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Prognosis of Colonic Carcinoma with Internal Fistula

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Introduction

During the past 22 years, 408 patients underwent surgery for cancer of the colon at Wakayama Medical College (Table 1).

While stenosis, perforation and intussusception are well-known complications of this disease, fistula formation to other parts of the gastrointestinal tract is considered rare. A retrospective analysis revealed that seven of 408 patients had fistula formation and a relatively good postoperative course[8]. We investigated the prognosis of these seven patients with reference to the peripheral lymphocyte count and the stromal reaction of the tumor.

Clinical cases

Table 2 summarizes the seven patients with fistula formation. Ages ranged from 29 to 72 years with an average of 49 years. Male to female ratio was 3 : 4. No significant distribution was seen with reference to either age or sex. The major presenting symptoms were diarrhea, abdominal pain and abdominal distension. Patients 4 and 5 manifested persistent diarrhea possibly due to a shunt or fistula formation. No characteristic symptoms were seen in the other patients. The site of the primary lesion was generally between the

Table 1. Number of cases of colonic carcinoma operated in our department of surgery (from 1956 through 1978)

Cecum & ascending colon	Transverse colon	Descending colon
66	12	11

Sigmoid colon	Retum	Anus	Total
76	226	17	408

Key words : Colonic carcinoma, Internal fistula.
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Table 2. Cases of colonic carcinoma with internal fistula to the other digestive tract

Case No.	Age	Sex	Initial symptom	Primary site of carcinoma	Type of int. fistula	Operative procedures	Histology	Prognosis
(1)	51	M	Abdominal distension	Descending colon	Colo-colic	Segmental resection of the colon	Adenocarcinoma (well)	Died of ileus (19 Months)
(2)	29	M	Left epigastralgia	Transverse colon	Gastro-colic	2/3 Gastrectomy & segment resection of the colon	Adenocarcinoma (moderate)	Alive (10 Years)
(3)	65	F	Epigastralgia	Transverse colon	Gastro-colic	Partial gastrectomy & segment. resection of the colon	Mucinous carci.	Dead (39 Months)
(4)	39	F	Diarrhea	Transverse colon	Jejuno-colic	Segment. resection of the jejunum & colon	Adenocarcinoma (moderate)	Alive (4 Years)
(5)	72	M	Diarrhea	Sigmoid colon	Colo-colic	Left hemicolectomy	Mucinous carci.	Alive (26 Months)
(6)	42	F	Lower abdominal pain	Sigmoid colon	Ileo-colic	Segment. resection of the ileum & colon	Adenocarcinoma (well)	Alive (8 Months)
(7)	45	F	Feacal fistula at the Ileocecal region	Cecum	Ileo-colic	Right hemicolectomy	Mucinous carci.	Alive

cecum and sigmoid colon. In six of the seven patients it was located in the left hemicolon near the splenic flexure. The portion of the gastrointestinal tract to which fistulization occurred included the stomach, jejunum, ileum and colon (Tabel 2). In each of these patients, the tumor grew to a large size with central necrosis. The fistula was located at the center of the tumor.

The definite diagnosis of an internal fistula was made preoperatively in patients 3, 4 and 5. Patient 3 underwent a bypass operation for cancer of the colon at another hospital 3 years ago, and a preoperative colonoscopic examination revealed a fistula to the stomach. In patients 4 and 5, preoperative upper gastrointestinal series and a barium enema confirmed the presence of fistula formation. In patient 4, fistula formation between the colon and the jejunum was demonstrated which is very rare.

Table 2 summarizes the operative procedures employed, histological diagnosis and prognosis in patients with internal fistula. Partial and segmental resection were frequently employed but the removal of lymph nodes was probably incomplete. The histological diagnoses consisted of moderate to highly differentiated adenocarcinoma and mucinous carcinoma with a relatively low grade of malignancy.

The prognosis of colonic carcinoma with fistula formation is relatively good. Five of the seven patients are still alive with the longest being Patient 2 who is 10 years postoperation. Patient 1 died of intestinal obstruction, 19 months postoperatively, while Patient 3 died of the original disease 39 months postoperatively

Prognosis

The prognosis has been favorable in our patients presenting with colonic carcinoma and

fistula formation despite marked extention of the tumor. The relationship between the peripheral lymphocyte count or stromal reaction and prognosis was investigated. The seven patients found to have fistula formation were matched with patients who underwent resection for colonic carcinoma in our department and were found to have tumor masses similar in size, degree of extention and histology.

It was determined that patients with a preoperative peripheral lymphocyte count above 1500 had a more favorable 3-and 5 year survival. A 5-year survival rate of 11% was determined in patients with a lymphocyte count less than 1500. In contrast, patients having an peripheral lymphocyte count above 2500 showed a 3-year survival rate of 100% and a 5-year survival rate of 80% (Table 3).

As outlined in Fig. 1, all seven patients manifesting fistula formation had a preoperative lymphocyte count between 1500 and 2500, thus suggesting a favorable prognosis. However, postoperatively there was a marked increase in the lymphocyte count in those patients that

Table 3. Peripheral lymphocyte count and prognosis of controlled cases of colonic carcinoma

Lymphocyte count/mm³	3-year-survival rate	5-year-survival rate	No. of cases
Above 1500	81%	63%	22
Under 1500	37%	11%	8
Above 2500	100%	80%	15
Under 2500	74%	48%	15

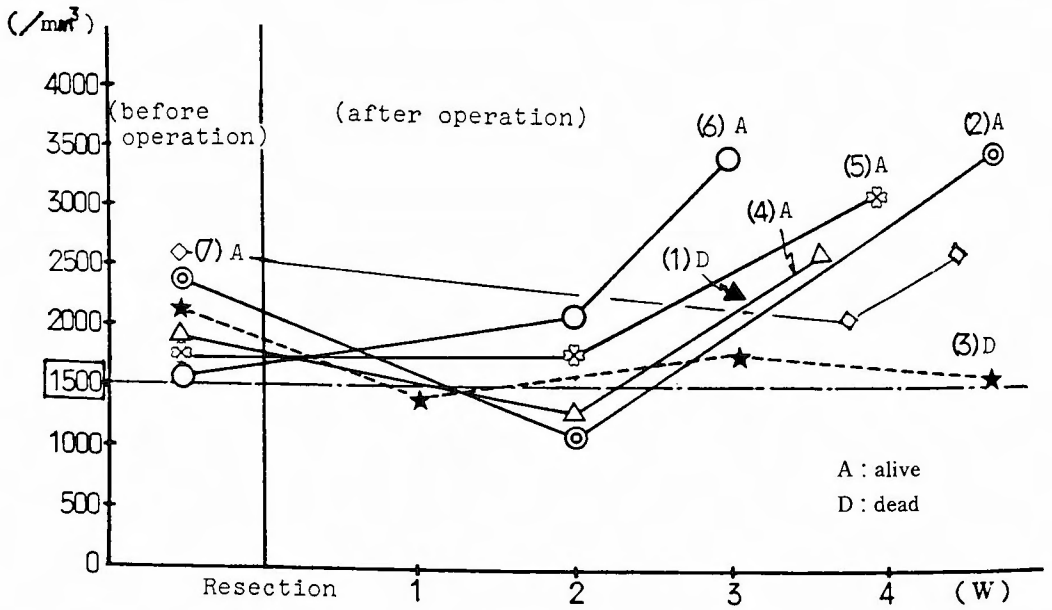

Fig 1. Relationship between peripheral lymphocyte count and prognosis of cases colonic carcinoma with fistula

Table 4. Relation of grade of stromal reaction in carcinoma to prognosis of controlled cases

	No. of cases	3-year-survival rate	5-year-survival rate
Strong (+++)	11	50%	41%
Moderate (++)	22	82%	65%
Weak (+)	5	66%	33%

Table 5. Fibrous and cellular stromal reaction in carcinoma and prognosis

	No. of cases	3-year-survival rate	5-year-survival rate
Fibrous	5	66%	33%
Cellular	6	100%	85%
Mixed	27	80%	60%

Table 6. Kind of cellular component and prognosis

	No. of cases	3-year-survival rate	5-year-survival rate
Eosinophil	8	100%	100%
Lymphocyte	22	81%	73%
Neutrophil	20	80%	70%
Lymphfollicle	10	90%	80%

Table 7. Relation of grade type of stromal reaction in carcinoma and regional lymphnode to prognosis in cases with fistula

	Cases	(1) F. N.	(2) H. K.	(3) M. Y.	(4) C. I.	(5) Z. N.	(6) K. S.
	Histology	adenocarci. (well)	adenocarci. (moderate)	mucinous carci.	adenocarci. (moderate)	mucinous carci.	adenocarci. (well)
stromal reaction	Strong		○				
	Moderate	○		○	○	○	○
	Weak						
	Fibrous						
	Cellular				○		
	Mixed	○	○	○		○	○
	Eosinophil						
	Lymphocyte	○	○	○	○	○	○
	Neutrophil	○	○		○		○
	Lymphfollicle				○		○
Lymphnode	Matastasis			+	−	−	−
	S. H			−	−	−	−
	G. C			−	##	−	+
	T-cell			−	−	−	−
	B-cell			−	+	−	+
	Prognosis	dead 1Y7M	alive 10Y	dead 3Y3M	alive 4Y	alive 2Y2M	alive 8M

survived, while no change was noted in the counts of those patients that died.

In assessing the degree and type of stromal reaction in relationship to prognosis in the control group the following results were observed. The prognosis was most favorable in the presence of a moderate reaction. In addition, the prognosis was best in patients manifesting an intense cellular reaction followed by those with a mixed reaction and those with a fibrous reaction (Table 6). It was also observed that the prognosis was most favorale in those patients demonstrating an intense eosinophillic response (Table 6) The patients with fistula formation were found to manifest the following characteristics (Table 7). The stromal reaction was intense in one and moderate in the remainder A mixed reaction was a consistent finding in all but one patient who manifested a cellular-type reaction. None of the patients manifested a fibrous reaction which in the control group was associated with a poor prognosis. All patients demonstrated a marked infiltration by lymphocytes and neutrophils. Metastases to lymph nodes were detected in only one of four patients in whom regional lymph nodes were totally dissected.

Discussion

In both the peripheral lymphocyte count and stromal reaction of the tumor, our patients with internal fistula appeared to have the condition required for favorable prognosis. There are numerous documentations in the literature of fistula formation associated with malignant tumors. In contrast there is a scarcity of reports describing fistula formation to various parts of the digestive tract associated with colonic carcinoma.

A review of the literature encompassing the last 20 years revealed 16 patients, including our own, with colonic carcinoma and fistula formation[1)~3)5)6)9)~13)]. The fistulae tended to occur most frequently in the left hemicolon (Table 8).

The mechanism of fistula formation has been purported to involve avascular necrosis due to infiltrative growth[1)7)] and a positional association due to anatomy and the accompanying inflammatory process. In view of the peripheral lymphocyte count and mode of stromal reaction reported above, the resistance against the tumor appears to be intense in patients with formation of internal fistula with consequent localized tumor growth without metastases to lymph nodes or remote sites. Though the tumor frequently appears unresect-

Table 8. Number of cases reported in the recent literature

Type of fistula	Japan	Foreign countries
Gastro-colic	5 (our case : 2)	42
Doudeno-colic	4	10
Jejuno-colic	2 (our case 1)	3
Ileo-colic	2 (our case 2)	—
Colo-colic	3 (our case : 2)	—
		(unknown 5)
Right Left	5 : 11	1 : 4

able in patients with internal fistula, its resection not only abolishes the symptoms due to shunting of the digestive tract but also provides a relatively favorable prognosis. It is, therefore, desirable to make every attempt possible to resect these tumors.

Conclusion

1. Internal fistula associated with colonic carcinoma tended to occur more frequently in the left hemicolon.

2. The prognosis of patients with colonic carcinoma and fistulae was better when (a) the preoperative absolute lymphocyte count was greater than 2500, and a postoperative rise was documented ; (b) a cellular-type stromal reaction was demonstrated ; (c) resection of the colonic carcinoma and fistula was performed.

Summery

While stenosis, perforation and intussusception are well-known complications of cancer of the colon, fistula formation to other parts of the gastrointestinal tract is considered rare. A retrospective analysis revealed that seven of 408 patients had fistula formation. These internal fistulae associated with colonic carcinoma tended to occur more frequently in the left hemicolon. The prognosis of patients with colonic carcinoma and fistulae was better when (a) the preoperative absolute lymphocyte count was greater than 2500, and a postoperative rise was documented ; (b) a cellular-type stromal reaction was demonstrated ; (c) resection of the colonic carcinoma and fistulae was performed.

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和文抄録

内瘻形成せる大腸癌の予後

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我々の教室において，過去22年間に手術を施行した大腸癌症例408例中に，大腸癌の合併症として従来比較的稀とされていた消化管への内瘻形成症例7例を経験した．これらの症例の原発癌の局在部位は6例が左側結腸であり，国内外の文献と併せ考え，内瘻形成は左側大腸癌の特長にあげられる．またこれらの症例では病期がかなり進行していたと思われるが，全例切除可能であり，その予後も比較的よい．そこでかかる症例の末梢リンパ球数，腫瘍の間質反応を検索し，これらの点からも内瘻形成大腸癌が予後の良い群に入ることを知りえた．結論として，内瘻形成大腸癌は予後が良いので，極力切除するように努めるべきであることを強調する．