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Increased Prevalence of Colorectal Neoplasia in Korean Patients with Sporadic Duodenal Adenomas: A Case-Control Study

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Background/Aims: Recent data from Western populations have suggested that patients with sporadic duodenal adenomas are at a higher risk for the development of colorectal neoplasia. In this study, we compared the frequency of colorectal neoplasia in patients with sporadic duodenal adenomas to healthy control subjects. **Methods:** This retrospective case-control study used the databases of 3 teaching hospitals in Gyeonggi-do Province, South Korea. The colonoscopy findings of patients with sporadic duodenal adenomas were compared with those of age- and gender-matched healthy individuals who had undergone gastroduodenoscopies and colonoscopies during general screening examinations. **Results:** Between 2001 and 2008, 45 patients were diagnosed endoscopically with sporadic duodenal adenomas; 26 (58%) of these patients received colonoscopies. Colorectal neoplasia (42% vs 21%; odds ratio [OR], 2.8; 95% confidence interval [CI], 1.1 to 7.4) and advanced colorectal adenoma (19% vs 3%; OR, 9.0; 95% CI, 1.6 to 50.0) were significantly more common in patients with sporadic duodenal adenomas than in healthy control subjects. **Conclusions:** Compared with healthy individuals, patients with sporadic duodenal adenomas were at a significantly higher risk for developing colorectal neoplasia. Such at-risk patients should undergo routine screening colonoscopies. **(Gut Liver 2011;5:432-436)**

Key Words: Duodenal neoplasms; Colorectal neoplasms; Colonoscopy; Endoscopy

INTRODUCTION

Duodenal adenomas are common in patients with genetic syndromes, such as familial adenomatous polyposis (FAP).[1] Sporadic duodenal adenomas are rare. Few endoscopic series have been published to date; these have reported a 0.1% to 0.3% incidence of duodenal adenomas.[2-5] Because duodenal adenomas have a high rate (35% to 85%) of malignant transformation, endoscopic or surgical removal is typically recommended.[6-8] Recent studies of Western populations[4,5,9-13] have suggested that patients with sporadic duodenal adenomas are at higher risk for the development of colorectal neoplasia.

The diagnosis and management of duodenal adenomas in Asia have been based solely on a few small case series.[14-17] Although colorectal neoplasia are thought to be less common among Asians than in Western populations,[18] recent studies[19,20] have shown an increasing trend for the development of this condition in Asian populations. However, the association between sporadic duodenal adenomas and the development of colorectal neoplasia in Asian populations has not been fully examined. The purpose of this study was to compare the frequencies of colorectal neoplasia in patients with sporadic duodenal adenomas to in age- and gender-matched healthy control subjects who had undergone routine gastroduodenoscopies and colonoscopies.

MATERIALS AND METHODS

1. Patients and study design

In this retrospective case-control study, we collected data from the endoscopy and pathology databases of 3 teaching hospitals (Uijeongbu and Incheon St. Mary's Hospitals, St. Vincent's Hospital) in Gyeonggi-do Province, South Korea. The Catholic University Institutional Review Board provided ethical approval

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for this study. Cases treated at these hospitals from 2001 to 2008 were considered for inclusion. Patients whose duodenal adenoma diagnosis had been confirmed by upper gastrointestinal (GI) endoscopy and histology, and who had undergone colonoscopy, were included in the study sample. Patients with ampullary tumors or personal and/or family histories of FAP, hereditary nonpolyposis colorectal cancer (HNPCC), or familial colorectal cancer were excluded.

The endoscopic and clinical data of patients in the study sample were examined to identify diagnoses of colorectal neoplasia. The location, number, size, and histological characteristics of duodenal and colorectal neoplasias were recorded, as were the indications for and interval of time between endoscopy and colonoscopy. Duodenal and colorectal adenomas were classified as low- or high-grade, according to the Vienna classification.[21] Patients with multiple lesions were classified according to the most advanced lesion. Advanced adenomas (duodenal and colorectal) were defined by size (≥10 mm), tubulovillous (villous component >20%) or villous histology, and/or high-grade dysplasia. Advanced colorectal neoplasm was defined as colorectal cancer or advanced adenoma. The findings in each patient with a duodenal adenoma were compared with those of 3 randomly selected age- and gender-matched asymptomatic subjects who had undergone upper GI endoscopies and colonoscopies during routine screening between January 2001 and December 2008. Control subjects with histories of colon-cancer surgery or polypectomy, or personal or family histories of FAP, HNPCC, or familial colorectal cancer were excluded.

2. Statistical analyses

Statistical analyses were performed using the SPSS software version 12.0 (SPSS Inc., Chicago, IL, USA). Data are expressed as proportions or medians/means and ranges, as appropriate. Predictors of colorectal neoplasia were tested using conditional logistic regression. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to compare the rates of colorectal neoplasia in patients with and without duodenal adenomas. p-values of less than 0.05 were considered to indicate statistical significance.

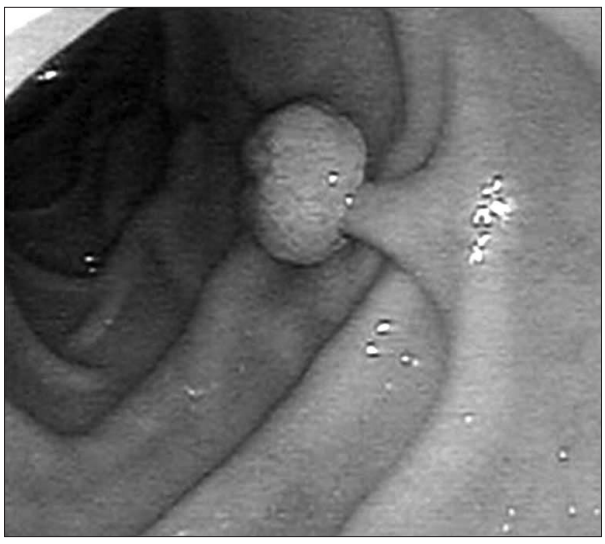

Fig. 1. Endoscopic view of a sporadic duodenal adenoma. A pedunculated tumor is located in the descending portion of the duodenum.

RESULTS

1. Sporadic duodenal adenomas

From January 2001 to December 2008, 45 patients (22 males, 23 females; mean age, 59.6 years; range, 33 to 86 years) were diagnosed with sporadic duodenal adenomas. Abdominal pain was the indication for upper GI endoscopy in more than half (51%) of these cases. Other indications were anemia (11%), melena (4%), nausea and vomiting (11%), diarrhea (4%), indications requiring endoscopic retrograde cholangiopancreatography (2%), and screening for gastric cancer (16%). A single duodenal adenoma was identified in each of the 45 patients; these lesions were located in the duodenal bulb (n=20, 44%), descending duodenum (n=16, 36%) (Fig. 1), and ampullary region (n=9; 20%). Adenoma size was reported for 38 patients (84%); mean size was 17.6 mm (median, 14.5 mm; range, 5 to 50 mm). Large (≥10 mm) duodenal adenomas were found in 33 patients (73%) and were classified as advanced, based on size (n=33), villous histology (n=3), and/or presence of high-grade dysplasia (n=11). There was no significant correlation among adenoma location, size, and histological stage.

2. Colorectal neoplasias associated with duodenal adenomas

Colonoscopies were performed in 26 (58%; 12 males, 14 females) patients with sporadic duodenal adenomas; colorectal neoplasia were diagnosed in 11 (42%) of these patients. The mean age of these patients was 58.4 (range, 37 to 76) years and none had a family history of colorectal cancer. Four patients with colorectal neoplasia had synchronous multiple lesions and 7 patients had a single neoplasm. Four colorectal neoplasia were located in the rectum or sigmoid colon, 2 were in the descending colon, and 5 were above the splenic flexure; proximal neoplasia occurred in 45% of cases. The mean size of the colorectal neoplasia was 11 mm (median, 8 mm; range, 5 to 23 mm). Ten patients (39%) had at least one adenoma; 8 of these showed low-grade dysplasia and 2 showed high-grade dysplasia. Of the 8 adenomas exhibiting low-grade dysplasia, three were advanced (size ≥10 mm, n=3; villous component, n=2). In total, 5 patients (19%) had advanced adenomas. One patient (4%) had a colorectal adenocarcinoma located in the cecum, which was diagnosed concurrently with duodenal adenoma. Advanced colorectal neoplasia (advanced adenoma+adenocarcinoma) was found in 6 of 26 patients (23%) with duodenal adenomas who had undergone colonoscopies. We found no significant

relationship between duodenal adenoma location and the presence or nature of colorectal neoplasia. Colonoscopies had been performed before the diagnosis of duodenal adenoma in 7 (27%) of 26 patients. In this group, the mean interval between colonoscopy and endoscopy was 11.6 (range, 3 to 22) months. The most common indication for colonoscopy was the occurrence of a duodenal adenoma (39%). Other indications were abdominal pain (19%), anemia (11%), altered bowel habits (8%), constipation (11%), and diarrhea (11%). We found no significant relationship between indications for colonoscopy and the presence or nature of colorectal neoplasia.

3. Control subjects

The control sample included 78 subjects (36 males, 42 females) who were matched by age and gender with the study sample (3 control subjects per case). Their mean age was 58.4 (range, 41 to 76) years. The control subjects were asymptomatic Korean adults who had undergone colonoscopies and upper GI endoscopies during routine screening at one of the participating hospitals during the study period. No control subject had a family history of colorectal cancer and none had previously undergone a colonoscopy. In the control group, 16 subjects (21%) presented with colorectal neoplasias (Table 1). Two (3%) adenomas were advanced (25 mm, low-grade dysplasia; 10 mm, high-grade dysplasia) and 14 (18%) were not. The mean size of the colorectal adenomas was 7.3 mm (median, 5 mm; range, 3 to 25 mm). No control subject had a colorectal adenocarcinoma. Comparison of the colonoscopy findings of patients with sporadic duodenal adenomas (n=26) with those of the control group (n=78) revealed that colorectal neoplasias (42% vs 21%; OR, 2.8; 95% CI, 1.1 to 7.4; p=0.032) and advanced colorectal adenomas (19% vs 3%; OR, 9.0; 95% CI, 1.6 to 50.0; p=0.012) were significantly more common in patients with duodenal adenomas (Table 2). We found no significant difference in the frequency of colorectal cancer diagnoses (4% vs 0%) between patients with duodenal adenomas and the control group.

Table 1. Incidence of Colorectal Neoplasia among Patients with Sporadic Duodenal Adenomas and Healthy Individuals

Colorectal neoplasia identified	Duodenal adenoma (n=26)	Controls (n=78)	p-value
All colorectal neoplasia	11 (42)	16 (21)	0.032
Nonadvanced adenoma	5 (19)	14 (18)	1.000
Advanced adenoma	5 (19)	2 (3)	0.012
Adenocarcinoma	1 (4)	0 (0)	1.000
Advanced neoplasia	6 (23)	2 (3)	0.004

Patients were classified according to the most advanced lesion identified at colonoscopy.
Data are presented as number (%).

DISCUSSION

This study was performed to determine whether the risk of colorectal neoplasia was higher in Korean patients diagnosed with sporadic duodenal adenomas. We identified 45 sporadic duodenal adenomas among the patients of 3 hospitals during an 8-year study period. Most (73%) of these adenomas were advanced at the time of diagnosis. Few studies[14-17] have examined duodenal adenomas and adenocarcinomas in Asian countries, and reported sample sizes have been small. Duodenal adenomas without FAP have not been previously reported in this region. Among the 45 patients identified in this study, 26 underwent colonoscopies and 11 (42%) had colorectal neoplasias. This incidence is consistent with that reported (31% to 56%) for Western populations.[4,5,9,10]

In this study, the randomly selected control group was age- and gender-matched to the study sample. The frequencies of colorectal and advanced neoplasias in healthy control subjects were 21% and 3%, respectively. These results are consistent with those of a previous Korean colonoscopy screening study,[22] which found colorectal neoplasia in 21.9% and advanced colorectal neoplasia in 2.4% of asymptomatic adults with no risk factor for colorectal cancer. In Western populations, the overall frequency of colorectal neoplasia has ranged from 20.4% to 37.5%, and that of advanced neoplasia has ranged from 4.9% to 10.5%.[23-25] The frequency of advanced neoplasia in average-risk Koreans may thus be slightly lower than in Western populations. Geographical differences may play an important role in the development of advanced colorectal neoplasia. However, the frequency of colorectal cancer is increasing in Korea; the incidence of this disease rose from 20.4/100,000 individuals in 1999 to 29.8/100,000 in 2005,[26] suggesting a transition from a low to a higher prevalence of advanced neoplasia in the Korean population.

The results of this study show that the risks for colorectal neoplasia (relative risk, 2.8; 95% CI, 1.1 to 7.4) and advanced colorectal adenoma (relative risk, 9.0; 95% CI, 1.6 to 50.0) increased significantly (vs control group) in patients with sporadic duodenal adenomas. The wide confidence intervals suggest that this series lacked the statistical power necessary to establish firm outcome findings. Nevertheless, our results are consistent with data from Netherlands,[5] where colorectal neoplasia were found in 21 of 49 (43%) patients who had undergone colonoscopies;

Table 2. Odds Ratios for Significant Differences between Patients with Sporadic Duodenal Adenomas and Healthy Individuals

Case vs Control	OR	95% CI	p-value
All colorectal neoplasia	2.8	1.1-7.4	0.032
Advanced adenoma	9.0	1.6-50.0	0.012
Advanced neoplasia	11.4	2.1-60.8	0.004

OR, odds ratio; CI, confidence interval.

13 (27%) of these cases were advanced neoplasias. In that population, patients with sporadic duodenal adenomas had significantly higher frequencies of colorectal neoplasias (OR, 3.6; 95% CI, 1.7 to 7.4) and advanced colorectal adenomas (OR, 7.8; 95% CI, 2.1 to 29.4) than observed in the symptomatic control group. An Australian study[4] showed a significant correlation between sporadic duodenal adenomas and colorectal neoplasia (OR, 2.4; 95% CI, 1.1 to 5.4), and reported a greater frequency of colorectal cancer in patients with sporadic duodenal adenomas than in the general population. In the present study, the absence of a significant difference in colorectal adenocarcinoma frequency between patients with duodenal adenomas (4%) and healthy control subjects (0%) may be due to the small number of cases or to ethnic differences.

The biological behavior of duodenal adenomas appears to be similar to that of colorectal adenomas; both show high rates of malignant transformation and recurrence after local excision.[7] Duodenal adenomas and colorectal neoplasias may thus share common pathophysiological mechanisms, including genetic and/or environmental factors. However, the mechanism underlying the association between sporadic duodenal adenomas and colorectal neoplasias has not been described to date. Although patients with diagnosed FAP were excluded from this study, some patients in the study sample may have had undiagnosed or attenuated FAP. However, this possibility seems unlikely to be a major factor affecting our results, because no patient in this study had 10 or more colorectal adenomas, characteristic of patients with FAP.[27,28] Patients with known HNPCC were also excluded from this study because HNPCC is associated with a higher risk of small bowel cancer.[29]

This study has some limitations. There were long intervals of time between upper GI endoscopies and colonoscopies in the study sample. Seven patients (27%) had undergone colonoscopies before the diagnosis of a duodenal adenoma, which should result in a lower apparent frequency of colorectal neoplasia with respect to age-matched control subjects. In the present study, we minimized the potential for selection bias by randomly selecting asymptomatic, average-risk, age- and gender-matched control subjects who had undergone routine colonoscopy screening. However, this control group was not representative of the general population because it consisted of self-referred asymptomatic subjects who were likely to be more health-conscious and from a higher socio-economic group. Furthermore, we did not assess other known risk factors for colorectal cancer, such as cigarette smoking, alcohol consumption, and dietary habits. Colonoscopies were performed in only 26 of 45 patients in the study sample; this limitation may be attributed to the rarity of duodenal adenoma diagnosis in clinical practice and the retrospective study design. A larger prospective study that provides colonoscopies to all patients with sporadic duodenal adenomas is needed.

In conclusion, patients with sporadic duodenal adenomas had significantly higher frequencies of colorectal neoplasia and advanced colorectal adenoma than the control group. Patients with sporadic duodenal adenomas should thus receive routine colonoscopy screening to increase the detection rate of colorectal neoplasias.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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