

Supra-angular biopsy is more reliable for atrophy recognition: analysis of 1598 cases for gastric mucosal histological examination

Ya Li Zhang¹, Zhuo Sheng Lai¹, Dian Yuan Zhou¹, Nobutaka Yamada² and Min Wen²

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INTRODUCTION

Chronic gastritis might be a disease of the highest morbidity in the world. Since Warren and Marshall successfully isolated and cultured *Helicobacter pylori* (*H. pylori*) from a gastric antrum biopsy^[1], intensive researches produced a historic change in the etiology and treatment of gastroduodenal diseases^[2-14]. Stimulated by this momentous discovery, a group of gastroenterologists mainly from Europe and pathologists presented a novel classification of gastritis (so-called the Sydney system) at the 9th World Congress of Gastroenterology in Sydney, Australia, in 1990^[15]. In the Sydney system, attempts were made to incorporate etiologic, topographic, and morphologic criteria into a clinically relevant scheme. It usually involves the histopathological analysis of the biopsy specimens obtained from the arbitrary sites in the antrum or corpus. In September 1994, a group of gastric pathologists from various parts of the world gathered in Houston, Texas, USA, to reprove the Sydney system 4 years after its introduction^[16]. One of the most controversial issues at the Houston Workshop was the concept of atrophy. Since the relationship of *H. pylori* with gastric adenocarcinoma rests on the natural history of atrophical gastritis induced by the bacterial infection^[17-23], it is very important to identify the histological lesions. According to the Sydney system, *H. pylori*, chronic and active inflammations were usually recognized and scored

with an agreement of degree of accuracy, but the judgments of the atrophy were often poor^[24-31]. Although many factors are involved in the failure of responsible detection of the atrophy, the biopsy sites in gastric mucosa may be one of most important factors for this lack of concordance. In this study, we collected biopsy specimens from the antrum, corpus and angularis simultaneously to compare the differences among the biopsy sites for the evaluation of mucosal atrophic inflammation.

MATERIAL AND METHODS

Patients

A total of 1598 cases underwent endoscopic and histological examinations. Among them, 1047 cases were male and 551 females (a male:female ratio of 1.9:1) with an average age of 53.2 years (ranged 11 to 94 years). All cases were diagnosed by endoscopy, which consisted of 76 normal subjects, 85 chronic superficial gastritis, 116 atrophic gastritis, 297 erosive gastritis (173 flat-erosive type and 124 elevated erosive type), 467 gastric ulcer, 175 duodenal ulcer, 77 gastroduodenal ulcer, 194 hyperplastic polyp, 23 adenoma, 74 carcinoma, and 14 submucosal tumors. The atrophic change in gastric mucosa by endoscopy was evaluated and scored as “-, -/+, +, ++, +++” by observing the location of the atrophic border in gastric supra-angulus on the mucosal changes, such as fine transparent capillaries in the pale colored and rather thin mucosa. Biopsies were obtained from the three fixed sites (3-points biopsy): the greater curvature of the lower antrum, the greater curvature of the corpus and the supra-angulus. All biopsies were taken from an area of intact mucosa at a distance from any focal lesion, such as an ulcer or erosion.

Assessment of *H. pylori* infection and mucosal inflammation

Biopsy specimens for histological examination were fixed in 10% formalin and processed routinely to paraffin and 3µm sections. *H. pylori* were identified as curved, rod or coccoid by toluidine blue and immunostaining according to our previous report^[32-34]. The biopsy sections were stained with haematoxylin-eosin. The histological chronic inflammation and activity were assessed and scored according to the Sydney system. Lymphocytes and plasmacytes were responded for chronic

¹PLA Institute for Digestive Diseases, Nanfang Hospital, Guangzhou 510515, Guangdong Province, China

²Department of Pathology, First Hospital of Nippon Medical School, Tokyo, Japan

Ya Li Zhang, Professor and tutor of doctorate students. Awardee of the State Council special allowance.

Correspondence to: Dr. Ya Li Zhang, PLA Institute for Digestive Diseases, Nanfang Hospital, Guangzhou 510515, Guangdong Province, China

Tel 0086-20-85141544

Email: zhangyl@fimmu.edu.cn

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inflammation and PMN for activity. It was scored based on the density of inflammatory cells in both lamina proprias and glandular epithelium. The histological atrophy was identified when the gastric glands were correspondingly shortened and widely separated^[15]. In order to avoid the variation, only the cases with muscularia mucosa were judged for histological atrophy, in which, the lower layer of glands almost touch the muscularia mucosa in normal mucosa.

Statistical analysis

The data were analyzed by the Student's *t* test and the *Chi*-square test. *P* values less than 0.05 were considered significant.

RESULTS

The infective rate of *Hp* evaluated by biopsy in different sites

By means of toluidine blue and *H. pylori* antibody staining, *H. pylori* was easily identified in the lower third of the superficial mucous layer and in the gastric pits. The prevalence of *H. pylori* evaluated by different biopsy specimens was not obviously different (Table 1). The positive cases of *H. pylori* infection were 983 (61.5%), 1196 (74.8%) and 994(62.2%), respectively in antrum, corpus and angulus. No significant difference was found in the detective rates among the different site biopsies.

Table 1 Infective rate of *Hp* evaluated by different site biopsy

	Cases	<i>Hp</i> infective rate (%)		
		Antrum	Corpus	Angulus
Normal	76	30(39.5)	35(46.1)	31(40.8)
Superficial gastritis	85	34(40.0)	42(49.0)	37(43.5)
Erosive gastritis	297	160(53.9)	164(55.2)	156(52.5)
Atrophic gastritis	116	90(77.6)	102(87.9)	79(68.1)
Gastric ulcer	467	314(67.2)	368(78.8)	326(69.8)
Gastric carcinoma	74	38(51.4)	43(58.1)	

Though the detective rate for *H. pylori* infection was slightly improved by combining the biopsy in the three sites of gastric mucosa (Table 2), the difference was not statistically remarkable among one point biopsy in the antrum and two-points in the antrum-corpus, or three points in the antrum-corpus-angulus ($P>0.05$).

Table 2 Infective rate of *Hp* evaluated by combined biopsies

	Cases	One point (Antrum)	Two points (Antr.corp.)	Three point (Antr.corp.angu)
Normal	76	39(51.3)	46(60.5)	47(61.8)
Superficial gastritis	85	34(40.0)	46(54.1)	48(56.5)
Erosive gastritis	297	160(53.9)	190(64.0)	195(65.7)
Atrophic gastritis	116	90(77.6)	107(92.2)	107(92.2)
Gastric ulcer	467	314(67.2)	399(85.4)	406(86.9)
Gastric carcinoma	74	38(51.4)	61(82.4)	64(86.5)

Mucosal inflammation and atrophy identified in the biopsy specimens from different sites

In the 1598 biopsy cases, the histological changes of gastric mucosa were evaluated by combining the results of observation in three different biopsy sites. It was found that there were 1413(88.4%) cases with mucosal chronic inflammation, in which, lymphocytes and plasmocytes were observed in both lamina proprias and glandular epithelium. PMN infiltration, which was responsible for the activity of chronic inflammation, was found in 1287 (80.5%) cases and intestinal metaplasia in 773 (48.8%) cases. A total of 1292 cases with muscularia mucosa met the standard for atrophy evaluation, histological atrophy was found in 489 (37.8%) cases.

By comparing the results of different sites biopsies, it was surprised to find that the mucosal inflammation and activity were in concordance evaluated among the antrum, corpus or angulus, but the detective rates for atrophy and intestinal metaplasia were remarkably higher in angulus. In the antrum biopsy specimen, 26.6% and 26.1% showed mucosal atrophy and intestinal metaplasia respectively, however, 65.4% and 31.8% were identified in angularis biopsy (Table 3) with significant difference ($P<0.05$) compared with those in antrum and corpus.

Table 3 Histological lesions identified in different biopsy sites

	Lesion identified		
	Antrum	Corpus	Angulus
Inflammation	1268(72.9)	1290(74.1)	1249(71.8)
Activity	1039(59.7)	1148(65.9)	1071(61.6)
Atrophy*	130(26.6)	96(19.6)	320(65.4) ^a
Intest.metaplasia	455(26.1)	137(17.7)	554 (31.8) ^a

* only 1292 cases in all three points judgable included.

^a $P<0.05$, vs the results of antrum and corpus.

The endoscopical atrophy and histological confirmation

Cases (1290) with muscularia mucosa examination were evaluated histologically and compared with the results of the judgment of endoscopy (Table 4). Among them, mucosal atrophy could be judged in 487 cases, 106 were negative and 697 cases were suspected. The biopsy specimens were further examined based on the correspondingly shortened and widely separated glands. Angular biopsy was found more available for the atrophical identification, in which, 48.3% endoscopical atrophy was confirmed, but in antrum or corpus biopsy, only 22.2% or 15.8% cases were verified. Better agreement of mucosal atrophy was reached in the cases with the 3+ score of endoscopical atrophy. Although the confirmation for endoscopical atrophy was slightly improved when the evaluation was made based on the different points biopsy, the difference was not statistically significant ($P<0.05$).

Table 4 The accuracy of endoscopic atrophy

Endoscopy atrophy	Cases	Evaluation by separate point		
		Antrum	Corpus	Angulus
Negative	106	10(9.4)	9(8.5)	15(14.2)
Suspected	697	124(17.8)	47(6.7)	171(24.5)
Positive	487	108(22.2)	77(15.8)	235(48.3)
+	252	47(18.7)	36(14.3)	103(40.9)
++	201	46(22.9)	35(17.4)	107(53.2)
+++	36	15(41.7)	6(16.7)	27(69.2)

Mucosal atrophy identified in different diseases

Histological atrophy not only occurred in the atrophic gastritis, but also in different gastric lesions, even in normal subjects (Table 5). The confirmation of mucosal atrophy in different diseases also varied with the biopsy specimens from different sites. In angular biopsy, the histological atrophy was much easier to be identified than in antrum. By the evaluation from the angular specimens, the occurrence of mucosal atrophy ranked the highest in the atrophic gastritis (82.2%), then in the carcinoma and adenoma and gastric ulcer. Though the occurrence of atrophy was lower in the endoscopic normal mucosa, superficial and chronic gastritis, there were still about 13.6% to 35.1% cases with the change of histological atrophy.

Table 5 The occurrence of histological atrophy in different diseases

Endoscopic diagnosis	Cases	Histological atrophy (%)		
		Antrum	Corpus	Angulus
Normal	69	6(8.7)	5(7.2)	15(21.7)
Superficial gastritis	79	15(18.9)	8(10.1)	23(29.1)
Flat erosion	152	26(17.1)	5(3.3)	33(21.7)
Elevated erosion	119	29(24.4)	7(5.9)	39(32.7)
Atrophic gastritis	107	59(55.1)	35(32.7)	88(82.2)
Gastric ulcer	387	134(34.6)	39(10.1)	175(45.2)
Duodenal ulcer	135	36(26.7)	8(5.9)	47(34.8)
Gastroduodenal ulcer	64	21(32.8)	5(7.8)	28(43.8)
Hyperplastic polyp	111	14(12.6)	8(7.2)	33(29.7)
Adenoma	11	3(27.3)	3(27.3)	6(54.5)
Carcinoma	46	22(47.8)	6(13.4)	27(58.7)
Submucosal tumors	12	3(25.0)	2(16.7)	3(25.0)

DISCUSSION

Since Warren and Marshall successfully isolated and cultured *H. pylori* from gastric antrum biopsy, the intensive researches into *H. pylori* infection during the past decade have provided important insights into the pathophysiology of gastric diseases^[1-16]. It was suggested that over the past years there was a slow progression of chronic gastritis with atrophy and intestinal metaplasia developing, and that the proportion of the population affected increased with age, and was high in geographical areas with a high risk of cancer^[35-45]. It is now generally supposed that *H. pylori* is one of the important factors in the etiology of chronic gastritis. Recently, a positive

relationship between *H. pylori* and gastric cancer was reported simultaneously by several authors^[45,46]. In light of these observations, it is important to determine the prevalence of atrophic gastritis and intestinal metaplasia since both of these lesions are closely related to the gastric cancer. There have been many reports as to the distribution of *H. pylori* colonization and atrophic gastritis, but usually only involve in small group of cases, and most researchers have not taken into consideration the effect of biopsy from the different sites of gastric mucosa on the atrophic evaluation^[47-52]. Though the Sydney system, a novel classification of gastritis usually based on the biopsy from antrum or corpus for histological analysis, can incorporate etiologic, topographic and morphologic criteria, the agreement for atrophic assessment is often poor^[15, 16]. Since many factors are involved in the failure of detection of the atrophy, the biopsy sites in gastric mucosa may be one of the most important factors responsible for this lack of concordance. In this study, we collected biopsy specimens from the antrum, corpus and angulus simultaneously in 1598 cases to compare the differences among the biopsy sites for the evaluation of mucosal atrophic inflammation.

As to the distribution of *H. pylori* and inflammation in the stomach, Genta *et al* reported that *H. pylori* was distributed evenly throughout the stomach^[26,27]. In this study, we found that the prevalence of *H. pylori* infection evaluated by different biopsy specimens was not obviously different. The positive cases of *H. pylori* infection were 61.5%, 74.8%, and 62.2%, respectively in antrum, corpus and angulus. This finding corresponds closely to Genta's. Since no significant difference was found in the *H. pylori* detective rates among the different site biopsies, it was suggested that one of the biopsies from antrum, corpus or angulus was enough for the evaluation of bacterial infection.

It is interesting to find that mucosal inflammation and atrophy identified in the biopsy specimens from different sites were varied. The evaluation for mucosal inflammation and activity was in concordance among the antrum, corpus or angulus, but the detective rates for atrophy and intestinal metaplasia were remarkably higher in angularis. In the antrum biopsy specimen, only 26.6% and 26.1% showed mucosal atrophy and intestinal metaplasia respectively, however, 65.4% and 31.8% were identified in angularis biopsy.

The endoscopic atrophy or metaplasia was suggested by a group of researchers for the chronological spread of atrophic gastritis and the evaluation of the entire stomach^[36,40]. A border between the normal mucosa and that showing atrophic gastritis was recognized by endoscopy, and this was designated as the endoscopic atrophic border. In this study, 1292 cases with muscularia

mucosa identification were evaluated histologically based on the correspondingly shortened and widely separated glands for the atrophical identification. The histological atrophy was only observed in half of the cases of the endoscopical atrophy, and in the cases without endoscopical atrophy, 20.8% cases still showed histological atrophy, though better agreement of mucosal atrophy was reached in the cases with the 3+ score of endoscopical atrophy. If biopsy was only taken from the antrum or corpus, the concordance of endoscopical atrophy with the histological atrophy was poor.

It is believed for a long time that the atrophic gastritis extends from the antrum to the body with age. Satoh *et al* indicated that *H.pylori* infection was usually associated with antral atrophic gastritis and intestinal metaplasia^[36]. In contrast to this concept, we found by analysis of 1598 cases that both atrophy and intestinal metaplasia were much more commonly identified in angularis than in antrum, no matter of the different number of *H.pylori* colonization or the different diseases. Although it remains to be further confirmed whether the real histological origin of atrophy or intestinal metaplasia developed first from the angulus, we should take this fact into consideration in evaluation on biopsy. Histological atrophy not only occurred in the atrophic gastritis, but also in different gastric lesions, even in normal subjects. The confirmation of mucosal atrophy in different diseases also varied with the biopsy specimens from different sites. In angular biopsy, the histological atrophy was much easier to be identified than in antrum. By the evaluation of the angular specimens, the occurrence of mucosal atrophy ranked the highest in the atrophic gastritis (82.2%), then in the carcinoma and adenoma and gastric ulcer. Although the occurrence of atrophy was lower in the endoscopical normal mucosa, superficial and chronic gastritis, still about 13.6% -35.1% cases had the change of histological atrophy.

In conclusion, our results based on the analysis of 1598 cases of gastric mucosal histology indicate that antrum biopsy is suitable for *H.pylori* evaluation, but supra-angular biopsy is more reliable for atrophy and intestinal metaplasia observation.

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