The analysis of pathological features of gastritis and Helicobacter pylori infection

Jianxian HUANG, Chao LIANG, and Tianzhi ZHANG*

Department of Pathology, The Seventh Affiliated Hospital of Sun Yat-sen University, Shenzhen, China
*Corresponding author. Email: zhangtzh@sysucc.org.cn, https://orcid.org/0009-0005-0953-9031

(Received 30 April 2023; revised 25 May 2023; accepted 5 June 2023; first published online 30 June 2023)

Abstract
Objective: To explore the correlation between helicobacter pylori infection and several pathological features of gastritis, and provide evidence for pathological features analysis and diagnosis in helicobacter pylori associated gastritis. Methods: We collected 180 patients with gastritis admitted to the Seventh Affiliated Hospital of Sun Yat-sen University from 2021 to 2022, and make a retrospective analysis of their status of H. pylori with PCR technology. Then we further detected the resistant results of clarithromycin and fluoroquinolone in H. pylori positive group. Chi-Squared Test were used to analyzed the relationship between helicobacter pylori status and pathological features of gastritis. Results: Erosion or ulcers in the H. pylori-positive group were significantly higher than those in the H. pylori-negative group (P<0.05). Meanwhile, H. pylori-positive group were tended to have more severe activity or inflammation in the biopsy specimen. However, there was no significant difference in resistance to clarithromycin or fluoroquinolone in H. pylori-positive group with erosion, ulcers, or active inflammation. Conclusion: Helicobacter pylori infection is correlated with gastritis pathological features such as erosion, ulcers, inflammation or activity, but the pathological features of H. pylori-positive patients could not predict the antibiotic resistance. The experiment of screening drug resistance still has important clinical significance.

Keywords: Helicobacter pylori; gastritis; antibiotic resistance

Introduction
Long-term infection of helicobacter pylori is a non-negligible factor leading to gastrointestinal diseases, including gastritis, gastric ulcer and gastric cancer. The occurrence of gastrointestinal diseases is also more likely to be infected with helicobacter pylori. Infection rate of H. pylori in Chinese is as high as 56.2% [1], so the study on the pathogenic mechanism and therapeutic effects of H. pylori is of universal significance. The most common type of gastrointestinal disease caused by H. pylori is gastritis. The general pathological features of gastritis include inflammation, ulceration, atrophy, and intestinal metaplasia. Among them, inflammation is the earliest sign of gastritis and the most common pathological feature. Ulceration is also a common feature of gastritis and is closely related to H. pylori infection. Atrophy and intestinal metaplasia are regarded as risk factors for the development of gastric cancer.

H. pylori infection is associated with various clinical outcomes, including peptic ulcer disease, gastric cancer, and other gastrointestinal disorders. The presence of H. pylori is associated with increased risk of gastric cancer, particularly in individuals with atrophic gastritis. Thus, it is essential to understand the pathological features associated with H. pylori infection to guide clinical management and treatment strategies.

In this study, we aimed to explore the correlation between H. pylori infection and several pathological features of gastritis, including erosion, ulcers, inflammation, and activity. We performed a retrospective analysis of 180 patients admitted to the Seventh Affiliated Hospital of Sun Yat-sen University from 2021 to 2022. The status of H. pylori was determined using PCR technology. In addition, we detected the resistant results of clarithromycin and fluoroquinolone in the H. pylori-positive group. Chi-Squared Test was used to analyze the relationship between H. pylori status and pathological features of gastritis.

The results showed that erosion or ulcers were significantly higher in the H. pylori-positive group compared to the H. pylori-negative group (P<0.05). Moreover, the H. pylori-positive group tended to have more severe activity or inflammation in the biopsy specimen. However, there was no significant difference in resistance to clarithromycin or fluoroquinolone between the H. pylori-positive group with erosion, ulcers, or active inflammation.

Our findings suggest that H. pylori infection is correlated with gastritis pathological features such as erosion, ulcers, inflammation or activity. However, the pathological features of H. pylori-positive patients could not predict the antibiotic resistance. This study highlights the importance of screening drug resistance and further research is needed to fully understand the clinical significance of these findings.

Keywords: Helicobacter pylori; gastritis; antibiotic resistance

© The authors. Creative Publishing Co., Limited 2023, mrhk26640333@gmail.com, mrhk@mrhk.cc. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.
features of gastritis are evaluated around erosion and ulcers on the tissue surface, as well as inflammation, activity, intestinal metaplasia, atrophy and atypia [2]. It was also seen that in gastritis, H. pylori, chronic inflammatory infiltrate, neutrophilic infiltration, presence of lymphoid follicles and aggregates and surface epithelial damage are strongly associated with each other [3]. Therefore, we attempt to measure the influence of H. pylori on gastritis. We review the relationship between pathologic features of a batch of H. pylori infected patients and gastritis semi-quantitatively, so as to provide morphological support for the radical treatment of H. pylori.

It is well known that clarithromycin and fluoroquinolone are two important drugs for the treatment of H. pylori infection, but with the abuse of antibiotics, many patients are resistant to these two drugs. In H. pylori-positive patients, can the evaluation of pathological features of gastritis predict drug resistance? Or to predict the severity of gastritis by testing for drug resistance? Some scholars believe that about 20% of H. pylori-positive people will develop stomach diseases, among which 2% may develop gastric cancer [4], indicating that H. pylori infection is related to the occurrence of stomach diseases. According to the latest research of resistance evolution trends of H. pylori, clarithromycin resistant rate in China counts for about 36%, while fluoroquinolone resistant rate in most WHO regions counts for more than 11-15% [5]. Based on this fact, we screened the H. pylori-positive group, detected their drug resistance by genetic testing, trying to find out the correlation between pathological characteristics and drug resistance of H. pylori-positive gastritis patients by statistical analysis.

Materials and methods

Participants and materials

During 2021 to 2022, 180 patients from the Seventh Affiliated Hospital of Sun Yat-sen University were recruited. All of them complained of dyspepsia, performed gastroscopic biopsy and have H. pylori test. The mean age of the patients were 48.9±12.8 years, including 117 males and 63 females. All gastric mucosal biopsy samples were preserved in 4% formalin, embedded in paraffin, and stained in Hematoxylin Eosin.

PCR test of H. pylori nucleic acid

H. pylori nucleic acid detection kit (Beijing Xinji Yongkang Biotechnology Company) was used to design specific primers for UreA gene and Taqman fluorescent probes, which were detected by fluorescent PCR technique. The specific probes and primers of wild type 2142∼2143AA, mutant A2142G, mutant A2142C and mutant A2143G were designed and matched into two reaction solution. The fluorescence PCR instrument was used to detect the drug
resistance mutation analysis when the sample was qualified. A2142C/G and A2143G were drug resistance mutations. Once there was more than 1 positive test result, the sample was judged to be clarithromycin resistant. Six types of mutation (A260T, T261G, T261A, G271A, G271T and A272G) also designed and detected, once FAM channel \( \leq 35.00 \), it was judged to be fluoroquinolone resistant.

**Statistical analysis**

Excel (Microsoft) was used to import the data and SPSS was used to statistical calculate. The statistical description of count data was expressed by frequency and percentage. The Chi-square test was used to analyze the prevalence of the characteristics of gastritis among different helicobacter pylori status.

**Results**

1. **Patient characteristics**

   There were 85 H. pylori-positive cases among the 180 samples in this study, and the ratio of male and female patients was close. There was no statistical difference in H. pylori positive rate between male and female patients (\( P > 0.05 \)). With the median age of 49 years old as the age dividing line, the positive rate of H. pylori in people younger than 49 years old (54.95%) was significantly higher than that in people older than 49 years old (38.64%), and the difference was statistically significant (\( P < 0.05 \)). At the same time, there was no significant difference in the positive rate of H. pylori between urban patients and rural patients (\( P > 0.05 \)).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>H. pylori expression</th>
<th></th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>117</td>
<td>54 (46.15%)</td>
<td>63 (53.85%)</td>
<td>0.696</td>
</tr>
<tr>
<td>Female</td>
<td>63</td>
<td>31 (49.21%)</td>
<td>32 (50.79%)</td>
<td></td>
</tr>
<tr>
<td>Age(years)*</td>
<td></td>
<td></td>
<td></td>
<td>0.029</td>
</tr>
<tr>
<td>( \leq 49 )</td>
<td>91</td>
<td>50 (54.95%)</td>
<td>41 (45.05%)</td>
<td></td>
</tr>
<tr>
<td>&gt;49</td>
<td>88</td>
<td>34 (38.64%)</td>
<td>54 (61.36%)</td>
<td>0.415</td>
</tr>
<tr>
<td>District</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Town</td>
<td>126</td>
<td>57 (45.24%)</td>
<td>69 (54.76%)</td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>54</td>
<td>28 (51.85%)</td>
<td>26 (48.15%)</td>
<td></td>
</tr>
</tbody>
</table>

*medium age of patient

2. **Pathological features of gastritis**

   As shown in Figure 2, the results showed that among several pathological criteria for gastritis, ulcer or erosion, inflammation, and activity had statistical significance in the difference of H. pylori infection (\( P < 0.05 \)), meaning that patients in the H. pylori-positive group were more likely to have ulcers or erosion, greater levels of inflammation, and greater levels of activity. However, there was no statistical difference between H. pylori positive and negative in the assessment of intestinal metaplasia and atrophy.
3. Antibiotic resistance among different population characteristics in H. pylori-positive group

Statistical analysis showed that there was no significant relationship between sex, age or regional distribution and drug resistance in the H. pylori-positive group, that is, the drug resistance rate in the H. pylori-positive group did not change due to demographic characteristics.

4. Antibiotic resistance to pathological features of gastritis in H. pylori-positive group

In the analysis of pathological features of gastritis in the HP-positive group, we found that no difference in Hp infection was statistically significant in ulcer or erosion, inflammation, activity, intestinal metaplasia, atrophy and other features (P > 0.05).
Discussion

Helicobacter pylori is a very common, carcinogenic gram-negative bacterium, which is highly infectious and has been reported to be positive in almost half of people in developing countries [6]. The positive rate of Helicobacter pylori in our country is about 50%-60%. With different regional distribution and degree of economic development, the positive rate of Helicobacter pylori in each region will also have great differences and overall infection shows a decreasing trend year by year [1]. Helicobacter pylori infection usually causes a series of changes in gastric tissues, ranging from gastritis, gastric ulcer to gastric cancer. Taking gastritis as an example, it has been reported that Helicobacter pylori destroys gastrin-producing cells and causes autoimmune gastric disease [7]. Gastritis is generally divided into atrophic type and non-atrophic type, among which a more complete assessment also includes inflammation, activity, intestinal metaplasia, atypical hyperplasia and other features. Many studies have shown that H. pylori infection is an important cause of chronic gastritis [8], but the relationship is less discussed quantitatively between H. pylori infection and pathological features of gastritis. Because there are various detection methods for H. pylori nowadays, such as C13 urea breath test in a non-invasive, rapid and simple way, or serological and fecal antigen tests. The diagnostic methods of endoscopic biopsy and pathological morphology detection are relatively invasive, so few people carry out this screening [9]. However, for some people with ulcers and serious stomach diseases, biopsy morphology can more directly reflect the relationship between H. pylori infection and stomach diseases, and reduce the probability of misdiagnosis [10]. Therefore, we hope to evaluate more features of H. pylori infection with semi-quantitative pathological features to help understand the mechanism of morphological change.

Based on the pathological characteristics, we discuss the most likely changes of gastric
mucosa when H. pylori is positive, such as ulcer erosion, inflammation, activity, etc. At the same time, we should also pay attention to the possibility of H. pylori infection when we observe the corresponding changes of chronic gastritis. Our results indicate that among 180 patients with gastritis, H. pylori-positive is most likely associated with active gastritis, and no relationship with intestinal metaplasia or atrophy has been found. However, we have reason to believe that without treatment, positive patients may also develop more severe gastric mucosal changes, and even malignant changes.

The consensus on the management of H. pylori infection is that drug sensitivity tests must be conducted regardless of the initial or recurrent infection [11]. Current scholars believe that the main mechanism of resistance to H. pylori-related antibiotics is the formation of biofilms, in which bacterial populations adhere to a substrate coated by extracellular polymeric substances (EPS). EPS is mainly composed of polysaccharides, proteins and extracellular DNA secreted by bacteria. It acts as a barrier for bacterial cells to defend against drugs and the host immune system [3]. In the case of H. pylori resistance, although there has been literature analysis on the classification of H. pylori and endoscopic gastritis, and it is believed that H. pylori is closely related to intestinal metaplasia and atrophy of gastritis, and H. pylori eradication therapy will block the development of gastric cancer and even gastritis [12], there is no conclusive evidence to prove that drug resistance can be deduced by observation of pathological characteristics under the microscope. Our negative experimental results in the H. pylori resistance group further confirmed that drug resistance in the H. pylori infection group would not cause differences in visible pathological features. In the future, we will further expand the observation number of specimens to find out whether there is the cause of sample error.

The current conclusion is that the eradication therapy of H. pylori still has a positive effect on the later stage of positive patients’ diseases such as gastric cancer, and the corresponding antibiotic resistance is becoming more and more common. It is suggested that each infected patient should be tested for drug resistance to improve the effectiveness and accuracy of treatment.

Summary
Our study showed that H. pylori infection was associated with ulcer, inflammation and activity in the occurrence of chronic gastritis, but had little correlation with intestinal metaplasia and atrophy. After H. pylori infection, its drug resistance is not related to the pathological characteristics of gastritis, so it is not possible to predict the drug resistance of H. pylori by pathological morphology under the microscope. Drug-sensitive experiments still play a very important role in the treatment and eradication of H. pylori.

Acknowledgment
None.

Statement
There is no conflict of interest in this article.
References


