Case Report

Multiple Early Gastric Cancer with Gastritis Cystica Profunda Showing Various Histological Types

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KEY WORDS:
Gastric cancer; Gastritis cystica profunda; GCP; Multiple early gastric cancer; *Helicobacter pylori*

ABBREVIATIONS:
Gastritis Cystica Profunda (GCP); *Helicobacter pylori* (*H. pylori*); Endoscopic Ultrasonography (EUS)

SUMMARY

We report a case of multiple early gastric cancer showing varied histological types associated with gastritis cystica profunda (GCP). A 61-year-old man who had early gastric cancer associated with GCP underwent a distal gastrectomy with lymphadenectomy. Histological examination showed various histological types of cancer -well differentiated, moderately differentiated, poorly differentiated adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma- that had developed independently in the mucosal and submucosal layers of the resected specimen. Furthermore, multiple cysts with a single layer of columnar epithelium were present in the submucosa around the cancerous lesions. However, no neoplastic changes were found in those epithelial cells. *Helicobacter pylori* was detected in the residual stomach 3 months after surgery. Although the mechanism of the relationship between gastric carcinoma and GCPs is obscure, we speculate that repeated erosion and regeneration induced by chronic inflammation causes multicentric carcinogenesis as well as an aberration of the gastric glands. GCPs may be a risk factor for multiple gastric cancer.

INTRODUCTION

Gastritis cystica profunda (GCP) has been characterized as a gastric pseudotumor associated with antecedent gastric surgery, which is observed at the gastroenterotomy site (1). It is relatively uncommon in the absence of previous gastrectomy (2,3). GCP has been suggested to be a predisposing condition for the development of gastric cancer, especially multiple cancers (4,5). Although most lesions in multiple early gastric cancers are differentiated (6), the histological types of multiple gastric cancers associated with GCP have not been reported. In this report, we present a patient with multiple early gastric cancers of various histological type associated with GCP.

CASE REPORT

A 61-year-old man with a history of gastric ulcer was referred to Wakayama Medical University Hospital with a chief complaint of epigastric pain. Physical examination yielded no abnormal findings, and results of laboratory examinations were within the normal range. Gastrointestinal endoscopy showed two depressed lesions (type IIc), which seemed to be separated by normal mucosa; one was at the anterior wall and the other was at the lesser curvature of the lower body of the stomach **(Figure 1a, b)**. Endoscopy also showed atrophic mucosa with intestinal metaplasia around the antrum and the body of the stomach. Endoscopic biopsies of the two depressed lesions showed moderately differentiated tubular adenocarcinoma. Endoscopic ultrasonography (EUS) showed that these two lesions had invaded the submucosal layer of the stomach and were surrounded by many hypo echoic lesions, suggesting GCP **(Figure 1c, d)**. Computed tomography and ultrasonography of the abdomen showed no abnormal findings. Distal gastrectomy with regional lymph node dissection was performed.

Pathological Findings

Macroscopically, two different depressed lesions were recognized at the anterior wall and at the lesser curvature of the body of the resected stomach. No abnormal findings were detected in the other parts of the specimen **(Figure 2)**.

The resected specimen was cut in serial sections parallel to the lesser curvature at 5-mm intervals, and each slice was further cut into standard-sized blocks. Microscopic examination demonstrated multiple cancerous lesions, including diffuse spreading flat-type tumors. Most lesions were confined to the mucosal layer, but some parts of depressed lesions extended to the submucosal layer. No tumor invasion was recognized beyond the submucosal layer **(Figure 3)**. Interestingly, five different histological types of tumor were recognized in these lesions: well differentiated tubular adenocarcinoma, moderately differentiated tubular

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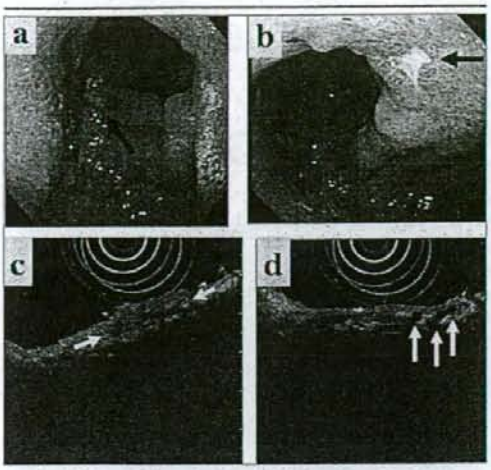

FIGURE 1 Preoperative gastrointestinal endoscopy and endoscopic ultrasonography. Gastrointestinal endoscopy showed a depressed lesion at the anterior wall of the lower body of the stomach **(a)** and a depressed lesion at the lesser curvature of the lower body of the stomach **(b)**. Endoscopic ultrasonography showed that these two lesions had invaded the submucosal layer of the stomach **(c)** and that many hypo echoic lesions, suggesting GCP, surrounded the depressed lesions **(d)**.

adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma; all lesions were separated by intervening areas of normal tissue **(Figure 4, 5)**. Furthermore, multiple cysts, which consisted of a single layer of columnar epithelium, were present in the submucosa around the cancerous lesions **(Figure 3, 5)**. However, no neoplastic changes were found in the epithelial cells of the submucosal cysts. No lymph node metastases were recognized.

Postoperative Course

The patient had a satisfactory postoperative course. Gastrointestinal endoscopy was performed 3 months after the operation, and *Helicobacter pylori* (*H. pylori*) was detected with urease tests in the residual stomach. Therefore, *H. pylori* was eradicated with lansoprazol, amoxicillin, and clarithromycin. No evidence of recurrence has been observed for 3 years after the operation.

DISCUSSION

GCP is found in 10.7% of resected stomachs (7). The congenital aberration hypothesis (8) and the acquired inflammation hypothesis (4) have been suggested as pathogenic mechanisms for GCP (9). According to the acquired inflammation hypothesis, epithelial components enter the submucosal layer as a result of repeated erosion and regeneration (9). In addition, GCP is occasionally associated with gastric carcinoma, and the prevalence of accompanying GCP among in patients with gastric carcinoma is 3.0% to 3.4% (4,5); however, whether gastric carcinoma and GCP are correlated remains unknown. In particular, GCPs are frequently accompanied by multiple gastric carcinomas (4,9). Mandai et al. have reported that 43% of gastric cancers with GCP are multiple gastric cancers (5). However, no reports have demonstrated that gastric carcinoma originates from the epithelial cells of GCP. Also, in the present case, neoplastic changes were not found in GCP but were found in the submucosal layer. The mechanism of the close relationship between gastric carcinoma and GCP is obscure. However, we speculate that both carcinoma and GCP tend to occur in similar environments (4,7,10). Chronic gastritis and intestinal metaplasia are often recognized in the mucosa around GCP (4,5,11). Recently, an extremely high percentage of cases of GCP are associated with *H. pylori* infection (9,12). *H. pylori* infection has been shown to be a major causative factor in chronic gastritis (13) and to induce gastric carcinoma (14). Indeed, *H. pylori* was also detected in the stomach of the present patient. Repeated erosion and regeneration

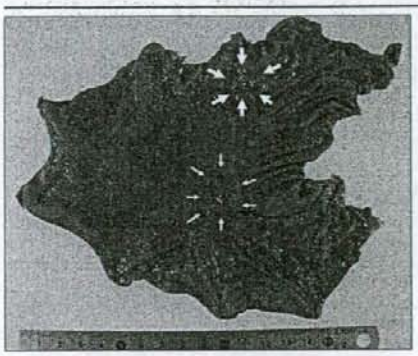

FIGURE 2
Macroscopic appearance of the resected specimen. Two different depressed lesions were recognized at the anterior wall (thick arrow) and at the lesser curvature of the body of the resected stomach (thin arrow).

FIGURE 3
Distribution of multiple cancers and GCP in the resected specimen.
The diagram shows the distribution of multiple early gastric cancers: m, cancer confined to the mucosal layer; sm, cancer in the submucosal layer; GCP, GCP in the submucosal layer.

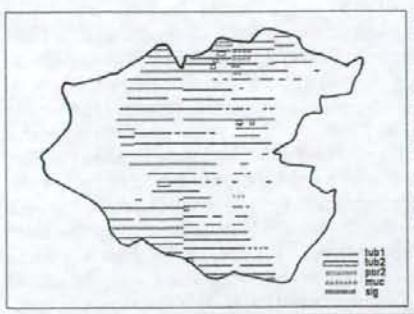

FIGURE 4
Distribution of histological types of cancer in the resected specimen. The diagram shows the distribution of various histological types of cancer: tub1, well - differentiated tubular adenocarcinoma; tub2, moderately differentiated tubular adenocarcinoma; por, poorly differentiated adenocarcinoma; muc, mucinous adenocarcinoma; and sig, signet ring cell carcinoma.

induced by chronic inflammation caused by *H. pylori* may cause cancer as well as an aberration of the gastric glands; therefore, GCP may be a paracancerous lesion rather than be a predisposing condition to gastric carcinoma (9). This possibility is consistent with the fact that GCPs are frequently accompanied by multiple gastric carcinomas.

The incidence of multiple gastric cancer is approximately 10%, and histopathological examinations of multiple gastric cancer have shown that most lesions are differentiated and are accompanied by intestinal metaplasia (15). However, no studies of the histological type of gastric cancer associated with GCP have been reported. In the present case, varied pathological types of cancers -well differentiated tubular adenocarcinoma, moderately differentiated tubular adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma- existed synchronously in the mucosal or submucosal layer. Although some of these cancers were diffusely distributed in the resected stomach, most lesions were separated by areas of normal tissue. This finding suggests that multiple cancer foci combined into large spreading tumors, rather than one cancer focus expanding widely. We can speculate that GCP is related to multicentric carcinogenesis of the gastric mucosa. In terms of clinical significance, the existence of varied and multiple gastric cancers should be considered when GCP is detected by preoperative examinations, such as EUS.

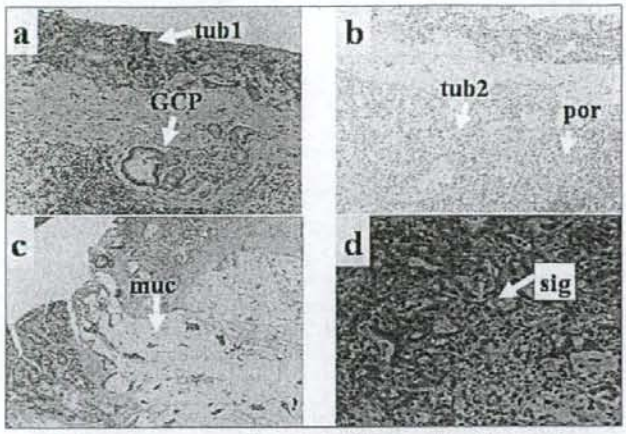

FIGURE 5 Histological appearance of the resected specimen. Five different histological types of tumor were recognized: well - differentiated tubular adenocarcinoma **(a)** (HE, x200), moderately differentiated tubular adenocarcinoma (tub2) **(b)**, poorly differentiated adenocarcinoma (por) **(b)** (HE, x200), mucinous adenocarcinoma **(c)** (H.E, x200) and signet ring cell carcinoma **(d)** (HE, x400). Furthermore, GCP was present in the submucosa around the cancerous lesions **(a)** (HE, x200).

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ORIGINAL ARTICLE

Analysis of the prognostic factors and evaluation of surgical treatment for synchronous liver metastases from gastric cancer

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Abstract
Background and aims Whether or not a synchronous resection of liver metastases from gastric cancer provides a survival benefit has been a key issue. We identify the significant prognostic factors and clarify the beneficial effect on the survival of liver surgical treatment.
Materials and methods We reviewed 72 patients who underwent a gastrectomy for gastric cancer with synchronous liver metastases and classified the liver metastases into three grades, such as H1: metastases were limited to one of the lobes, H2: there were a few scattered metastases in both lobes, and H3: there were numerous scattered metastases.
Results H1, 2 metastases, and an absence of peritoneal dissemination (P0) were significantly independent prognostic factors for liver metastases of gastric cancer. In addition, the cumulative 1 and 5-year survival rates of liver surgical treatment (hepatic resection and/or microwave coagulation therapy) were 80.0% and 60.0%, whereas the survival rates for non-hepatic surgical treatment were 36.4% and 0% in 26 patients with H1, 2, and P0. In those patients, the radical operation, the solitary metastatic liver tumor, and no-distant lymph node metastases were independent prognostic determinants of survival.
Conclusion The radical operation including the surgical treatment for metastatic liver tumors should be performed to improve the prognosis in gastric cancer patients with synchronous H1, 2, and P0.

Keywords Gastric cancer · Synchronous liver metastases · Prognostic factors for survival · Hepatic surgical treatment

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Introduction

Gastric cancer is the second most common cancer worldwide and has a substantial mortality for distant metastases in the liver, peritoneum, or extensive lymph nodes despite technical advances in surgery and the use of adjuvant therapy [1]. Of all patients with gastric cancer, 2–9% have synchronous liver metastases that are a frequent and crucial problem [2–5] because patients with metachronous metastases have a longer survival (5-year survival, 29%) than those with a synchronous disease (5-year survival, 6%) [6], and a synchronous resection of metastatic liver tumors does not contribute to a survival benefit [7]. In fact, a lot of studies have reported that the effect of hepatic resection for gastric liver metastases on survival was dubious [8–11], whereas some reports have demonstrated that only a hepatic resection for liver metastases with gastrectomy was able to obtain a long-term survival when both the primary tumor and metastatic lesions were potentially respectable [7, 12–14]. It is, thus, a key question whether or not a synchronous resection of liver metastases provides a survival benefit. The reason for this is that patients with liver metastases from gastric cancer often have other simultaneous or future

incurable factors, such as peritoneal dissemination, widespread lymph node metastases, and direct invasion to adjacent organs [7, 13, 14]. In addition, the clinicopathological characteristics related to the prognosis of gastric cancer with synchronous liver metastases have not been comprehensively identified. Therefore, the surgical indications for synchronous liver metastases from gastric cancer are very important and must be carefully determined.

In this study, we retrospectively reviewed 72 patients who underwent gastrectomy for gastric cancer with synchronous liver metastases during the last 15 years and identified which population of the patients obtained a clinical benefit from multimodality treatment for synchronous metastases.

Materials and methods

At the Second Department of Surgery of Wakayama Medical University Hospital, 1,602 gastric cancer patients were surgically treated between January 1991 and December 2005. Of these patients, 81 patients (5.1%) had synchronous liver metastases, which were found with routine abdominal computed tomography before gastrectomy. Among these 81 patients, we retrospectively reviewed the records of 72 patients (88.9%) who underwent a gastrectomy for primary gastric carcinoma. The group consisted of 58 men and 14 women ranging from 25 to 85 years of age (median 67.0 years). None of the patients died of postoperative complications, and the follow-up and outcome of all of the patients were completed by clinical visits, telephone interviews, or correspondence until December 2006.

The classifications of the degree of liver metastases (H1: metastases were limited to one of the lobes, H2: there were a few scattered metastases in both lobes, and H3: there were numerous scattered metastases in both lobes), which were determined from the first English edition of the Japanese Classification of Gastric Carcinoma [15], were used for a prognostic estimation in the gastric cancer patients with synchronous liver metastases. It is thought that the radical operation would be possible against H1 and H2 metastases, and we defined H2 metastases as the number of metastases which was less than five in this study. The following clinicopathological risk factors were also examined for prognostic influence: age, gender, histological differentiation, tumor size, tumor depth of invasion, lymphatic invasion, venous invasion, lymph node metastases, the absence (P0) or presence (P1) of peritoneal dissemination based on gross intraoperative finding and peritoneal cytology, serum carcinoembryonic antigen (CEA), and serum carbohydrate antigen 19-9 (CA-19-9) level before operation. The pathological diagnosis and classification of the resected specimens were performed according to the General Rules for Gastric Cancer Study and Pathology in Japan [16].

Overall survival was analyzed from the date of surgical treatment to the date of death or the last follow-up and was estimated according to the Kaplan–Meier method and compared using the log-rank test. A multivariate analysis was performed to identify the significant contributors that were independently associated with the prognosis among the factors that were found to be significant in the univariate analysis using the Cox proportional hazards model. Statistical significance was defined as a p value of less than 0.05. All statistical analyses were performed with the Statview software program (Version 5.0; Abacus Concepts Inc., Berkeley, CA, USA).

Table 1 Clinicopathological characteristics of gastric cancer patients with synchronous liver metastases (n=72)

Characteristics		Total (n=72) (%)	H1, 2 (n=34)	H3 (n=38)
Age (years)	<65	29 (40.3)	15	14
	≥65	43 (59.7)	19	24
Gender	Male	58 (80.6)	27	31
	Female	14 (19.4)	7	7
Histologic differentiation	Diffe.	46 (63.9)	34	23
	Undiffe.	26 (36.1)	11	15
Tumor size (cm)	<5	15 (20.8)	7	8
	≥5	52 (72.2)	24	28
	Unknown	5 (7.0)	3	2
Tumor depth of inversion	T1,2	27 (37.5)	14	13
	T3,4	45 (62.5)	20	25
Lymphatic invasion	ly0,1	13 (18.1)	10	3
	ly2,3	56 (77.8)	21	35
	Unknown	3 (4.1)	3	0
Venous invasion	V0,1	22 (30.6)	15	7
	V2,3	46 (63.9)	16	30
	Unknown	4 (5.5)	3	0
Lymph node metastases	N0,1	22 (30.6)	14	8
	N2,3	46 (63.9)	19	27
	Unknown	4 (5.5)	1	3
Peritoneal dissemination	P0	50 (69.4)	26	24
	P1	22 (30.6)	8	14
CEA level (ng/ml)	<5	23 (33.0)	12	11
	≥5	46 (63.9)	21	25
	Unknown	3 (4.1)	1	2
CA19-9 level (ng/ml)	<37	34 (47.2)	19	15
	≥37	32 (44.4)	11	21
	Unknown	6 (8.4)	4	2

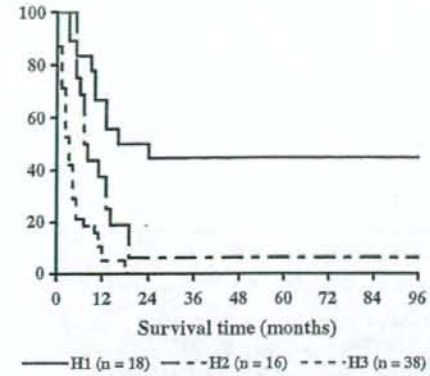

Fig. 1 The overall survival curve for 72 gastric cancer patients with H1, H2, and H3 metastases. Comparison of actuarial survival rates (Kaplan–Meier) for H1 group (n=18) vs. H2 (n=16): P=0.0120 (log-rank test); H1 group vs. H3 group (n=38): p<0.0001; H2 group vs. H3 group: p=0.0005

Results

Clinicopathological data in 72 gastric cancer patients with synchronous liver metastases

The clinicopathological characteristics of 72 gastric cancer patients with synchronous liver metastases are summarized in Table 1. Of the patients, 34 (47.2%) had H1 or H2 metastases, whereas 38 (52.8%) patients had H3 metastases. Tumor size, tumor depth of invasion, extent of lymph node metastases, and lymphatic and venous invasion of the primary gastric cancer were high grade in more than 60% of all patients. Twenty-two patients (30.6%) were positive for peritoneal dissemination, and 63.9% and 47.2% of the patients had abnormally elevated CEA and CA19-9 levels, respectively. In addition, the median survivals of the H1, H2, and H3 groups were 16.6, 10.2, and 4.4 months, and the difference in these groups' curves was statistically significant (p<0.02), as shown in Fig. 1.

Univariate and multivariate analyses of prognostic factors

The univariate analysis was performed for all the clinicopathological factors in Table 1 to further elucidate the prognostic factors. As shown in Table 2, degree of liver metastases (H1, H2/H3), tumor depth of invasion, lymphatic invasion of primary gastric cancer, lymph node metastases, absence (P0) or presence (P1) of peritoneal dissemination, and CA19-9 level were found to be univariately related to patient survival (p<0.05). Next, a multivariable analysis was performed to determine the independent prognostic factors among those six factors that were found significant on the univariate analysis, as shown in Table 2. It was demonstrated that the degree of liver metastases (p<0.0001) and the presence of peritoneal dissemination (p=0.0033) were significantly high risk factors for liver metastases of gastric cancer.

Treatment methods of liver metastases in patients with H1, H2, and P0

The treatment methods for the 26 patients with H1, 2, and P0 are summarized in Table 3. Twelve patients underwent a hepatic resection in the same time of gastrectomy, and a radical operation was performed in 11 of these patients. Of these 12 patients, five patients received hepatic artery infusion (HAI) chemotherapy after the operation, and two patients with H2 metastases were additionally treated with microwave coagulation therapy (MCT) [17, 18]. Three patients received MCT+HAI, and of these three, two patients also received a radical operation.

The overall survival curves of the liver surgery (hepatic resection and/or MCT) group (n=15) and the non-liver surgery group (n=11) are shown in Fig. 2. The cumulative 1, 2, and 5-year survival rates of the liver operation group were 80.0%, 60.0%, and 60.0%, whereas the 1-year survival rate of the non-hepatic treatment group was only 36.4%, and the patients in this group did not survive for more than 2 years. The difference in these survival curves

Table 2 Univariable and multivariate analyses of the risk factors for a prolonged overall survival

Risk factors		Univariable analyses		Multivariable analyses	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Tumor depth	T1,2/T3,4	1.710 (1.008–2.900)	0.0466	1.149 (0.547–2.413)	0.7137
Lymphatic invasion	ly0,1/ly2,3	3.654 (1.644–8.124)	0.0015	2.036 (0.731–5.677)	0.1739
Lymph node metastases	N0,1/N2,3	2.228 (1.240–4.002)	0.0074	1.385 (0.701–2.739)	0.3489
Liver metastases	H1,2/H3	4.102 (2.386–7.053)	<0.0001	3.819 (2.004–7.278)	<0.0001
Peritoneal dissemination	P0/P1	3.121 (1.777–5.482)	<0.0001	3.070 (1.454–6.479)	0.0033
CA19-9 level	<37/≥37 ng/ml	1.718 (1.018–2.898)	0.0426	0.845 (0.415–1.723)	0.6436

Table 3 Therapeutic methods of patients with H1, 2, and without peritoneal dissemination

Liver treatment	Total	Liver metastases		Radical operation	
		H1	H2	R 0	R 1
Hepatectomy	12	9	3	11	1
Lobectomy	4	4	0		
Segmentectomy	1	1	0		
Partial resection	7	4	3		
Combination of HAI	5	4	1		
Hepatectomy + MCT	2	0	2		
MCT+HAI	3	1	2	2	1
HAI alone	5	2	3	0	5
No treatment	6	1	5	0	6

MCT microwave coagulation therapy, *HAI* hepatic artery infusion chemotherapy

was statistically significant (p=0.001). In addition, these 26 patients were divided to four groups: liver surgery + HAI group (n=8), liver surgery alone group (n=7), HAI alone group (n=5), and non-hepatic treatment group (n=6), and the overall survival curves are shown in Fig. 3. The cumulative 1, 2, and 5-year survival rates of the liver surgery + HAI group were 87.5%, 75.0%, and 75.0%, whereas those of the liver surgery alone group were 57.1%, 42.9%, and 42.9%, respectively. The difference between these two groups was not statistically significant (p= 0.2255). The 1-year survival rates of the HAI alone and non-hepatic treatment groups were 60.0% and 16.7%, and the HAI alone group had a tendency toward better survival

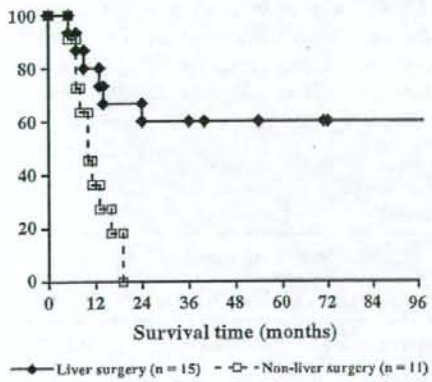

Fig. 2 The overall survival for the 26 patients with H1 or H2 metastases without peritoneal dissemination. A comparison of the actuarial survival rates (Kaplan–Meier) for liver surgery including hepatic resection and/or microwave coagulation therapy (*MCT*, n=15) vs. non-liver surgery at the operation (n=11): p=0.001 (log-rank test)

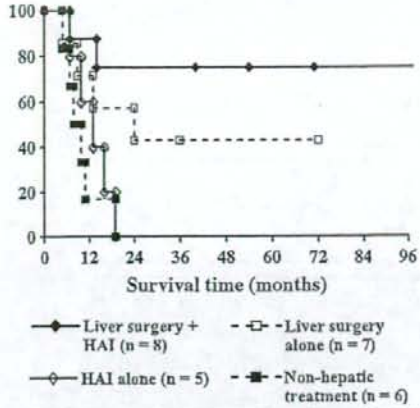

Fig. 3 The overall survival for the 28 patients with H1 or H2 metastases without peritoneal dissemination. Comparison of actuarial survival rates (Kaplan–Meier) for hepatic resection and/or microwave coagulation therapy (Liver surgery) + hepatic artery infusion chemotherapy after the operation (*HAI*; n=8) vs. liver surgery alone (n=7): P=0.2255 (log-rank test); liver surgery + HAI vs. HAI alone (n=5): p=0.0113; liver operation + HAI vs. non-hepatic treatment (n=6): p= 0.0009; liver surgery alone vs. HAI alone: p=0.1317; liver surgery alone vs. non-hepatic treatment: p=0.0380; HAI alone vs. non-hepatic treatment: p=0.4309

than the non-hepatic treatment group; however, the difference between those two groups was not statistically significant (p=0.4309). These results suggested that only liver surgery, but not HAI, could significantly prolong the survival period of patients with H1, 2, and P0.

Analysis of risk factors for prolonged overall survival in patients with H1, 2, and P0

To examine the risk factors for prolonged overall survival in patients with H1, 2, and P0, univariate and multivariate analyses using the Cox proportional hazards model were performed as shown in Table 4. The radical operation (p= 0.0133), the solitary metastatic liver tumor (p=0.0224), and N0, 1 of lymph node metastases (p=0.0260) were independent prognostic determinants of survival.

Characteristics of patients who survived more than 5 years

Furthermore, we reviewed the data on five patients who survived more than 5 years after operation and are alive at present as shown in Table 5. In all of the patients, a radical operation for primary gastric cancer and liver metastases had been performed, and the maximum size of the liver metastases was less than 3 cm. Interestingly, two of the five patients received only MCT and not hepatic resection for liver metastases, and HAI had not been performed after the radical operation in one of the five patients.

Table 4 Univariable and multivariate analyses of the risk factors for a prolonged overall survival in patients with H1, 2, and without peritoneal dissemination

Characteristics		Number	Univariable analyses		Multivariable analyses	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value
Radical operation	R0	13	9.693 (2.685–34.989)	0.0005	33.339 (2.073–536.269)	0.0133
	R1	13				
Treatment method						
Hepatic resection	(−)	14	3.304 (1.141–9.569)	0.0276	0.375 (0.047–2.982)	0.354
	(+)	12				
MCT	(−)	21	0.839 (0.240–2.925)	0.7825		
	(+)	5				
HAI	(−)	13	1.916 (0.727–5.052)	0.1885	0.576 (0.185–1.795)	0.3414
	(+)	13				
Systemic chemotherapy	(−)	6	1.422 (0.500–4.044)	0.5092		
	(+)	20				
Liver metastases						
Number of liver tumor	Solitary	11	4.364 (1.390–13.700)	0.0116	7.218 (1.323–39.370)	0.0224
	Multiple	15				
Size of liver tumor (cm)	<3	11	6.696 (1.878–23.870)	0.0034	1.884 (0.378–9.403)	0.4398
	≥3	15				
Gastric carcinomas						
Histologic differentiation	Diffe.	20	0	0.4823		
	Undiffe.	5				
	Unknown	1				
Tumor size (cm)	<5	6	1.358 (0.433–4.260)	0.5999		
	≥5	18				
	Unknown	2				
Tumor depth of inversion	T1,2	13	1.759 (0.665–4.651)	0.2548		
	T3,4	13				
Lymphatic invasion	ly0,1	10	2.801 (0.887–8.846)	0.0792	2.010 (0.676–5.971)	0.209
	ly2,3	14				
	Unknown	2				
Venous invasion	v0,1	12	0.649 (0.233–1.807)	0.4084		
	v2,3	12				
	Unknown	2				
Lymph node metastases	N0,1	12	2.296 (0.825–6.392)	0.1115	8.159 (2.076–32.076)	0.026
	N2,3	12				
	Unknown	1				

Discussion

The clinicopathological factors of primary gastric cancer may influence survival in gastric cancer patients with liver metastases. It was previously reported that the pathological factors associated with the primary tumor, such as serosal invasion and lymphatic and venous invasion, are significant prognostic factors [14, 19]. However, the impact of these factors was not significant in this study, although tumor depth of invasion (≤T2) and lymphatic invasion (≤ly1) were picked up for the predictor of survival by a univariate analysis. Most authors have reported that these are not predictive factors for the prognosis of patients with liver metastases [3, 5, 6, 13]. Therefore, the clinicopathological factors of the primary tumor may be not directly related to the prognosis and the surgical indications of a hepatic resection. We have demonstrated that the degree of liver metastases (H1, 2) and the absence of peritoneal dissemination (P0) were significant prognostic factors for survival after surgery in patients with liver metastases according to a multivariate analysis. These results emphasize that the indication of the surgical treatment for synchronous liver metastases from gastric cancer is H1, 2 metastases, and P0, and of course, the curative operation for primary and metastases tumors should be treated. We have also found that in those patients, the number of liver metastases (solitary versus multiple) and lymph node metastases (N0, 1 versus N2, 3) were independent prognostic factors of

Table 5 Data on patients who survived more than 5 years after surgery

Patient No.	1	2	3	4	5
Gender, age	M, 54	M, 58	F, 72	F, 74	M, 65
Survival time (months)	136	107	100	72	71
Radical operation	R0	R0	R0	R0	R0
Degree of liver metastases	H1	H1	H2	H1	H1
Number of liver tumor	1	1	3	1	1
Size of liver tumor (cm)	2.5	2.5	2.3	1.5	0.8
Hepatic operation	Right lobectomy	Partial resection	MCT	Left lobectomy	MCT
HAI	CDDP+5FU+MMC	MMC+5FU	MMC+CDDP+5FU	No treatment	CDDP+5FU
Histology	PAP	PAP	PAP	TB1	TB2
Lymphatic invasion	ly1	ly2	ly1	ly2	ly1
Venous invasion	v1	v3	v2	v3	v2
Tumor depth of inversion	T2	T2	T2	T3	T3
Lymph node metastases	n0	n1	n1	n2	n2
CEA (ng/ml)	0.5	2.1	144.9	0.5	10.3
CA19-9 (ng/ml)	7.0	Unknown	18.0	2.0	1.0

survival according to a multivariate analysis. It has also been reported that the number of metastatic tumors is a significant prognostic factor [3, 5, 13] and that the favorable survival outcome for patients with solitary metastases has been no worse than that for a solitary metastases of colorectal cancer [20–22]. In addition, it has been reported that extended lymph node metastases lead to difficulty in radical operations and that the proportion of liver metastases increases with an increased degree of lymph node metastases [19, 23]. Therefore, we strongly indicate that a solitary liver metastatic tumor and no-distant lymph node metastases (≤N1) are good candidates for surgical resection.

Our study demonstrated that in patients with H1 and 2 synchronous metastases without peritoneal dissemination who received the surgical treatment for the metastatic tumors, the cumulative 1- and 5-year survival rates were 80.0% and 60.0%, and this survival period of a surgical treatment for liver metastases is dramatically elongated in comparison to those that have been previously reported [3–5, 7, 13, 14, 24]. In addition, the radical operation including the surgical treatment for liver metastases is a significantly independent prognostic factor of survival according to our univariate and multivariate analyses. Furthermore, it has recently been reported that there were no significant differences in the effect of hepatectomy between synchronous and metachronous metastases [5]. Therefore, synchronous liver metastases from gastric cancer are not necessarily a contraindication for attempts at curative resective therapy of both the primary site and the metastatic site.

Whether the surgical margin is a prognostic factor of survival in gastric cancer patients with metastatic liver tumors remains controversial [5, 6, 13, 19]. On the other hand, in patients with liver metastases from colorectal cancer, a wedge resection with a tumor-free margin of less than 5 to 10 mm is justified because the occurrence of satellite nodules around the main metastatic lesion is reportedly rare [22] and a non-anatomically limited liver resection has become a standard surgical procedure [20, 21]. In the present study, two patients treated for H1 and 2 metastases with only MCT, of which the surgical margin may be less than that of a hepatic resection, [18] survived more than 5 years. In addition, other authors have reported that MCT is equally effective as a hepatic resection in the treatment of two to nine hepatic metastatic tumors from colorectal carcinoma [17, 18]. Therefore, we recognized that a limited resection including MCT may be enough in the treatment of liver metastases from gastric cancer, although the positive surgical margins should be avoided.

Conclusion

Our findings indicate that a radical operation including the surgical treatment for metastatic liver tumors should be performed to improve the prognosis in gastric cancer patients with synchronous H1 and 2 metastases if there is no peritoneal dissemination. A minimum surgical margin is sufficient for a resection of liver metastases, and furthermore, a solitary liver metastatic tumor and no-distant lymph node metastases are the preferable prognostic factors for survival.

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Scientific Paper (Experimental)

Laparoscopic resection for gastrointestinal stromal tumors of the stomach

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KEYWORDS:
Gastrointestinal tumor;
Recurrence;
Laparoscopic surgery

Abstract

BACKGROUND: We reviewed our experience with primary gastrointestinal tumors (GISTs) after surgical treatment.

METHODS: Between 1998 and 2003, 56 patients who underwent surgical treatment for primary GIST of the stomach were enrolled in this study. Statistical analyses of the risk factors for recurrence were assessed.

RESULTS: The proportion of cases undergoing laparoscopic surgery was 25 of 56 (44%) in these retrospective data. The site of recurrence was only the liver in all cases. These recurrent cases were defined as high-risk category. Tumors measuring over 2 cm in size tended to recur earlier, namely within 32 months. A statistical analysis showed a statistically significant correlation between the disease progression and the pathological phenotype.

CONCLUSIONS: This retrospective study has shown that an initial laparoscopic resection of gastric GISTs is feasible even when the tumor size is relatively small (2–5 cm). The pathological phenotype (especially tumor mitosis) directly correlates to the patient's survival even if the resected tumor size was relatively small.

Gastrointestinal stromal tumor (GIST) is one of the many subsets of different types of histology of soft-tissue sarcomas, resulting from a mutation in one of the receptor protein tyrosine kisase (KIT, also called CD117).[1,2] GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract. Most GISTs are KIT positive (approximately 85%–95%). A few GISTs (approximately 5%–15%) may be KIT negative; morphologically typical is not precluded by an absence of KIT staining.[3] GISTs can arise anywhere along the gastrointestinal tract but are most common in the stomach and small intestine. In patients with clinically significant GISTs, the symptoms may include early satiety, bloating, gastrointestinal bleeding, or fatigue-related anemia. Liver metastases and/or peritoneal dissemination are the most common clinical manifestations of malignancy.

Two pivotal sets of guidelines for the treatment of GISTs have already been published from the United States[4] and the European Union.[5] However, there are some differences between the treatments proposed in these guidelines and the results of GIST treatment in Japan. Adenocarcinoma of the stomach is a disease of wide prevalence in East Asia. Routine upper gastrointestinal endoscopy including endoscopic

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ultrasonography (EUS) is well established in Japan. For these reasons, relatively small and asymptomatic GISTs are frequently detected and diagnosed.[6] This retrospective analysis provides data regarding the outcome of patients undergoing a surgical resection for GISTs at our institution.

Patients and Methods

Patient characteristics

Between January 1998 and December 2003, 56 consecutive patients undergoing a surgical resection of primary gastric GISTs were identified in a retrospectively collected database at Wakayama Medical University Hospital.

Diagnostic procedure and tumor evaluation

To assess the clinical stage of the gastric GISTs, an upper gastrointestinal series, endoscopy, and computed tomography scan were performed preoperatively in all patients. EUS was also performed when necessary. Our criteria for determining the endoscopic or EUS findings as possibly malignant were as follows: ulcer formation, tumor size (>30 mm), asymmetric margin, heterogeneous ultrasonographic pattern, existence of an echo-free area, and rapid growth within a short period, as previously described.[6]

Lesions in which the immunohistochemical staining was positive for CD117 (KIT) were diagnosed as GISTs. The resected tumors were divided into 4 groups according to the Risk Assessment Classification proposed by Fletcher.[7] Tumors less than 2 cm in diameter and a mitotic count (MC) of less than 5 of 50 high-power fields (HPFs) was classified as very low risk, low risk was identified when the size ranged from 2 to 5 cm and the MC was less than 5 of 50 HPFs, intermediate risk when the tumor size was less than 5 cm and 6 to 10 of 50 HPFs or the tumor size was 5 to 10 cm and the MC was less than 5 of 50 HPFs, and high risk was determined when the tumor size was greater than 10 cm or the MC was greater than 10 of 50 HPFs or the tumor size was greater than 5 cm and the MC was greater than 5 of 50 HPFs.[7] The mitotic figures were counted in 50 randomly selected HPFs by an experienced pathologist for all samples.

Statistics

The quantitative results were expressed as the mean ± standard deviation of the mean. The statistical significance of the difference between the 2 groups was analyzed by a Student *t* test. The SPSS 15.0 software program (Chicago, IL) was used for all statistical analyses. *P* values of less than .05 were considered to indicate statistical significance.

Table 1 Clinical characteristics of 56 resected GISTs

Age (y)	64.1 ± 12.9	(mean ± SD)
Sex		
Male	23	(41%)
Female	33	(59%)
Clinical symptoms		
Bleeding	6	(11%)
Discomfort	16	(28%)
Asymptomatic	34	(61%)
Tumor location		
Proximal stomach	30	(53%)
Gastric body	25	(45%)
Distal stomach	1	(2%)
Growth pattern		
Intragastric	17	(30%)
Intramural	14	(25%)
Extragastric	25	(45%)

Results

Patient characteristics

From January 1998 to December 2003, 56 consecutive patients undergoing surgical resection of gastric GIST were reviewed (23 men and 33 women). The average age was 64.1 ± 12.9 years (range, 23–83 years). The clinical and pathological characteristics are summarized in Table 1. It is striking that about 60% of the patients were asymptomatic. The tumors of 6 patients had increased in size within 6 months by repeat endoscopy. In addition, 56 (100%) patients underwent an abdominal computed tomography scan, and 29 patients (52%) had endoscopic ultrasonography.

Perioperative outcomes

The operative approaches used were laparoscopic partial resection of the stomach (n = 17), laparoscopic/intragastric resection (n = 8), open partial gastric resection (n = 24), and open gastrectomy (proximal, distal, or total; n = 7). The proportion of laparoscopic surgery was 25 of 56 (44%) in this retrospective data. The average operative time was 165 ± 34 minutes. The mean estimated blood loss was a little less than 50 mL. Moreover, there were no episodes of tumor rupture or spillage, no major intraoperative complications, and no conversions to open surgery during laparoscopic surgery. Postoperatively, some patients after a proximal gastrectomy required a nasogastric decompression tube beyond a 24-hour period. No patient had any evidence of either a staple-line or anastomotic leakage. The average length of hospitalization was 6.6 ± 0.5 days. There were no major postoperative complications or mortalities.

Tumor gross and microscopic characteristics

The majority (98%) of tumors were located in the proximal two thirds of the stomach (Table 1). The average tumor

Table 2 Characteristics of 10 patients with metastatic disease

Patient #	Metastasis (mm)	Size	Risk category	TTR	Operation treatment	Imatinib
1	Liver	70	High	15	GR	No
2	Liver	30	High	18	LPR	No
3	Liver	60	High	24	GR	Yes
4	Liver	56	High	24	GR	No
5	Liver	35	High	26	LPR	Yes
6	Liver	38	High	32	OPR	No
7	Liver	100	High	30	OPR	Yes
8	Liver	55	High	22	OPR	No
9	Liver	46	High	31	OPR	No
10	Liver	150	High	14	OPR	No

TTR = time to recurrence (months); GR = open gastrectomy; LPR = laparoscopic partial resection; OPR = open partial resection.

Table 4 Evaluation of patients and tumor characteristics predictive of the recurrence (univariate analysis)

Patients/tumor characteristics	No recurrence (n = 46)	Recurrence (n = 10)
Age (y)	64.0 ± 11.8	64.7 ± 17.9
Tumor size (mm)	46.8	64.0*
Mitotic index	4.3	26.7*
CD117 positive	45 (98%)	10 (100%)
CD34 positive	44 (96%)	10 (100%)
Asymptomatic	26 (60%)	6 (60%)
Tumor ulceration	10 (21%)	5 (50%)
Tumor necrosis	5 (10%)	7 (70%)*
Macroscopic surgical margin (mm)	33.3 ± 7.9	23.2 ± 8.6*

Mitotic index means number of mitosis per 50 HPFs.
*$P < .05$.

size was 50.1 ± 30.7 mm (range, 10–150 mm). All lesions had a negative resection margin of 31.6 ± 8.9 mm (range, 12–57 mm). Mucosal ulcer formation was detected in 15 (26%) of the lesions. In immunohistochemical staining, a CD117- positive rate was detected in 55 (98%), and CD34 was positive in 54 (96%) patients. The risk categories were as follows: very low, 4 (7%); low, 9 (16%); intermediate, 23 (41%); and high, 20 (36%), respectively.

Recurrent pattern and characteristics

With a median follow-up of 37 months (range, 26–79 months), recurrence occurred in 10 (18%) patients, 4 of whom died of the disease. The site of recurrence was only the liver in all cases. These 10 recurrent cases are summarized in Table 2. These recurrent cases had already been defined as high risk. There was no recurrence of tumors less than 2 cm in a diameter, whereas in case of relatively small tumors (2–5 cm in diameter) had tumor recurrence in 13% (Table 3). The average time of recurrence was 23.6 ± 6.4 months.

Recurrent risk assessment

Patients' characteristics (age and sex), tumor size and resection margin, and microscopic (including mitotic index, cellular maker, presence of necrosis, or ulcer formation) features were analyzed as prognostic factors of disease progression (Table 4). We considered both recurrence and metastasis during the follow-up period as evidence of disease progression. A statistical univariate analysis showed that there was a statistically significant correlation between disease progression and tumor size, mitotic count, tumor ulcer necrosis, and macroscopic surgical margin. On a multivariate analysis of these 4 significant factors detected on a univariate analysis, however, only the tumor mitotic index proved to be a significant independent predictive variable affecting survival (hazard ratio = 10.546; confidence interval, 2.313–45.167, $P = .007$).

Table 3 Relatively small (2–5 cm) GISTs have the potential recurrence

Tumor diameter	Total cases	Recurrence
<2 cm	5	0
2–5 cm	30	4 (13%)
5–10 cm	15	4 (26%)
>10 cm	6	2 (33%)

Comments

GISTs of the stomach are one of the most important submucosal tumors becoming more frequently encountered because of the rising incidence of upper gastrointestinal endoscopy. In particular, routine upper gastrointestinal endoscopy including EUS is well established for asymptomatic patients in Japan. For these reasons, small (<2 cm) or relatively small (2–5 cm) GISTs may be frequently detected and diagnosed.[6] This article summarizes the outcome of surgically resected GISTs of the stomach in our institution.

Defining meaningful prognostic factors of surgically resected GISTs of the stomach has been historically elusive. This may be because of the inconsistent pathological diagnosis before the recognition of KIT as well as the grouping of GISTs from various areas of the gastrointestinal tract. Several recent studies have shown a comprehensive relationship between the clinical and pathological data of gastric GISTs. The emerging consensus favors risk optimization of the tumors over absolute distinction of benign versus malignant.[7,8] Based on a large retrospective analysis, for example, Meiettien et al[8] recently showed the classification of the gastric GISTs as benign, very low, low, low-to-moderate, and high malignant potential. Similar to other previous reports,[9,10] they used the tumor size and mitotic

activity as the most predictive prognostic factors. They also showed that even patients with large (>10 cm) GISTs of the stomach and with a low (<5 per 50 HPF) mitotic index have a 12% to 15% tumor-related mortality, often after a prolonged survival. In contrast, even relatively small (<5 cm) tumors in the presence of a high mitotic index result in tumor-related deaths in more than 50% of patients.[8] Another multivariate analysis of 140 surgically resected GISTs of the stomach showed that male sex, a tumor size of over 10 cm, and a mitotic index of 10 or more were all significant predictors of a poor prognosis.[9] In this retrospective analysis, we also found tumor size, mitotic index, and tumor necrosis to be statistically correlated with recurrence after a surgical resection.

A surgical resection of localized GISTs of the stomach is the preferred treatment modality.[11,12] Recently, a 1- to 2-cm margin was thought to be necessary for an adequate resection.[13,14] DeMatteo et al,[15] however, recently showed tumor size, not a negative microscopic surgical margin, to determine survival. Therefore, it is accepted that the goal of a surgical resection of gastric GISTs should be a complete resection including gross negative margins without lymph node dissection. Our retrospective analysis showed that a relatively large surgical margin had the possibility to avoid tumor recurrence after surgery. On a multivariate analysis of significant factors detected on univariate analysis, however, only tumor mitotic index proved to be a significant independent predictive variable affecting survival. We speculate that resected surgical margin may therefore not be directly correlated with tumor recurrence.

Because a simple and less invasive resection, including a laparoscopic resection, is the preferred endoscopic surgical technique of gastric surgeons, the reliability of laparoscopic surgical devices and the fact that gastric GISTs can be easily reached using intraoperative endoscopy, a laparoscopic approach, and the resection to GISTs of the stomach has therefore become very appealing.[13,14,16] Although the National Comprehensive Cancer Network Clinical Practice Guidelines for the Optimal Management of Patients with GIST suggests that laparoscopic techniques should be limited to tumors less than 2 cm, many surgical investigators have reported successful and safe resection of larger GISTs of the stomach.[4] This recommendation regarding size criteria amendable to laparoscopic techniques does not appear to be evidence based. In our series, 44% of the patients received laparoscopic surgery, and no patients had operative lacerations or rupture of the tumor. In our previous report, we proposed that laparoscopic resection be considered the treatment of choice for small (<3 cm) gastric GISTs.[6] In addition, the prospective study from Carolina's Medical Center has recently shown that laparoscopic and laparoendoscopic resection of gastric GISTs of sizes up to 8.5 cm was associated with low morbidity, short hospital stays, and the long-term disease-free survival.[16] In our present analysis, the tumor mitotic index only proved to be a significant independent predictive variable affecting survival. Given the degree of efficacy and the advantages afforded by laparoscopic techniques, therefore, we recommend that a laparoscopic approach may be the preferred resection strategy in most patients with from small- to medium-sized gastric GISTs. With recent trials confirming the safety of laparoscopic techniques in colon and gastric oncologic surgeries,[17,18] the role of laparoscopic surgery in the resection of GISTs of the stomach should therefore be further clarified in the near future.

In conclusion, this retrospective study has shown that an initial laparoscopic resection of a gastric GIST is feasible even when the tumor size is relatively small (2–5 cm). A complete resection, including adequate surgical margins, may therefore be an important treatment to avoid liver metastases. However, the pathological phenotype (especially tumor mitosis) is directly correlated to the patient's survival even when the resected tumor size was relatively small. A laparoscopic approach may be the preferred resection strategy in most patients with medium-sized gastric GISTs in the future.

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症例報告

幽門側胃切除術後過食を契機とした胃破裂の1例

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症例は67歳の男性で，胃癌の診断で幽門側胃切除術，D2リンパ節郭清術，Billroth I法による再建が施行され，14病日に軽快退院となった．25病日，すしを大量摂取した後に上腹部の激痛を訴え近医受診し，急性腹症にて当院紹介となった．来院時，腹部は板状硬で，CTでは上腹部を中心とした遊離ガスを認め，上部消化管穿孔の疑いにて緊急手術となった．開腹所見では，腹腔内には多量の無臭で混濁した腹水と米粒を認めた．胃は体上部大彎で長軸方向に約3cmの裂創が認められた．同部に明らかな炎症所見や潰瘍の形成は認められなかった．また，胃十二指腸吻合部にも明らかな異常を認めなかった．破裂部を縫合閉鎖し，腹腔内を洗浄，ドレナージを行った．術後約2週の透視でも，胃十二指腸吻合部に明らかな狭窄は認められなかった．過食による過膨張のために起こった胃破裂と考えられた．幽門側胃切除後の胃破裂は報告がなく，若干の考察を加えて報告する．

はじめに

特発性胃破裂は外傷や酸アルカリの服用など明らかな素因のない胃破裂をいい[1]，まれな疾患である．今回，我々は幽門側胃切除術後に発症した特発性胃破裂の症例を経験したので，若干の文献的考察を加えて報告する．

症　例

症例：67歳，男性

主訴：上腹部痛

既往歴：高血圧症，高脂血症，不眠症にて内服加療中．

現病歴：当院にて幽門前底部小彎の胃癌に対し幽門側胃切除術，D2リンパ節郭清，Billroth I再建が施行された（Fig. 1）．術後病理組織学的診断はmp，n1，P0H0M0 p-Stage IIであった．術後経過良好にて術後14病日に退院となった．退院時の経口摂取は常食の1/3程度を分割摂取していた．

術後25病日にすし屋にてすしを約20分で10貫以上摂取した．この直後より上腹部に激痛が出現し，救急車にて近医を受診した．急性腹症と診断され当院紹介受診となった．発症より4時間であった．

入院時現症：身長165cm，体重52kg，血圧143/80mmHg，脈拍135回/分，呼吸35回/分，SpO_2 91％ 腹部は板状硬で著明な腹膜刺激症状を認めた．圧痛の最強点は心窩部にあった．

入院時検査所見：白血球数が2,800/μと低下し，ヘモグロビン11.1g/dlの軽度の貧血および血清クレアチニン値1.34mg/dlと上昇が認められた．CRPの上昇は認められなかった．

胸部X線検査所見：明らかな異常陰影は認められなかった．

腹部単純CT所見：残胃には大量の食物残渣が存在し，一部上腹部を中心とした腹水と腹腔内遊離ガスが認められ，上部小腸には炎症性の壁肥厚が認められた（Fig. 2a，b）．

術前診断：以上より，急性腹症，その原因として吻合部潰瘍や十二指腸潰瘍などの上部消化管穿孔が疑われた．

手術所見：上腹部正中切開にて開腹した．腹腔内には無臭で混濁した腹水を約500ml認めた．上

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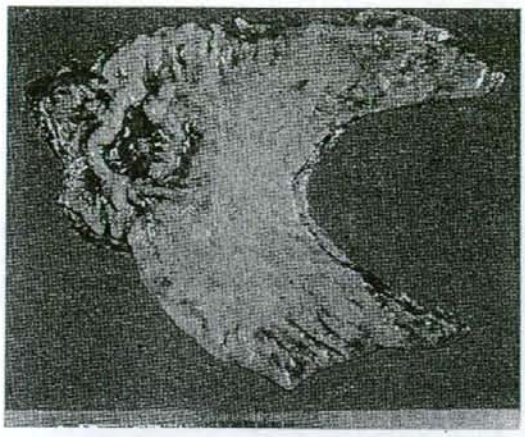
Fig. 1　The resected specimen showed type 2 gastric cancer.



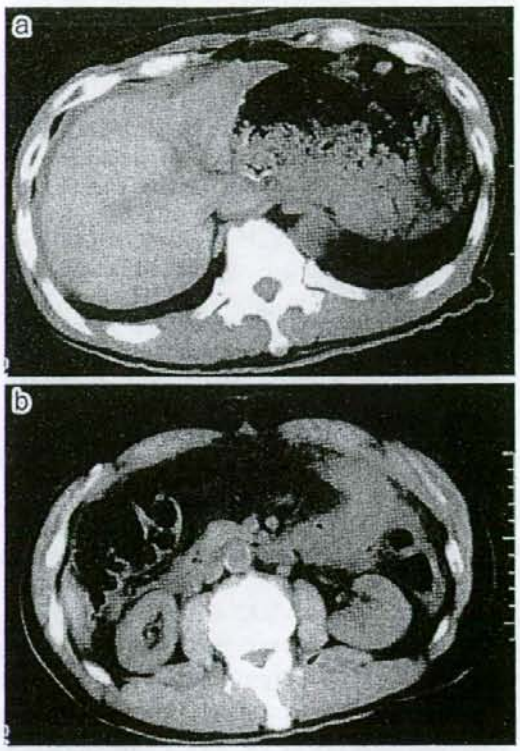
腹部を中心とした腹腔内には多量の米粒が認められた．残胃の体上部大彎に長軸方向に約3cmにわたる裂創が認められた．同部には明らかな潰瘍形成や粘膜の色調の変化は認められなかった（Fig. 3）．胃十二指腸吻合部に明らかな異常は認められなかった．以上より，過食を契機とした特発性胃破裂と診断した．腹腔内を十分に洗浄した後に，同穿孔部を2層に縫合閉鎖し，大網で被覆した．腹腔内ドレナージを行い手術を終了した．

術後経過：3日間の集中治療室での全身管理を要した．術後，肺炎や創離開が認められたが，保存的に軽快した．今回の術後14病日の胃透視を示す（Fig. 4）．胃十二指腸吻合部に明かな通過障害を認めなかった．術後87病日に退院となった．

考　察

特発性胃破裂は，spontaneous ruptureやunexpected ruptureともいわれ[1]，外傷や酸アルカリの服用などの明らかな素因のない胃破裂をいう[2]．原因としては，胃の菲薄化を伴う過膨張があげられており，その誘因として過飲，過食，sodium bicarbonateの服用，胃出血，酸素カニューレによる酸素投与などが報告されている[2)-6)]．また，十川ら[6]の本邦12例の検討によると，7例で精神疾患の関与が認められている．術後に発症した報告は少なく，Nissenのfundoplication術後の報告があるものの[7]，幽門側胃切除術後の報告は非常にまれである．医学中央雑誌で「胃破裂」「胃切除」をキーワードとして1983年から2007年までにつき検索したところ2例の報告[8)9)]（会議録）を認めるのみであった．

Fig. 2　Abdominal CT showed free air, ascites, dilatation of the stomach due to meal (a) and wall thickness of upper small intestine (b). A small part of the meal seemed to be out of the stomach.

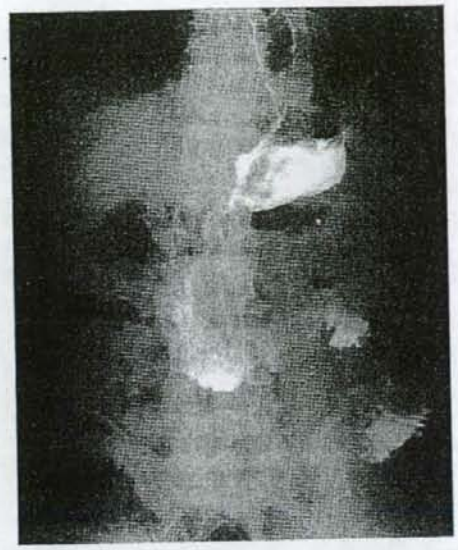


奥村ら[2]によると過膨張状の胃が破裂する原因として物理的な要因と血流障害による要因の二つが考えられている．

物理的要因とは，過膨張した胃が嘔吐などのために，幽門と食道噴門接合部の閉鎖を生じ，胃内圧が急激に上昇し，主として伸展性の少ない小彎側に緊張が集中して破裂する場合を言う．Jefferis[10]は，食道胃接合部や小網により固定され膨張性に乏しい小彎や前壁が一般的に破裂しやすいと報告している．具体的には，4L以上の液体で胃が充満した場合[10]や，内圧が120～150mmHgを超えた場合[11]に胃破裂が起こるとされている．

Fig. 3 Operative findings revealed an apporoximately 3-cm logitudinal tear of the greater curvature of upper stomach body. There was neither ulceration nor inflammation at the lesion.

Fig. 4 Roentgenoscopy showed : There was no stenosis at the gastrojejunostomy on 14th postoperative day.



血流障害による要因とは，過膨張のため胃壁静脈圧を超える胃内圧の上昇が遷延し胃壁の血流障害，壊死が起こり破裂する場合を言う[12]．胃壁には血流障害が起こりやすい場所はないとされるため[13]，この機序では胃破裂は小彎以外にも発生するといわれている．

本症例の胃破裂の原因としては，すしの過食により胃が急速に過膨張したことによる物理的要因が主であると推察された．すしは一口で，出されたらすぐに食べるのが粋な食べ方とされている．この食べ方では，食物が短時間で多量摂取され，胃切除後のため容量の減少した残胃が過膨張を容易に引き起こすことが推察される．また，よく咀嚼されなかった米飯（しゃり）がブロック状の個体として胃に蓄積され，術後25病日で胃十二指腸吻合部が浮腫により狭窄していた可能性も考えると，これも原因の一因となったことは否めない．また，物理的要因による胃破裂は一般に小彎に多いとされているが[10]，本症例は大彎に裂創を来していた．これまでに報告された2症例も原因は物理的要因と推察されたが，大彎に穿孔を来していた[8][9]．この理由として，手術により胃の固定が胃食道接合部，体上中部大彎，胃十二指腸吻合部と変更されたこと，胃十二指腸吻合は大彎側に作成するため，大彎側が最も進展され，菲薄化しやすい状態となっていたことなどが考えられた．また，本症例を含めいずれの症例でもD2リンパ節郭清が行われており[8][9]，左胃大網動脈領域のリンパ節郭清が胃破裂に影響をおよぼしていることも推察された．

本疾患の診断は，術前に確定することが難しく，その重症度，緊急度が高く急性腹症として手術されることが多い．本症例でも急性腹症として緊急手術が行われた．突然出現する腹痛，腹部膨満，腹腔内遊離ガスなどともに病歴の聴取が診断の決め手となると思われる[2]．

本疾患の治療に関しては，汎発性腹膜炎に対する手術，併発するショックに対する全身管理の正否が治療成績を左右すると思われる．胃切除の必要性については議論があると思われるが，本症例のように縫合閉鎖することで治癒する症例もあり[4][8][9]，穿孔部に明らかな血流障害がなければ，縫合閉鎖も一つの選択肢となりうると思われた．

胃切除術後の穿孔に対しては，最も重要なことは予防，すなわち食事指導と思われた．当院では，1) 1回食事量は術前食事量の1/3程度とする，2) おやつを含めて1日5から6回の食事回数とす

る，3)1回の咀嚼は10回以上行う，ということを胃切除の食事方法として推奨している．この少量頻回摂取の食事指導が守られていれば，本症例の発症は予防できたと考えられ，本人の嗜好などに合わせた食事指導の重要性が再認識された．

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Spontaneous Gastric Rupture triggered Overextension due to Excessive Oral Intake following Distal Gastrectomy：A Case Report

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We report a case of spontaneous gastric rupture following distal gastrectomy. A 67-year-old man who underwent distal gastrectomy for gastric cancer and discharged our hospital on postoperative day (POD) 14, ate a large amount of sushi, then experienced severe enough gastric pain to be admitted in an emergency. Physical examination showed muscular defense in the upper abdomen. Computed tomography (CT) showed abdominal free air and ascites, necessitating emergency surgery for acute abdomen. Laparotomy findings included turbid ascites and numerous grain of rice in the upper abdomen. The upper gastric body had a 3-cm longitudinal tear at the greater curvature. Neither ulceration nor inflammation was seen, and diagnosing spontaneous gastric rupture, we sutured the lesion primarily in two layers and lavaged and drainaged the abdomen. No stenosis had been seen in X-ray imaging at the gastrojejunostomy on POD 14, so we concluded that excessive oral intake had overextended the stomach, triggering spontaneous gastric rupture.

Key words：spontaneous gastric rupture, distal gastrectomy, complication

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3. 胃癌手術とリンパ節郭清

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はじめに

胃癌は所属リンパ節に転移が認められても手術による制御がある程度までは可能であり，われわれ消化器外科医にとっては，リンパ節郭清のやり甲斐がある癌腫である。本稿においては，進行胃癌に対してわが国で標準的と考えられているD2郭清の実際，大動脈周囲リンパ節郭清の意義，早期胃癌に対する縮小手術について概説する。

胃癌に対する標準的D2郭清の実際

欧米においてはいくつかの臨床試験の結果から，D1郭清が胃癌に対する標準的術式と考えられている[1]。一方，わが国においてはこれまでD1とD2を比較した検討はなされていないものの，安全に実施可能で郭清効果も高いことからD2郭清が標準的術式と考えられている[2]。確実なリンパ節郭清を実施するには，上腹部の解剖と郭清の手順について習熟しておく必要がある。本稿では，とくに重要なリンパ節について郭清手技を解説する。

A. No.6，14vの郭清

『胃癌取扱い規約』では，No.14vリンパ節は上腸間膜静脈（SMV）前面にあり，上縁は膵下縁，右縁は右胃大網静脈と下（上の誤り）前膵十二指腸静脈の合流部，左縁はSMVの左縁，下縁は中結腸静脈分岐部とされている。したがって，No.14vの郭清に際しては，はじめに中結腸静脈の根部付近で腹膜を切離しSMVの前面に達する。次いでSMVの左縁を同定し，膵下縁との間の組織を右方に向かって剝離していく。通常SMV前面には血管が存在しないので，鈍的操作で容易に右縁に達することが可能である。ここで胃結腸静脈幹を確認し，右胃大網静脈の根部まで血管の前面を剝離し，膵臓との間にある組織を切除することによりNo.14vの郭清は終了する。この際，膵の下縁をしっかり露出しておくことが肝要である。

No.6と14vの境界は同様に，『胃癌取扱い規約』では右胃大網静脈と下（上の誤り）前膵十二指腸静脈との合流部とする。ただし，合流部のものはNo.6に含むとされている。すなわち，No.6の郭清を確実にするためには膵前筋膜を剝離し，上前十二指腸静脈を確実に離出しておく必要がある。われわれは，胃結腸間膜前葉の剝離に際して，膵前筋膜を十二指腸右縁まで剝離し，さらにその層を十二指腸上縁まで左側に向かって膵臓，十二指腸から剝離する。この左右からの剝離操作により，右胃大網静脈を含む層だけが残るため確実な郭清が可能となる（図1）。次いで，膵頭部前面の被膜をさらに十二指腸側に向かって剝離し胃十二指腸動脈を露出し，これを末梢に向かって剝離し右胃大網動脈を確認，根部で結紮切離する。最後に，十二指腸下縁にて下十二指腸動脈，幽門下動脈を切離し，郭清を終了する（図2）。

B. No.8a，No.9右側の郭清

No.8aリンパ節は，脾動脈分岐部から胃十二指腸動脈分岐部までの総肝動脈の前面・上面に存在するリンパ節である。郭清操作は通常右側から開始し，胃十二指腸動脈から固有肝動脈を露出し，郭清の右縁を決定する。さらに郭清の背側縁を決める目的で，右側では門脈に沿って，総肝動脈の背側を剝離し，右腹腔動脈神経叢の前面で後腹膜を食道裂孔付近まで切離する。この際，いわゆるNo.8aと8pには解剖学的な境界が存在しないので，一部リンパ節を切り込んでいく可能性がある。太いリンパ管も存在する部位なので，郭清の