Gastroduodenal Polyps in Patients with Familial Adenomatous Polyposis

James M. Church, M.D., Ellen McGannon, B.S.W., Sharon Hull-Boiner, Michael V. Sivak, M.D., Rosalind Van Stolk, M.D., David G. Jagelman, M.D., Victor W. Fazio, M.D., John R. Oakley, M.D., Ian C. Lavery, M.D., Jeffrey W. Milsom, M.D.

From the Departments of Colorectal Surgery and Gastroenterology, Cleveland Clinic Foundation, Cleveland, Ohio

A review of the endoscopy reports and pathology results from esophagogastroduodenoscopy (EGD) of all patients with familial adenomatous polyposis (FAP) undergoing such an examination was performed. Two hundred forty-seven patients were identified, with an overall prevalence of duodenal adenomas of 66 percent and of fundic gland polyps of 61 percent. Analysis of our more recent experience (1986 to 1990) shows the prevalence to be 88 percent and 84 percent, respectively. A normal-appearing papilla was adenomatous in 50 percent of cases. No case of periampullary carcinoma developed in patients under surveillance. Routine EGD is indicated for patients with FAP. Duodenal adenomas and fundic gland polyps will occur in the majority of patients. [Key words: Familial polyposis; Duodenum; Adenomas; Fundic gland polyp; Esophagogastroduodenoscopy]

Church JM, McGannon E, Hull-Boiner S, Sivak MV, Van Stolk R, Jagelman DG, Fazio VW, Oakley JR, Lavery IC, Milsom JW. Gastroduodenal polyps in patients with familial adenomatous polyposis. Dis Colon Rectum 1992;35:1170–1173.

Familial adenomatous polyposis (FAP) is an inherited growth disorder manifested by the development of multiple colorectal adenomas, one or more of which will inevitably become malignant with the patients at a relatively young age. Most patients with FAP are now diagnosed by surveillance endoscopy because their risk status is known. In such patients, removal of the large bowel prevents death from colorectal cancer but allows expression of the genetic defect in other organs. Tumors in extracolonic sites have been well documented in FAP patients,[1,2] with the upper gastrointestinal (GI) tract the most common location. Over the last 10 years, esophagogastroduodenoscopies (EGDs) performed in FAP patients have revealed a high prevalence of gastric polyposis (usually hamartomatous or fundic gland polyps [FGPs]) and of duodenal polyposis (usually adenomas).[3–17] The prevalence of adenomas in this area is of prime concern, because carcinoma in the duodenum and periampullary area is the most common cause of death, after colorectal cancer, in FAP patients.[18] In 1986 we presented our initial EGD results in 100 patients with FAP.[14] In this paper we augment the earlier report with our last five years of experience.

Read at the meeting of The American Society of Colon and Rectal Surgeons, Boston, Massachusetts, May 12 to 17, 1991.
Address reprint requests to Dr. Church: Colorectal Surgery Department, A111, Cleveland Clinic Foundation, Cleveland, Ohio 44195.

METHODS

Over the decade 1981 to 1991, all patients presenting to the Colorectal Surgery Department with FAP were referred for EGD as part of their initial diagnostic workup. EGD was performed using a combination of an end-viewing gastroscope and a side-viewing duodenoscope. The presence, number, size, and appearance of any abnormality of the stomach, duodenum, or papilla were noted. Representative biopsies of polypoid lesions and routine biopsies of the papilla were taken. Data were entered into the FAP Registry computer program and have been abstracted for this study using DATATRIEVE™.

EGDs were performed by one of six endoscopists in the Department of Gastroenterology at the Cleveland Clinic. Since 1986, attempts have been made to standardize reporting as far as this was possible, and a specially designed reporting form has been used.

Biopsy material was interpreted by one of several Clinic pathologists. Histologic examinations performed at institutions other than the Cleveland Clinic have been excluded from this study.

RESULTS

Our total series consists of 745 EGDs performed in 247 patients from 202 FAP kindreds. An average of three EGDs were performed per patient, although 82 patients had only one examination. The

average age of patients at diagnosis of FAP was 25.4 years, while the average age at first EGD was 33.5 years, a difference of eight years. Overall results of the EGD examinations are shown in Table 1. The histology of the polyps found at various sites is described in Table 2.

The appearance and histology of the duodenal papilla are shown in Table 3. It can be seen that a normal-looking papilla is often adenomatous on histologic examination. In Table 4, we have separated our early experience (1980–1986) from our more recent results (1987–1991). The results of the first 100 patients are compared with those of the more recent 147. In Table 5 the Cleveland Clinic results are compared with other data available in the literature.

Table 1.
Prevalence of Polyps

	No. of Patients	%
No polyps	54	22
Both gastric and duodenal polyps	121	49
Gastric polyps alone	30	12
Duodenal polyps alone	42	17

Table 2.
Histology of Polyps by Site

	Adenomas		Fundic Gland		Normal	
	No.	%	No.	%	No.	%
Stomach	10	7	141	93	0	0
Duodenum	162	99	0	0	1	1
Papilla	115	61	0	0	74	39

Table 3.
Appearance and Histology of the Duodenal Papilla

Appearance	Adenomatous	Normal Histology
Normal	65	64
Abnormal	50	10

Table 4.
Comparison of Prevalence Data Before and After 1986

	Before 1986		1986–1990		Total	
	n	%	n	%	n	%
Normal	54	54			54	22
Gastric polyps	28	28	123	84	151	61
Duodenal polyps	33	33	130	88	163	66

Table 5.
Combined Series of EGD Findings in Polyposis Patients

Reference	Date	No. of Patients	Gastric Polyps		Duodenal Polyps	
			n	%	n	%
3	1983	34	21	62	20	61
4	1985	26	7	39	12	46
5	1984	11	6	55	8	73
6	1981	9	9	100	8	89
7	1974	15	10	67		
8	1978	22	15	68		
9	1984	34	16	47		
10	1984	31	12	39		
11	1976	24	15/22	68	9/10	90
12	1977	14			13	93
13	1987	41	14	34	10	24
14	1986	100	28	28	33	33
15	1985	14	8	57	9	64
16	1985	24	6	25	14	58
17	1989	102	56	55	88	86
Present study	1991	147	123	84	130	88
Total		648	346/632	55	354/532	67

DISCUSSION

The results shown here demonstrate the frequency with which both gastric and duodenal polyps can be found in patients with FAP. Almost all of these patients were asymptomatic, and all of those with adenomas are potentially at risk for the development of duodenal or gastric cancer, although the actual risk is unknown.

The difference between a retrospective approach to screening EGDs in FAP patients and a prospective, planned recording of EGD findings has been demonstrated in this report and in that by Spigelman *et al.*[17] Although the current study suffers from the use of multiple endoscopists and pathologist, efforts have been made to minimize the effect of this. The standardization achieved within the one institution with common data recording sheets and the exclusion of more subjective data such as degree of dysplasia and numbers or sizes of polyps were intended to improve the reliability of the data. The similarity of these results to those produced by a single endoscopist[17] suggests that these measures have been successful. The apparent rise in prevalence of adenomas from 33 percent in 1986 to 88 percent in 1991 now reflects the difference in methodology and probably also a tendency for FAP patients to develop adenomas that increases with age. Very similar data were produced by Spigelman *et al.*,[17] who noted a marked increase in

adenoma prevalence (190 percent) and FGP prevalence (540 percent) with a prospective study design and detailed data recording. Such high prevalence rates mean that almost all FAP patients are likely to develop duodenal adenomas and that these adenomas are present not only in the Gardner's syndrome variant of FAP. This has been our experience, as there was no difference in adenoma prevalence between patients with and without other extracolonic manifestations of FAP.

Historically there has been a marked variation in reported prevalence rates of adenomas and FGPs, as can be seen in Table 5. Part of this is likely due to the generally small numbers of patients studied, and part is due to a difference in approach to EGDs. In addition, it is apparent that studies from Japan, where gastric neoplasia in non-FAP patients is much more common than in the Western countries, show a higher prevalence of gastric and duodenal adenomas.[11,12] The Japanese prevalence of FGPs is not different from that in Western countries, however, providing further suggestive evidence that these are more due to an inherited factor while adenomas reflect a combination of heredity and carcinogen.

The stomach and duodenum in FAP patients may possibly illustrate the genetic model of colorectal tumorigenesis proposed by Kinzler *et al.*[19] This postulates that colorectal epithelial cells drift toward neoplasia as a result of the cumulative effect of a series of genetic mishaps, starting with deletion of the MCC[19] gene (or APC gene in FAP) on chromosome 5q and continuing with *ras* oncogene activation, DCC gene loss (chromosome 18q), and finally the loss of the p53 gene on chromosome 17p. As Spigelman *et al.*[17] have pointed out, bile is likely to contain a carcinogen that promotes this genetic cascade, and the effects of this are seen in the upper GI tract of FAP patients. The FGPs seen in the stomach may be caused by the inherited genetic event, the APC deletion on 5q seen in FAP patients. The duodenal papilla, the duodenum itself, and, to a much lesser extent, through bile reflux the gastric antrum are thus primed for the tumor-promoting effect of bile. This effect, the development of dysplasia and adenomas, appears most severe where bile is most concentrated (ampulla, second part of duodenum) and becomes increasingly less severe as bile is diluted (rest of duodenum, gastric antrum, jejunum). Perhaps these phenomena represent merely the effect of different pH on the genetic sequence, rather than a specific carcinogen. This and the carcinogenic effect of bile itself remain potentially fruitful subjects for further investigation.

The variation from one patient to another in number and size of polyps, both FGPs and adenomas, reported by others[3–5,13,17] and noted also by ourselves, is likely to represent differences in the expression of genetic abnormalities and differences in environmental carcinogens. It should be possible to use these differences in polyp presentation when examining bile from FAP patients to help identify potential substances that are promoting neoplasia.

The best form of treatment for gastroduodenal adenomas in FAP patients is not yet known. The incidence of cancer in this area, while high, is not yet high enough to warrant an aggressive surgical approach.[18] Endoscopic treatment of adenomas has not proved effective, as would be expected given the universal nature of the underlying genetic abnormality. Data in preparation from the Cleveland Clinic on 33 patients treated with polyp ablation confirm this lack of long-term effect. For the moment, the best option seems to be surveillance, using increase in adenoma area and dysplasia and endpoints. Carpet-like, villous lesions, or those with severe dysplasia, should probably undergo some sort of surgical excision. Ultimately, the best treatment of these worrisome lesions is likely to be manipulation of the upper GI environment so as to reduce or completely remove the carcinogenic stimuli present there.

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