Clinical Characteristics of Gastric Cancer in Patients with Familial Adenomatous Polyposis

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Familial adenomatous polyposis is an autosomal dominant hereditary disease leading to the development of numerous colorectal polyps with malignant potential. Extra-colonic neoplasms are observed often in patients with familial adenomatous polyposis, but clinical characteristics of gastric cancer associated with familial adenomatous polyposis are not well understood. We studied the clinical characteristics of five Japanese patients who developed gastric cancer after undergoing colectomy for familial adenomatous polyposis. Gastric cancer was found on gastroduodenal endoscopy performed during postoperative follow-up in all five patients. Mean ages at the time of colectomy and at the time of diagnosis of gastric cancer were 39.2 and 58 years, respectively. Importantly, gastric fundic gland polyps were undetectable in these five patients. The mean duration between colectomy and diagnosis of gastric cancer was more than 20 years in three of five patients (mean: 19 years and 1 month). Cancers were multiple in three of five patients. Two patients developed metachronous gastric cancer in the gastric remnant. All five patients presented with well to moderately differentiated adenocarcinoma; four of the five patients were stage IA. Characteristics of the gastric cancer with familial adenomatous polyposis include a long duration between occurrence of gastric cancer and colectomy, metachronous cancers, multicentric lesions, and a high rate of well to moderately differentiated adenocarcinoma. Long-term and periodic gastroduodenal surveillance endoscopy is recommended for patients with FAP who underwent colectomy.

Keywords: colectomy; familial adenomatous polyposis; gastric cancer; gastroduodenal endoscopy; multiplicity

Familial adenomatous polyposis (FAP) is an autosomal dominant hereditary disease leading to the development of numerous colorectal polyps with malignant potential (Debinski et al. 1996). Although extra-colonic neoplasms are observed often in patients with FAP, desmoids and upper gastrointestinal malignancies are considered important as causes of death (Tulchinsky et al. 2005; de Campos et al. 2010). Gastric fundic gland polyps (FGPs), gastric cancer, duodenal adenoma, and ampullary adenoma complicate in patients with FAP (Kashiwagi and Spiegelman 2000). Among these lesions, the frequency of gastric cancer associated with FAP is not high, but its incidence differs between Western countries and Japan and Korea (Jagelman et al. 1988; Park et al. 1992; Iwama et al. 1993). This difference could be attributed to the increased occurrence rate of gastric cancer in Asian countries. Clinical characteristics of gastric cancer associated with FAP remain obscure because of the few number of patients described previously.

In our department, we routinely perform preoperative gastroduodenal endoscopy when performing colectomy for FAP. We recommend patients to undergo surveillance gastroduodenal endoscopy once every year after colectomy, and gastric cancer was found in several patients with FAP. We investigated the clinical characteristics of gastric cancer that developed after colectomy in patients with FAP.

Clinical Reports

Clinical records were reviewed of 42 patients with FAP who underwent colectomy and postoperative endoscopic examination of the upper gastrointestinal tract between 1980 and 2011. Mean follow-up time was 122 ± 14 (range: 9-337) months. Three of 42 patients (7.1%) developed gastric cancer during follow-up after colectomy. Clinical characteristics were studied in these three patients (Patients 1-3) and additional two patients who underwent colectomy at another institution and were referred to our institution for the treatment of gastric cancer that developed after colectomy for FAP. In these five patients, we studied family history for FAP, patients’ sex, age at the time of colectomy, age at the time of diagnosis of gastric cancer, site...
of gastric cancer, treatment, and histopathologic findings of gastric cancer.

The clinical characteristics of five patients are shown in Table 1. Ages at the time of colectomy and of diagnosis of gastric cancer ranged from 26-45 (mean: 39.2) and 49-72 (mean: 58.0), respectively, and the duration between colectomy and diagnosis of gastric cancer was 21 years 2 months, 4 years 8 months, 9 years, 30 years 6 months, and 30 years 2 months (mean: 19 years 1 month). Although gastric FGPs were observed in 22 of 42 patients (52%), none of five patients with gastric cancer had gastric FGPs.

Patient 1 had the gastric cancer in the cardia and underwent proximal gastrectomy with reconstruction after esophagogastrosotomy 21 years and 2 months after total proctocolectomy with end-ileostomy.

Patient 2 developed unicentric gastric cancer in the gastric antrum, and distal gastrectomy with Billroth-I reconstruction (an end-to-end gastrojejunostomy) was performed. In Patient 2, early gastric cancer was found in the gastric remnant on surveillance gastroduodenal endoscopy 4 years and 6 months after total gastrectomy; endoscopic resection was performed for this lesion.

Patient 3 underwent distal gastrectomy with Billroth-II reconstruction (an end-to-side gastrojejunostomy with closure of the proximal end of the duodenum) for gastric cancer 1 year and 5 months before colectomy at the age of 40; two early stage cancers at sites close to a prior gastrojejunostomy in the gastric remnant were detected on surveillance gastroduodenal endoscopy 9 years after colectomy. She has been managed by endoscopic resection and laser ablation for these lesions for 23 years, but total gastrectomy was finally performed 32 years after colectomy because of difficulty in continuing endoscopic treatment. She had undergone gastroduodenal endoscopy 85 times before total gastrectomy.

In Patient 4, 10 separate lesions were diagnosed as the gastric cancer throughout the stomach, and cancer of the duodenal ampulla was also suspected at the time of diagnosis of gastric cancer. Therefore, we at first performed an endoscopic ampullectomy and confirmed that a complete endoscopic resection had been possible before performing total gastrectomy. Patient 4 underwent total gastrectomy, and jejunal interposition between the esophagus and duodenum (an end-to-side esophagojejunostomy and an end-to-end jejunojunoendostomy) was performed as a reconstruction to make endoscopic duodenal examination possible. Conventional Roux-en-Y anastomosis was not done, in which endoscopic duodenal examination is impossible, because an end-to-side esophagojejunoendostomy and an end-to-side jejunojejunoendostomy are performed as a reconstruction with closure of the proximal end of the duodenum.

In Patient 5, four cancer lesions were distributed in the fundus, cardia, and antrum. He simultaneously had gastric cancer and advanced ileal cancer causing intestinal obstruction. He at first underwent ileal resection as an emergent operation to treat intestinal obstruction, because patient’s condition did not allow us to perform ileal resection and total gastrectomy at the same time. Multiple liver metastases became evident soon after ileal resection, and the gastric cancer was considered as out of surgical resection.

Four of five patients had well differentiated adenocarcinoma on histopathologic examination, while one patient (Patient 3) had moderately differentiated adenocarcinoma. The final pathologic stage of gastric cancer was IA in four patients except for Patient 5, and all these four patients are alive without recurrence.

**Discussion**

The rate of FAP-associated gastric cancer differs between USA and Japan or Korea. Gastric cancer was
found in 27 of 1,050 (2.6%) patients with FAP registered in Japan (Iwama et al. 1993), while the rate of FAP-associated gastric cancer was 7.1% in our study. Park et al. (1992) reported that three patients with gastric cancer were identified in 72 (4.2%) patients with FAP in Korea. Jagelman et al. (1988) described the rate of gastric cancer associated with FAP as low as 0.6% (7 of 1,255 patients) in the USA. This rate in the USA is obviously less than that in Japan and Korea. This difference is presumed related to the high incidence of gastric cancer in Japan and Korea. The rate of gastric cancer in patients with FAP in Japan (2.6-7%) is greater than that of the overall incidence of gastric cancer in the Japanese population (Parkin et al. 1992). One reason for the greater rate of gastric cancer in the present study compared to previous reports from Japan and Korea is probably related to the long-term follow-up (122 months in mean and 337 months at the maximum) in our study.

Results in our study suggest that gastric cancer after colectomy for FAP is characterized by 1) a long duration between the development of gastric cancer and colectomy, 2) metachronous lesions, and 3) predisposition to multicentric lesions, and 4) high rate of well - moderately differentiated adenocarcinoma. Kamoi et al. (1997) summarized Japanese patients with gastric cancer and FAP in their case series in a Japanese literature and concluded that the incidence of gastric cancer in patients with FAP is much greater than that in patients without FAP. In a case report, Shimoyama et al. (2004) characterized gastric cancer in patients with FAP as onset at relatively young age, tendency of multiple gastric cancer, and high rate of well differentiated adenocarcinoma. Our findings were consistent with these 2 previous reports except that the diagnosis of gastric cancer was made at a mean age of 58 in our study, rather than at younger age. This difference must be related to the fact that we focused on patients with FAP only after colectomy and having long-term surveillance with gastroduodenal endoscopy. The interval between occurrence of gastric cancer and colectomy in patients with FAP has not been studied in previous reports. The mean interval as long as 19 years and 1 month in five patients in our study indicates that long-term surveillance with gastroduodenal endoscopy is important for the detection of gastric cancer.

Multicentric gastric cancers were detected in three of five patients (60%), and gastric cancer reoccurred in the gastric remnant in the two patients treated by distal gastrectomy for prior gastric cancer. In these two patients, one patient underwent total gastrectomy after endoscopic treatment, and endoscopic treatment continues in the other patient. The frequency of multicentric gastric cancer is estimated overall as 2-19% (Arai et al. 1992; Suzuki et al. 1995), and rate of metachronous gastric cancer after gastrectomy for early gastric cancer is estimated to be 0.5-3% (Ikeda et al. 2005; Nozaki et al. 2010). Results in the present study indicate a predisposition to multicentric gastric carcinogenesis in patients with FAP. In the present study, all five patients with gastric cancer had well to moderately differentiated adenocarcinoma which is present in approximately 50% of gastric cancers overall in Japan. The gastric cancer was stage I in four of five patients, and all of them are alive without recurrence. It is likely that gastric cancer developing in patients with FAP is usually well to moderately differentiated adenocarcinoma and probably confers a better prognosis. This observation also emphasizes the importance of diagnosis at early stage by endoscopic surveillance examination. We believe that gastroduodenal endoscopic surveillance should be performed once every year.

Gastric FGP is a frequently encountered abnormality as shown in the present study and had been regarded as hyperplastic polyps without a malignant potential (Bianchi et al. 2008; Teichmann et al. 2008). A patient with FAP, however, was reported whose gastric cancer must have arisen from FGP (Garrean et al. 2008). Because none of five patients had FGP in the present study, gastric cancers in our series do not seem to have something to do with FGP.

Adenomas of the duodenum and especially in the periampullary region frequently complicate FAP. Therefore, when performing gastrectomy for patients with FAP, methods of gastrointestinal reconstruction should allow for endoscopic surveillance of the duodenum whenever feasible. In Patient 4 in whom endoscopic duodenal ampullectomy was performed before gastrectomy, jejunal interposition and not conventional Roux-en-Y anastomosis was performed as a reconstruction after total gastrectomy for this reason.

Conclusion

Characteristics of the gastric cancer with FAP include a long duration between occurrence of gastric cancer and colectomy, metachronous cancers, multicentric lesions, and a high rate of more well to moderately differentiated adenocarcinoma. We would like to emphasize the importance of long-term and periodic gastroduodenal surveillance endoscopy in their high-risk patient population with FAP.

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Conflict of Interest

The authors declare no conflict of interest.

References