Two Cases of Early Gastric Carcinoma with Synchronous Liver Metastasis

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Summary: We have experienced two cases of early gastric cancer with synchronous liver metastasis. One patient was a 64-year-old man diagnosed as having early gastric cancer type 0 Ila at 15×10 mm on the lesser curvature of the cardia. The other patient was a 58-year-old man diagnosed as having early gastric cancer type 0 Ila+IIc at 24×18 mm on the posterior wall of the antrum. The histological findings showed that proliferation of moderately differentiated tubular adenocarcinoma with hepatoid pattern was massively invading to the deep layer of the submucosa, with positive lymph vessel, vein invasion and lymph node metastasis, in both cases. These results suggested that elevated or mixed macroscopic type, differentiated adenocarcinoma massively invading to the deep layer of submucosa, positive lymph vessel and vein invasion, lymph node metastasis, and hepatoid adenocarcinoma were risk factors for liver metastasis from early gastric cancer.

Key words gastric carcinoma, submucosal cancer, liver metastasis, hepatoid picture, differentiated adenocarcinoma

INTRODUCTION

Early gastric carcinoma is defined as a carcinoma limited to within the mucosa or submucosa of the stomach with or without lymph node metastasis, according to the Guidelines of the Japanese Gastric Cancer Association for Gastric Cancer [1]. Recently, the proportion of early gastric cancer has increased among cases of gastric cancer. The prognosis of early gastric cancer is good. And recurrence or distant metastasis from early gastric cancer is rare. The 5-year-survival-rate after resection of early gastric cancer is 96%-99% [2-4]. The most frequent site of distant metastasis from early gastric cancer is the liver [5,6]. Here, we present two rare cases of submucosal gastric cancer with synchronous liver metastasis.

CASE REPORT

Case 1

A 64-year-old man visited a private hospital because of weight loss and general fatigue on 27 June 1989. An abnormal shadow in the stomach was recognized on a routine X-ray examination and upper gastrointestinal endoscopic examination. The patient was referred to Kurume University Hospital for further examination and treatment on 28 July. An X-ray examination and an upper gastrointestinal endoscopic examination showed a type I tumor on the lesser curvature of the EG junction. The pathological diagnosis based on a biopsy specimen from the tumor lesion was tubular adenocarcinoma moderately differentiated type. On admission, the liver, spleen, and tumor were not palpable on physical examination. The serum levels of carbohydrate antigen (CA 19-9), carcinoembryonic antigen (CEA), a-fetoprotein; CA19-9, carbohydrate antigen; CEA, carcinoembryonic antigen; CT, computed tomography; EGF, epidermal growth factor; EGFR, epidermal growth factor receptor.
and α-fetoprotein (AFP) were normal. Computed tomography (CT) showed low-density masses at S3 and S7. Surgery was performed through a median laparotomy on 22 August. The operative procedure was total gastrectomy, with D2 lymph node dissection, Roux-Y method reconstruction, cholecystectomy, and right gastric artery cannulation. The primary tumor was palpable on the lesser curvature of cardia, but no exposed tumor was seen on the serosa. Macroscopic metastasis was found in the No. 3, 7, 8a, 8p, 12 lymph nodes, and in the liver (S3, S7), but not recognized in the peritoneum. The surgical diagnosis was gastric cancer type 0I and H1, P0, N3, T1 Stage IV. The macroscopic findings of the resected specimen were an irregular shaped elevated lesion type 0 Ila 15×10 mm in size on the lesser curvature of the cardia. The histological findings showed proliferation of moderately differentiated tubular adenocarcinoma massively invading to the deep layer of the submucosa, with positive lymph vessel and vein invasion. Metastases were recognized in one No. 8p lymph node and in the liver, histologically (Fig. 1). A hepatoid pattern was recognized in the tumor (Fig. 2). No AFP was found in the cancer tissue, immunohistochemically. Combination of intra-hepatic arterial infusion of 5-FU (250 mg/day ×15 doses), MMC (20 mg×1 dose) was begun from 29 August. Administration of 5-FU (250 mg/day iv ×13 doses) was begun from 14 September, and MMC (6 mg iv) was given on 3 October. Peroral administration of 5-FU (200 mg/day) was begun on 3 October. CT showed multiple metastatic tumors in the liver and ascites on 23 October (Fig. 3). At 14 months after the surgery, the patient eventually died of liver metastasis.

Case 2

A 58-year-old man visited a private hospital
EARLY GASTRIC CARCINOMA WITH LIVER METASTASIS

Fig. 5. Trabecular or small glandular pattern of tumor cells which had a large nucleus with eosinophilic cytoplasm was recognized in the liver (H & E ×200).

Fig. 6. Cobble stone pattern of tumor cells which had a large or a bizarre nucleus with eosinophilic cytoplasm (H & E ×100).

Fig. 7. CT showed low density areas at S7 and S8 in the liver.

because of dysphagia in June 1991. Gastric cancer was diagnosed based on gastrography and endoscopy. The patient was referred to Kurume University Hospital for further examination and treatment on 2 September. An upper gastrointestinal endoscopic examination showed type 0 Ila+Ilc tumor on the greater curvature in the posterior wall of the antrum (Fig. 4). The pathological diagnosis based on a biopsy specimen from the tumor lesion was tubular adenocarcinoma moderately differentiated type. On admission, the liver, spleen, and tumor were not palpable on physical examination. The serum level of CA19-9 was normal, but the level of CEA was elevated at 4.1 ng/ml. Surgery was performed through a median laparotomy on 26 September. The operative procedure was distal gastrectomy, with D2 lymph node dissection, Billroth-I method reconstruction, cholecystectomy, and wedge resection of the liver. No exposed tumor was seen on the serosa. Macroscopic metastasis was found in the No. 4d and 6 lymph nodes, and in the liver (S4, S7), and not found in the peritoneum. The surgical diagnosis was gastric cancer type 0 Ila+Ilc and H1, P0, N1, T1 Stage IV. The macroscopic findings from the resected specimen were an irregular shaped elevated lesion type 0 Ila+Ilc 24×18 mm in size on the posterior wall of the antrum. The histological findings showed proliferation of moderately differentiated tubular adenocarcinoma massively invading to the deep layer of the submucosa, with positive lymph vessel and vein invasion. Metastases were recognized in two No. 4d lymph nodes and in the liver, histologically (Fig. 5). A hepatoid pattern was recognized in the tumor (Fig. 6). No AFP was found in the cancer tissue, immunohistochemically. MMC (20 mg iv) was given on 26 September. CDDP (100 mg iv) and MMC (10 mg iv) were given on 19 October. Peroral administration of UFT (400 mg/day) and PSK (3.0 g/day) was begun on 1 November. CT showed multiple low density areas in the liver on 16 October (Fig. 7). At 13 months after surgery, the patient eventually died of liver metastasis.

DISCUSSION

Most frequent site of distant metastasis from early gastric cancer is the liver. Nevertheless, reports of liver metastasis from early gastric cancer are few. The features of a gastric cancer having liver metastasis are a cancer in the atrophic mucosal area of the lower regions of the stomach, macroscopic type 2 advanced gastric cancer and elevated or mixed
macroscopic type early gastric cancer, differentiated type adenocarcinoma or poorly differentiated adenocarcinoma with massive invasion, and positive lymph vessel, vein invasion and lymph node metastasis [7-10]. The features of an early gastric cancer with liver metastasis are invasion to the deep layer of the submucosa without superficial spreading growth, localized elevated or Ila+IIc macroscopic type [11,12]. We have previously reported that EGF, EGFR and c-erbB-2 positive cases were preferentially found in penetrating type rather than in superspreading, and that the autocrine mechanism of the growth factors and c-erbB-2 were correlated to the degree of gastric wall invasion [13]. Concerning submucosal cancer with lymph node metastasis, we have concluded that vertical submucosal infiltration was a more important factor to lymph node metastasis than horizontal infiltration [14]. In our two cases, the macroscopic type was elevated or Ila+IIc macroscopic type, the histological findings showed proliferation of moderately differentiated tubular adenocarcinoma with a hepatoid pattern, and was massively invading to the deep layer of the submucosa without superficial spreading growth, with positive lymph vessel, vein invasion and lymph node metastasis. The histological features of a hepatoid adenocarcinoma is a solid or trabecular pattern of tumor cells which have a large nucleus with clear or eosinophilic cytoplasm, and is very similar to hepatocellular carcinoma [15]. Liver metastasis from a hepatoid adenocarcinoma of the stomach is frequent recognized, and many of cases of hepatoid adenocarcinoma are AFP producing tumors [15], but we could not find any AFP in either case, immunohistochemically. These results suggested that elevated or mixed macroscopic type, differentiated adenocarcinoma massively invading to the deep layer of submucosa, positive lymph vessel and vein invasion, lymph node metastasis, and hepatoid adenocarcinoma were risk factors for liver metastasis from early gastric cancer.

REFERENCES