A 2-Year Study of Helicobacter Pylori in Children

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From September 1990 to October 1992, Helicobacter pylori was searched for in 426 children, 2 days to 16 years old, requiring upper fibroscopy for various symptoms. H. pylori was detected in 77 children (18.1%). Recurrent abdominal pain was present in 63.3% of the patients with H. pylori versus 48.6% of a control group of 74 age-matched children negative for H. pylori, weight loss was present in 6.5% of the patients versus 0% of the control subjects, and a family history of peptic ulcer was present in 14.2% of the patients versus 5.4% of the controls. Micronodular gastritis was observed in 31 children with H. pylori infection (40.2%). Among the 24 children (31.1%) with H. pylori infection and a normal mucosa at endoscopy, 18 (75%) complained of recurrent abdominal pain. H. pylori was also found in 21 of 38 children (55.2%) being examined because of short stature. These findings indicate that H. pylori should be looked for in children with recurrent abdominal pain with or without weight loss or a family history of peptic ulcer. Its relevance in short-stature syndrome requires further clarification.

The association between gastric colonization by Helicobacter pylori, gastritis, and peptic ulcer is now strongly established for adults, whereas only a few reports describe the culture of the bacteria in gastric mucosal samples from children (5, 14, 15). In large studies, only serological tests were done (2). The present work, using a large number of patients, was undertaken to evaluate by culturing gastric biopsy specimens (as a "gold standard") the incidence of H. pylori and its association with antral gastritis in a French pediatric population requiring upper fiber endoscopy for various symptoms. In addition, the clinical features of H. pylori infection in children were evaluated.

MATERIALS AND METHODS

During a 2-year period, from September 1990 to October 1992, all children requiring endoscopy were eligible to enter this study. The total number of children was 426. Their ages ranged from 2 days to 16 years (mean, 8.9 years); 388 had endoscopy for various upper intestinal tract disorders, and 38 were examined because of short stature with a documented absence of growth hormone deficit. For the latter group, endoscopy was performed to diagnose damage to the intestinal mucosa, such as coeliac disease.

Clinical data were prospective and were obtained from records by practitioners who were not aware of the H. pylori status of the patients. In order to evaluate the clinical manifestations specific to H. pylori infection in children, 74 age-matched subjects negative for H. pylori were used as a control group.

Upper endoscopy was performed with an Olympus GIF X P10, and three biopsy specimens were taken. The biopsy specimen for histology was fixed in Bouin, embedded in paraffin, sectioned, and stained with hematoxylin-eosin. A pathologist determined the presence and degree of gastritis and the presence or absence of H. pylori.

The second specimen was smeared onto a glass slide and stained with Gram stain with 1% concentrated Fuchsine (RAL, Paris, France). Slides were examined for up to 10 min for characteristic curved bacterial cells. The specimen was then crushed in 0.5 ml of Christensen's 2% urea broth and examined after 1 h of incubation at 37°C for urea hydrolysis. The third biopsy specimen was suspended in 0.5 ml of meat-liver broth (Pasteur, Marne la Coquette, France) and homogenized by using a glass Griffith's tube. All of the homogenate was cultured on Columbia sheep blood agar and chocolate agar (Merieux, Lyon, France) and incubated at 37°C under microaerophilic conditions (15% O2, 10% CO2, 85% N2), achieved with a gas generator envelope, for at least 7 days (Generbag-microaer; Merieux). The organisms produced characteristic light brown convex colonies and were identified as H. pylori by their typical cell morphology; rapid positive urease test; positive oxidase, catalase, gamma glutamyl transferase, and alkaline phosphatase tests; and negative nitrate reductase test. (API; Merieux).

Antibiotic susceptibility testing by the disc diffusion method was performed with chocolate agar incubated under microaerophilic conditions.

Statistical analysis was performed by using the χ2 test for nonparametric values.

RESULTS

H. pylori was detected in 77 (18.1%) of the 426 children included in the study; 48 (62.3%) of these patients were male and 29 (37.3%) were female. In 51 cases (66.2%), both culture and histology were positive, whereas in 26 cases (33.8%), one of the two methods failed to reveal the organism. Among the 77 patients positive for H. pylori, 24 (31.1%) had a normal antral mucosa, 31 (40.2%) had a micronodular gastritis, and 16 (20.7%) had a congestive mucosa. Atrophic gastritis was found in one case, gastric ulcer was found in one case, and duodenal ulcer was found in two cases.

Clinical data are shown in Table 1. Abdominal pain, weight loss, and a family history of ulcer were more frequent in patients positive for H. pylori, although these higher frequencies were not statistically significant (P = 0.09, P = 0.05, and P = 0.10, respectively).
TABLE 1. Clinical symptoms in patients positive for H. pylori in gastric samples and in controls

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. (%) with symptom among:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients positive for H. pylori (n = 77)</td>
</tr>
<tr>
<td>Recurrent pain</td>
<td>48 (62.3)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>20 (26)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>5 (6.5)</td>
</tr>
<tr>
<td>Anemia</td>
<td>5 (6.5)</td>
</tr>
<tr>
<td>Peptic ulcer in family</td>
<td>11 (14.2)</td>
</tr>
<tr>
<td>Short stature</td>
<td></td>
</tr>
<tr>
<td>With abdominal pain</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Without abdominal pain</td>
<td>14 (18.1)</td>
</tr>
</tbody>
</table>

* The total number of occurrences of symptoms is greater than the total number of subjects because symptoms can be associated.

Of the 38 patients being examined because of short stature, 21 children (55.2%) were positive for H. pylori; among these, 7 had clinical symptoms (abdominal pain), which were associated with histological signs in 5 cases. The 14 patients without clinical symptoms had a mucronulor or hyperemial mucosa.

Among the 24 patients with a normal mucosa at endoscopy, 18 (75%) had recurrent abdominal pain with or without vomiting, 1 was anemic, 1 was anorexic, 2 had dyspepsia symptoms, and 2 were being examined because of short stature and had abdominal pain.

The ages of the 77 children positive for H. pylori ranged from 13 months to 16 years with two peaks of frequency, one in the range of 6 to 8 years and the other in the range of 10 to 12 years (Fig. 1).

Children were treated with two different regimens: (i) amoxicillin and metronidazole or (ii) amoxicillin, metronidazole, and a proton pump blocker. Only 23 patients were given a new endoscopy. Among 14 children treated with amoxicillin-metronidazole, H. pylori was definitively eliminated in only 1 case. When the proton pump blocker was added (nine cases) after relapse or failure of the two-drug treatment, bacteriological and histological elimination of the pathogen were observed, together with the disappearance of clinical symptoms (abdominal pain and vomiting), and three children appeared to put on weight rapidly (more than 4 lb [ca. 2 kg] in 2 months).

**DISCUSSION**

The interest in an infectious cause of gastric disorders was enhanced since H. pylori was isolated in up to 100% of adults with duodenal ulcer (13). This association was confirmed for children in several studies, but these studies included only a few cases (11, 14, 15). Our study relies on a larger group and provides a good evaluation of the main clinical manifestations in children with H. pylori infection.

The incidence of H. pylori is 18.1% in the present study, a frequency higher than those previously described for children, probably because of the method of selection of patients. The incidence of H. pylori infection appears to be 20 to 30% (7, 10) in the general population; this number is strongly dependent on age and geography. H. pylori is reported to be less common in the developed world (incidence of 5%) (7, 8, 16) than in developing countries (8).

The predominance of H. pylori infection among male rather than female children, previously described by Oderda et al. (11) and Drumm et al. (4), is confirmed here. In accordance with these reports, we found a higher frequency of the infection in children aged 10 to 12 years. This could correspond to the age for peak frequency of infection in children.

Recurrent abdominal pain with or without vomiting was a common manifestation of H. pylori in this study, as previously described (4, 17). Similarly, like in previous studies (3, 9, 11), several cases of ulcer in the family were found in patients positive for H. pylori.

The difference between children in the short-stature group positive for H. pylori and the control group is not significant. All children positive for H. pylori had either an abnormal mucosa or clinical symptoms. Some cases of protein-losing enteropathy, with or without diarrhea, associated with H. pylori have been described (1, 6). Likewise, Sullivan and Thomas (18) suggest that H. pylori may predispose individuals to having bacterial overgrowth in the small intestine and induce malabsorption. However, children in the short-stature group did not exhibit any sign of hypoproteinemia or malabsorption, so the relationship between short stature in children and H. pylori infection requires further clarification.

In this study, 40.2% of children positive for H. pylori had a mucronulor gastritis, an incidence lower than that reported by other authors (11, 14). The 24 children with a macroscopically normal mucosa did not have silent infections, since 18 children (75%) had abdominal pain. Six of these children recovered after treatment. The presence of H. pylori in children with a normal endoscopy has been described by Price et al. (12). In these children the mucosa might not yet have reacted immunologically to H. pylori, or, possibly for genetic reasons, these children might not be prone to develop gastritis.

This normal gastric mucosa might also represent an early stage of the infection. An alternative explanation is that in some children, H. pylori causes a much less marked active chronic antritis, as described for children by Rosh et al. (15). Our experience proves that, even with a normal gastric endoscopy, biopsies must be taken when clinical symptoms are present.

The absence of H. pylori in numerous children with abdominal pain may have several reasons. Apart from possible other pathologies, the biopsy could be inadequate because of an inequally shared repartition of the organism in the mucosa. More important, the method may not be sensitive enough; a role for PCR could be indicated, even though

**FIG. 1. Ages of patients tested for H. pylori by culture of gastric mucosa.** Open bars, all patients; solid bars, patients positive for H. pylori. A total of 426 children were tested.
a recent study showed that culture was as sensitive as PCR for the detection of *H. pylori* (19).

Our preliminary results showing the elimination of *H. pylori* and the disappearance of clinical symptoms in nine cases after the combination of amoxicillin, metronidazole, and proton pump blockers versus the elimination of *H. pylori* in only one case after dual therapy with amoxicillin and metronidazole confirm those obtained for adults and indicate the need for further studies with children.

In conclusion, we found a prevalence of *H. pylori* gastric infection of 18.1% in a general pediatric population. The clinical symptoms leading to endoscopy and biopsy were recurrent abdominal pain with or without vomiting, weight loss, or a family history of peptic ulcer. As described in previous reports, we observed that *H. pylori* can be the causative agent of gastritis in children as well as in adults, and must be searched for, even when the mucosa is macroscopically normal.

REFERENCES