

ORIGINAL ARTICLE

위내시경검사에서 간과된 진행성 위암의 특징

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Characteristics of Advanced Gastric Cancer Undetected on Gastroscopy

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Background/Aims: Stomach cancer can be easily diagnosed via endoscopy, but also possible to be missed. The aim of this study was to investigate the clinical and endoscopic characteristics of advanced gastric cancers that were not diagnosed based on endoscopic examination.

Methods: We evaluated patients who had newly diagnosed advanced gastric cancer that was undetected via endoscopy within the last six months.

Results: Sixteen patients were included in this study. The locations of the cancers were the cardia in six cases, the greater curvature side of the body in eight cases and the antrum in two cases. The histological findings were tubular type adenocarcinoma in 11 cases, with ten cases of moderately to poorly differentiated adenocarcinoma and five cases of signet ring cell type adenocarcinoma.

Conclusions: Even advanced gastric cancer lesions may not be detected during endoscopy. If a patient continues to complain of upper gastrointestinal symptoms, even though endoscopy does not find abnormal findings, repeated endoscopy and/or additional diagnostic studies should be considered. (Korean J Gastroenterol 2011;57:288-293)

Key Words: Gastric cancer; Gastroscopy

INTRODUCTION

The incidence of stomach cancer has decreased worldwide, but it remains the most common cancer in Korea, Japan and China.¹ Many patients visit gastroenterology departments with upper gastrointestinal symptoms that cannot be used to discriminate stomach cancer from various benign

disorders. Because of the relatively high incidence of stomach cancer in these far eastern countries, even patients under the age of 40 must be considered for endoscopic evaluations.²⁻⁴

To detect stomach cancer, endoscopic examination is the diagnostic tool of choice.⁵⁻⁷ However, perfect diagnostic tool is not available, currently. Early gastric cancer can be missed

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because it is usually small and may not be ulcerated or elevated, and therefore may not be differentiated from the normal surrounding tissue.⁸ In general, advanced gastric cancer is large and the lesion is generally ulcerated or protruding, or has an irregular surface and therefore, it can easily be detected, even by an inexperienced endoscopist. However, some advanced gastric cancers are not ulcerated or protruded. For example, a Borrmann type IV advanced gastric cancer infiltrates diffusely and may not be visualized even by an expert endoscopist.

Missed or delayed the diagnosis of an advanced gastric cancer can be fatal. In addition, a delay in the diagnosis of an advanced gastric cancer may become a legal problem. There are no data on advanced gastric cancers that were not detected during recent endoscopic examinations. The aim of this study was to analyze the clinical and endoscopic characteristics of advanced gastric cancers that were not diagnosed by an endoscopic examination within the previous six months and to determine why the cancers were not detected.

SUBJECTS AND METHODS

We prospectively collected cases of advanced gastric cancer that were not diagnosed on recent endoscopic examinations from 1997 to 2008. In addition, we reviewed the medical records of previously diagnosed advanced gastric cancers from 1991 to 1996. In total, 2,310 cases of stomach cancer were analyzed. We defined 'undetected advanced gastric cancer' as cases in which advanced gastric cancer was diagnosed at our hospital, which had not been detected

via previous endoscopy at an outside hospital within the previous six months. We identified 26 cases of undetected advanced gastric cancer, but only 16 cases were available for analysis. All of the gastroenterologists in our hospital reviewed the endoscopic findings of the latter and prior endoscopic examinations. All of the lesions were classified endoscopically according to the Borrmann classification: type I was polypoid, type II was ulcerative, type III was ulcero-infiltrative, and type IV was diffuse infiltrative. We attempted to determine why the lesions were not detected using chart review and telephone interviews with the endoscopists. One gastrointestinal pathologist reviewed the biopsy specimens.

RESULTS

Seven patients were male, and nine patients were female. The age distribution ranged from 36 to 68 years, and the average age was 49.2 years. The chief complaints were epigastric pain in eight cases, epigastric soreness in six cases, and the remaining cases complained of weight loss and dysphagia.

The hospitals in which the prior endoscopic examinations were performed included general hospitals in six cases, a community hospital in one case, private clinics in eight cases, and an unidentified location in one case. The prior endoscopists were gastroenterologists in four cases, internists in six cases, family physicians in two cases, and unidentified in four cases (Fig. 1).

Histologically, 11 cases were tubular type adenocarcinoma and five cases were signet ring cell type adenocarcinoma. Among the cases with the tubular type of adeno-

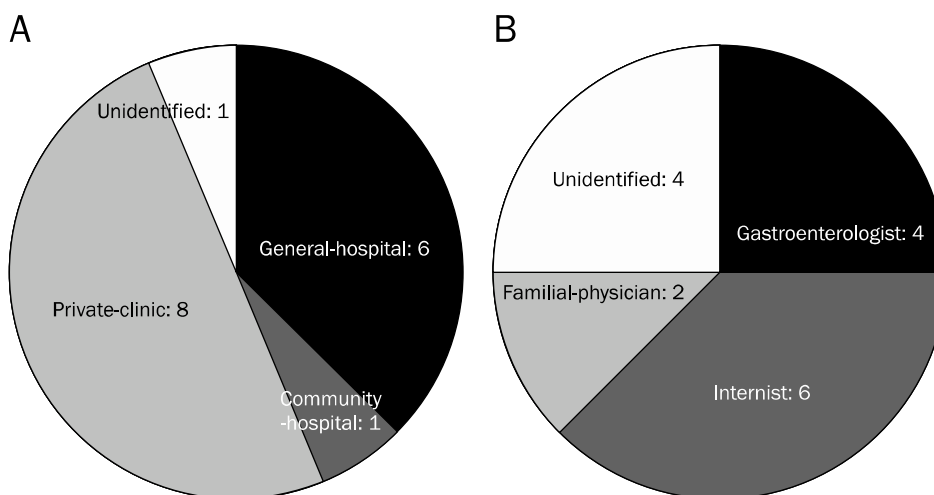


Fig. 1. Hospitals and endoscopists of prior endoscopic examinations which could not detect gastric cancer. (A) Most of the hospitals were general hospitals or private clinics. (B) Most of the prior endoscopists were gastroenterologists or internists.

carcinoma, one was well differentiated, five were moderately differentiated and five were poorly differentiated (Fig. 2).

Endoscopically, six cases were located around the cardia, and they were classified as Borrmann type III. Eight cases were found on the greater curvature side of the body, and they were Borrmann type IV in seven cases and Borrmann type III in one case. Two cases had lesions on the antrum; one was a Borrmann type II, and the other one was a Borrmann type III (Fig. 3A). Microscopically, the cancers around the cardia were moderately differentiated in four cases, a signet ring cell type in one case and a well differentiated type in one case. The cancers on the greater curvature side of the body were signet ring cell types in four cases and poorly differentiated in four cases. On the antrum, one was moderately differentiated and the other one was poorly differentiated (Fig. 3B).

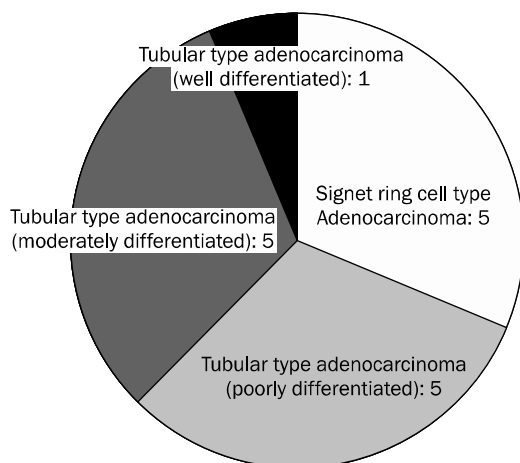
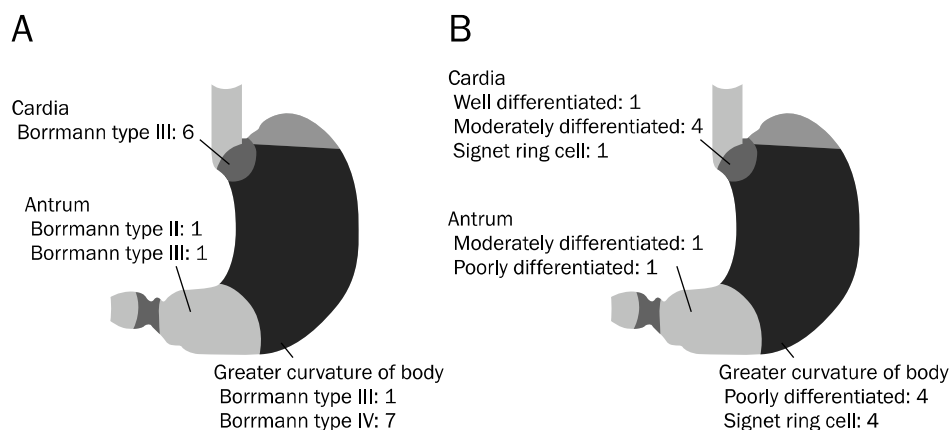


Fig. 2. Histological characteristics of misdiagnosed advanced gastric cancer.



DISCUSSION

In this study, more than one-third of the cases with advanced gastric cancers that were not detected with previous endoscopic examination were located around the cardia. Because the cardia is not easily accessible during endoscopy, even with modern flexible endoscopes, lesions around the cardia are difficult to identify. To examine the cardiac re-

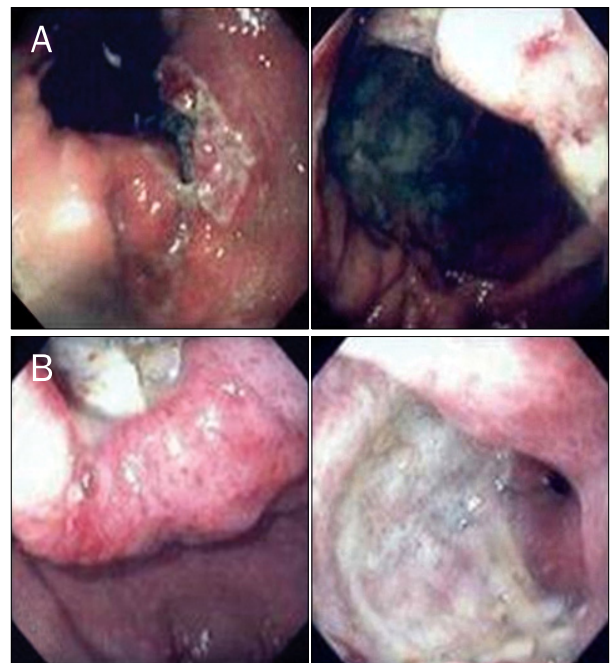


Fig. 4. Endoscopic finding of misdiagnosed advanced gastric cancer around the cardia (A) and antrum (B). (A) The endoscopic findings on later examination showed a large ulceroinfiltrative lesion around the cardia. (B) A very large ulcerative lesion was observed on the second endoscopic examination. The prior endoscopist misdiagnosed the encircling antral ulcerative cancer lesion as a duodenal ulcer within the duodenal bulb.

Fig. 3. Endoscopic and histological classifications of misdiagnosed advanced gastric cancer according to the location in the stomach. (A) Most cancers were located around the cardia and greater curvature side of the body. Endoscopically, the cancers around the cardia are Borrmann type III, and the cancers on the greater curvature side of the body were Borrmann type IV. (B) Microscopically, the cancers around the cardia were moderately differentiated, and the cancers on the greater curvature side of body were signet ring cell and poorly differentiated.

gion, it is necessary to bend the tip of the endoscope, which causes patient discomfort. Frequent belches and retches during the examination of the cardia can be considered as a limitation that can result in missed detection. Sometimes, the shaft of the endoscope may hide the lesion around the cardia, especially when the examiner has the endoscope in a U shape. Thus, the examination of the cardia requires special attention due to the difficulties of visualization. In our review, the cardiac lesions were not small, and they were classified endoscopically as ulceroinfiltrative types (Fig. 4A); therefore, on the assumption that the advanced gastric cancer (AGC) did not grow rapidly, they would likely be easily detected if they were located on the antrum rather than the cardia. Needless to say, it is possible that there was no clue of AGC on previous endoscopy and it grew rapidly. Because this study was limited to only patients with advanced gastric cancer, the number of missed cases involving the gastric cardia may be even higher. Therefore, all endoscopists must make an effort to examine the cardia.

As expected, most of the advanced gastric cancers located on the greater curvature side of the body that were not observed during a recent endoscopic examination were diffuse

infiltrative Borrmann type IV cancers (Fig. 5). As many endoscopists have pointed out, lesions on the greater curvature side of the body may not be visualized, even in an advanced form, especially if the lesions are hidden by the gastric folds of the body. Histologically, all of the cases were signet ring cell types and poorly differentiated adenocarcinomas. Because these lesions usually spread along the submucosa without any noticeable lesions on the mucosa, except for thickening of the gastric folds, advanced lesions may be missed.^{9,10} Some studies have reported that an indicator of Borrmann type IV advanced gastric cancer might be a tiny shallow ulcer on the greater curvature side of the upper body on a prior endoscopy, which may heal and disappear over time.^{11,12} Such lesions can be easily missed. Occasionally, the stomach with gastric cancer may show only thickening of the gastric folds in the body with poor expansibility and no mucosal lesion. This can result in misdiagnosis as a normal stomach or hypertrophic gastritis. In this situation, even an expert endoscopist may not correctly diagnose gastric cancer, and the biopsy frequently reveals only normal mucosa. Additional investigations with an upper gastrointestinal study using barium gastrography or computed tomography may be helpful in ad-

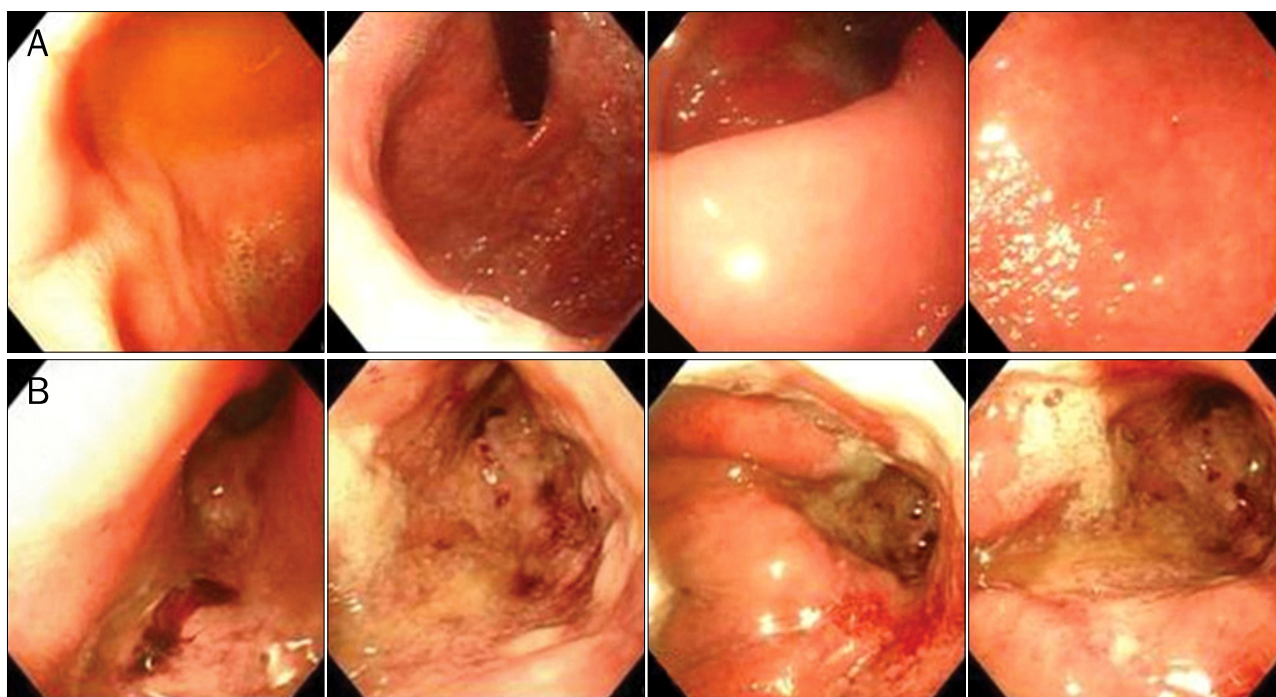


Fig. 5. Endoscopic finding of misdiagnosed advanced gastric cancer on the greater curvature side of the body. (A) On the first endoscopic examination, there was no remarkable lesion on the greater curvature side of body except for an ulcer scar on the duodenal bulb. (B) However, three months later, endoscopic examination showed a very large irregularly shaped ulcer with thickened mucosal folds and poor expansibility along the greater curvature side of stomach from the antrum up to the mid-body.

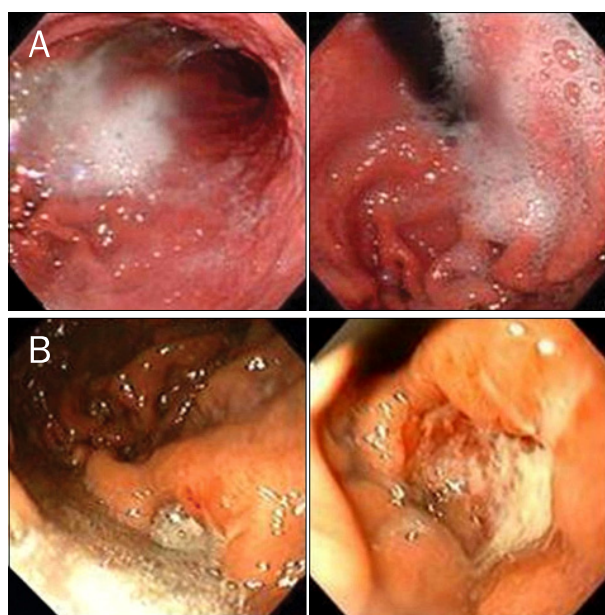


Fig. 6. Endoscopic finding of misdiagnosed advanced gastric cancer of the upper body. (A) On the previous endoscopic photograph, there appeared to be no abnormal lesion; there were gastric secretions and air bubbles on the greater curvature side of the upper body. (B) Follow-up endoscopic examination revealed a large round ulcerative cancer lesion on the greater curvature side of the upper body. This lesion was missed because of inadequate removal of gastric secretions during the first endoscopic examination.

dition to the repeated endoscopic examination.¹³⁻¹⁵ In one case, even repeated biopsy failed to obtain cancer cells from the suspicious lesion due to submucosal spreading of the cancer cells covered by normal mucosa. In that case, the cancer was ultimately diagnosed via strip-off biopsy.

Because most advanced gastric cancers of Borrmann type IV are signet ring cell types or poorly differentiated adenocarcinomas, they usually progress rapidly. Therefore, missing such a lesion may be fatal.^{16,17} The endoscopist should carefully examine the gastric body after full expansion of the gastric folds with sufficient air inflation, and fluid should be suctioned out of the body. In addition, adequate time should be spent on the endoscopic examination. In one case, the examiner performed the procedure in a few minutes and did not completely aspirate the fluid from the body; the patient was later found to have advanced gastric cancer (Fig. 6).

In two cases of missed advanced gastric cancers, the cancer was located in the antrum. In one case, the cause could not be found; the prior diagnosis for the other case, which was performed by an unidentified endoscopist, was a duodenal

ulcer. However, the lesion observed on our endoscopic examination was located in the antrum, not in the duodenum. Therefore, this case was misdiagnosed. The narrowing of the antral lumen by the encircling mass appeared to be the pyloric canal (Fig. 4B), and the ulcer was mistaken as a duodenal ulcer; we think the reason the advanced gastric cancer lesion was missed in this case was lack of experience of the endoscopist.

More than one-third (six cases) of the missed cases occurred in general training hospitals. Therefore, we cannot rule out the possibility that the lesions were missed by residents in training who had inadequate faculty supervision. However, the possibility of a selection bias exists with our data because it was easier to get information and to analyze the data on endoscopic examinations from general hospitals compared to private clinics. Most of the prior endoscopists were gastroenterologists or internists who would be expected to be expert endoscopists. Therefore, it is likely that some of the undetected lesions were missed because of the limitations of endoscopy during the examination or the characteristics of the lesions and thus might have been unavoidable.

The usual doubling time of advanced gastric cancer varies from one month to six months. One study reported that the doubling time of advanced gastric cancer was only nine days.¹⁸ In such a case, even though the second endoscopic examination revealed a very large advanced gastric cancer, the first endoscopic examination, only a few months earlier, may have been normal.

In the patients studied, most did not complain of alarming symptoms. Therefore, physicians should be alert to any persistent upper gastrointestinal symptoms, even if the prior endoscopic examination was normal.

The limitations of this study are as follows. 1) the presence of several endoscopists, so there was possibility of inter-observer bias. 2) We do not know for sure whether AGC was present at the time of previous examination, but there was no way to exclude this limitation. 3) Although we collected data prospectively, it is ambiguous whether it is a prospective or retrospective study because we analyzed the data from previous endoscopic results retrospectively. 4) Small sample size, although even in Korea, which has a high incidence of gastric cancer, we could not collect sufficient advanced gastric cancer cases which satisfied our criteria.

Although this study had many limitations, some valuable

information was procured. Because we believe that some advanced gastric cancer can be undetected during endoscopy, we suggest the following. 1) Adequate time and care, including aspiration of fluid and sufficient air inflation and deflation, must be routine during endoscopic examinations, especially in the evaluation of the cardia and greater curvature side of the body of the stomach. 2) If a patient with a normal endoscopic finding complains of persistent gastrointestinal symptoms, the physician should consider a repeat endoscopy or other diagnostic evaluation, especially in nations such as Korea and Japan where the prevalence of gastric cancer is high.

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