Mp Colorectal Cancer Should Be Defined as Early Colorectal Cancer

KAZUYA KITAMURA, SATOKI NISHIDA, KAZUHITO YAMAMOTO, DAISUKE ICHIKAWA, KAZUMA OKAMOTO, KIYOSHI SAWAI, TOSHIHARU YAMAGUCHI and TOSHIO TAKAHASHI

The First Department of Surgery, Kyoto Prefectural University of Medicine, Kyoto 602-0841

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—— Little is known about the clinicopathologic features of mp colorectal cancer, defined as a cancer where the depth of invasion is limited to within the mucosa, the submucosa and the proper muscle. This study was designed to determine the clinicopathologic features of mp colorectal cancers. From 1973 to 1993, 83 mp colorectal cancer and 66 sm colorectal cancer patients were treated in our department and were enrolled in this study. During the same period, 66 patients with sm colorectal cancer defined as a cancer where the depth of invasion is limited to within the mucosa and the submucosa, were treated. The clinicopathologic findings of these patients were determined retrospectively from their hospital records. Clinicopathologic differences in sm and mp colorectal cancers were compared with sm and mp gastric cancers. The incidence of mp colorectal cancer increased from 7.9% in 1973–1977 to 16.2% in 1988–1993. An advanced macroscopic appearance, a larger tumor size, lymph node metastasis and lymph vessel invasion were more predominant in mp than sm colorectal cancer. Multivariate analysis demonstrated that these clinicopathologic factors were not statistically independent prognostic factors for mp colorectal cancer patients. There was no statistical difference in postoperative survival between sm and mp colorectal cancer patients. Mp colorectal cancer should be defined as early colorectal cancer, because the postoperative survival rate does not differ between mp and sm colorectal cancers, and the clinicopathologic differences between these two are negligible. ——— colorectal cancer; mp cancer; early colorectal cancer; surgery
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Recent advances in diagnostic techniques have increased the early detection of colorectal malignancies (Kitamura et al. 1997). The accumulating number of early-staged colorectal malignancies has allowed us to determine the clinicopath-

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Address for reprints: Kazuya Kitamura, The First Department of Surgery, Kyoto Prefectural University of Medicine, 465 Kawaramachi Hirokoji, Kamigyo-ku, Kyoto 602-0841, Japan.

ologic features of early-staged cancers, which were previously considered to be rare (Shimoda et al. 1989). Mp colorectal cancer, defined as a cancer where the depth of invasion is limited to within the mucosa, the submucosa, and the proper muscle of the colorectal wall, is one such variant. Despite the increasing incidence of mp colorectal cancer, little is known about its clinicopathologic features. This study was designed to clarify the clinicopathologic features of mp colorectal cancer and to determine the most appropriate surgical treatment for this cancer.

PATIENTS AND METHODS

From 1973 to 1993, a total of 765 patients with colorectal cancer were treated at The First Department of Surgery, Kyoto Prefectural University of Medicine, and were enrolled in this study. The clinicopathologic features of these 765 patients were reviewed retrospectively on the basis of their hospital records, using the general rules for Colorectal Cancer Study in Japan (Japanese Research Society for Cancer of the Colon and Rectum 1983). Of the 765 patients, 66 (8.63%) and 83 (10.9%) were diagnosed with sm and mp colorectal cancers, respectively. The clinicopathologic features of both groups were compared.

From 1969 to 1995, a total of 1795 patients with gastric cancer were treated at our department, and were also enrolled in this study. The clinicopathologic features of these 1795 patients were reviewed retrospectively from their hospital records. The macroscopic and microscopic classifications for these gastric cancers were based on the general rules for Gastric Cancer Study in Japan (Japanese Research Society for Gastric Cancer 1981). Of these 1795 patients, 323 (18.0%) and 133 (7.41%) patients were diagnosed with sm and mp gastric cancers, respectively.

The postoperative survival curves were calculated by both the actuarial life table method and the Kaplan-Meier method. All data from both groups were analyzed and compared with a generalized Wilcoxon test. Other statistical analyses were performed by the chi-square test, multivariate adjustment were performed by Cox regression analysis.

RESULTS

Chronological changes in the incidence of mp colorectal cancer

The incidence of mp colorectal cancer had increased significantly from 7.9% in 1973–1977 to 16.2% in 1988–1993 (Table 1).

TABLE 1. *Chronologic change in the number of cases of mp colorectal cancers*

	1973–1977	1978–1982	1983–1987	1988–1993
Rectal cancer	4/36	8/47	16/75	37/176
Colon cancer	3/53	0/43	5/90	31/245
Total (%)	7/89 (7.9)	8/90 (8.9)	21/165 (12.7)	68/421 (16.2)

Clinicopathologic findings of sm and mp colorectal cancers

The clinicopathologic features of patients with mp colorectal cancer were compared with those of patients with sm colorectal cancer (Table 2). For the macroscopic appearance, the superficial type was found more predominantly in sm colorectal cancers than in mp colorectal cancers ($p < 0.01$). The tumor size was smaller for sm colorectal cancers than for mp colorectal cancers ($p < 0.01$). Minimally invasive surgery, including a partial resection and limited lymph node dissection, was performed frequently on patients with sm colorectal cancers than those with mp colorectal cancers ($p < 0.01$). Lymph node metastasis and lymph vessel invasion were more prevalent in mp colorectal cancers than in sm colorectal cancers ($p < 0.05$ and $p < 0.01$, respectively).

TABLE 2. *Clinicopathologic findings of sm and mp colorectal cancers*

Variable	sm cancer (%)	mp cancer (%)	chi-square test
Case number	66	83	
Gender			n.s.
Male	38 (57.6)	41 (49.4)	
Female	28 (42.4)	42 (50.6)	
Macroscopic appearance			
Early			$p < 0.01$
Superficial	35 (54.7)	7 (9.5)	
Advanced			
Borrmann 1	12 (18.8)	16 (21.6)	
Borrmann 2	17 (26.6)	49 (66.2)	
Borrmann 3	0	1 (1.4)	
Borrmann 4	0	1 (1.4)	
Unknown	2	9	
Tumor size			$p < 0.01$
<1.0	8 (12.7)	2 (2.6)	
1.1-3.0	37 (58.7)	40 (51.9)	
3.1-5.0	10 (15.9)	25 (32.5)	
5.1-	8 (12.7)	10 (13.0)	
Unknown	3	6	
Location			n.s.
Cecum	3 (4.5)	3 (3.6)	
Ascending	7 (10.6)	7 (8.4)	
Transverse	4 (6.1)	5 (6.0)	
Descending	6 (9.1)	3 (3.6)	
Sigmoid	21 (31.8)	16 (19.3)	
Rectosigmoid	3 (4.5)	4 (4.8)	
Upper rectum	6 (9.1)	15 (18.1)	
Lower rectum	16 (24.2)	30 (36.1)	

TABLE 2. *Continued*

Variable	sm cancer (%)	mp cancer (%)	chi-square test
Lymph node dissection			$p < 0.01$
Limited			
D0	5 (7.7)	5 (6.4)	
D1	20 (30.8)	8 (10.3)	
Extensive			
D2	29 (44.6)	42 (53.8)	
D3 or greater	11 (16.9)	23 (29.5)	
Unknown	1	5	
Surgery			n.s.
Polypectomy	10 (15.2)	0	
Partial resection	12 (18.2)	7 (8.4)	
Ileocecal resection	2 (3.0)	3 (3.6)	
Right hemicolectomy	3 (4.5)	4 (4.8)	
Transverse colectomy	2 (3.0)	5 (6.0)	
Left hemicolectomy	2 (3.0)	4 (4.8)	
Sigmoid colectomy	14 (21.2)	15 (18.1)	
Anterior resection	12 (18.2)	21 (25.3)	
Pullthrough resection	7 (10.6)	3 (3.6)	
Miles operation	2 (3.0)	21 (25.3)	
Histology			n.s.
Well	44 (71.0)	62 (77.5)	
Mod	18 (29.0)	14 (17.5)	
Por	0	1 (1.3)	
Muc	0	3 (3.7)	
Unknown	4	3	
Lymph node metastasis			$p < 0.05$
Positive	7 (10.6)	20 (24.1)	
Negative	59 (89.4)	63 (75.9)	
Lymph vessel invasion			$p < 0.01$
Positive	14 (25.9)	40 (48.2)	
Negative	40 (74.1)	43 (51.8)	
Unknown	12	0	

Well, well differentiated adenocarcinoma; Mod, moderately differentiated adenocarcinoma; Por, poorly differentiated adenocarcinoma; Muc, mucinous carcinoma.

Clinicopathologic findings of sm and mp gastric cancers

The clinicopathologic findings of sm and mp gastric cancers are shown in Table 3. The tumor size was smaller in sm gastric cancers than in mp gastric cancers ($p < 0.01$). Lymph node metastasis, lymph vessel invasion and vascular invasion were more prevalent in mp gastric cancers than in sm gastric cancers ($p <$

TABLE 3. Clinicopathologic findings of sm and mp gastric cancers.

Variable	sm cancer (%)	mp cancer (%)	chi-square test
Case number	336	138	
Gender			n.s.
Male	235 (69.9)	92 (66.7)	
Female	101 (30.1)	46 (33.3)	
Tumor size			$p < 0.01$
– 2.0	116 (34.8)	28 (20.7)	
2.1–4.0	144 (43.2)	55 (40.7)	
4.1–6.0	58 (17.4)	34 (25.2)	
6.1–	15 (4.5)	18 (13.3)	
Unknown	3	3	
Location			n.s.
Upper third	36 (10.9)	24 (18.3)	
Middle third	151 (46.2)	48 (36.6)	
Lower third	141 (42.9)	59 (45.0)	
Unknown	7	7	
Gastrectomy			n.s.
Partial resection	8 (2.4)	0	
Distal gastrectomy	272 (82.7)	100 (73.0)	
Proximal gastrectomy	14 (4.3)	11 (8.0)	
Total gastrectomy	35 (10.6)	26 (19.0)	
Unknown	7	1	
Lymph node metastasis			$p < 0.01$
Positive	50 (15.0)	54 (39.7)	
Negative	284 (85.0)	82 (60.3)	
Unknown	2	2	
Lymph vessel invasion			$p < 0.01$
Positive	51 (24.5)	36 (46.1)	
Negative	157 (75.5)	42 (53.8)	
Unknown	134	60	
Histology			n.s.
Diffuse	117 (37.9)	55 (40.7)	
Intestinal	192 (62.1)	80 (59.3)	
Unknown	27	3	

0.01). The extent of lymph node metastasis in the mp colorectal cancers was as follows: n1 positive in 16 cases, and n2 positive in 4 cases.

Postoperative survival

There was no significant difference in postoperative survival between patients with mp colorectal cancer and those with sm colorectal cancer (Fig. 1). The five

Fig. 1. Postoperative survivals of sm or mp colorectal cancer patients.

year survival rates were 96.0%, 92.3%, 88.7% and 87.2% in patients with sm colon cancer, mp colon cancer, sm rectal cancer, and mp rectal cancer, respectively. Postoperative death was found in 13 patients with mp cancer, and in 5 patients with sm cancer. The details were as follows: a) mp cancer: Death due to cancer in 6 cases, and other disease deaths in the other 7 cases; b) sm cancer: Death due to cancer in 3 cases, and other disease deaths in the other 2 cases.

Patients with mp gastric cancer showed a poorer postoperative survival than those with sm gastric cancer (Fig. 2). The five year survival rates were 88.5% and 74.1% in patients with sm and mp gastric cancer, respectively. A generalized

Fig. 2. Postoperative survivals of sm or mp gastric cancer.

Wilcoxon test revealed a statistical difference in the postoperative survival curves between both groups ($p < 0.001$).

There was no difference in survival rate between mp colorectal cancer patients undergoing limited lymph node dissection (D0, D1) and those undergoing extensive lymph node dissection (D2, D3).

Multivariate analysis

To determine the independent prognostic factors of the clinicopathologic factors examined, a multivariate analysis was performed by Cox regression analysis. Lymph node metastasis and lymph vessel invasion were significant prognostic factors in mp gastric cancers (regression coefficients: 0.6940688 [$p = 0.01837$] and 0.7455405 [$p = 0.01942$], respectively), but no other any clinicopathologic findings were independent prognostic factors for mp colorectal cancers.

DISCUSSION

It is commonly held by physicians that the majority of early gastrointestinal cancers can be cured by some form of treatment. In Japan, early colorectal cancer is defined as cancer in which the depth of invasion is limited to within the mucosa or the mucosa and submucosa of the colorectal wall. This definition was presented in accordance with the Japanese definition for early gastric cancer. However, this definition of colorectal cancer does not cover all of the tumors which should be defined as early-staged colorectal cancers. Recent advances in therapeutic techniques have improved the postoperative clinical outcome for colorectal cancer patients (Koyama et al. 1984; Iwatsuki et al. 1986; Martin et al. 1990) and have led to a complete cure for most advanced colorectal cancer patients. This fact, as well as the significant increase in early-staged cancers, indicates that early colorectal cancers should be re-defined to reflect the changing times.

The apparent clinicopathologic differences found between sm and mp gastric cancers are as follows: mp gastric cancers readily produced larger tumors, greater lymph node metastasis and lymph vessel invasion as compared to sm gastric cancers. These factors significantly affected the postoperative survival rate of mp gastric cancer patients according to the results of the multivariate analysis. Thus, mp gastric cancer should be discriminated from sm gastric cancer. In colorectal cancers, the advanced macroscopic appearance, a larger tumor size, lymph node metastasis and lymph vessel invasion were more predominant in mp colorectal cancers than in sm colorectal cancers. Patients with mp colorectal cancers showed a similar survival rate to those with sm colorectal cancers and those rates were significantly higher in the survival rate of patients with colorectal cancer in which the depth of invasion was beyond the proper muscle of the colorectal wall (data not shown). The clinicopathologic differences between sm and mp colorectal cancers were statistically significant, but these differences were

less pronounced than those between sm and mp gastric cancers. The multivariate analysis demonstrated that the clinicopathologic factors of the sm and mp colorectal cancers were not prognostic factors. In other words, the clinicopathologic differences between these colorectal cancers can be ignored from the viewpoint of postoperative survival, as long as the depth of invasion is confined to the proper muscles; thus, mp colorectal cancers can be defined as early cancer.

The present study demonstrated that the incidence of mp cancers in proportion to all colorectal malignancies has recently increased: The overall rate of mp colorectal cancers has been reported to vary from 8% to 14% and the current rate exceeds 10% in Japan (Moriya et al. 1982; Yamaguchi et al. 1990; Itoh et al. 1997). This increase appears to be strongly associated with the increase in early colorectal cancers. The nationwide institution of mass screening and colonoscopy has also facilitated the detection of early and mp colorectal cancers (Registry Committee, Japanese Society for Cancer of the Colon and Rectum 1995).

Advances in endoscopic ultrasonography have allowed us to preoperatively diagnose the depth of invasion, which contributed greatly to determining the best operative procedure for colorectal cancers (Hodgman et al. 1986; Saitoh et al. 1986). However, it remains controversial whether lymph node dissection for mp colorectal cancers should be limited or extensive. Several retrospective analyses concluded that D3 lymph node dissection was imperative for mp colorectal cancer patients based on the results of the anatomical distribution of lymph node metastases (Yamada et al. 1990; Tsunoda et al. 1992). In contrast, other reports have recommended D2 lymph node dissection for these cancer patients (Yasui et al. 1995). The latter opinion is based on the notion that the lymph node metastases were largely limited to n2 regional lymph nodes and that patients with n3 lymph node metastasis showed an extremely poor postoperative prognosis despite the D3 dissection. Our results demonstrated that lymph node metastases were confined to the n2 nodes, and none of the patients with n2 lymph node metastases had any recurrence. Thus, we support the latter notion that mp colorectal cancer patients should undergo a D2 lymph node dissection.

In conclusion, mp colorectal cancers should be defined as a type of early colorectal cancer based on their clinicopathologic findings and postoperative survival rate, and D2 lymph node dissections should be performed on these cancers.

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