Hiroshima Journal of Medical Sciences
Vol.35, No.4, 303~308, December, 1986
HIJM 35-44

Distribution of G-Cells in the Gastric Mucosa in Peptic Ulcer

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(Received July 31, 1986)

Key words: G-cell, Peptic ulcer, Peroxidase antiperoxidase method, Intestinal metaplasia

ABSTRACTS

The distribution of G cells in mucosa of the resected stomachs from patients with peptic ulcer was investigated using the peroxidase-antiperoxidase immunohistochemical method. Moreover, the specimens were stained additionally with hematoxylin and eosin to determine the condition of background gastric mucosa.

G cells were present chiefly in the glandular cervix of the pyloric gland area. They were also seen in the intermediate area and, although small in number, in the area adjoining the f-line. The number of G cells per unit area in DU was three times higher than that in GU. The significant inverse relation was found between G cell density and the degree of intestinal metaplasia. And in each case, mean values of uG were estimated for unit areas on the greater and lesser curvature lines as well as the unit areas on the mid-line of the anterior and posterior walls. The G cell density was higher on the greater curvature and in the posterior wall than the other.

Recently gastrointestinal hormones have drawn increasing attention, and many new findings have been obtained. In 1967, basal granule cells in the pyloric vestibular portion of the stomach were designated by Solcia as G cells which produce and release gastrin[17]. McGuigan identified G cells using the immunofluorescence direct immunoperoxidase methods[7,8]. G cells were also identified by Creutzfeldt using an indirect immunoperoxidase method[2].

As compared with the immunofluorescence method, the immunoperoxidase method is advantageous since various post staining methods including hematoxylin and eosin (HE) staining are available to observe the background gastric mucosa simultaneously. The authors stained G cells in resected stomachs from patients with peptic ulcers by the peroxidase-antiperoxidase (PAP) method and prepared maps showing the distribution of G cells in the gastric mucosa. Moreover, the specimens are stained additionally with HE to determine the condition of the background gastric mucosa.

MATERIALS AND METHODS

Resected stomachs from fours patients with gastric ulcer (GU) and four patients with duodenal ulcer (DU) were examined. All of these patients had recurring peptic ulcers, for which the stomach was extensively resected. Cases which had ulcers in both stomach and duodenum were excluded. There were 7 male cases and 1 female case. Cases of gastric ulcer included 3 male cases and 1 female case with a mean age of 49.0 ± 15.6 years (mean ± SD). In the cases of duodenal ulcers, the mean age was 34.8 ± 14.0 years.

In preparing specimens for observation, freshly obtained materials were fixed in 10% buffered formalin, sectioned totally at intervals of 5 μm

parallel with the longer axis, and embedded in paraffin. Each block thus obtained was sliced to obtain two thin sections of about 4 μm thickness. One of the sections was used for examination of G cells. The other was stained with HE to examine the degree of intestinal metaplasia of the background gastric mucosa and determine glandular borderline between the pyloric gland area and the gastric fundic gland area. As the negative control, the large intestine was used after the silimlar preparation.

For immuno-staining of G cells, PAP method using anti-gastrin antibody (17-I) of DAKO Co. Ltd. (Denmark) was employed[9].

For observation, the stained preparations were used as one unit, and the number of G cells per unit area (uG) was counted.

The degree of intestinal metaplasia was assessed for each unit area by classification into three grades: none to slight, moderate and marked.

In addition, the glandular borderline between the pyloric gland area and the gastric fundic gland area was determined and indicated in the maps.

For statistical analysis, Student's t-test was used.

RESULTS

G cells were present chiefly in the glandular cervix of the pyloric gland region. They were also seen in the duodenal mucosa. In addition, they were observed in the intermediate area and, although small in number, in the gastric fundic glandular mucosa adjoining the f-line (histological borderline between fundic glandular area and pyloric glandular area). However, no G cell was found in the large-intestinal mucosa used as the control preparation.

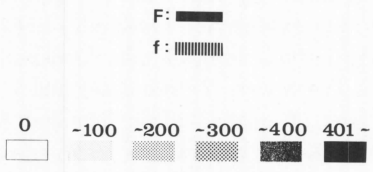

Fig. 1. Classification of G-cell density

F line: Macroscopic borderline between fundic glandular mucosa and pyloric glandular mucosa.

f line: Microscopic borderline between fundic glandular mucosa and pyloric glandular mucosa.

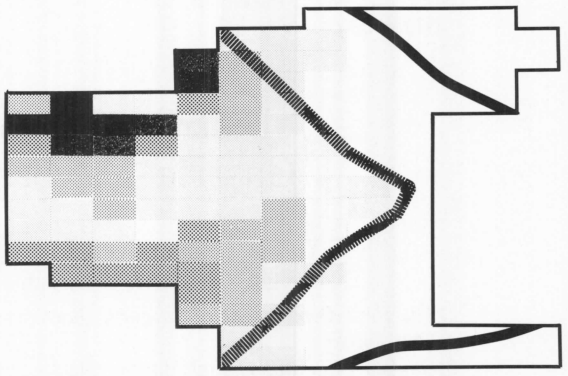

Fig. 2. Case 1 (GU)

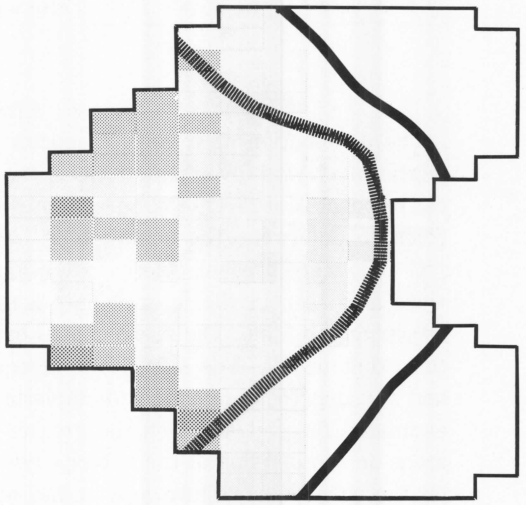

Fig. 3. Case 2 (GU)

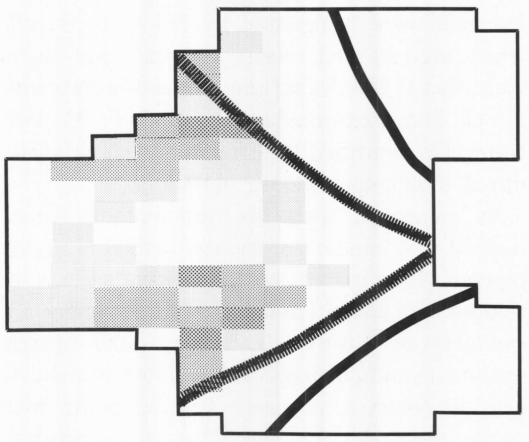

Fig. 4. Case 3 (GU)

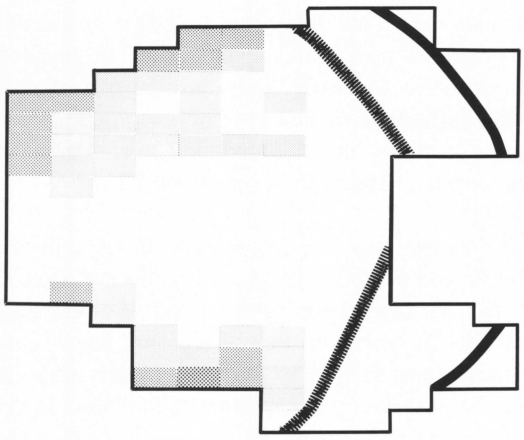

Fig. 5. Case 4 (GU)

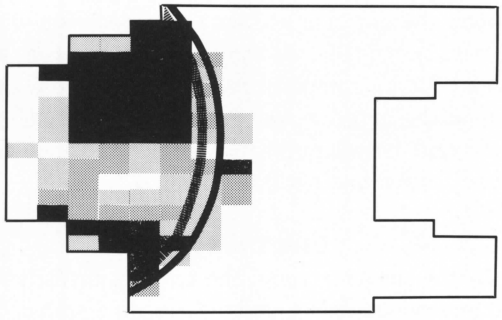

Fig. 6. Case 5 (DU)

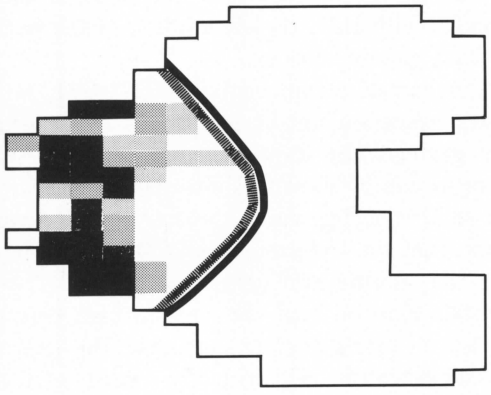

Fig. 7. Case 6 (DU)

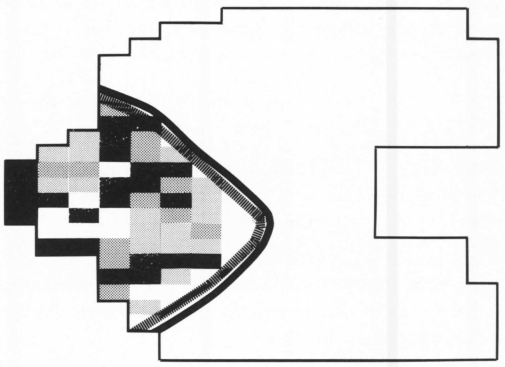

Fig. 8. Case 7 (DU)

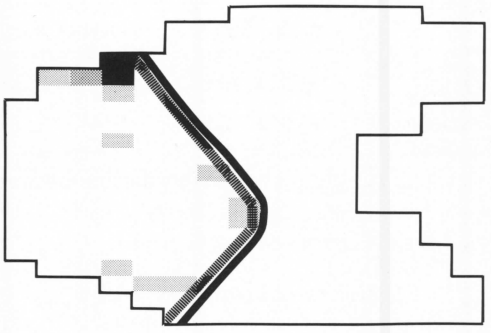

Fig. 9. Case 8 (DU)

1) Distribution of G cells

In each case, uG was determined and classified into six grades of 0, 1-100, 101-200, 201-300, 301-400 and more than 400, for which color was assigned for identification (Fig. 1). Using these colors, a map was prepared to show distribution of G cells (Figs. 2-9). Moreover, the glandular borderline was shown for each case.

As shown in these figures, there was no uniformity in distribution and density of G cells. However, as a constant tendency was observed, we searched for the factor which controls distribution and density of G cells.

2) Distribution of G cells in terms of the disease (GU and DU)

The total number of G cells in the pyloric region was 6,494.3 ± 1,669.8 (Mean ± SD) cells for GU (4 cases) and 14,230.5 ± 4.045.0 cells for DU (4 cases), with significantly higher value for the latter ($p<0.001$). When inspected by unit number, the number of G cells per unit was 82.1 ± 24.0 cells for GU and 258.7 ± 104.5 cells for DU, with the density being about 3 times higher for the latter (Table 1).

3) Intestinal metaplasia and number of G cells

The degree of intestinal metaplasia was grad-

Table 1. Mean number of G-cells which were identified with the immunohistochemical method

	GU (n = 4)	DU (n = 4)
No. of G-cells		
Total area	7129.5 ± 1655.0	16456.3 ± 5592.4
Pyloric gland area	6494.3 ± 1669.8	14230.5 ± 4045.0
uG*	82.1 ± 24.0	258.7 ± 104.5

* uG=(total number of G-cells in pyloric gland area) / (total length of the pyloric gland area on the sections expressed in cm)

Table 2. Relationship between No. of G-cells and the grade of intestinal metaplasia (I.M.) in pyloric gland area

	gastri ulcer	duodenal ulcer
Grade of I.M.		
no-slight	191.5 ± 19.2	277.2 ± 15.8
moderate	85.9 ± 6.2*	110.9 ± 32.8**
marked	28.1 ± 3.7***	———

Values are mean ± S.E. (No./cm)
*, ***: Significantly different from no-slight I.M. groups of gastric ulcer. ($p<0.001$)
**: Significantly different from no-slight I.M. groups of duodenal ulcer. ($p<0.01$)

Table 3. Distribution of G-cells in pyloric gland area

	gastric ulcer	duodenal ulcer
greater curvature	145.9 ± 15.6*	353.8 ± 56.6
lesser curvature	32.8 ± 6.2	140.0 ± 20.5
anterior wall	86.0 ± 13.4	276.8 ± 44.0
posterior wall	63.0 ± 10.5	118.0 ± 15.8

1) Significantly different gastric ulcer from duodenal ulcer at each position. ($p<0.01$)
2) Significantly different between each position except anterior wall VS. posterior wall of gastric ulcer. ($p<0.01$)
3) Significantly different between each position except anterior wall VS. greater curv. and posterior wall VS. lesser curv. of duoenal ulcer. ($p<0.01$)
* Values are mean ± S.E. (No./cm)

ed into three categories: none to slight, moderate and marked. In each case, the degree of intestinal metaplasia per unit was assessed according to the above described criteria. Mean values of uG were determined for each grade of intestinal metaplasia (Table 2). In cases of GU, a significant difference ($p<0.001$) was seen between mean uG for none to slight intestinal metaplasia and that for moderate or marked metaplasia. Similarly, there was also a significant difference ($p<0.01$) between mean uG for none to slight intestinal metaplasia and that for moderate metaplasia in cases of DU.

4) Site (greater and lesser curvatures, and anterior and posterior walls) and number of G cells

In each case, mean values of uG were estimated for the units on the greater and lesser curvature lines as well as the units on the mid-line of the anterior and posterior walls (Table 3). At any of the sites examined, mean uG values were significantly lower in GU than in DU ($p<0.01$). In GU, a significant difference was observed for all comparisons except for the comparisons between the anterior wall and the posterior wall ($p<0.01$). In DU, a significant difference as found for all comparisons except for those between the anterior wall and the greater curvature and between the posterior wall and the lesser curvature ($p<0.01$).

DISCUSSION

In the present study, the authors investigated gastric mucosal G cells of resected stomachs from cases of gastric ulcer and those of duodenal ulcer by staining them by PAP method. Moreover, the preparations were stained additionally with H.E. for observation of the background gastric mucosa.

The human serum contains G17, G34, G13, and a trace amount of component 1 called big big gastrin. The former mentioned three substances can be classified into gastrin 1 having no sulfuric acid group in tyrosin, the 6th amino acid from the C terminal, and gastrin 11 having the sulfuric acid group on tyrosine[4,5,14,24,25]. Gastric mucosal cells are seen in high density in the pyloric glandular segment. The gastrin contained in this region chiefly consists of G17. The anti-gastrin antibody (G17-1) used in this study is able to bind to GM-11 and G34. From these findings, it may be reasonable to consider that the distribution of gastric mucosal G cells could be grasped more accurately by the staining method used in this study compared with other methods[22].

This study involves a problem technically in that uncontinuous and qualitative findings were

assessed quantatively. However, it is extremely difficult to overcome this problem completely in a study to determine distribution of G cells in the gastric mucosa[10,15,18,19,23]. Since our purpose is not to grasp the precise number of G cells but to compare the number of G cells in terms of disese, site and condition of the background gastric mucosa, the condition due to fixation and the thickness of the lamina propria mucosa were not taken into consideration.

In all of the cases studied, G cells were distributed densely with prevalence in the grandular cervix of the pyloric glands. They were also seen, although in lower density, in the transitional zone and the duodenal bulbar area[15]. In case 5, a number of G cells are found even in the gastric fundic gland adjoining the f-line. It has been reported that G cells are seen in the area apart from the transitional zone, namely the gastric fundic glands which have changed into the pyloric gland[13,15]. Similar findings were obtained for one site in case 5.

When the number of G cells was compared between GU and DU, the number of G cells per unit in DU was three times greater than that in GU. Takahashi[23] also described that the density of G cells was higher in DU than in GU. However, some investigators described that they failed to find any differences between GU and DU[3]. This discrepancy may be partly explained by difference in distribution of G cells according to site. It is assumed that the higher density of G cells in DU refrects, as shown from the present study, strong influence from the intestinal metaplasia. This concept is also supported by Cox[1] and Takahashi[23]. When the intestinal metaplasia involves whole lamina propria mucosa, no G cells were detected[23].

When the density of G cells was examined in terms of the site, it was found that the density was higher for the greater curvature and the anterior wall and lower for the lesser curvature and the posterior wall[6]. Takahashi[23] suggested higher density for the greater curvature and lower density for the lesser curvature. He explained this by greater thickness and less intestinal metaplasia of the greater curvature.

We attempted to examine the relationship between the width of the transitional zone and G-cell density. However, all of the specimens with transitional zone of the shortest width of less than 1 cm were from DU and all of those more than 1 cm were from GU. Thus this comparison became similar to the comparison in terms of the disese. In this respect, further studies in accumulated number of cases are required[20]. In this study, no functional assessment was made because of the small number of cases. In general, the gastrin content in the serum and the mucosa is lower in case of GU than in cases of DU[2]. As described before, it is considered that this observation of gastrin content related closely with the decrease in number of G cells in the pyloric sinus with progression in intestinal metaplasia and atrophy[16]. An additional investigation is required for the identification of the relation between the functional aspects of the gastric asid secretion and the G cell distribution in the stomach[11].

ACKNOWLEDGEMENT

The authors gratefully acknowledge the expert technical assistant of M. NISHII and Y. KATOH.

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