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A Study of the Correlation between Endoscopic and Histological Diagnoses in Gastroduodenitis

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Serial histological specimens from 14 patients with the endoscopic diagnosis of erosive gastritis and/or duodenitis were examined for correlation between endoscopic and histological findings. All patients were symptomatic outpatients without history of alcoholism or usage of aspirin or nonsteroidal antiinflammatory drugs. After the initial diagnosis, the patients underwent follow-up endoscopy until healing of erosions at 1, 4, and 8 wk. Pairs of biopsies from the gastric fundus, body, and antrum, and the duodenum were obtained at each endoscopy. Agreement between histological and endoscopic findings occurred in only 56% of the 161 sites studied. The best correlation occurred in the duodenum when there was endoscopic disease (89%) and was worst in the stomach at all sites regardless of endoscopic findings (46%). A normal histology in the face of abnormal endoscopic changes was seen in only 16% of all biopsies. Histological inflammation occurred in 27% of all biopsies with a normal endoscopic appearance and in 55% of the normal endoscopic areas in the stomach. Histological appearances at each biopsy site remained constant in individual patients throughout the study. The specific histological findings, such as activity and severity, did not correlate with the endoscopic severity of inflammation or with any specific endoscopic appearances, such as erosions, petechiae, or nodules. In conclusion, the histological and endoscopic findings in the stomach from patients with symptomatic erosive gastroduodenitis correlate poorly while good correlation occurs in the duodenum.

INTRODUCTION

The diagnoses of gastritis and duodenitis are frequently made both endoscopically and histopathologically, but it is not clear if these diagnoses are equivalent. Two previous studies of endoscopically diagnosed duodenitis had histological abnormalities in 70–80% of the duodenal biopsies (1, 2). In contrast, a study of endoscopically diagnosed "acute gastritis" had only 36% of specimens showing abnormal histological findings (3). In two studies of histologically diagnosed gastroduodenitis, significant inflammation was defined as having a neutrophilic infiltrate (4, 5). We have examined serial biopsy specimens from 14 patients with endoscopically diagnosed erosive gastroduodenitis in order to further assess the correlation between specific histological and endoscopic changes. We have also examined the differences in correlation between four areas; the gastric fundus, body, and antrum, and the duodenum and the consistency of these histological and endoscopic findings in serial endoscopies.

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METHODS

Fourteen patients presenting with epigastric pain who had the endoscopic diagnosis of erosive gastroduodenitis were studied over a 12-month period. They were selected for this histological study on the basis of their endoscopic diagnosis and their willingness to participate in a placebo-controlled therapeutic trial. There were five women and nine men with an age range of 18–77 yr and a median age of 40. Erosive gastroduodenitis was defined as an area of inflammation containing at least one erosion in either the stomach, the duodenum, or both. A history of alcoholism or the recent use of aspirin or nonsteroidal antiinflammatory drugs excluded patients from the study. Patients with previous gastric surgery or with active ulcer craters were excluded as were those who had used antiulcer medications during the 5 days before entry.

After the diagnosis, the patients were entered into a placebo controlled double-blind trial using ranitidine. Follow-up endoscopic examinations were performed until healing of the erosion(s) at 1, 4, and 8 wk. The average number of endoscopies performed per patient was 2.9. One of three staff gastroenterologists performed 40 of the 41 endoscopic studies using the Olympus XQ10 or Q10 endoscopes. Endoscopic changes that were specifically evaluated include: erosions, erythema, hemorrhages, petechiae, and nodules. Erosions were defined as small mucosal defects <5 mm in size with no appreciable depth. Erythema was included as an

abnormality only when it was intense in color and involved at least one-third of the area examined. For the data analysis, endoscopic findings were considered to be abnormal if any of the following were present: erosions, hemorrhages, petechiae, or marked erythema. Symptoms were graded on the following scale: 0 = none, 1 = few episodes (1–3 days per 2 wk) of mild severity, 2 = several episodes (4–7 days per 2 wk) of mild to moderate severity, 3 = many episodes (8–10 days per 2 wk) of moderate to severe intensity, and 4 = many episodes or continual pain of severe intensity. Improvement or worsening of symptoms were determined if the symptom score changed by two points in either direction or if the patient became asymptomatic.

At each endoscopy, at least two pinch biopsies were obtained from each of four areas, the gastric fundus, body, and antrum, and the duodenum. The biopsies were directed at the endoscopically abnormal mucosa in each site or randomly in that site if the mucosa appeared normal. On one endoscopy, only the duodenum was biopsied leading to a total of 161 gastric and duodenal sites being studied. All histological evaluation was performed blind to the endoscopic diagnosis by one staff pathologist. Histological appearances were classified as: normal, superficial gastritis, mild duodenitis, severe inactive gastritis or duodenitis, severe active (with neutrophils and epithelial damage) gastritis or duodenitis. Superficial gastritis is defined as an infiltrate of mainly plasma cells in the lamina propria between gastric pits and necks with sparing of the glandular compartment (Fig. 1). Severe gastritis includes findings of superficial gastritis, as defined above, plus extension of infiltrate into the glandular compartment (Fig. 2). Since the biopsies were all pinch type and therefore superficial, atrophy was generally difficult to identify. Mild duodenitis is defined as expansion of the lamina propria by plasma cells. Severe duodenitis is further expansion of the lamina propria with plasma cells with the addition of architectural distortion (Fig. 3). Activity is defined as infiltration of neutrophils in the adjacent epithelial structures (surface epithelium, pits, necks, and glands in the stomach, crypts, and surface epithelium in the duodenum) resulting in epithelial damage (Fig. 2). Activity could be superimposed on any of the above types of gastritis and duodenitis. The consistency of histological findings in serial biopsies in each patient were analyzed. We also examined the concordance between each pair of specimens obtained from each location. For the data analysis, any biopsy finding other than normal was classified as abnormal.

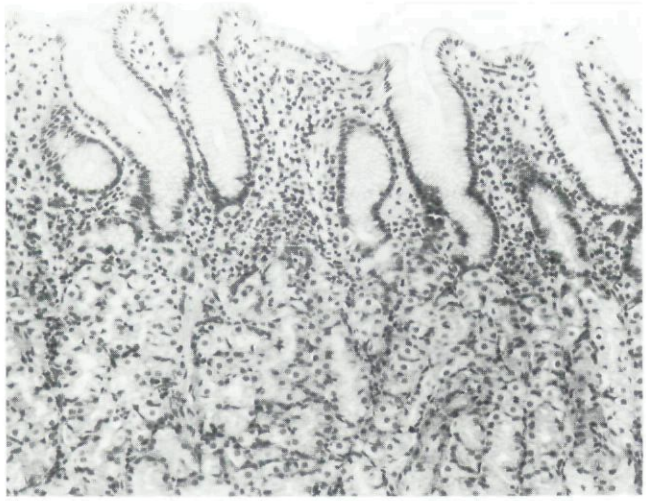

FIG. 1. Superficial body gastritis. The lamina propria between the pits is filled with plasma cells. The glandular compartment contains very few such cells among the glands (×132).

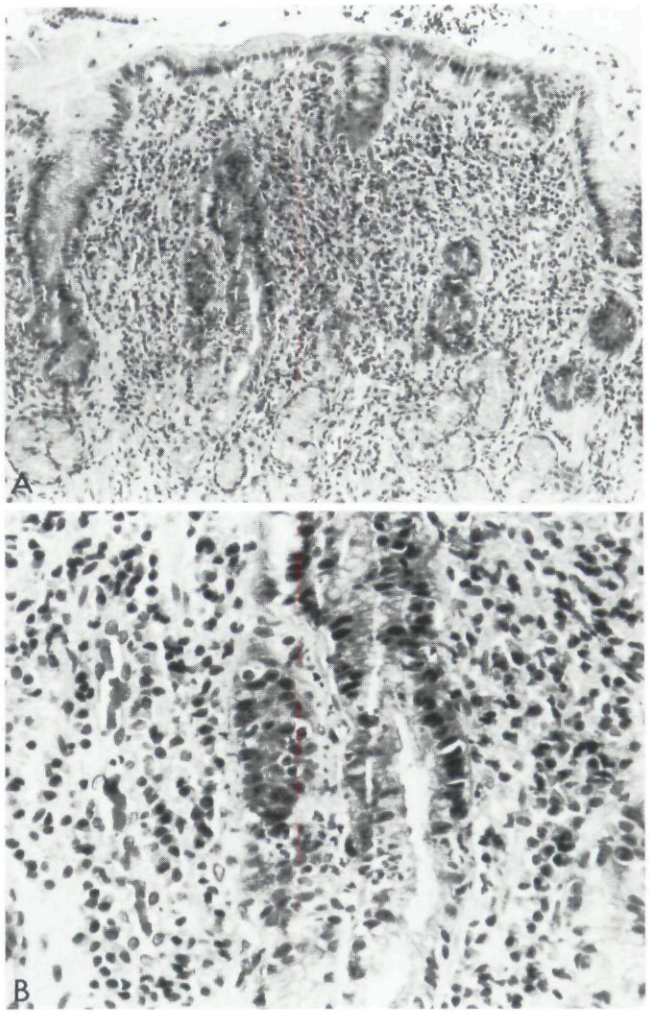

FIG. 2. Severe, active antral gastritis. *A*, the pits are separated by a highly cellular lamina propria with extension of these inflammatory cells into the deep glandular compartment (×132). *B*, higher power of two pits infiltrated by neutrophils with associated epithelial disruption (×330).

RESULTS

Agreement between histological and endoscopic evidence for inflammation or normalcy in patients with

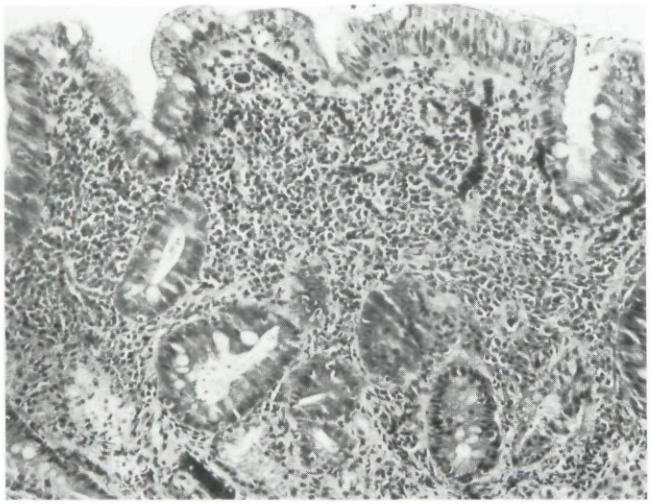

FIG. 3. Severe duodenitis is characterized by partial loss of villi and expansion of the lamina propria by inflammatory cells, mainly plasma cells, resulting in separation of the crypts (×132).

endoscopic erosive gastroduodenitis occurred in only 91 of the 161 specimens (56%). Of these positive correlations, 53 of the 91 were abnormal histology combined with abnormal endoscopy while 38 of the 91 had both normal histology and endoscopy. This positive correlation occurred more often in the duodenum (85%) than in the stomach (43 to 55% depending on the site). In the endoscopically abnormal areas in the stomach, histological findings were as likely to be normal as abnormal (Table 1). That is, of the 44 abnormal endoscopic gastric areas, 50% had normal histology. In the duodenum, this correlation was much better with 31 of the 35 abnormal endoscopies showing abnormal histology (89%). Normal endoscopic findings in our patients were as likely to have abnormal histology as they were normal, especially in the gastric body and fundus mucosa (Table 2). Fifty-five percent of the 76 normal endoscopic gastric sites had abnormal histology.

All biopsies from each area with specific endoscopic diagnostic features, such as erosions, petechiae, nodules, and hemorrhages were examined to assess possible histological counterparts to these gross findings. No consistent histological changes were found to correlate with these endoscopic appearances. The severity of histological inflammation, specifically the presence or absence of a neutrophilic infiltrate with epithelial damage, was also compared to endoscopic severity. Again, no correlation could be found (Table 3).

The severity of histological findings was consistent in individual patients in the follow-up biopsies. The number of endoscopies per patient was between two and four with an average of three. Only one of the 14 patients' fundus and body biopsies changed in subsequent biopsies (both in the worsening direction). Only two of the 14 patients' antral biopsies changed. In the duodenum, five of 14 patients had either histological worsening or improvement while in nine patients the biopsies remained much the same (Table 4).

All 161 sites biopsied had at least two specimens

TABLE 1
Endoscopic and Histological Agreement in Sites with Abnormal Endoscopy

Abnormal Endoscopy by Site	Abnormal Histology	Normal Histology
Fundus (n = 3)	1 (33%)	2 (66%)
Body (n = 10)	6 (60%)	4 (40%)
Antrum (n = 31)	15 (48%)	16 (52%)
Duodenum (n = 35)	31 (89%)	4 (11%)

TABLE 2
Endoscopic and Histological Agreement in Sites with Normal Endoscopy

Normal Endoscopy by Site	Normal Histology	Abnormal Histology
Fundus (n = 37)	16 (43%)	21 (57%)
Body (n = 30)	16 (53%)	14 (47%)
Antrum (n = 9)	2 (22%)	7 (78%)
Duodenum (n = 6)	4 (67%)	2 (33%)

TABLE 3
Comparison of Severity of Histological Inflammation with Endoscopic Findings

	Endoscopic Findings		
	Normal	Erythema	Erosions
Mild inflammation on histology			
Fundus and Body			
Antrum	20	0	2
Duodenum	2	1	2
	4	3	7
n = 41	26 (63%)	4	11
Severe inflammation with activity			
Fundus and Body			
Antrum	7	1	3
Duodenum	3	1	8
	0	2	3
n = 28	10 (36%)	4	14

TABLE 4
*Consistency of Histological Findings in Follow-Up Endoscopies**

	Fundus	Body	Antrum	Duodenum
No change† in histological diagnosis	13	13	12	9
Improvement in histology	0	0	0	2
Worsening of histology	1	1	2	3

* No. of endoscopies, 2 3 4; no. of patients, 5 5 4.

† Change in histological diagnosis is defined as a change from three histological categories: normal, mild, or severe during the two to four endoscopies in each patient.

obtained from the same area, but in 20 pairs, one of the specimens was too small to evaluate fully. Variation between histological evidence of inflammation and severity of inflammation between these two pinch biopsies was examined in the remaining 141 pairs in an attempt to assess the importance of sampling error. Significant variation between histological interpretation was present in only two of the 141 pairs of biopsies.

Over the course of the study, symptom scores improved in four individuals, remained unchanged in nine, and became worse in one. Of the four patients who were clinically improved, one had both histological and endoscopic improvement, two had endoscopic improvement without histological change, and one patient had worsening of both endoscopic and histological appearances. Of the nine patients without significant change in symptom score, five had no change in either histological or endoscopic appearances, three had endoscopic improvement without histological change, and one patient had endoscopic worsening without histological change. The single patient with worsened symptoms developed both histological and endoscopic worsening.

When patients were stratified by age (seven patients less than 40 yr old and seven more than 40 yr old), no correlation between abnormal histology and age was found.

DISCUSSION

This study was actually weighted toward finding a strong endoscopic-histological correlation since all patients had to have endoscopic findings of erosions and the biopsies were directed at the specific endoscopic abnormalities. Despite these factors, this study showed a poor correlation between endoscopic and histological evidence of inflammation in the stomach, but a good correlation in the duodenum. Previous studies in this area have shown variable results, probably due to different populations studied and varying criteria for both endoscopic and histological diagnoses. Cotton *et al.* (1) studied nonerosive duodenitis only and found histological agreement with the endoscopic appearance in 80%. However, even in their group of 28 normal controls without dyspepsia, only 71% had completely normal biopsies. McCallum *et al.* (2) found histological evidence of duodenitis in 70% of duodenal bulbs with abnormal endoscopy. This study included only 14 patients of whom six had moderate to severe endoscopic changes. Gregg and Garabedian (6) found that nine of 11 patients with nonerosive duodenitis had histological abnormalities. Greenlaw *et al.* (4) studied 100 dyspeptic patients of whom 59 had a histological diagnosis of gastroduodenitis. Of this 59, 25% had a normal endoscopy. An early endoscopic study of gastritis by Adkins and Benedict (3) of 78 patients showed only 38% with microscopic evidence of inflammation. In a more recent study, there was an 86% incidence of histological inflammation in 119 patients with endoscopically diagnosed gastritis (7).

Sampling error between the actual site biopsied and the endoscopic abnormality could explain some of the poor correlations we obtained. To examine this possibility, we compared the two or more biopsies obtained from the same area at each endoscopy and found that only two of 141 (1%) pairs of biopsies showed significant variation. Therefore, sampling error in this study cannot explain the poor endoscopic and histological correlation.

The best agreement between histological and endoscopic appearances in our study occurred in the duodenum (86%). This distribution of correlation may be explained in part by a much higher incidence of endoscopic abnormality in the duodenum [35 of 41 examinations (85%)] than in the stomach [42 of 120 examinations (35%)]. Thus, the poorer gastric correlation could be due to the frequent association of normal endoscopy with abnormal histology in the stomach. One explanation for this association in the stomach may be that mild superficial gastritis is a normal histological variant as was found in the study by Kreuning *et al.* (8). However, when our data were reanalyzed combining the mild gastritis histological diagnoses with the normals, the correlation between the gastric endoscopic and histological changes remained poor.

Previous studies have stressed the clinical significance of a neutrophilic infiltrate in gastroduodenal biopsies. Greenlaw *et al.* (4) found that patients with histological features of acute inflammation in biopsies of stomach and duodenum were much more likely to have endoscopic duodenal than gastric abnormalities. A recent report of patients with nonulcer dyspepsia suggests that a neutrophilic infiltrate is more common in gastroduodenal biopsies from dyspeptics than from normal controls (5). We were unable to find a correlation between the presence of such inflammatory activity and the endoscopic severity of disease. In addition, individual analysis of endoscopic findings, *e.g.*, erosions or hemorrhages, did not correlate with a specific histological change.

Clinical gastroduodenitis is presumably part of the spectrum of peptic ulcer disease (9). The relationship between endoscopic or histological abnormalities and clinical symptoms remains unclear. On the one hand, it has been shown that evidence for histological inflammation occurs in 36% of stomachs and 12% of duodenums in asymptomatic normals (8). It is also well accepted that extensive peptic disease diagnosed endo-

scopically, including duodenal ulcer, may be asymptomatic (10). In addition, it is possible that true dyspepsia may occur in a patient with both normal histology and endoscopy (11). Therefore, to date we are unable to determine which diagnostic technique, endoscopy or biopsy, relates better to the patient's symptoms. It is clear that these two methods of diagnosis are often in disagreement. The reasons for this lack of correlation are unclear, but do not appear to include sampling error. Variations in endoscopic interpretation may be partly responsible as may the existence of a true discrepancy between histological inflammation and endoscopic changes considered to be inflammatory.

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