-producing cancers have been associated with a higher incidence of concomitant lymph node metastasis, lymphatic and venous invasion in gastric wall, liver metastasis, lower radical resectability rates, and a poorer prognosis than ordinary advanced gastric cancers. Liver metastasis has been reported to occur in as many as 70% to 80% of cases. Approximately half of these are metachronous, with serum AFP usually elevating to abnormal levels before the lesions are detected by imaging[20,21].

Metastatic liver tumors from AFP-producing

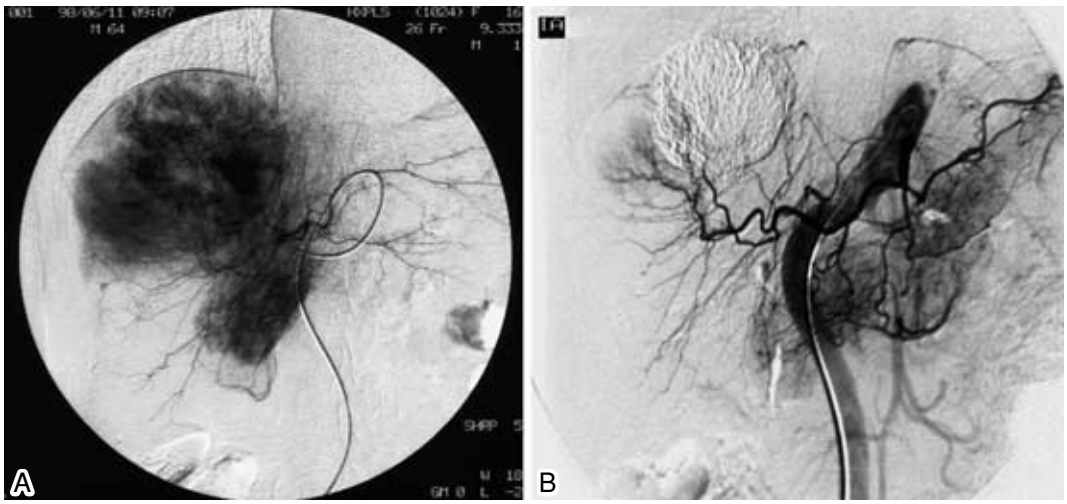

Fig. 5 Emergency arteriography revealed a huge hypervascular tumor in segment 8 (A) and TAE was performed. Another angiography performed 2 months after the TAE, revealed a residual hypervascular area in the liver tumor, prompting us to perform a second TAE (B).

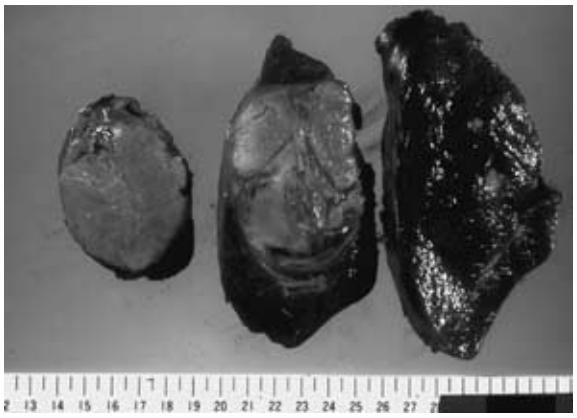

Fig. 6 The resected specimen contained a well-defined tumor, measuring 6×6 cm.

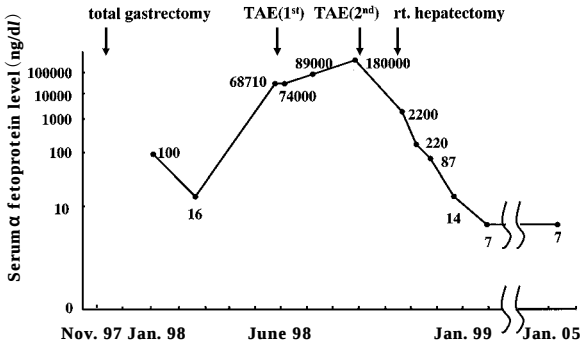

Fig. 7 Changes in the serum α-fetoprotein level

gastric cancer are usually unresectable due to the multiplicity of metastases. In fact, only 4 liver resections for synchronous or metachronous metastases have been previously reported[21–23]. A synchronous case reported by Tsurumachi et al.[21] showed no sign of recurrence for 1 year after hepatectomy, while a metachronous case reported by Chang et al.[22], underwent two hepatectomies on separate occasions. The tumor recurred and serum AFP rose sharply in Chang's patient 3 months after hepatic resection, and the patient died 23.5 months after the initial gastrectomy. When Sato et al.[23] partially resected a liver metastasis, they noted no sign of recurrence at 1 year after this operation[23]. In our case, the ruptured liver metastasis from an AFP-producing gastric cancer was treated by hepatic resection, and no tumor recurrence has been detected in the ensuing 6 years. Curative treatment was performed by TAE followed by hepatic resection.

In conclusion, we encounterd a ruptured liver metastasis from an AFP-producing gastric carcinoma. The metastasis was successfully treated with TAE followed by hepatic resection, and no tumor recurrence has been detected over the 6 years since the hepatectomy. TAE followed by hepatectomy is an effective treatment even for ruptured liver metastasis.

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