Clinicopathologic Characteristics of Barrett's Cancer in Korea

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Background/Aims: The incidence of Barrett's cancer is increasing in Western countries, but there have been only a few case reports of this condition in Korea. The aim of this study was to elucidate the endoscopic and pathologic characteristics of Barrett's cancer in a single center in Korea. **Methods:** We retrospectively reviewed the demographic, endoscopic, and pathologic characteristics of six patients with Barrett's cancer, defined as a tumor centered above the esophagogastric junction and surrounded by Barrett's esophagus. **Results:** All six patients were male, and three (50%) were symptomatic. Barrett's cancer had developed from short-segment Barrett's esophagus in all patients. All tumors were located on the right side of the lower esophagus and showed hyperemic mucosal changes. Three patients were treated surgically and three by endoscopic resection. All cases had pathologic evidence of Barrett's cancer. **Conclusions:** Early detection of Barrett's cancer requires meticulous endoscopic observations of subtle mucosal color and morphological changes around the esophagogastric junction. (*Gut and Liver* 2008;2:193-198)

Key Words: Barrett esophagus; Esophageal neoplasms

INTRODUCTION

The incidence of distal esophageal adenocarcinoma has been increasing, especially in Western countries.^{1,2} Barrett's esophagus (BE), a condition in which the squamous epithelial lining of the distal esophagus is replaced by specialized columnar epithelium, is thought to be the

precursor of distal esophageal adenocarcinoma. BE is diagnosed using a combination of endoscopic and histologic criteria. In Western countries, a 4-quadrant biopsy of the columnar-lined esophagus has been used for the diagnosis of BE.³ This procedure, however, is time consuming and has a high risk of bleeding.⁴ Moreover, the low reproducibility of the procedure makes it difficult to perform endoscopic resection.

While Barrett's cancer is associated with both the presence of GERD and older age, little is known about the characteristics of Barrett's cancer in Korea.⁵⁻⁹ Early endoscopic detection of Barrett's cancer may lead to successful endoscopic treatment with favorable clinical outcomes, avoiding aggressive surgical esophagectomy. The aims of this study were to characterize the endoscopic features and to analyze the histopathologic findings of Barrett's cancer in Korea.

MATERIALS AND METHODS

1. Patients

Six patients diagnosed with Barrett's cancer from January 1998 to July 2007 at Asan Medical Center, Seoul, Korea, were retrospectively evaluated. Medical records were retrospectively reviewed for year of diagnosis, age, sex, smoking habit, body mass index, clinical presentation. This study was granted by the institutional review board at our center.

2. Definition of Barrett's esophagus and cancer

The esophagogastric junction (EGJ) was defined as the proximal end of the gastric mucosal fold.¹⁰ The diagnosis

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of Barrett's cancer required that adenocarcinoma centered above the endoscopic EGJ and adjacent to Barrett's esophagus.

Barrett's esophagus was pathologically diagnosed by the presence of (1) submucosal esophageal glands covered by columnar mucosa, (2) a remnant of squamous epithelium island between the columnar mucosae, and (3) double muscularis mucosae beneath the columnar line mucosa.^{11,12}

3. Endoscopic and pathologic features

Endoscopic features reviewed included the presence of BE, color, shape and clockwise direction of tumor, squamous island, presence of reflux esophagitis and hiatal hernia whereas the pathological features reviewed included the macroscopic type, depth, and size of each tumor. We also analyzed this features of previously reported cases in Korea.

RESULTS

1. Demographic characteristics

The mean $\pm$ SD age of the six patients, all male, was 60.1 $\pm$ 7.5 years. Three patients had symptoms such as epigastric pain at the time of presentation. None of the patients had undergone surveillance endoscopy for Barrett's esophagus. Their clinical presentation, demographic features, and year of diagnosis are summarized in Table 1.

2. Endoscopic review of early Barrett's cancer

All of the Barrett's mucosa was short segmented and five of them was non-circular. No long segment Barrett's mucosa was identified. Reflux esophagitis was present in three patients. The common endoscopic features of the

Barrett's cancer were right sided (12 to 3 o'clock) and hyperemic change (Fig. 1-4). Otherwise, there were no common endoscopic features for all. However, it was very difficult to differentiate reflux esophagitis in some case (case 3). Two cases had the squamous island and three of the tumor had recta-angular shaped and round shaped. Three patients were treated surgically (Fig. 1) and three by en-

Fig. 1. Endoscopy images of surgically treated Barrett's cancer. (A) A type 0-IIa hyperemic elevated lesion on the right side. (B) A type 0-IIc+IIa rectangular lesion that developed from the short-segment Barrett's esophagus, accompanied by reflux esophagitis (arrowhead). A whitish squamous island was also evident (arrow). (C) A round hyperemic 0-IIb lesion similar to deep erosion.

Table 1. Demographic Characteristics of Six Korean Patients with Barrett's Cancer

Factor	
Number of patients	6
Male/female	6/0
Age, yr, mean $\pm$ SD	60.1 $\pm$ 7.5
Body mass index, kg/m ² , mean $\pm$ SD	25.1 $\pm$ 2.6
Reason for examination	
Screening	3
Epigastric pain	3
Smoking history	
Current smoker	4
Non smoker	2
Year of diagnosis	
1998	1
2004	1
2006	1
2007	3

Fig. 2. Case of mucosal Barrett's cancer treated by endoscopic submucosal dissection. (A) A hyperemic depressed lesion above the esophagogastric junction. A whitish squamous island was evident in the middle of the Barrett's cancer (arrow). (B) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident under the Barrett's cancer (H&E stain, $\times 40$). (C) Dysplastic epithelial cells mixed with glands containing sparse goblet cells (H&E stain, $\times 400$).

Fig. 3. Type 0-IIa Barrett's cancer invading the mucosa that was treated by endoscopic submucosal dissection. (A) Hyperemic elevated lesion above the esophagogastric junction. (B) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident under the columnar lined esophagus (H&E stain, $\times 40$).

Fig. 4. Type 0-I+IIb Barrett's cancer invading the mucosa that was treated by endoscopic submucosal dissection. (A) A hyperemic polypoid lesion with exudates just above the esophagogastric junction. (B) Image obtained after endoscopic submucosal resection. A protruding lesion (arrow) was detected around Barrett's epithelium, which had an irregular fine mucosal pattern. (C) Histopathologic view of the endoscopically resected specimen. The esophageal gland (arrow) was evident beneath the disrupted squamous epithelium (H&E stain, $\times 100$).

Table 2. Endoscopy Findings of Barrett's Cancer

Case	Presence of BE (mm)	Color	Shape of tumor	Squamous island	RE	HH	Type of BE	Endoscopic impression	Clockwise direction	Treatment
1	SSBE	Reddish	Rectangular		+	+	Noncircular	Barrett's cancer	1°	Surgery
2	SSBE	Reddish	Rectangular	+	+	+	Noncircular	RE	3°	Surgery
3	SSBE	Reddish	Round		—	—	Noncircular	Erosion	1°	Surgery
4	SSBE	Reddish	Rectangular	+	—	+	Circular	RE	12°	EMR
5	SSBE	Reddish	Round		—	+	Noncircular	EGJ cancer	1°	EMR
6	SSBE	Reddish	Round		+	—	Noncircular	Barrett's cancer	3°	EMR

SSBE, short segment Barrett's esophagus; EMR, endoscopic mucosal resection; location: clockwise direction of tumor; RE, reflux esophagitis; HH, hiatal hernia.

Table 3. Pathologic Characteristics of Barrett's Cancer

Case	Macroscopic type	Size	Depth	Evidence of Barrett's epithelium around the tumor
1	Ila	20	sm1	Submucosal esophageal gland
2	Ilc+IIa	20	m	Remnant of squamous epithelium
3	IIb	6	sm1	Double muscularis mucosae
4	Ilc	15	m	Submucosal esophageal gland
5	Ila	13	m	Submucosal esophageal gland
6	I+IIb	13	m	Submucosal esophageal gland

m, mucosa; sm1, submucosa invasion less than 500 μ m.

Endoscopic mucosal resection (Fig. 2-4). Endoscopic features are listed in Table 2.

3. Pathologic review of early Barrett's cancer

The size of tumor ranged from 6 to 20 mm. Four tumors were diagnosed as mucosal cancer and 2 as sm1 cancer (within 500 μ m into the submucosal layer). As a evidence of Barrett's esophagus around the tumor, there were four submucosal esophageal gland, one remnant of squamous island, and one double muscularis mucosae, respectively. All of the treated patients showed no evidence of lymph node metastasis. The pathologic features of the 6 Barrett's cancers are listed in Table 3. Previously reported cases in Korea are summarized in Table 4.

DISCUSSION

Recently, the incidence of distal esophageal adenocarcinoma has been found to increase dramatically, accounting for almost 50% of esophageal carcinomas, while the incidence of esophageal squamous cell carcinoma has decreased.² In Korean populations, however, the relative proportion of these tumors has not changed, although there have been no well designed population based studies.¹³ In our center, the ratio of esophagogastric junction

Table 4. Result of Previously Reported Cases in Korea

Case	Endoscopic findings			Pathology			Treatment
	Length of BE	Color	Type of BE	Macroscopic type	Size	Depth	
1 ⁵	SSBE	NA	NA	Ilc	5	sm	Surgery
2 ⁶	SSBE	NA	Non-cir	Ila	8	m	EMR-C
3 ⁶	SSBE	Reddish	Non-cir	I	8	m	EMR-C
4 ⁷	SSBE	Reddish	Non-cir	Ila	8	m	EMR-C
5 ⁸	LSBE	Reddish	Cir	Ila	10	m	Surgery
6 ⁹	SSBE	NA	Non-cir	Ila	8	sm	Surgery

BE, Barrett's esophagus; NA, not available; LSBE, long segment Barrett's esophagus; SSBE, short segment Barrett's esophagus; EMR-C, cap assisted endoscopic mucosal resection; m, mucosa; sm, submucosa; Cir, circular; Non-cir, non-circular.

adenocarcinoma versus gastric noncardiac cancer has not changed over the 15 years prior to 2006 (unpublished observation). Due to the poor prognosis of patients with esophageal adenocarcinoma, however, early diagnosis is essential.¹⁴

In our study, all 6 patients were male. In addition, 5 of the previous 6 Korean patients described in case reports were also male, making the overall male to female ratio of this tumor 11:1, consistent with reports in Western countries.^{15,16} In all of the patients in our series, tumors developed from the right aspect of the lower esophagus with hyperemic mucosal change, a finding consistent with the Japanese study of Barrett's cancer patients.¹¹

Moreover, all of our patients and 5 of 6 of the other Korean patients with Barrett's cancer showed development from short segment Barrett's esophagus. In Western reports, esophagogastric junction tumors over 6 cm in diameter were found to have significantly fewer changes of the surrounding Barrett's epithelium because larger cancers overgrow and destroy the underlying specialized columnar epithelium from which they arise.¹⁷ Most Korean patients, however, have been found to have short segment

Barrett's epithelium, with long segment Barrett's esophagus being quite rare.^{18,19} If a tumor is not detected early, the chance of finding the specialized intestinal metaplasia (SIM) was very low. This may explain why most Barrett's cancers in Korean patients were small sized (less than 20 mm sized) and shallow depth of invasion.

Barrett's cancer was defined as an adenocarcinoma centered at the proximal tip of the gastric fold and adjacent to BE. Accurate endoscopic localization of the EGJ is pivotal in the diagnosis of Barrett's cancer as well as Barrett's epithelium. We have previously reported that use of the lowest extent of the palisade vessel as a marker of the EGJ is not adequate for Korean patients, although it showed substantial agreement between observers.²⁰ To date, no guidelines have been developed for detecting the EGJ in Korean patients. Our results indicate that, as in Western patients, the most reliable marker of the EGJ in Korean patients is the proximal end of the gastric fold.³ In contrast, it is very difficult to identify the EGJ in resected pathologic specimens and to differentiate cardiac intestinal metaplasia from specialized intestinal metaplasia.

To date in Korea, no cases of Barrett's cancer were detected by the surveillance program. Even if they had been diagnosed by the presence of Barrett's epithelium before the diagnosis of cancer, most of these tumors were partial and short segmented. Hence, application of Western protocols in Korean patients seems impractical. Narrow band imaging of mucosal and capillary patterns, with or without magnifying endoscopy, was shown to be useful in visualizing special intestinal metaplasia and early adenocarcinoma in patients with columnar-lined esophagus.²¹⁻²³ Although promising in Korean patients, this approach requires further evaluation.

In conclusion, endoscopic review of six patients with Barrett's cancers found that these tumors usually develop from short segment Barrett's epithelium, with hyperemic and right side predilection. Meticulous examination of esophagogastric junction focused on subtle mucosal change with high index of suspicion may be a key to the early detection of these tumors.

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