Digestive Diseases and Science, Vol. 34, No. 2 (February 1989), pp. 167–170

High Prevalence of Adenomatous Polyps of the Duodenal Papilla in Familial Adenomatous Polyposis

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Eighteen consecutive asymptomatic patients with familial adenomatous polyposis (both familial polyposis coli and Gardner's syndrome) were studied over a 12-month period; side-viewing upper endoscopy and biopsy were used to assess the frequency of adenomatous polyps of the duodenal papilla. Nine of the 18 patients demonstrated adenomatous polyps of the papilla, varying in size and appearance from microadenomas in normal-appearing duodenal papillae (two) to a sessile polyp 3 cm in diameter. Two were tubulovillous adenomas (0.5 cm and 2 cm in diameter) and the remainder were tubular adenomas. Severe atypia and malignancy were not encountered. These findings reveal that adenomas of the duodenal papilla are common in individuals with familial adenomatous polyposis. Because of these findings and because of the known risk of periampullary adenocarcinomas and nonmalignant complications of polyps of the duodenal papilla in patients with familial adenomatous polyposis, upper gastrointestinal screening of such patients should include examination of the duodenal papilla with a side-viewing endoscope.

KEY WORDS: adenomatous polyps; duodenal papilla; familial denomatous polyposis; Gardner's syndrome.

Familial polyposis coli (FPC) and Gardner's syndrome (GS) are associated with gastric fundic gland polyps and duodenal adenomatous polyps (1–8). Studies have shown that duodenal adenomas occur in 24–90% of subjects screened (4–10). These duodenal polyps most frequently occur in the second portion of the duodenum near the duodenal papilla (4–6, 11, 12). The periampullary region is also the most common location for upper gastrointestinal malignancy in individuals with familial adenomatous polyposis (13–15). These observations, and a recent report of pancreatic duct obstruction from an adenoma at the ampulla of Vater in a patient with GS (16), suggest that polyp formation at the papilla may be of particular clinical significance in familial adenomatous polyposis. This study sought to establish the prevalence of adenomatous polyps of the duodenal papilla in asymptomatic patients with familial adenomatous polyposis.

MATERIALS AND METHODS

Between March 1986 and March 1987, 18 consecutive patients with FPC or GS were studied. The patients came from 14 different kindreds, and the largest number of patients from a single kindred was three. The diagnosis of familial adenomatous polyposis had been previously documented in each case by family history and by the presence of colonic adenomatous polyposis at colectomy or colonoscopy. None of the patients had symptoms of upper gastrointestinal, biliary, or pancreatic disease. Gastroduodenoscopy was performed on each patient using a side-viewing endoscope (Olympus JF 10). The stomach

Manuscript received January 26, 1988; revised manuscript received August 1, 1988; accepted August 5, 1988.

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Supported by NIH grant CA 40641.

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TABLE 1. SUMMARY OF ENDOSCOPIC AND HISTOLOGIC FINDINGS OF DUODENAL PAPILLA

Patient	*Age*	*Sex*	*Appearance of papilla*	*Microscopic*
1	20	F	normal	tubular
2	21	M	normal	tubular
3	51	M	slightly irregular	tubular
4	22	M	slightly irregular	tubular
5	57	M	irregular, polypoid	tubular
6	74	M	3-cm sessile polyp	tubular
7	28	F	1.5-cm sessile polyp	tubular
8	47	F	0.5-cm sessile polyp	tubulovillous
9	56	F	2-cm sessile polyp	tubulovillous
10	45	M	normal	normal
11	20	F	normal	normal
12	48	F	normal	normal
13	42	F	normal	normal
14	19	M	normal	normal
15	31	F	normal	normal
16	27	F	normal	normal
17	31	F	normal	normal
18	28	M	normal	normal

and duodenum were evaluated, particularly for the presence or absence of polyps. Biopsies were taken of representative gastric and duodenal polyps with standard fenestrated biopsy forceps. The duodenal papilla was identified and biopsied regardless of its endoscopic appearance, and multiple biopsies were taken if the papilla had a polypoid appearance.

Each biopsy specimen was processed for routine cell and tissue examination and was reviewed independently by two pathologists (J.M.A. and R.G.L.). The biopsy specimens of the duodenal papilla were examined for the presence of adenomatous changes and atypia.

Multivariate analysis of the data was performed.

RESULTS

Eighteen patients were evaluated; 10 were women and eight, men, with a mean age of 37 years (range 20–74). Gastric fundic gland polyps were found in eight patients. All had multiple 1- to 8-mm polyps located in the proximal stomach. Fifteen patients exhibited duodenal polyps; these were most often multiple, small (0.5–3 mm) tubular adenomas largely confined to the second portion of the duodenum.

Nine of the 18 patients had adenomatous tissue on the duodenal papilla (Table 1). In two of these the papillae appeared normal endoscopically. In three patients, although discrete polyps were not seen, the papillae were prominent with abnormal-appearing mucosa (Figure 1A). The abnormal mucosa in these three was pale or white with a slightly irregular surface and covered all or part of the papilla, usually including the orifice of the ampulla of Vater. The remaining four patients had visible

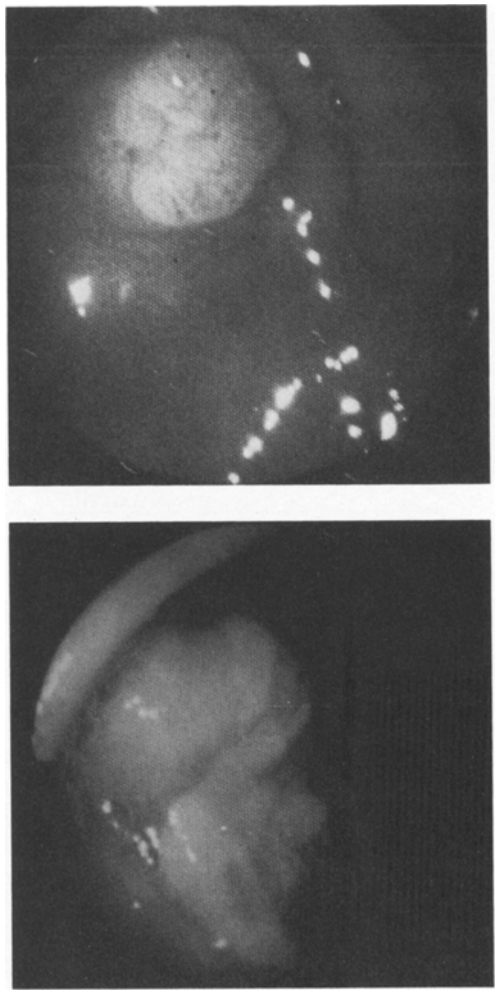

Fig 1. The duodenal papillae of two patients. (A) The papilla in patient 4 appeared slightly irregular, but not distinctly pathologic. (B) In patient 7, much of the papilla was draped with whitish tissue, which proved to be a sessile tubular adenoma.

polyps on the papilla ranging from 0.5 cm to 3 cm in size (Figure 1B). Microscopic examination of the papillae of seven of these nine patients revealed tubular adenoma without atypia. Two of the nine adenomas (0.5 cm and 2 cm in size) were tubulovillous without atypia. No adenocarcinomas were discovered.

Multivariate analysis revealed no significant correlation of the adenomatous changes involving the duodenal papilla with the sex of the patient, with the presence of gastric fundic gland polyps, or with the presence of duodenal polyps. The mean age of the patients with adenomatous tissue of the papilla was 42 years, compared to 32 years for patients with histologically normal papillae. This difference was also not statistically significant.

DISCUSSION

Adenomatous polyps of the duodenum are uncommon in the general population. When they do occur, they are usually single polyps randomly dispersed in the duodenum. In familial adenomatous polyposis, both FPC and GS, adenomatous polyps of the duodenum are very common, with a prevalence in excess of 50% in some series (4–10). Polyps in patients with familial adenomatous polyposis are predominantly found in the second portion of the duodenum with an apparent clustering of polyps in the periampullary region.

It is unclear how often adenomatous polyps involve the duodenal papilla. Knowing the frequency of lesions involving the duodenal papilla is of particular importance because standard upper gastrointestinal examination with an end-viewing endoscope results in poor visualization of the papilla. If polyps of the duodenal papilla are common in patients with familial adenomatous polyposis, then better screening techniques for visualizing the papilla would be indicated. This is an important issue, as evidenced by case reports of pancreatic or biliary obstruction caused by benign polyps involving the duodenal papilla (16). In addition, it is known that adenocarcinomas of the papilla or periampullary area are more common in patients with familial adenomatous polyposis (13–15). The lifetime occurrence of adenocarcinoma of the papilla is only 0.01% in the general population (13). Estimates of the lifetime incidence in patients with familial adenomatous polyposis have ranged as high as 12% (13, 14).

The findings in the present study indicate that a significant number of lesions of the duodenal papilla would be missed if only symptomatic subjects were studied. A previous study by Iida et al (17) assessed the appearance of the duodenal papilla in asymptomatic subjects with FPC: Using side-viewing duodenoscopy with biopsies of the papilla, they also found adenomatous tissue in 50% of their subjects. No patient had measurable polyps, although 42% had prominent papillae with "granular"-appearing mucosa. Of those with normal-appearing papillae, 14% contained adenomatous tissue, and these microadenomas comprised 17% of all the adenomas found. The high frequency of adenomatous polyps and microadenomas found in the present study confirms the Japanese findings in a Caucasian population, although it should be noted that visible polyps were encountered only in the present study. These studies support the need for screening the upper gastrointestinal tract of asymptomatic polyposis patients. They further suggest that side-viewing endoscopy should be employed as part of this screening.

The importance of these data to the clinical management of familial adenomatous polyposis is still unclear. The clinical significance of microadenomas and the frequency with which they progress to visible adenomas and adenocarcinomas are not yet known. In the present series, the two subjects with microadenomas were young, with a mean age of 20.5 years. Those with visible polyps had a mean age of 52 years, thus suggesting but not proving a progression from microadenomas to visible adenomas.

There is growing evidence that the adenoma-to-adenocarcinoma sequence is operational in the upper gastrointestinal tracts of patients with familial adenomatous polyposis, just as it is known to occur in the colon (18). These patients exhibit both a high prevalence of duodenal adenomas and a lifetime risk of duodenal adenocarcinoma that may be as much as 1000-fold greater than that of the general population (13, 14). There are also reports of duodenal adenomas and periampullary adenomas containing adenocarcinomas (18).

In view of the cancer risk and the risk of biliary or pancreatic duct obstruction, it is significant that the present study demonstrated visible adenomas, some with villous histology, in a large proportion of the asymptomatic subjects. Given the high frequency of duodenal polyps, all patients with familial adenomatous polyposis (both FPC and GS) should undergo screening duodenoscopy. Although polyps of the stomach and duodenum may occur at a young age, clinical problems arising in the upper gastrointestinal tract have not been reported to occur in patients with familial adenomatous polyposis prior to the occurrence of colonic polyps (18). Therefore, upper gastrointestinal screening should begin only after colonic polyps appear. Side-viewing endoscopy is essential, since the duodenal papilla is not always well visualized with an end-viewing instrument.

Until prospective studies elucidate the clinical course of polyps of the duodenal papilla, any recommendations regarding subsequent evaluation and therapy are empiric, based on knowledge of the behavior of adenomas elsewhere in the upper gastrointestinal tract. If the initial screening examination is normal, interval screening should be per-

formed every three years, as previously suggested for the stomach and duodenum (19). This is the time interval thought to be required for the polyp–carcinoma sequence to occur in previously normal colonic mucosa (20). Until more information is gathered about the significance of microadenomas, routine biopsy of a normal-appearing duodenal papilla does not appear indicated, except in the setting of prospective studies. Multiple biopsies should be obtained from any abnormal mucosa or visible polyps on the duodenal papilla. Whenever possible, adenomatous polyps should be removed. Endoscopic removal with biopsy forceps may be attempted for smaller adenomas, but the use of electrocautery for removal of larger polyps near the papillary orifice would seem imprudent, given the risk of ampullary obstruction and its attendant complications. Surgery would, therefore, seem more appropriate for polyps that encase the ampulla of Vater, large villous adenomas (>1 cm), or malignant polyps. Benign tumors should be locally excised with sphincteroplasty if possible. Pancreaticoduodenal resection would be indicated for any larger polyp that could not be locally excised and for potentially curable adenocarcinomas.

The present study demonstrates a high frequency of adenomatous polyps of the duodenal papilla in asymptomatic patients with familial adenomatous polyposis. Longitudinal studies of such patients are needed to verify the validity of any empiric screening and therapeutic strategies.

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