Helicobacter heilmannii gastritis: a histological and immunohistochemical trait

E Ierardi, R A Monno, A Gentile, R Francavilla, O Burattini, S Marangi, L Pollice, A Francavilla

Abstract

Aim—Biopsies of the gastric antrum were reviewed over a period of 10 years to determine the prevalence of Helicobacter heilmannii in symptomatic subjects from this geographical area and to relate its presence to distinctive histopathological and immunohistochemical features.

Methods—Biopsies from 7926 symptomatic patients were reviewed. Ten serial sections were stained with haematoxylin and eosin for conventional histology. Another 10 sections were stained with the Gram method for spiral bacteria. When H heilmannii was suspected, 10 additional serial sections were stained with methylene blue to obtain homogeneous colouring. An equal number of sections from patients affected by isolated H heilmannii or H pylori gastritis were analysed by immunohistochemistry to evaluate lymphoid aggregate/mucosal lymphocyte clonality (CD20 and CD3) and tumour necrosis factor alpha (TNF-α) in stromal cells.

Results—The prevalence of H heilmannii was 0.1% (eight of 7926), whereas H pylori was present in 60.7% of patients (4813 of 7926). In two of the eight H heilmannii positive patients both helicobacters were found. In all subjects infected by H heilmannii only, distinctive histology (lymphocyte exudation into gastric foveolae) was seen. Lymphoid aggregates, chronic mucosal inflammation with patchy activity, and the absence of epithelial mucus depletion were regular features of H heilmannii gastritis. Immunohistochemistry did not reveal different lymphocyte clonal patterns between H pylori and H heilmannii gastritis: CD20 positive cells were predominant in the centre of aggregates and mucosal infiltrates, whereas CD3 positive cells were prevalent at the periphery of follicles. Only H pylori gastritis showed a significant increase in TNF-α positive stromal cells.

Conclusion—These data suggest that an unusual lymphocyte reaction, with the tendency to invade the foveolar lumen, is a distinctive histopathological aspect of H heilmannii chronic gastritis, although further studies in a larger series are necessary to confirm this fact. Nevertheless, lymphocyte clones do not differ qualitatively from those found in H pylori infection. Moreover, compared with H heilmannii, H pylori provokes a more intense release of TNF-α, suggesting that different inflammatory responses exist to these two organisms.

Keywords: Helicobacter heilmannii; Helicobacter pylori; tumour necrosis factor α

In 1987, Dent et al reported the finding of a bacterium different from H pylori in the human gastric mucosa; this organism was named GASrosprillum hominis. 8 Since then, other cases have been described in association with gastritis, confirming the worldwide distribution of this microorganism. Most infected patients had been in contact with dogs, cats, and even pigs, thus suggesting an animal transmission of this infection. 3, 4 Various attempts to grow the microorganism in vitro failed, until Andersen et al isolated it in an artificial medium in 1999. 5 Moreover, it was propagated and maintained by taking gastric biopsies from patients and feeding them to mice. Finally, by cloning and sequencing the bacterial 16S rRNA gene, G hominis was shown to be a helicobacter, 7 and the name of Helicobacter heilmannii was proposed in honour of the German histopathologist K Heilmann. 8 The low prevalence of H heilmannii infection in histopathological series reflects the small number of cases published until now. 7

Following on from our previous reports, 10 11 we have reviewed endoscopic biopsies of the gastric antrum over the past 10 years. Aims of the study were to detect the histological prevalence of H heilmannii in symptomatic subjects in our geographical area (Puglia, southern Italy) and to relate the presence of this bacterium to distinctive histopathological and immunohistochemical changes in the gastric mucosa.

Material and methods

STUDY DESIGN

A retrospective study was performed on biopsy specimens taken at the level of the gastric antrum at a distance of 3 cm from the pylorus. Our series comprised 7926 patients (4131 men and 3795 women; age range, 17–75 years; mean age, 44.8) undergoing oesophagogastroduodenoscopy for upper gastrointestinal symptoms over a total period of 10 years (1989–99) in the section of gastroenterology of the department of emergency and organ transplantation of the University of Bari, Italy. At least two biopsy specimens had been taken for each patient. Routinely, 10 serial sections had been stained with haematoxylin and eosin for

Department of Emergency and Organ Transplantation, Section of Gastroenterology, University of Bari, 70124 Bari, Italy
E Ierardi
O Burattini
S Marangi
A Francavilla

Department of Internal Medicine and Public Health, Section of Hygiene, University of Bari
R A Monno

Department of Human Pathology, University of Bari
A Gentile
L Pollice

Department of Paediatrics, University of Bari
R Francavilla

Correspondence to: Professor Francavilla
Cattedra di Gastroenterologia, Università di Bari, Policlinico V.le Ennio, 70124 Bari, Italy
afrancavilla@gastro.uniba.it

Accepted for publication
17 January 2001
histological examination of gastric mucosa and an additional 10 with the Gram stain for the detection of spiral bacteria.

**Helicobacter Heilmannii Gastritis**

The morphological criteria for *H heilmannii* identification that we used for this study and our previous ones were in agreement with those described by Dent and colleagues and successively stated by Heilmann and Borchard. In particular, “tightly spiral shaped bacteria (corkscrew shape)” were suspected to be *H heilmannii*. They were characterised by their predominantly straight appearance and large size (about 10 µm). When *H pylori* was also present, the distinction was based on the smaller dimensions and curved shape of this last bacterium when compared with *H heilmannii*.

When the presence of *H heilmannii* was suspected, 10 additional serial sections were cut and stained with methylene blue which, in our experience, yields a more homogeneous colouring of bacteria. Finally, the histological picture was accurately reviewed in these sections to detect any distinctive histopathological features.

**Immunohistochemistry**

Sections from all six patients with isolated *H heilmannii* infection and an equal number of *H pylori* positive subjects, with chronic gastritis with moderate–severe activity, were studied by means of immunohistochemistry. The two groups were matched for sex, age, and endoscopic picture.

Clonal lymphocyte populations CD20 and CD3 were detected using monoclonal antibodies (Dako, Copenhagen, Denmark) and the labelled streptavidin–biotin technique, according to Saxena et al.

Tumour necrosis factor alpha (TNF-α) was stained using a polyclonal rabbit antibody (PromoCell, Heidelberg, Germany). The reaction was visualised using a peroxidase/antiperoxidase (PAP) technique with goat anti-rabbit immunoglobulins (Dako) and a complex of rabbit antibodies and horseradish peroxidase (Dako).

**Statistics**

The TNF-α labelling index (LI) was expressed as per cent of stromal positive cells (at least 1000 cells were counted for each specimen) as described by Baert et al. The Student’s *t* test for unpaired data was used to compare the values of LI in *H pylori* and *H heilmannii* gastritis.

**Results**

The prevalence of *H heilmannii* in our series of gastric biopsies was 0.1% (eight of 7926), whereas the prevalence of *H pylori* was 60.7% (4813 of 7926). In two of the eight *H heilmannii* positive patients both helicobacters (*H pylori* and *H heilmannii*) were present. Helicobacter *heilmannii* were seen as single elements or clumps of spiral bacteria. They had the typical feature of “corrugated cigars/corkscrew shape” and were found both in the gastric foveolar lumen and within the mucus. In some instances bacteria were seen in close association with the gastric epithelium (fig 1A and B).

The details of the *H heilmannii* positive patients are as follows: five men and three women with a median age of 40.3 years and a range of 20–64. Contacts with domestic animals (cats and/or dogs) were reported by six of the eight patients. Table 1 details the endoscopic features of the patients. All patients were treated with conventional triple therapies. Eradication was achieved in all but one patient who dropped out for unknown reasons.

**Histopathology**

The presence of *H heilmannii* was always associated with chronic gastritis (an increase of lymphocytes and plasma cells in the lamina

---

**Table 1  Endoscopic features in patients with Helicobacter heilmannii chronic gastritis**

<table>
<thead>
<tr>
<th>Endoscopic feature</th>
<th>Prevalence (positive patients/total patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypaeremia/oedema</td>
<td>5/8</td>
</tr>
<tr>
<td>Antral chronic erosions</td>
<td>5/8</td>
</tr>
<tr>
<td>Duodenal erosions</td>
<td>1/8</td>
</tr>
<tr>
<td>Desophagitis</td>
<td>3/8</td>
</tr>
<tr>
<td>Normal</td>
<td>2/8</td>
</tr>
</tbody>
</table>
propria). Active inflammation (polymorphonuclear cells) showed a diffuse distribution in the lamina propria and epithelial cells only in the two patients affected by combined (H pylori/heilmannii) infection. In all six subjects with isolated H pylori infection, a small number of polymorphonuclear cells with a patchy distribution was always seen. Moreover, in these patients distinctive histology (lymphocyte exudation into gastric foveolae) was seen (fig 2A and B). This feature was never found in H pylori gastritis, in which the inflammatory cell exudate in the gastric foveolae, when present, was made up of polymorphonuclear cells (crypt abscesses).

Lympoid aggregates were seen regularly in H heilmannii chronic gastritis and were predominantly located in the basal portion of the lamina propria.

A depletion of epithelial cell mucus was often seen in H pylori gastritis and its extent was related to the degree of inflammation. This feature was never seen in H heilmannii infection.

Table 2 summarises the differences in histopathology seen in H pylori and H heilmannii gastritis.

<table>
<thead>
<tr>
<th>Feature</th>
<th>H pylori</th>
<th>H heilmannii</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic inflammation</td>
<td>+±</td>
<td>+±</td>
</tr>
<tr>
<td>Active inflammation</td>
<td>+± + (patchy)</td>
<td>±</td>
</tr>
<tr>
<td>Epithelial mucus depletion</td>
<td>+±</td>
<td>−</td>
</tr>
<tr>
<td>Lymphoid aggregates</td>
<td>+± +±</td>
<td>± +±</td>
</tr>
<tr>
<td>Lymphocyte exudation into gastric foveolae</td>
<td>− ± + +</td>
<td>+ ±</td>
</tr>
<tr>
<td>Foveolar abscesses</td>
<td>+ + ±</td>
<td>−</td>
</tr>
</tbody>
</table>

Discussion

It is well known that H heilmannii is an uncommon cause of chronic gastritis. The first cases of infection by this bacterium in Italian patients were described by Figura and colleagues14 and our laboratory.15 We have since reported other cases of isolated and H pylori associated H heilmannii gastritis.11 Following on from these previous reports, we have reviewed endoscopic biopsies of the gastric antrum over a period of 10 years with the aim of detecting the histological prevalence of H heilmannii in...
A variety of factors contribute to the induction and persistence of Helicobacter pylori gastritis. In the period 1989 to 1999, we have seen eight cases of Helicobacter heilmannii infection with a prevalence of 0.1% in symptomatic subjects in our geographical area. In Italy, the prevalence of Helicobacter heilmannii is higher than in other regions of Europe. For this reason, we have decided to include this bacterium in our immunohistochemical study.

Helicobacter heilmannii gastritis is a distinctive histopathological entity. It is characterized by a paucity of inflammatory cells, with a predominant T helper 1 type response, which is important for the development of related gastric disease and is predominantly mediated by TNF-α release. In conclusion, our results suggest that Helicobacter heilmannii gastritis is associated with some unusual histopathological and immunohistochemical features, which may render it a distinctive histopathological entity.
Helicobacter heilmannii gastritis: a histological and immunohistochemical trait

E Ierardi, R A Monno, A Gentile, R Francavilla, O Burattini, S Marangi, L Pollice and A Francavilla

J Clin Pathol 2001 54: 774-777
doi:

Updated information and services can be found at:
http://jcp.bmj.com/content/54/10/774

References

These include:

This article cites 20 articles, 5 of which you can access for free at:
http://jcp.bmj.com/content/54/10/774#BIBL

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

Stomach and duodenum (105)
Immunology (including allergy) (1664)
Inflammation (173)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/