Impact of Helicobacter pylori infection on histological changes in non-erosive reflux disease

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Abstract

AIM: The evidence for an association between Helicobacter pylori (H pylori) and gastroesophageal reflux disease, either in non-erosive (NERD) or erosive esophagitis (ERD) remains uncertain. The available data on the histological changes in NERD and the effect on H pylori infection on them are elusive. The aim of this study therefore was to prospectively evaluate the histological findings and the impact of H pylori infection on a group of symptomatic patients with NERD.

METHODS: Fifty consecutive patients were prospectively evaluated for symptoms compatible with GORD. In all cases, routine endoscopy and lugol directed biopsies were performed and assessed histologically in a blinded manner.

RESULTS: The overall prevalence of H pylori infection was 70%. Twenty-nine patients out of 50 (58%) were NERD patients. No statistical significance was observed between the H pylori status and NERD. The remaining 21 (42%) were diagnosed as follows: 13 (26%), 6 (12%), 2(4%) with esophagitis grade A, B and C respectively. A statistically significant correlation was observed between the H pylori+ and esophagitis grade A, as well as between H pylori- and grade B. Biopsies from 2 patients were not included because of insufficient materials. Histologically, a basal zone hyperplasia was found in 47 (97.91%) patients, alterations of glycosgen content in 47 (97.91%), papillae elongation in 33 (68.75%), blood vessels dilatation in 35(72.91%), chronic inflammation in 21 (43.75%), infiltration with eosinophils, neutrophils and T-lymphocytes in 4 (8.33%), 6 (12.5%) and 39 (81.25%) respectively. No correlation was observed between the H pylori status and the histological parameters studied either in NERD or GERD.

CONCLUSION: Histological assessment can not differentiate symptomatic patients with erosive versus non-erosive reflux disease. Moreover, H pylori infection may not act as an important factor in patients with NERD.

INTRODUCTION

Helicobacter pylori (H pylori) is a prevalent pathogenetic factor associated with ulceration, dyspepsia, and adenocarcinoma[1,2]. The role of H pylori in gastroesophageal reflux disease (GORD) has only recently received attention, with the evidence for an association between H pylori and GORD remaining uncertain[3]. Diminution of peptic ulcer disease and adenocarcinoma of the distal stomach have paralleled the decreasing prevalence of H pylori infections in the developed world. At the same time, there has been an increase in GORD, Barrett’s esophagus, and adenocarcinoma of the distal esophagus and proximal stomach, suggesting that H pylori protects against these esophageal diseases[4,5].

Adequate assessment of reflux esophagitis has proved difficult to be assessed by endoscopy only, as the endoscopic appearance of the esophageal mucosa may be normal despite the presence of reflux symptoms[6-7]. Non-erosive gastroesophageal reflux disease (NERD) is the most common diagnosis in patients with reflux symptoms when organic diseases such as ulcers, esophageal erosions, and carcinomas, have been excluded by esophagogastroduodenoscopy[8].

Histological abnormalities have been described in GORD[9-11], and hence it seems reasonable to diagnose non-erosive reflux disease by simple esophageal biopsies during endoscopy. These mild histological findings are mainly basal zone thickening, elongated papillae, alterations in intracellular glycogen content, infiltration with neutrophils, eosinophils and T-lymphocytes, and submucosal blood vessel dilatation[6-8,9]. However, the available data on the diagnostic value of these histological criteria are contradictory[9]. This study therefore evaluated prospectively the histological findings and the impact of H pylori infection in a group of symptomatic patients with erosive and non-erosive reflux disease.

MATERIALS AND METHODS

Patients

Fifty patients (29 men, 21 women; mean age 49.9 years) were evaluated prospectively in our endoscopic unit for symptoms compatible with GORD, namely heartburn, acid regurgitation, and/or epigastric pain. A standardized questionnaire was completed for each patient during an interview with an experienced gastroenterologist. Demographic details of the GORD patients were recorded, including age, sex, smoking and drinking habits, tea and coffee consumption, and concurrent medical conditions including hypertension and diabetes mellitus. None of the patients included in this study had a...
Methods
A routine endoscopy was performed by the same endoscopist on all patients using an (GIF-Q145) Olympus flexible endoscope. The distance between the esophagogastroduodenal junction and the incisor teeth was recorded. Reflux esophagitis was graded in accordance with the Los Angeles classification[12]. H pylori status was determined by the rapid urease test and histological examination of biopsies taken from the antrum and the corpus[13,14].

At least 4 biopsy specimens were taken 3 cm above the lower esophageal sphincter with Olympus biopsy forceps in a cross-fashion manner. In order to improve endoscopic visualization and provide biopsy orientation, 20 mL of 20 mg/L potassium iodine’s solution (Lugol) was applied through a “spray” catheter[15-17]. To obtain sufficient material and to ensure an almost vertical pinch biopsy specimen, the opened forceps were withdrawn towards the tip of the scope, which was bent towards maximally, and hence the forceps were pressed vertically against the esophageal wall. Specimens were fixed in 40 g/L formaldehyde[18]. When all sections had been selected they were assessed histologically in a blinded manner (without endoscopic or clinical information). A standardized report completed by the histopathologist comprised an evaluation of the following histological parameters: basal zone hyperplasia, papillary length, dilatation of intraepithelial blood vessels, and semi-quantitative cellular infiltration with T-lymphocytes, neutrophils, eosinophils. Alterations of glycogen content, erosion, ulceration and chronic inflammation were also assessed[6,9-11].

Statistical analysis
Statistical analysis was performed using SPSS (version 11.0 for Windows) on data from all 50 patients. The analysis was based on demographic characteristics, such as age, sex, and presence of H pylori infection, as well as endoscopic and histological findings. Differences in the distribution of the variables of interest between subgroups of patients were examined by Pearson chi-square test or Fisher’s exact test (the latter when small frequencies were present). Comparison between proportions in 2 independent groups was performed with the z-test statistic. P-values less than 0.05 were considered significant.

RESULTS
The relationship between endoscopic findings and the presence (H pylori+) or absence (H pylori-) of H pylori infection is shown in Figure 1.

The overall prevalence of H pylori+ was 70% (35 out of 50 patients). A normal appearance of esophageal mucosa (non-erosive esophagitis) was observed in 29 out of 50 (58%) patients. No statistical significance was observed between H pylori+ and NERD patients [H pylori+ in 20 out of 35 (57.1%) vs H pylori- in 9 out of 15 (60%) patients P>0.05]. The remaining 21 (42%) patients with erosive esophagitis were diagnosed as follows: 13 (26%), 6 (12%) and 2 (4%) with esophagitis grade A, B and C respectively. None of the patients in our series suffered from esophagitis grade D. A statistically significant correlation was observed between the H pylori+ and esophagitis grade A [H pylori+ in 11 out of 35 (31.4%) vs H pylori- in 2 out of 15 (13.3%) patients, P<0.05]. Similarly, a statistical difference was observed in the group of patients with esophagitis grade B [H pylori+ in 2 out of 35 (5.7%) vs H pylori- in 4 out of 15 (26.7%) patients, P<0.05].

Figure 2 summarizes the distribution of patients according to biopsy findings and the existence of H pylori. Biopsies from 2 patients were not included because of insufficient materials. No difference was observed between the 2 variables of interest. As expected, the majority of patients examined (46 of 48, 95.8%) were diagnosed histologically as having esophagitis, despite the esophageal mucosa appearing normal under endoscopy.

Figure 1 Findings at endoscopy. Note: H pylori (+): Helicobacter pylori positive patients; H pylori (-): Helicobacter pylori negative patients.

Figure 2 Findings at biopsy. H pylori (+): Helicobacter pylori positive patients; H pylori (-): Helicobacter pylori negative patients.

Table 1 Correlation of H pylori infection with the histological parameters esophagitis in NERD and GERD

| Histological parameters | Total (n) | NERD Patients (n) (%) | ERD Patients (n) (%) | P |
|-------------------------|----------|----------------------|---------------------|---|
| Basal zone hyperplasia  | 47       | 28 (59.6)            | 19 (67.9)           | 0.462 |
| Loss of glycogen        | 47       | 28 (59.6)            | 19 (67.9)           | 0.462 |
| Papillae elongation     | 33       | 18 (54.4)            | 11 (61.1)           | 0.357 |
| Blood vessels dilatation| 35       | 20 (57.1)            | 15 (75.0)           | 0.527 |
| Oesinophils infiltration| 4        | 2 (50.0)             | 1 (50.0)            | 0.500 |
| Neutrophils infiltration| 6        | 2 (33.3)             | 1 (50.0)            | 0.600 |
| T-lymphocytes infiltration| 39     | 24 (61.5)            | 17 (70.8)           | 0.582 |
| Chronic inflammation    | 21       | 13 (61.9)            | 10 (76.9)           | 0.410 |
Finally, Table 1 outlines the histological parameters of esophagitis with the presence or absence of erosions during endoscopy. We focused on patients with H pylori infection. No statistically significant difference was observed between H pylori (+) patients with erosive (ERD) and non-erosive esophagitis (NERD) for any of the histological parameters examined (P values refer to the numbers in italics).

DISCUSSION

This study investigated the impact of H pylori infection on the histological changes of non-erosive esophagitis. Our study was performed prospectively in a series of 50 patients with reflux symptoms. Esophageal erosions were found during endoscopy in 21 of these patients. The overall prevalence of H pylori+ was 70% (erosive: 15/21, 71.5%; non-erosive: 20/29, 68.9%). As expected, histological changes were noted in the majority of biopsies (95.8%) despite a normal appearance of esophageal mucosa under endoscopy in half of the cases.

In the group of patients with erosive esophagitis, H pylori+ was correlated with grade A esophagitis, whereas H pylori- was correlated with grade B disease. This probably indicates that H pylori- is a risk factor for ERD and aggravates the endoscopic appearance. This finding of a close association between H pylori+ and less serious endoscopic findings is consistent with other studies[14,18-21]. Some studies have found an inverse relation between H pylori and esophagitis, once H pylori has been eradicated[22,23]. In our series no patient had previously received eradication therapy. Furthermore, we confirmed previous findings that H pylori infection was not associated with positive or negative esophagitis findings in biopsies[24,25].

In the second group of patients (those with non-erosive esophagitis), no correlation was observed between the H pylori+ and the histological parameters studied. Little is known about the relationship between H pylori infection and the histological variables in non-erosive esophagitis. The fact that there appears to be no correlation between the H pylori+ and any of the aforementioned mild changes probably implies that these are provoked by mechanisms other than H pylori infection[26,27] (perhaps acid or bile reflux).

In conclusion, H pylori probably plays a statistically unimportant role in the histological changes seen in patients with non-erosive reflux disease, since similar histological alterations were detected in biopsies of both erosive and non-erosive esophagitis. Further research is required to identify other pathogenetic factors responsible for the histological parameters found in this group of patients.

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