Simultaneous Occurrence of Multiple Gastric Carcinomas and Familial Polyposis of the Colon

Keiichi OHSATO, Hidenobu WATANABE, Hideaki ITOH,
Tsuneyoshi YAO, and Masaya NISHIMURA

ABSTRACT: Upper gastrointestinal survey in ten patients with familial polyposis of the colon revealed the presence of polyps and/or carcinomas of the stomach or duodenum in eight, including two cases of associated multiple gastric carcinomas with concomitant presence in one case of multiple gastroduodenal adenomatous polyps and in the other without presence of polyp. The rather frequent association of gastroduodenal polyps and cancerous lesions in familial polyposis suggests such association to be a part of the manifestation of this inherited disease and possible malignant change occurring in gastroduodenal mucosa as is generally supposed to be the case in large intestine.

KEY WORDS: familial polyposis, multiple gastric cancers, polyp, upper gastrointestinal survey, total colectomy, gastrectomy, gastrointestinal cripples.

INTRODUCTION

Familial polyposis is characterized by the occurrence of multiple adenomas with malignant potential in the colon and rectum[6,11,13]. Recently, however, accompanying upper gastrointestinal polyposis as well as extraalimentary growth, such as bone and soft tissue tumor in Gardner's syndrome,[8] has been described[1,9,10,18,20]. Furthermore, the occurrence of carcinoma of the stomach or duodenum in familial polyposis is increasingly reported. The purpose of the present study is to report rather high incidence of such associated gastrointestinal lesions and to emphasize the importance of routine upper gastrointestinal survey in familial polyposis.

MATERIALS AND METHODS

This report is based on the 10 cases of familial polyposis admitted to the Department of Surgery I, Kyushu University Faculty of Medicine during the past 10 years. Heredity was confirmed in 9 of the 10 cases. In all cases, detailed study by upper gastrointestinal X-ray series, endoscopy and histological examination was carried out on the stomach and duodenum for associated lesions. All cases except for one were treated surgically with single or multiple stage procedures. Total colectomy with or without resection of the rectum was

From the Department of Surgery I, Department of Pathology II and Department of Internal Medicine II, Kyushu University Faculty of Medicine, Fukuoka 812, Japan.

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done followed by ileorectal anastomosis in 6, and permanent ileostomy in 3. New polyps arising in the preserved rectum after ileoproctostomy have been fulgurated or extirpated. There was no surgical death. The presence of numerous adenomas was confirmed in resected and autopsy specimens of the colon and rectum. Adenocarcinoma(s) were present in 9 of the 10 cases.

Results

Accompanying Gastrointestinal Lesions

In 8 of the 10 cases subjected to detailed study on upper gastrointestinal tract, polyp(s) and/or carcinomas were detected in the stomach and/or duodenum. Gastric and/or duodenal polyp(s) were found in 7, including one case with concomitant presence of multiple gastric carcinomas. In the remaining one case, only carcinomas in the stomach were detected. Histological studies on these polyps revealed all to be adenomas except for one case of hamartomatous polyposis (Table 1). Polyps were not found in small intestine upon X-ray examination.

Table 1. Accompanying gastroduodenal lesions in familial polyposis of colon

Case Number	Patient	Age	Sex	Confirmed by	Pathological findings	
					Stomach	Duodenum
1	S.T.	52	M	X-ray endoscopy gastrectomy	three adenocarcinomas multiple adenomas	adenoma
2	Y.K.	17	F	X-ray endoscopy gastrectomy	fourteen carcinomas composed of signet-ring cells	not found
3	E.K.	19	F	X-ray endoscopy biopsy	not found	two adenomas
4	Y.N.	30	M	X-ray autopsy	multiple hamartomas	adenoma
5	K.N.	31	M	X-ray endoscopy	not found	not found
6	M.K.	42	M	X-ray endoscopy biopsy	adenoma	not found
7	M.K.	22	F	X-ray endoscopy biopsy	not found	adenoma
8	S.T.	41	M	X-ray endoscopy biopsy	adenoma	multiple adenomas
9	Y.S.	38	M	X-ray endoscopy biopsy	multiple adenomas	multiple adenomas
10	M.F.	20	F	endoscopy	not found	not found

Cases 2–3, cases 4–5, and cases 6–7 belong to the same pedigree respectively.

Report of Cases with Multiple Gastric Carcinomas

Case 1, S. T., a 57-year-old male, was admitted to the department on June 18, 1970, with chief complaints of diarrhea and bloody stool. Sigmoidoscopy and double contrast barium enema revealed numerous sessile or pedunculated polyps throughout the whole large intestine and an ulcerative tumor in the rectum. A diagnosis of diffuse polyposis of colon with rectal cancer was made. An upper gastrointestinal series revealed two shallow, irregular depressed lesions on each of the anterior and posterior walls of the angulus, with multiple sessile polyps in the antrum. These lesions were confirmed by endoscopy. Endoscopic biopsy showed the two depressed lesions to be adenocarcinomas, while the polyps were adenomas. No bone or soft tissue tumor was found. His niece was recently found to have polyposis of the colon.

The surgery was made in two stages. On July 3, 1970 subtotal gastrectomy and abdominoperineal resection of the rectum were carried out. On October 23, 1970 total colectomy with permanent ileostomy was performed. The patient made a satisfactory recovery with loose stool lasting only 2 weeks but the body weight fell by 4 Kg compared to the preoperative level. For three years postoperatively, he was quite healthy, and digestion and absorption tests were normal. In September 1973, however, lung and bone metastases were noted and the patient died on February 27, 1974. No autopsy was done.

Numerous polyps were found diffusely over the whole resected colon and rectum macroscopically. Polyps were with or without pedicles and their size ranged from 0.3 to 3.0 cm in diameter. Histologically, adenomas were demonstrated. Two ulcerative tumors were found

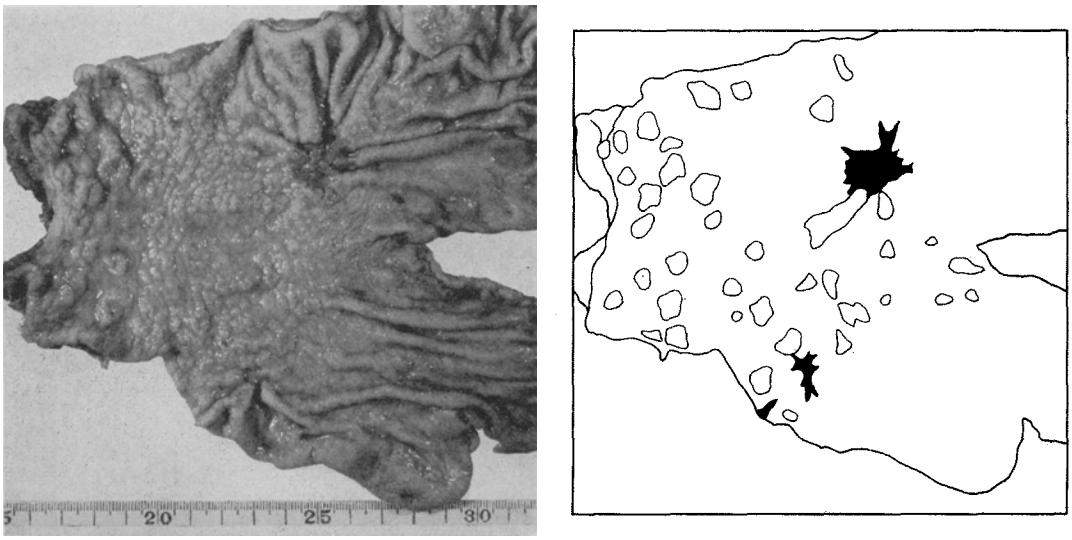

Fig. 1. Left: Two visible, depressed cancerous lesions located symmetrically in the intermediate zone and multiple sessile polyps in the pyloric glandular area of the resected stomach. Right: Cancers including the one detected microscopically shown with the dark areas and polyps with the open circles (case 1).

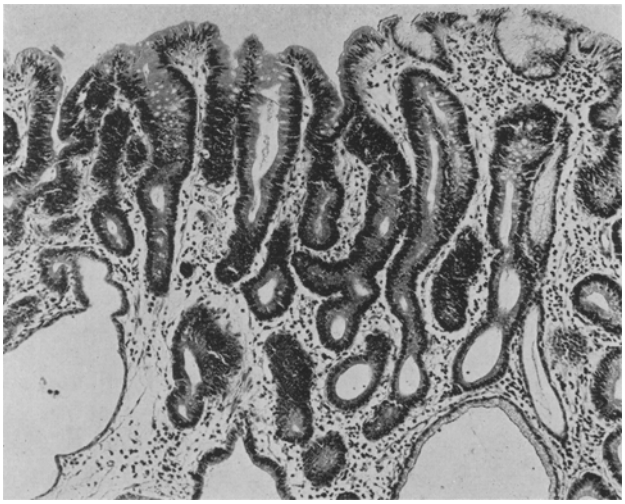

Fig. 2. One of the multiple gastric adenomas in case 1 (S-1326–8, H. E., ×78).

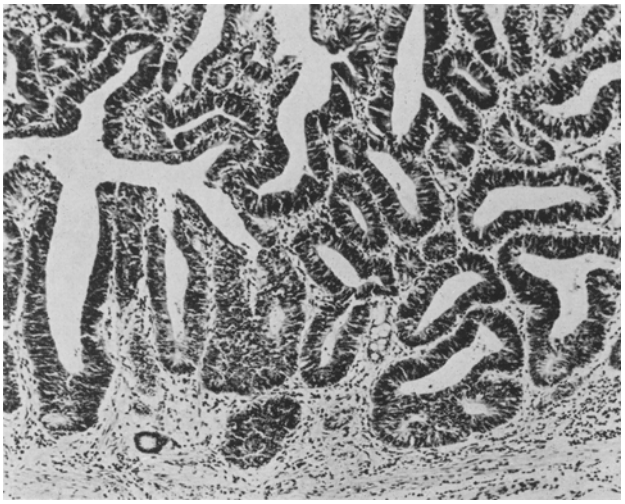

Fig. 3. A well-differentiated intramucosal adenocarcinoma of the stomach in case 1 (S-1326-22-7, H. E., ×78).

in the rectum, both being adenocarcinomas infiltrating beyond the muscular layer, giving rise to metastases to lymph nodes. In the intermediate zone of the resected stomach, two depressed lesions (2.0×2.0, and 1.0×1.0 cm) were noted with approximate symmetry. In the pyloric glandular area, multiple sessile polyps were noted (Figure 1). Histologically, all polyps were adenomas with atypical epithelium (Figure 2) and several flat lesions with same appearance were also demonstrated. Marked intestinal metaplasia was noted in the remaining antral mucosa. An adenoma with similar findings was noted in the duodenum.

Two depressed lesions in the stomach were adenocarcinomas, one confined within the mucosa and the other invading the submucosa. Another microscopic intramucosal adenocarcinoma was detected in the greater curvature of the intermediate zone (Figure 3). In addition, adenomatous foci were noted among the cancer tissues. The metastatic bone involvement probably arose from rather advanced lesions of the rectum infiltrating beyond the muscularis propria with lymph node metastases than from early lesions of the stomach confined within the submucosa without lymph node involvement, although definite identification of the primary lesion from the histological appearance, whether gastric or rectal origin, was difficult, because of the close histological similarity of the both possible primary sites, i.e. both being well-differentiated adenocarcinoma.

Case 2, Y. K., a 17-year-old girl, has a two years older sister with multiple polyposis of the colon, duodenal polyps and possible presence of the brain tumor which was later removed by surgery and was found to be astrocytoma. She was admitted to the department on January 13, 1972, with complaints of poorly formed stools and some anal bleeding. Double contrast barium enema revealed numerous polyps scattered over the whole colon and rectum. An upper gastrointestinal series revealed two small shallow depressed lesions on the anterior wall and the greater curvature of the gastric corpus. These lesions were confirmed by endoscopy. Biopsy revealed anaplastic carcinomas composed of signet-ring cells in each of these lesions. Three small subcutaneous tumors were found in the left thigh and one of these proved to be lipoma histologically after the removal. In addition, there were several café-au-lait spots on the skin. No gastric cancer was found in the family pedigree.

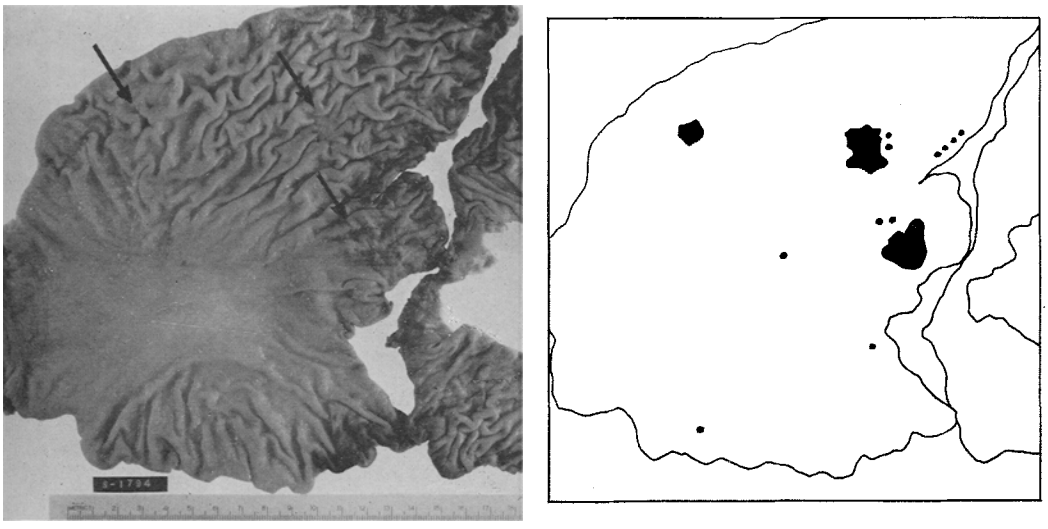

Fig. 4. Left: Three visible, depressed cancerous lesions shown by the arrows. Right: Location of 14 carcinomas shown by the dark areas and dots. Eleven dots representing macroscopically invisible microcarcinomas detected only by a detailed histological examination (case 2)

On February 7, total gastrectomy and total colectomy with temporary ileostomy were carried out. The rectum was left for future use in ileoproctostomy. Extirpation of the right ovarian cyst was also performed. Profuse diarrhea persisted and fluid and electrolyte supplementation of more than 2,000 ml per day was required for 2 months postoperatively to prevent dehydration. The body weight decreased by 6 Kg from the preoperative level. Studies on digestion and absorption performed 5 months postoperatively revealed a dis-

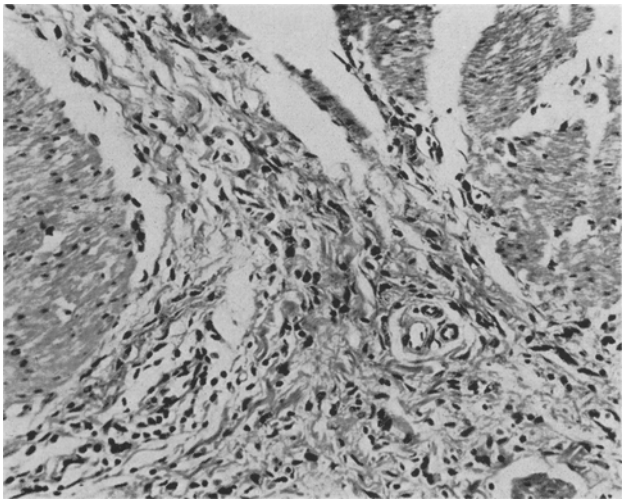

Fig. 5. A part of scirrhous carcinoma invading the muscularis propria in case 2 (S-1794-9, H. E., ×190).

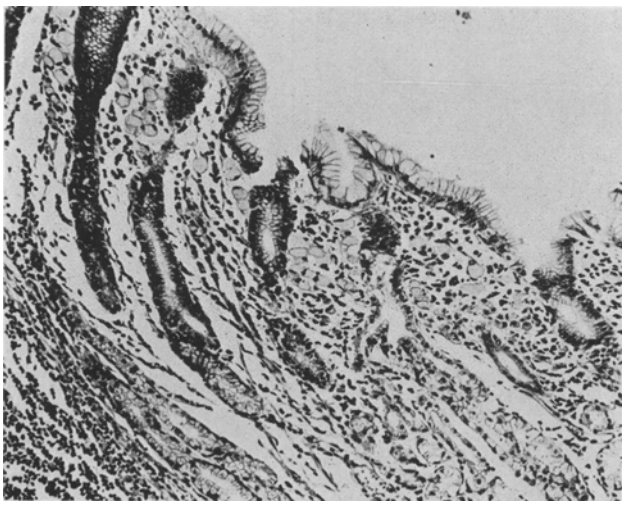

Fig. 6. A microcarcinoma composed of signet-ring cells and confined within the upper mucosa in case 2 (S-1794-60-20, H. E., ×112).

turbance of fat absorption, the rate of ^{131}I-Triolein excretion being 11 per cent (normal value: less than 4 per cent). Serum total lipids (normal value: 600–800 mg/dl) decreased to 475 mg/dl. After discharge, the frequency of diarrhea gradually decreased, and ^{131}I-Triolein excretion rate was improved to 4.6 per cent; and serum total lipids, 695 mg/dl, 2 years later. Thus, ileorectal anastomosis was performed on July 1, 1974 with a satisfactory result.

About 80 polyps with or without pedicles, ranging in size from 0.3 to 5.0 cm in diameter were distributed over the whole resected colon. Histologically, carcinoma was demonstrated in part of the two polyps in the ascending colon but all other polyps were adenomas. Numerous small polyps due to lymphoid hyperplasia were also found in the terminal ileum. In the resected stomach, 3 shallow, irregularly shaped, depressed lesions were noted macroscopically (1.6×1.7, 1.5×1.2, and 0.3×0.4 cm). No polyp was found in the specimen (Figure 4). A detailed histological examination performed on the serial sections of the whole resected specimen revealed 14 primary carcinomas in the gastric fundic glandular area, all being signet-ring cell carcinoma. Among 3 visible lesions, cancerous invasion was found to reach the subserosa in one (Figure 5), and the submucosa in the other two. The other 11 carcinomas were macroscopically invisible, with a microscopic appearance of microcarcinoma of less than 1 mm in the neck zone of the gastric fundic glands (Figure 6). Neither intestinal metaplasia, epithelial atypia, nor metastasis to lymph nodes was noted.

Discussion

Devic and Bussy[5] were the first to describe the extracolonic adenomas accompanying familial polyposis in 1912. Mayo et al[13] in 1951 found polyps in the stomach and small intestine in 2 of 9 cases studied by the upper gastrointestinal series among 95 cases with familial polyposis. Duncan et al[7] in 1968 reported the frequency of polyps in the duodenum and small intestine in Gardner's syndrome as 12 per cent. However interest in such association was thereafter rather slow to grow as pointed out by Hoffmann and Goligher[10] and Schnur et al[20] that scarcely any examinations were carried out in this condition for the associated upper gastrointestinal lesion in the past.

Recently great stride has been made in the early diagnosis of gastric cancer because of the rather high incidence in this country. The upper gastrointestinal series and endoscopy thus became a routine procedure in patients with digestive symptoms. The detection of frequent gastroduodenal lesions with the incidence of 80 per cent in our series of familial polyposis is probably based on such background. Utsunomiya et al[21] reported gastric polyposis accompanying familial polyposis in 10 of 15 cases indicating that our results are not incidental.

Three cases of gastric cancer and 10 cases of duodenal cancer in familial polyposis have hitherto been reported in the literature (Table 2). In 8 cases, coexistence of cancer and polyps in duodenum has been observed. In the present series, such association was found in one case (case 1) in which numerous adenomas composed of atypical epithelium and three adenocarcinomas containing foci of adenomatous pattern coexisted in the pyloric glandular region. Although whether or not the gastroduodenal polyps in familial polyposis have a malignant potential has not been decided, such association suggests the possible malignant change occurring in gastric or duodenal adenomas as is generally supposed to be

Table 2. Reported cases of gastric and duodenal carcinomas accompanying familial polyposis of colon

Author	Year	Site	Pathological findings	Surgical procedures
Cabot[2]	1935	duodenum	carcinoma of papilla of Vater and polyposis of duodenum	none
Murphy[17]	1962	stomach	adenocarcinoma of stomach	partial gastrectomy
Macdonald[12]	1967	duodenum	adenocarcinoma of ampulla of Vater and two adenomas of duodenum	pancreatico-duodenectomy
Capps[3]	1968	duodenum	adenocarcinoma of ampulla of Vater	pancreatico-duodenectomy
Duncan[7]	1968	duodenum	adenocarcinoma and several polyps of duodenum	polypectomy
McFarland[14]	1968	duodenum	periampullary carcinoma	pancreatico-duodenectomy
Coli[4]	1970	duodenum	adenocarcinoma and multiple polyps of duodenum	gastrojejunostomy
Parks[18]	1970	duodenum	adenocarcinoma of ampulla of Vater and numerous hamartomas of stomach and duodenum	pancreatico-duodenectomy
Yamada[22]	1971	stomach	carcinoma of stomach	partial gastrectomy
		stomach	carcinoma of stomach	none
Melmed[15]	1972	duodenum	adenocarcinoma and multiple polyps of duodenum	partial resection of duodenum
Schnur[20]	1973	duodenum	adenocarcinoma and two adenomas of duodenum	pancreatico-duodenectomy
		duodenum	adenocarcinoma and eight adenomas of duodenum	pancreatico-duodenectomy

the case in large intestine[6,13]. On the other hand, cancer of the stomach or duodenum without coexistence of polyps as in case 2 of the present series has been detected in 5 cases. In these two cases, the criteria for multiple gastric cancers by Moertel et al[16] was met and the cancers probably occured in a multicentric fashion from the adenomas of the pyloric glandular area (case 1) or from the mucosa of the fundic glandular area (case 2). The coexistence of gastric adenomas and adenocarcinomas containing foci of adenomatous pattern (case 1) and the occurrence of multiple gastric carcinomas composed of signet-ring cells in young patient (case 2) with familial polyposis seem to be rather unusual and have never been reported. These patients may have yet undefined systemic disposition for oncogenesis or cancerogenesis. Malignant potential may exist, if it ever does, not only in polyps but also in the gastrointestinal mucosa itself in familial polyposis. Polyps and/or carcinomas of the upper gastrointestinal tract may very well be a part of the manifestation of familial polyposis. In view of the rather frequent occurrence of such association, upper gastrointestinal survey is mandatory in the treatment of familial polyposis. Furthermore because of the possible malignant change of the mucosa itself, in addition to adenoma, in the gastrointestinal tract, the patients should be followed postoperatively even though no polyps were found in upper gastrointestinal tract at the time of the operation.

Because of the frequent occurrence of carcinoma in the large intestine, total or subtotal colectomy is a rule in the treatment of familial polyposis[11,13]. Therefore, in dealing with associating gastric or duodenal lesions careful consideration is necessary to prevent the occurrence of "gastrointestinal cripples". In those with apparently benign polyps of the upper gastrointestinal tract, follow-up with X-ray, endoscopy and biopsy is advisable. Preventive gastrectomy as suggested by Boley et al[1] is deterred. However, once the coexistence of carcinoma of the stomach or duodenum is established, radical operation must be done even in the face of grave danger of producing gastrointestinal cripples. Fortunately total colectomy coupled with partial gastrectomy resulted in remarkably little disturbance in postoperative recovery, nutrition and daily living in case 1 in concordance to the earlier reports[1,17,19,22]. In case 2, even total gastrectomy with total colectomy carried out simultaneously did not produce gastrointestinal cripples. Of 6 cases of pancreaticoduodenectomy carried out subsequent to colectomy for Gardner's syndrome with cancer of the duodenum, Macdonald et al,[12] Capps et al,[3] Parks et al,[18] and Schnur et al[20] reported a success in one case each (Table 2).

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