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The Comparison of Histologic Gastritis in Patients with Duodenal Ulcer, Chronic Gastritis, Gastric Ulcer and Gastric Cancer

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Abstract

This study was designed to investigate the differences of histologic gastritis according to the endoscopic diagnosis, and between *H. pylori* positive and negative gastritis, using the Sydney system. A total of 122 patients (42 duodenal ulcer, 31 chronic gastritis, 35 gastric ulcer and 14 gastric cancer) underwent endoscopy with biopsies from the antrum and body. Among the 122 patients, 104 (85%) were *H. pylori* positive. *H. pylori* density of the antrum was significantly higher in duodenal ulcer than in chronic gastritis, gastric ulcer, and gastric cancer. The positivity of intestinal metaplasia was lowest in duodenal ulcer and highest in gastric cancer. *H. pylori* density as well as the grade of activity, inflammation and atrophy were significantly higher in the antrum than in the body in duodenal ulcer, while in chronic gastritis, gastric ulcer and gastric cancer there was no difference of *H. pylori* density, activity, inflammation and atrophy between the antrum and body. The grade of activity and chronic inflammation were significantly higher in *H. pylori* positive patients than in *H. pylori* negative patients in both the antrum and body. In conclusion, the gastritis of duodenal ulcer was mainly localized to the antrum, while the gastritis of chronic gastritis, gastric ulcer or gastric cancer was rather uniform in the antrum and body. *H. pylori* seemed to be related to the development of chronic inflammation and activity.

Key Words: Gastritis, *H. pylori*, Sydney system

INTRODUCTION

Since the advent of the endoscopic biopsy technique in 1947, pathologists and gastroenterologists have attempted to devise a uniform classification of gastritis, but they have been unsuccessful.[1] In 1983, *Helicobacter pylori* (*H. pylori*) was discovered and the role of this bacterium in the etiology of most patients of chronic gastritis, previously considered idiopathic, became rapidly apparent.[2]

The discovery of *H. pylori* prompted the investigation of gastritis. In an attempt to remove diagnostic confusion, a working party met before the World Congress of Gastroenterology in Sydney in 1990 to establish guidelines for the classfication and grading of gastritis.[3] The resulting "Sydney system" had both endoscopic and histologic divisions, and the latter had five grade variables; *H. pylori* density, activity, chronic inflammation, atrophy, and intestinal metaplasia.

Peptic ulcer always accompanies histologic gastritis. Whitehead pointed out that whatever the etiology, "ulcer and gastritis are invariably present in the same stomach".[4] *H. pylori* is known to cause chronic active gastritis, characterized by the histologic features of polymorphonuclear cell infiltration in lamina propria. However, there have been few reports about how the patterns of histologic gastritis are different among various gastroduodenal diseases. The aim of this study was to investigate the differences of histologic gastritis evaluated by the Sydney system in patients with duodenal ulcer, chronic gastritis, gastric ulcer and gastric cancer, and the differences between *H. pylori* positive and *H. pylori* negative patients.

MATERIALS AND METHODS

Patients

This study consisted of 122 patients. All patients underwent routine upper gastrointestinal endoscopic examination with Olympus XQ200 or XQ230 for the investigation of epigastric soreness, hunger pain or dyspepsia. During endoscopy, two biopsy specimens each were obtained from the antrum and body at the

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anterior and posterior wall. Among the 122 patients, 79 (65%) were males and 43 (35%) females. Their average age was 47.6 years (range; 19-81). Forty-two (34%) had duodenal ulcer, 31 (25%) had chronic gastritis, 35 (29%) had gastric ulcer and 4 (12%) had gastric cancer (Table 1).

Methods

Histological assessment of *H. pylori* and gastritis: For the assessment of *H. pylori* and the histologic grading of chronic gastritis, sections of the biopsy specimens were stained with hematoxylin and eosin. The histopathologic features of gastric biopsy specimens were evaluated according to the Sydney classification[3] by one pathologist and *H. pylori* density, chronic inflammation, activity and atrophy were each graded into none, mild, moderate or severe (Table 2).

Statistical analysis: Each item of histologic gastritis was compared among duodenal ulcer, chronic gastritis, gastric ulcer and duodenal ulcer and then compared between *H. pylori* positive and negative patients. Chi-square test was used to determine the difference of the grade of gastritis.

RESULTS

The status of *H. pylori* infection of patients

Among the 122 patients, 104 (85%) were *H. pylori* positive and 18 (15%) were *H. pylori* negative in histopathologic examination. The positive rate of *H. pylori* status was 96% in duodenal ulcer, 78% in

Table 1. Demographic Data and *H. pylori* Status of Patients

Diagnosis	No.	M:F	Mean age	H&E (+) (%)	H&E (−) (%)
Duodenal ulcer	42	34/8	39.4	40 (96)	2 (4)
Chronic gastritis	31	12/19	48.8	24 (78)	7 (22)
Gastric ulcer	35	21/14	52.5	28 (80)	7 (20)
Gastric cancer	14	12/2	57.7	12 (86)	2 (14)
Total	122	79/43	47.6	104 (85)	18 (15)

H&E, Hematoxylin and Eosin stain for *H. pylori*.

Table 2. Definitions and Grading Guidelines for Each of the Histological Features to Be Graded According to the Sydney Classification

Feature	Definition	Grading guidelines
H. pylori	Density of *Helicobacter*-like organisms overlying epithelium	none : no curved bacilli mild : scattered organisms covering <1/3 of the surface moderate : intermediate numbers severe : large clusters or a continuous layer over >2/3 of the surface
Activity	Neutrophil polymorph infiltration of the lamina propria, pits or surface epithelium	none : polymorphs difficult to find mild : <1/3 of pit and surface infiltrated moderate : 1/2-2/3 of pit and surface infiltrated severe : >2/3 of pit and surface infiltrated
Chronic inflammation	Increase in lymphocytes and plasma cells in the lamina propria	none : lymphocytes and plasma cells present normal in numbers mild : mild increase in density moderate : moderate increase in density severe : severe increase in density
Atrophy	Loss of specialized glands from either antrum or body	none : absent mild : mild loss moderate : moderate loss severe : severe loss

chronic gastritis, 80% in gastric ulcer and 86% in gastric cancer (Table 1).

The comparison of histologic gastritis among duodenal ulcer, chronic gastritis, gastric ulcer, and gastric cancer

Both the overall positivity and density of *H. pylori* in the antrum were significantly higher in duodenal ulcer than in chronic gastritis ($p<0.05$), gastric ulcer ($p<0.05$), and gastric cancer ($p<0.05$) (Fig. 1).

Grade of inflammatory activity of the antrum was no different among diseases, but grade of activity of the body was lower in duodenal ulcer than in chronic gastritis ($p<0.05$), gastric ulcer ($p<0.01$), and gastric cancer ($p<0.05$) (Fig. 2).

Grade of chronic inflammation of the antrum was no different among diseases, but grade of chronic inflammation of the body was lower in duodenal ulcer than in chronic gastritis ($p<0.01$), gastric ulcer ($p<0.01$), and gastric cancer ($p<0.05$) (Fig. 3).

Grade of atrophy of antral mucosa was no different among diseases, but grade of atrophy of body mucosa was significantly higher in chronic gastritis ($p<0.05$) and gastric ulcer ($p<0.01$) than in duodenal ulcer (Fig. 4).

The positivity of intestinal metaplasia was lowest in duodenal ulcer (17% in the antrum and 7% in the body) and highest in gastric cancer (57% in the antrum and 56% in the body), but there was no significant difference of the positivity of intestinal metaplasia among diseases (Fig. 5).

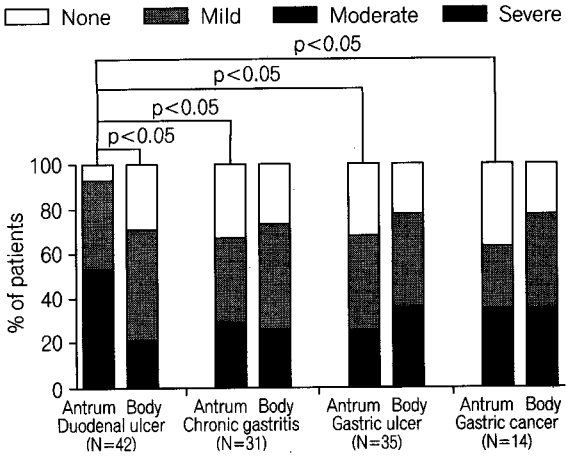

Fig. 1. The grade of H. pylori density in duodenal ulcer, chronic gastritis, gastric ulcer and gastric cancer in accordance with the Sydney system.

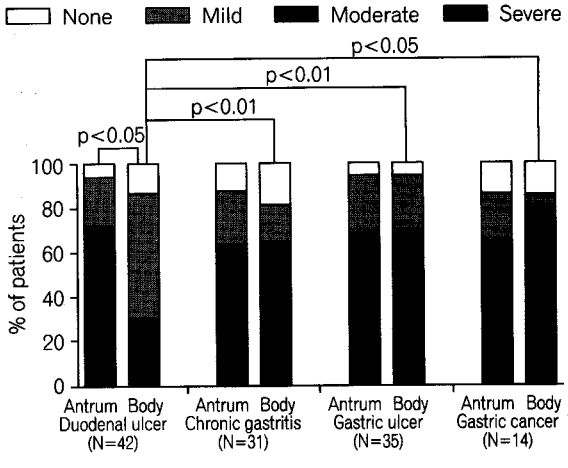

Fig. 3. The grade of chronic inflammation of gastric mucosa in duodenal ulcer, chronic gastritis, gastric ulcer and gastric cancer in accordance with the Sydney system.

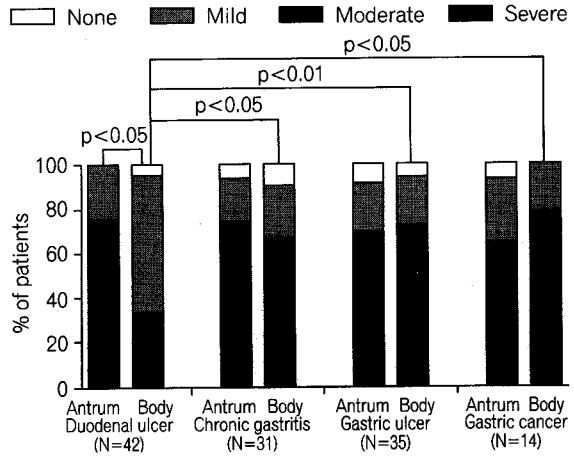

Fig. 2. The grade of inflammatory activity in duodenal ulcer, chronic gastritis, gastric ulcer and gastric cancer in accordance with the Sydney system.

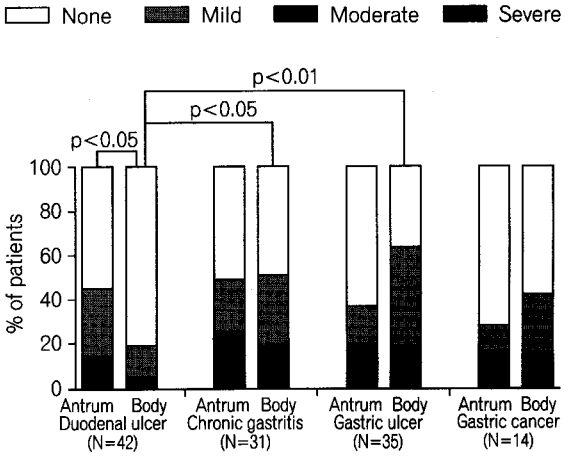

Fig. 4. The grade of gastric mucosal atrophy in duodenal ulcer, chronic gastritis, gastric ulcer and gastric cancer in accordance with the Sydney system.

Comparing between the antrum and body in each disease, only in duodenal ulcer, the *H. pylori* density ($p<0.05$) as well as the grade of inflammatory activity ($p<0.05$), chronic inflammation ($p<0.05$) and atrophy ($p<0.05$) were significantly higher in the antrum than in the body; while in chronic gastritis, gastric ulcer and gastric cancer, there was no difference of *H. pylori* density, activity, inflammation and atrophy between the antrum and body (Fig. 1−4).

The comparison of histologic gastritis between H. pylori positive and H. pylori negative patients

Comparing the gastritis between *H. pylori* positive patients (n=104) and *H. pylori* negative patients (n=18), the grade of activity and chronic inflammation were significantly higher in *H. pylori* positive patients than in *H. pylori* negative patients both in the antrum and body, while there was no difference in grade of atrophy between *H. pylori* positive patients and *H. pylori* negative patients (Fig. 6 and 7). The positivity of intestinal metaplasia of *H. pylori* positive patients in the antrum was lower than that of *H. pylori* negative patients (28% vs. 53%, $p<0.05$); while in the body there was no difference of the positivity of intestinal metaplasia between *H. pylori* positive patients (27%) and *H. pylori* negative patients (33%) (Fig. 8).

Comparing between the antrum and body in *H. pylori* positive patients and *H. pylori* negative patients, only in *H. pylori* positive patients, the grades of activity ($p<0.05$) and chronic inflammation ($p<0.05$) were significantly higher in the antrum than in

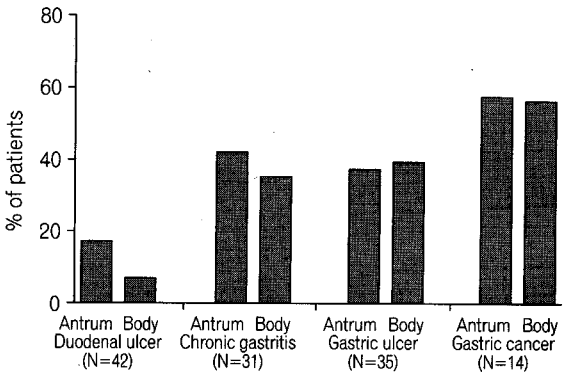

Fig. 5. The positivity of intestinal metaplasia of gastric mucosa in duodenal ulcer, chronic gastritis, gastric ulcer, and gastric cancer.

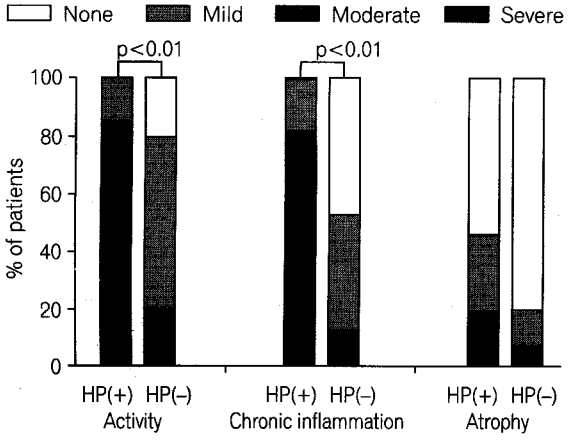

Fig. 6. The comparison of degree of inflammatory activity, chronic inflammation and gastric mucosal atrophy of the antrum between H. pylori positive and negative patients in accordance with the Sydney system. HP, H. pylori.

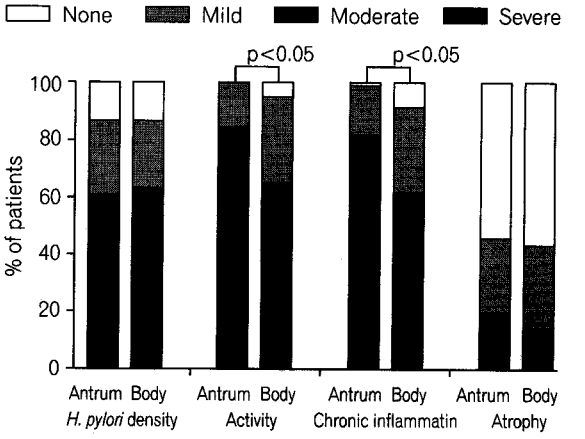

Fig. 7. The comparison of degree of inflammatory activity, chronic inflammation and gastric mucosal atrophy of the body between H. pylori positive and negative patients in accordance with the Sydney system. HP, H. pylori.

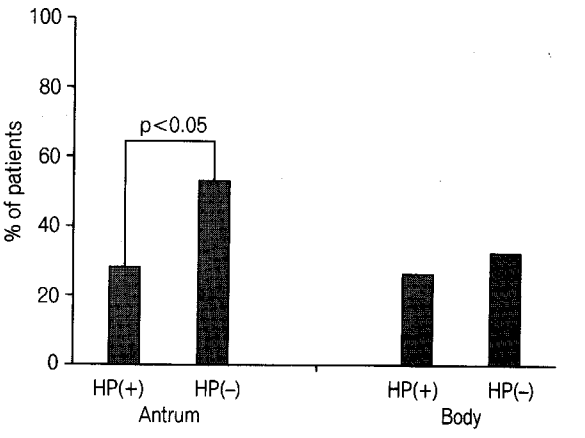

Fig. 8. The prevalence of intestinal metaplasia of H. pylori positive and negative patients in antrum and body. HP, H. pylori.

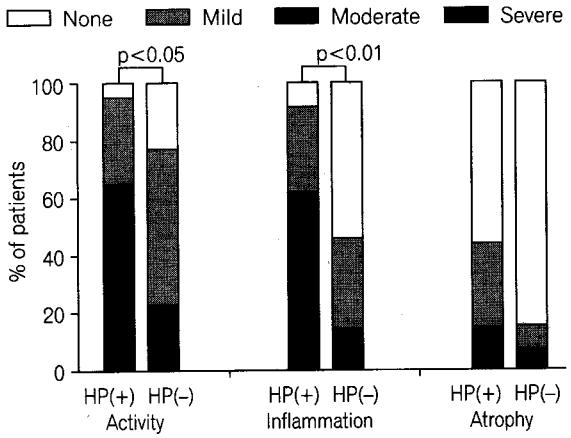

Fig. 9. The comparison of H. pylori density, activity, chronic inflammation and atrophy between antrum and body in H. pylori positive patients.

the body; while in *H. pylori* negative patients, there was no such difference of activity and chronic inflammation between the antrum and body (Fig. 9).

DISCUSSION

In duodenal ulcer in this study, the *H. pylori* density of the antrum was significantly higher compared to chronic gastritis, gastric ulcer and gastric cancer. Comparing between the antrum and body in duodenal ulcer, *H. pylori* density as well as grade of activity, chronic inflammation and atrophy were significantly higher in the antrum than in the body. These results indicated that the gastritis accompanied in duodenal ulcer is mainly antrum localized and body spared and they are consistent with Alam et al.[5] Correa and Yardley suggested that the duodenal ulcer is accompanied by diffuse antral gastritis (DAG) which involves diffusely the full thickness of the mucosa exclusively in the antrum.[6]

However, in other diseases such as chronic gastritis, gastric ulcer and gastric cancer in this study, there were no differences of these grades of histologic gastritis and they showed similar grades between the antrum and body in each disease, suggesting pangastritis of these diseases.

In gastric ulcer, the grade of activity and chronic inflammation was similar between the antrum and body, meaning that the gastritis accompanied by gastric ulcer is diffuse in distribution. Compared with duodenal ulcer, chronic gastritis, and gastric cancer, the grade of activity and chronic inflammation in gastric ulcer was not significantly different. Because the *H. pylori* density of the antrum was lower in gastric ulcer than in duodenal ulcer, other factors except *H. pylori* might be related to the development of the gastritis in gastric ulcer. Martin et al. have shown that *H. pylori* and NSAID are the two independent risk factors for gastric ulcer.[7]

The grade of mucosal atrophy in gastric ulcer was higher than that in duodenal ulcer. Gastric ulcer was reported to be accompanied by multifocal atrophic gastritis (MAG).[6]

Comparing between *H. pylori* positive and *H. pylori* negative patients, activity and chronic inflammation were more severe in *H. pylori* positive patients than in *H. pylori* negative patients in both the antrum and body. The positive relationship beteen the grade of acute and chronic inflammation of gastric mucosa and the grade of *H. pylori* density has been reported by others.[8,9] Clearing of *H. pylori* resulted in improvement of both acute and chronic gastritis.[10] Therefore, these reports support the view that *H. pylori* plays a causal role in the pathogenesis of chronic gastritis.

The secretion of cytokines such as interleukin-8 is increased in gastric epithelium by *H. pylori* infection, especially in chronic active gastritis of which the histologic characteristic is increased infiltrations of polymorphonuclear cells.[11] Activity of chronic gastritis is known as a useful measure of response to therapy and can be particularly related to the presence and concentration of *H. pylori*.[12-14]

In *H. pylori* positive patients of this study, the activity and inflammation were more severe in antrum than in body, while in *H. pylori* negative patients, there was no such difference. This result was consitent with Stolte et al.[15] However, in *H. pylori* positive patients of this study, though the activity and chronic inflammation were more severe in the antrum than in body, *H. pylori* density was no different between the antrum and body. This result means, as Bayerdörffer et al. suggested, that the different expression of gastritis in the antrum and body is due to increased reactivity of the antral mucosa to the infection, possibly on the basis of an enhanced immunologic response to *H. pylori* in this region.[11]

The glandular atrophy of gastric mucosa was reported to be more severe in *H. pylori* positive patients than negative patients.[12,14] However, in this study, there was no difference in the grade and positivity of atrophy between *H. pylori* positive and *H. pylori* negative patients. This inconsistency may be due to the small number of patients in this study and another possibility is that, as Park et al. suggested, the role of *H. pylori* on the pathogenesis of chronic gastritis in endemic countries of *H. pylori* may differ from that in western countries.[13] So, further studies

about the relationship between *H. pylori* and atrophy will be needed.

Intestinal metaplasia is generally recognized as a precancerous lesion of intestinal-type gastric carcinoma.[16] In this study, the positivity of intestinal metaplasia in gastric cancer was highest among four diseases, while that in duodenal ulcer was lowest. However, there was no significant difference among diseases. This result can be related to the small number of patients in this study and remains to be further investigated.

Comparing the positivity of intestinal metaplasia between *H. pylori* positive and *H. pylori* negative patients in this study, the positivity of intestinal metaplasia in the antrum of *H. pylori* positive patients was lower than that of *H. pylori* negative patients. This result can suggest a negative correlation between *H. pylori* and intestinal metaplasia and was consistent with the fact that *H. pylori* does not colonize epithelium that has undergone intestinal metaplasia.[17,18] Furthermore, Kim et al. reported that the distribution of *H. pylori* was not observed on metaplastic mucosa.[9] However, no association[19] or positive association[16,20] between *H. pylori* and intestinal metaplasia has been reported. Therefore, the present concept of *H. pylori* and intestinal metaplasia is still a subject of much debate.

In conclusion, the gastritis of duodenal ulcer was mainly localized to the antrum, which may be related to the higher density of *H. pylori* in this area, while the gastritis of chronic gastritis, gastric ulcer or gastric cancer was rather uniform in the antrum and body. *H. pylori* is related to chronic inflammation and activity, but its relationship with atrophy and intestinal metaplasia should be further investigated.

REFERENCES

1. Genta RM. Recognizing atrophy: another step toward a classification of gastritis. Am J Surg Pathol 1996;20 Suppl 1:23-30.
2. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984;1:1311-5.
3. Price AB. The Sydney system. Histologic division. J Gastroenterol Hepatol 1991;6:209-22.
4. Whitehead R. Mucosal biopsy of the gastrointestinal tract. 3rd ed. Philadelphia: Saunders Inc; 1985. p.41-85.
5. Alam K, Schbert TT, Bologna SD, Ma CK. Increased density of *Helicobacter pylori* on antral biopsy is associated with severity of acute and chronic inflammation and likelihood of duodenal ulceration. Am J Gastroenterol 1992;87:424-8.
6. Correa P, Yardley JH. Grading and classification of chronic gastritis: one American response to the Sydney system. Gastroenterology 1992;102:355-9.
7. Martin DF, Montgomery E, Dobek AS, Patrissi GA, Peura DA. *Campylobacter pylori*, NSAIDS and smoking: Risk factors for peptic ulcer disease. Am J Gastroenterol 1989; 84:1268-72.
8. Satoh K, Kimura K, Yoshida Y, Kasano T, Kihira K, Taniguchi Y. A topographical relationship between *Helicobacter pylori* and gastritis: quantitative assessment of *Helicobacter pylori* in the gastric mucosa. Am J Gastroenterol 1991;86:285-91.
9. Kim KM, Lee AH, Shim SI, Chae HS. Gastric lymphoid follicles in *Helicobacter pylori* infection: Frequency, distribution and relationship to inflammation in 331 gastric biopsy material. Korean J Pathol 1995;29:442-9.
10. Valle J, Seppala K, Sipponen P, Kosunen T. Disappearance of gastritis after eradication of *Helicobacter pylori*. A morphometric study. Scand J Gastroenterol 1991;26:1057-65.
11. Bayerdörffer E, Lehn N, Hatz R, Mannes GA, Oertel H, Sauerbruch T, et al. Difference in expression of *Helicobacter pylori* gastritis. Gastroenterology 1992;102:1575-82.
12. Kuipers EJ, Uyterlinde AM, Pena AS, Roosendaal R, Pals G, Nelis GF, et al. Long-term sequelae of *Helicobacter pylori* gastritis. Lancet 1995;345:1525-8.
13. Park JW, Kim MW, Park SM. Influence of *Helicobacter pylori* colonization on histologic grading of chronic gastritis in Korean patients with peptic ulcer. Korean J Intern Med 1995;10:125-9.
14. Kim CH, Kim IG, Kim TS, Kim CG, Shon HS, Choe JY, et al. Relationship between *H. pylori* infection and severity of gastritis, serum IgG antibody titer against *H. pylori*, and fasting serum gastrin in the upper gastrointestinal disease patients. Korean J Gastroenterol 1996; 28:311-9.
15. Stolte M, Eidt S, Ohnsmann A. Differences in *Helicobacter pylori* associated gastritis in the antrum and body of the stomach. Gastroenterology 1990;28:229-33.
16. Craanen ME, Dekker W, Blok P, Ferwerda J, Tytgat GNJ. Intestinal metaplasia and *Helicobacter pylori*: an endoscopic bioptic study of the gastric antrum. Gut 1992; 33:16-20.
17. Carrick J, Lee A, Hazell S, Ralston M, Daskalopoulos G. *Campylobacter pylori*, duodenal ulcer and gastric metaplasia: Possible role of functional heterotopic tissue in ulcerogenesis. Gut 1989;30:790-7.
18. Coelho LG, Das SS, Payne A, Karim QN, Baron JH, Walker MM. *Campylobacter pylori* in esophagus, antrum, and duodenum. A histological and microbiological study. Dig Dis Sci 1989;34:445-8.
19. Lee HJ, Yu ES, Lee IC. Histopathologic analysis of *Helicobacter pylori* associated gastritis. Korean J Pathol 1996;30: 764-74.
20. Ko GH, Park CK, Choi CS, Park HB, Lee JH, Lee HJ, et al. *Helicobacter pylori* infection and histopathological features of gastric mucosa. Korean J Pathol 1996;30: 199-209.