

Lymph Node Metastases and Recurrence of Rectal Submucosal Invasive Carcinoma

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 (Accepted Feb. 9, 2006)

[Background] It has been possible to resect early colorectal cancer by endoscopy because of the progress of colonoscopic diagnosis and technology. Therefore most cases of colorectal mucosal cancer and benign tumor have been resected by endoscopy only. Surgical procedures for rectal submucosal invasive carcinoma include transanal tumor resection and abdominoperineal resection of the rectum. Therefore, there is a variation in quality of life. The aim of this study was to evaluate the management of rectal submucosal invasive carcinoma by analyzing lymph node metastases and recurrence of rectal submucosal carcinomas.

[Methods] From 1988 to 2003, 108 patients who had rectal submucosal invasive carcinoma were studied clinicopathologically. Fifty-three patients underwent endoscopic resection (ER), 11 patients underwent local resection, and 44 patients underwent surgical resection with lymph node dissection. Patients with recurrence after resection and patients with lymph node metastasis after surgical resection were analyzed.

[Results] ① Of 53 patients who underwent ER, 14 underwent additional bowel resection, and one (7.1%) had lymph node metastasis. Histopathological findings showed well-differentiated tubular adenocarcinoma and lymphatic invasion. No recurrence occurred in the patients who underwent additional bowel resection. Recurrence was seen in 2 (5.1%) of 39 patients who had been followed up without additional bowel resection. ② Of 11 patients who underwent local resection, one had recurrence after transsacral tumor resection. ③ Of 44 patients who underwent surgical resection with lymph node dissection, 4 patients (9%) had lymph node metastasis. All 4 patients had submucosal invasion deeper than sm2 and positive lymphatic invasion. Recurrence after surgical resection occurred in 2 patients.

[Conclusion] In patients with rectal submucosal invasive carcinoma, additional bowel resection after ER or local resection is thought to be indicated if histopathological findings reveal submucosal invasion deeper than sm2 and positive vascular invasion. Patients who underwent endoscopic piecemeal resection should be followed up carefully. It was often difficult to diagnose lymph node metastasis intra-operatively. Therefore, radical resection with adequate lymph node dissection for advanced cancer is indicated if lymph node metastasis is positive on quick histopathological diagnosis.

Key words: rectal submucosal invasive carcinoma, lymph node metastasis, recurrence

Introduction

It has become possible to resect early colorectal carcinoma by endoscopy because of the progress of colonoscopic diagnosis and technology. Some cases of colorectal submucosal invasive carcinoma have been resected curatively by endoscopy. Complete endoscopic resection (ER) of intramucosal carci-

noma is accepted as curative, as there is no risk of lymph node metastasis¹⁾²⁾. Conversely, submucosal invasive carcinoma shows lymph node metastasis in 6-12% of cases^{3)~7)}. Therefore, in some patients who had colorectal submucosal invasive carcinoma, ER has been performed curatively. However in some cases of colorectal submucosal invasive carcinoma

Table 1 Rectal submucosal invasive carcinoma (n=108)

	Case	Followed up	Surgical resection (additional bowel resection)
Endoscopic resection	53	39	14
Local resection	11	10	1
Surgical resection	44	—	—

Table 2 Rectal submucosal invasive carcinoma resected by ER (n=53)

	Case	Residual tumor	Lymph node metastasis	Recurrence
ER and cut end (-)				
Additional bowel resection	6	0	0	0
Follow up	23	—	—	0
EPMR or cut end (+)				
Additional bowel resection	8	0	1	0
Follow up	16	—	—	2
Total	53	0	1	2

after surgical resection with lymph node dissection, recurrence has been seen. On the other hand, surgical procedures for rectal submucosal invasive cancer include transanal tumor resection and abdominoperineal resection of the rectum (APR), and therefore there is a variation in quality of life (QOL). The aim of this study was to evaluate the management of rectal submucosal invasive carcinoma by analyzing lymph node metastases and recurrence of rectal submucosal cancer.

Patients and Methods

From 1988 to 2003, 108 patients who had rectal submucosal invasive carcinoma were studied clinicopathologically at the Institute of Gastroenterology, Tokyo Women's Medical University. Fifty-three patients underwent ER, 11 patients underwent local resection (transanal tumor resection; 8 and transsacral tumor resection; 3) and 44 patients underwent surgical resection with lymph node dissection (Table 1).

Patients with recurrence after ER, local resection or surgical resection, and patients with lymph node metastasis after surgical resection with lymph node dissection were analyzed. We recommended additional bowel resections after ER to patients who had the risk factor of lymph node metastasis (①submucosal massive invasive carcinoma, ②vascular invasion, ③poorly differentiated adenocarcinoma, ④

positive surgical margin). We used the classification of submucosal invasion according to the vertical invasive level of the submucosal layer between the muscularis mucosae and muscularis propria into three grades (sm1, infiltration into the upper third of the submucosal layer; sm2, middle third; sm3; lower third)⁸⁾. Patients who had been diagnosed submucosal slightly invasive cancer were indicated ER and patients who had been diagnosed submucosal massive invasive cancer were indicated surgical bowel resection with lymph node dissection. But the incidence of lymph node metastasis was low, APR should be indicated carefully. In these cases, local resection, such as transanal tumor resection often was selected.

Results

1. Patients who underwent ER (Table 2)

Fourteen of 53 patients underwent additional bowel resection after ER. One patient (7.1%) had lymph node metastasis. This patient had a sessile lesion (20 mm in diameter) which was not lifted after submucosal injection (non-lifting sign positive⁹⁾) and was resected by endoscopic piecemeal polypectomy. Histopathological findings yielded a diagnosis of well-differentiated tubular adenocarcinoma and lymphatic invasion. No recurrence occurred in patients who underwent additional bowel resection. Recurrence was seen in 2 (5.1%) of 39 patients who

Table 3 Rectal submucosal invasive carcinoma resected by local resection (n=11)

	Transanal resection case (recurrence)	Transsacral resection case (recurrence)
sm1	2 (0)	1 (0)
sm2	1 (0)	0 (0)
sm3	4 (0)	2 (1)
Uncertain	1 (0)	—
Total	8	3

Table 4 Rectal submucosal invasive carcinoma resected by surgical resection (n=44)

	AR case (recurrence)	APR case (recurrence)	Hartmann case (recurrence)
sm1	9 (0)	1 (0)	0 (0)
sm2	14 (0)	0 (0)	0 (0)
sm3	18 (3)	1 (0)	1 (0)
Total	41	2	1

Table 5 The cases of lymph node metastasis

No.	Location	Size (mm)	Type	Pathological finding	Submucosal invasion	Lymphatic invasion	Lymph node metastasis	Recurrence
1	Ra	14	Ila+IIc	wel	sm3	ly2	n1	+
2	Rs	25	Is	mod	sm3	ly3	n1+n2	+
3	Rb	26	Is	wel	sm2	ly1	n1	-
4	Rb	25	Ila+IIc	wel	sm3	ly1	n1	-

had been followed up without additional bowel resection. One patient had a nodular aggregating tumor (20 mm in diameter) which was resected by endoscopic piecemeal mucosal resection (EPMR). This patient had no lymphatic invasion and sm massive invasive cancer. Eighteen months after EPMR, local recurrence occurred. This tumor was resected completely by endoscopic resection again using a transparent cap. The other patient had a sessile lesion (20 mm in diameter) which was resected by EPMR. Four years after EPMR, recurrence of lymph node metastasis occurred. This tumor was resected curatively by transsacral tumor resection.

2. Patients who underwent local resection (Table 3)

Eight patients underwent transanal tumor resection, and 3 underwent transsacral tumor resection. One patient who had lymphatic invasion underwent additional bowel resection and had no lymph node metastasis. One patient had recurrence two years after transsacral tumor resection, which was re-

sected curatively by APR.

3. Patients who underwent surgical resection with lymph node dissection

Forty-one of 44 patients underwent anterior resection (AR), 2 underwent APR, and one underwent Hartmann's operation (Table 4). Four patients (9%) had lymph node metastasis (Table 5). Two patients had sessile lesions and two patients had superficial depressed lesions. Histopathological findings revealed that 3 patients had well-differentiated tubular adenocarcinoma and one had moderately-differentiated tubular adenocarcinoma. All 4 patients had submucosal invasion deeper than sm2 and positive lymphatic invasion. Recurrence after surgical resection occurred in 3 patients. Of 44 patients who underwent surgical resection, 10 patients underwent dissection of lymph node group 1, 18 patients underwent dissection of lymph node group 2 and 16 patients underwent dissection of lymph node group 3. Two of 3 patients that had recurrence after surgical resection underwent dissec-

tion of lymph node group 2 and one patient underwent dissection of lymph node group 3.

Of 40 patients who had no lymph node metastasis, the depth of cancer invasion of 10 patients were sm1 that of 13 were sm2 and that of 17 were sm3.

Discussion

Submucosal invasive colorectal carcinoma shows lymph node metastasis in 6-12% of cases^{3)~7)}. Therefore, patients who have submucosal invasive carcinoma without lymph node metastasis should undergo ER. The risk factors of lymph node metastasis are known to be the depth of submucosal invasion and vascular invasion⁷⁾¹⁰⁾. The other risk factor is known poorly differentiated adenocarcinoma, but poorly differentiated adenocarcinoma is very rare in the patients who had undergone ER. For non-pedunculated submucosal invasive colorectal carcinoma, the rate of lymph node metastasis was also 0% if the depth of submucosal invasion was $<1,000 \mu\text{m}$ ¹⁰⁾.

Patients who have these risk factors should undergo additional bowel resection. However, there are differences between cases of surgical resection and cases of ER in practice. The risk of lymph node metastasis after ER is thought to be lower than after surgical resection. Therefore, patients who have these risk factors often reject additional bowel resection. We studied 33 patients who had submucosal massive invasive carcinoma endoscopically resected and who did not be received the additional bowel resection¹¹⁾. Sixteen patients rejected to received the additional bowel resection and 14 patients did not received the resection because of the other disease.

ER alone is thought to be curative in the case of endoscopic one-piece resection with a negative margin¹²⁾. On the other hand, of patients who underwent endoscopic piecemeal resection, one patient had lymph node metastasis after additional bowel resection and 2 patients who were followed up had recurrence. One patient with lymph node metastasis after additional bowel resection had vascular invasion. Therefore, endoscopic piecemeal resection should be indicated cautiously for submucosal invasive carcinoma.

Seven patients who had submucosal invasion deeper than sm2 underwent local resection. The incidence of lymph node metastasis was low; therefore, radical resection, such as APR, should be avoided¹³⁾. In such case, local resection is the procedure of choice. Recurrence 2 years after transsacral tumor resection was seen in one patient, and was resected by APR. Histopathological findings revealed a positive margin and vascular invasion, however this patient declined additional bowel resection (APR). Patients who had the risk factors of lymph node metastasis should be received the additional bowel resection.

The depth of cancer invasion of 10 patients who underwent surgical resection was sm1. In these patients, 5 patients underwent surgical resection because of tumor size, but 5 patients were overdiagnosed by usual endoscopy. It is thought be necessary to diagnose more exactly by using magnifying endoscope and endoscope ultrasonography.

Four patients (9%) who underwent surgical resection had lymph node metastasis. Two patients had sessile lesions and 2 patients had superficial depressed lesions. Histopathological findings revealed that 3 patients had well-differentiated tubular adenocarcinoma and one had moderately-differentiated tubular adenocarcinoma. All 4 patients had submucosal invasion deeper than sm2 and positive lymphatic invasion. Our study shows that recommended indications for additional bowel resection are submucosal invasion deeper than sm2 and vascular invasion⁷⁾. Three patients had recurrence after surgical resection. The recurrence of submucosal invasive carcinoma occurred higher in the patients who had moderately differentiated tubular adenocarcinoma, lymph node metastasis and vascular invasion¹⁴⁾. One patient underwent dissection of lymph node group 1 for heart disease and had lymph node group 2 recurrence. The average metastasis lymph node diameter was $<5 \text{ mm}$ ⁷⁾. Therefore, it was thought to be difficult to diagnose lymph node metastasis intra-operatively. Therefore dissection of lymph node group 2 is indicated for patients with submucosal invasive carcinoma who undergo surgical resection. Radical resection with adequate

lymph node dissection for advanced cancer is indicated if lymph node metastasis is positive on quick histopathological diagnosis in resected specimen.

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直腸粘膜下層浸潤 (sm) 癌リンパ節転移例および再発例に関する検討

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[目的] 直腸 sm 癌は、内視鏡切除で根治可能なものから外科切除後再発するものと多様で、外科切除の術式も、経肛門的腫瘍切除術から腹会陰式直腸切斷術と多岐にわたり、術後 QOL にも大きな差異が生ずる。そこで今回、直腸 sm 癌のリンパ節転移例および再発例の検討を行い、治療方針に関して考察した。[対象と方法] 1988~2003 年までに経験した直腸 sm 癌 108 例を初回治療別に、内視鏡切除 53 例、局所切除 11 例および外科切除(リンパ節郭清を含めた腸管切除術) 44 例に分け、リンパ節転移例と再発例を検討した。[成績] ①内視鏡切除: 53 例中 14 例に追加腸切除を行い、リンパ節転移は 1 例 (7.1%) みられた。この症例は Is 病変 (20mm) で non-lifting sign 陽性の分割摘除例 (高分化腺癌, ly (+)) であった。追加腸切除例に再発はなく、経過観察した 39 例中 2 例 (5.1%) に再発を認め、いずれも分割切除例であった。②局所切除: 11 例中 1 例に追加腸切除を行った。経過観察した 10 例中、経肛門的切除の 1 例に 2 年後局所リンパ節再発を認めた。③外科切除: 44 例中リンパ節転移を 4 例 (9%) に認めた。全例 sm2 以深癌でかつ脈管侵襲陽性であった。再発は 2 例 (5%) に認めた。[まとめ] 内視鏡切除および局所切除例で、sm2 以深癌かつ脈管侵襲を有している場合は追加腸切除を考慮すべきで、とくに内視鏡的分割切除の適応は慎重にすべきである。sm 癌はリンパ節転移術中診断は困難で、迅速病理診などを行い、転移陽性の場合には十分なリンパ節郭清を行うべきと考えられる。