Risk of Gastric Cancer Among Korean Familial Adenomatous Polyposis Patients

Report of Three Cases

Jae-Gahb Park, M.D., Kyu Joo Park, M.D., Yoon-Ok Ahn, M.D., In Sung Song, M.D., Kyoo Wan Choi, M.D., Hong Young Moon, M.D., Sang-Yong Choo, M.D., Jin-Pok Kim, M.D.

From the Korean Polyposis Registry and Cancer Research Center, Seoul, Korea

Gastric cancer has been recognized as an extracolonic manifestation in patients with familial adenomatous polyposis (FAP). In Korea, gastric cancer is the most common malignant neoplasm. In a recent survey, we collected data from 72 Korean patients with FAP. Among them, three (4.2 percent) were found to have associated gastric cancer. This incidence of gastric cancer in our series is much higher than the previous reports from Japan and other countries. The expected cumulative incidence of gastric cancer among these 72 patients was 0.44, which gives the standardized incidence ratio of 6.9 (95 percent CI, 1.4–20.1). This difference in incidence of gastric cancer was statistically significant ($P < 0.05$), which implies that patients with FAP are at significantly higher risk of developing gastric cancer compared with the general population in Korea. These findings confirm an increased risk of gastric cancer in FAP patients, even in a region where gastric cancer is highly prevalent. [Key words: Gastric cancer; Familial adenomatous polyposis]

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Familial adenomatous polyposis (FAP) is a genetically determined disease that leads to the development of multiple intestinal polyps that eventually degenerate into carcinoma of the large intestine. There are a variety of associated extracolonic features, both benign and malignant, that may affect a patient with FAP.

Gastric lesions in FAP include fundic gland polyposis, adenomas, and carcinomas.[1–4] The incidence of gastric cancer in patients with FAP shows a marked difference between Westerners and Japanese. Jagelman *et al.*[4] reported a 0.6 percent incidence of gastric cancer among 1,255 patients from 10 separate, non-Oriental registries, compared with a 2.1 percent incidence reported by the Japanese Polyposis Center.[5] It has been suggested that the function of the FAP gene may be modified to produce cancer under the relevant environmental circumstances.

In Korea, gastric cancer is the most common malignant neoplasm, with the age-standardized incidence rate of 57.9 and 25.1 per 100,000 in males and females, respectively.[6] The point prevalence rate was reported to be 74 per 100,000 in males and 45 per 100,000 in females.[7] It accounts for 30 percent of male cancer and 17 percent of female cancer according to the report of the Ministry of Health and Social Affairs in 1989.[8]

FAP has been considered as a rare disease entity in Korea. Before 1990, there were only scattered case reports of the disease, but, in July 1990, the Korean Polyposis Registry (KPR) was newly organized and collected the FAP data from major general hospitals throughout Korea.[9]

The aim of this study was to find out whether patients with FAP are at significantly higher risk for developing gastric cancer compared with the general population, even in a country where gastric cancer is highly prevalent.

PATIENTS AND METHODS

In July 1990, we established the KPR and carried out a retrospective survey on FAP throughout 40 major general hospitals in Korea. A Korean version of the registry form of the Leeds Castle Polyposis Group was used to obtain medical records of the patients.

Review of each record was performed, and diagnosis of FAP was confirmed by barium enema

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Address reprint requests to Dr. Park: Department of Surgery, Seoul National University Hospital, 28 Yongon-dong, Chongno-gu, Seoul 110-744, Korea.

and colonoscopic findings, along with pathologic reports.

Data from a total of 72 patients with FAP, diagnosed during the period of 1981 to 1990, were collected. Mean age at diagnosis of these patients was 38 (range, 14–78 years). Forty-seven percent of these patients had family history of colorectal polyposis and/or cancer. Associated colorectal cancer was detected in 60 percent of these patients. Among these 72 patients, three (4.2 percent) were found to have associated gastric cancer.

The cumulative incidence of gastric cancer in 72 FAP patients was calculated based on the age-specific annual incidence rate of gastric cancer among Koreans[6] to determine the expected number of cases.

Statistical tests for the standardized incidence ratio (SIR; number of observed cases/number of expected cases) were performed by using Poisson distribution.

REPORT OF THREE CASES AND RESULTS

The first male patient, born in 1948, developed symptoms of epigastric pain and indigestion at the age of 35. On clinical examination, he was found to have advanced gastric cancer in the antrum. He underwent radical subtotal gastrectomy, and the pathologic specimen revealed that he had adenocarcinoma extending to the serosa with regional lymph node metastasis. Three years later a sigmoid colon cancer was detected, and he underwent abdominoperineal resection. Pathologic examination revealed numerous adenomatous polyps scattered throughout the specimen and a Dukes C colon cancer located in the sigmoid colon.

The second male patient, born in 1933, was examined for diffuse abdominal cramping pain at the age of 55. He was found to have right colon cancer and gastric cancer and underwent right hemicolectomy and radical subtotal gastrectomy. Pathologic examination of the stomach revealed adenocarcinoma invading the serosa with regional lymph node metastasis. There were underlying tubular adenomas in the stomach. In the colon, he had Dukes C colon cancer of the ascending colon in the background of diffuse tubular adenomas.

The third patient, a female born in 1947, was examined for diarrhea and abdominal pain at the age of 36. Her mother had died of colon cancer, and her older sister had been diagnosed as having FAP. After examination, she was found to have FAP and underwent total proctocolectomy with Kock ileostomy. She had diffuse polyposis throughout the entire colon and *in situ* carcinoma. At the age of 44, on routine gastrofiberscopic examination, she was found to have early gastric cancer and underwent radical subtotal gastrectomy. The pathologic specimen showed that she had adenocarcinoma invading the submucosal layer without regional lymph node metastasis. She also had multiple tubular adenomas in the stomach.

The expected cumulative incidence of gastric cancer among these 72 patients was 0.44, and the SIR, defined as the number of observed cases divided by the number of expected cases, was 6.9; the 95 percent confidence interval of the SIR was estimated to be 1.4 to 20.1 using Poisson distribution. This SIR was statistically significant ($P < 0.05$).

DISCUSSION

An increased risk for benign and malignant upper gastrointestinal neoplasm has long been recognized in FAP.[3, 4] Cancer incidence of the upper gastrointestinal tract as a whole does not show a significant difference between Japanese and Western FAP patients, but there is a striking difference in site of cancer in the upper gastrointestinal tract.[5] Jagelman *et al.*[4] reported a 0.6 percent incidence of gastric cancer in contrast to a 2.9 percent incidence of duodenal cancer. In a Japanese series,[5] the incidence of gastric cancer was 2.1 percent, while duodenal cancer was found in only 0.6 percent of patients. In our series, in addition to three patients (4.2 percent) with gastric cancer, there was one patient (1.4 percent) who had duodenal cancer.

In Korea, gastric cancer is the most common malignant neoplasm. In a recent report by Ahn *et al.*,[6] estimated cumulative rates of gastric cancer for age spans 0 to 64 and 0 to 74 are 3.8 percent and 7.3 percent in males and 1.8 percent and 3.0 percent in females, which are among the highest in the world. Diet and environmental factors possibly have an important role in such a high incidence of gastric cancer among Koreans. Utsunomyia[10] stated that gastric cancer was at least 10 times as likely to occur in FAP patients than in the general population. It was our intention to determine whether FAP patients are really at significantly higher risk for developing gastric cancer

in a region where gastric cancer is highly prevalent. We were able to estimate the expected cumulative incidence of gastric cancer among our 72 FAP patients using the age-specific annual incidence rate of stomach cancer among Koreans by using the data provided by Ahn *et al.*[6] in 1991. The SIR of 6.9 indicates that Korean FAP patients are, on the average, at about a sevenfold increased risk of developing gastric cancer compared with the general population. Our data are comparable to a 10-fold increased risk for developing gastric cancer in FAP patients in Japan, as previously stated by Utsunomyia.[9] Our data confirm that the incidence of gastric cancer among FAP patients is significantly higher than in the general population, even in a country where the incidence rate of gastric cancer is one of the highest in the world.

FAP has been considered a rare disease entity in Korea. Until recently there has been neither a polyposis registry nor a central surveillance program in Korea to manage FAP patients, and some Korean patients were mismanaged. In two male patients with gastric cancer, the preoperative diagnosis of FAP was not confirmed, and they were only thought to have colon cancer, which may explain why total colectomy was not performed. Tubular adenomas in the stomach were identified in two of our three patients, which explains the adenoma-carcinoma sequence in the gastric mucosa.

Since we have just recently established the polyposis registry, and hence only a short follow-up period is available, longer duration of follow-up in the future may reveal more cases of gastric cancer.

Our data confirm that patients with FAP are at a significantly higher risk, sevenfold on the average, for developing gastric cancer compared with the general population, even in a region where gastric cancer is highly prevalent. It can be stated that the incidence of gastric cancer among Western FAP patients does not confirm that gastric cancer is an extracolonic manifestation in Western FAP patients, but, on the other hand, in Korean and Japanese FAP patients, gastric cancer can be considered as an extracolonic manifestation. These differences may reflect the role of dietary and environmental factors associated with the carcinogenesis of gastric mucosa. It may be stated that the FAP gene is also influenced by the relevant environmental circumstances that produce a higher incidence of gastric cancer.

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