Unique Features of \textit{Helicobacter pylori} Disease in Children

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In a six-year period, 41 children had endoscopically documented duodenal ulcer disease or primary \textit{H. pylori} antral gastritis without duodenal ulcer. Of 37 children with \textit{H. pylori} gastritis, group 1 comprised 23 patients with duodenal ulcer disease and group 2 had 14 patients without ulcers (primary \textit{H. pylori} gastritis). Group 3 comprised four children with duodenal ulcer disease and \textit{H. pylori}-negative antral biopsies. During the study period, all primary chronic ulcer disease was duodenal; no primary chronic gastric ulcer was present. Two distinct types of duodenal ulcer disease were identified; the majority (85\%) was always associated with significant active \textit{H. pylori} antral gastritis (group 1). The minority (15\%) had virtually absent gastritis and no \textit{H. pylori} (group 3). Native Indian children were represented in group 1 quite out of proportion to the referral population and had the most severe disease. While it is established that a higher prevalence of asymptomatic \textit{H. pylori} infection exists in non-Caucasians, this appears to be the first demonstration of a higher prevalence of symptomatic ulcer disease in non-Caucasian children or adults. Caucasian children tended to have primary \textit{H. pylori} gastritis (group 2) or duodenal ulcer without \textit{H. pylori} (group 3). Antral nodularity was found to be an important specific endoscopic sign, unique to those children with \textit{H. pylori} disease. It has not been described in adult \textit{H. pylori} disease. Non-Caucasian children, especially Native Indians, in British Columbia have more prevalent and more severe \textit{H. pylori} disease than Caucasians. Endoscopy with gastric antral biopsies is necessary to distinguish different types of duodenal ulcer disease and to diagnose primary \textit{H. pylori} gastritis.

KEY WORDS: \textit{Helicobacter pylori}; \textit{Campylobacter pylori}; duodenal ulcer; nodularity; lymphoid nodular hyperplasia; gastritis; peptic ulcer.

In 1983 Warren and Marshall (1) described the association of spiral-shaped bacteria on the antral mucosa with gastritis in adults. This association has been well documented subsequently in reports from several parts of the world (1–7). The organisms, gram-negative rods with three to four flagella, were previously known as \textit{Campylobacter}-like organisms, \textit{C. pyloridis}, \textit{C. pylori}, and now \textit{Helicobacter pylori} or \textit{H. pylori}.

Recently, studies in small numbers of patients have verified the association between \textit{H. pylori} and antral gastritis in children (4–11). We describe the distinctive clinical, endoscopic and histologic findings in 37 children with \textit{H. pylori} in the gastric antrum, and four children with duodenal ulcers, no antral \textit{H. pylori} present. This group of children differs significantly in several respects from those in other reports and shows important differences from \textit{H. pylori} disease in adults.

MATERIALS AND METHODS

Patients are those referred to the Division of Gastroenterology of B.C. Children's Hospital, which is the only tertiary referral children's hospital for the Province of
British Columbia. Of the 2.9 million population of B.C., approximately 4.5% are Chinese and 3.9% Native Indian (12). Other non-Caucasian groups (e.g., East Indian 2.9%, Japanese 0.6%, Filipino 0.6%) comprise 6-7%, with 85% of the population being Caucasian (12). Patients referred to the Division are seen in the same ethnic proportions as the provincial profile, with two exceptions: Chinese patients comprise 6-7% of gastroenterology referrals, and Native Indians 2%. This reflects geographic distribution; the Native Indian population is lower in the Vancouver area than in the rest of the province, and the reverse is true for the Chinese population. Although the referral base for Gastroenterology is province-wide, referral patterns are influenced by distance from Vancouver.

Over a six-year period following the inception of a new gastrointestinal endoscopy unit at B.C. Children's Hospital, data concerning peptic ulcer disease were documented prospectively. All data refer to patients diagnosed at endoscopy. This study concerns chronic ulcers, and therefore excludes any data on acute or "stress" or drug-related gastric ulceration/erosive disease.

During this period 1293 children under the age of 18 years had upper gastrointestinal flexible fiberoptic endoscopy performed by one pediatric gastroenterologist. Of these, 1190 were diagnostic procedures. Two or more biopsies from the gastric antrum were taken in 803 children. Under endoscopy was performed for all of the usual childhood indications, those being abdominal pain, nausea, vomiting, gastroesophageal reflux, failure to thrive, possible upper gastrointestinal tract Crohn's disease, gastrointestinal bleeding, and dysphagia. Diagnostic procedures refer to those procedures performed for indications other than variceal sclerotherapy, percutaneous endoscopic gastrostomy or foreign body removal. Examination to the third part of the duodenum was performed in all patients. One gastroenterologist performed all of the procedures and documented his findings immediately following endoscopy, before the biopsies were reviewed.

In the last four years it has been routine practice to take two to four biopsies from the gastric antrum whether or not an abnormality was present at endoscopy. Biopsies were fixed in Bouin's solution and stained with hematoxylin and eosin (H&E) and with Steiner's stain. All biopsies were examined independently by two pathologists who were unaware of the patient's clinical history or endoscopic findings. The presence of *H. pylori* in all positive patients was considered to be unequivocal by each pathologist independently. Only pretreatment biopsies were evaluated for inflammation, organisms, and lymphoid hyperplasia. Antritis was classified as chronic (plasmacellular and lymphocytic infiltration) and active (polymorphonuclear infiltration) and assessed as to extent of mucosal involvement (focal or diffuse, superficial or panmucosal). A superficial pattern indicated inflammation predominating in the upper half of the mucosa occupied by antral pits; panmucosal denoted inflammation involving, additionally, the antral glandular mucosa. Lymphoid hyperplasia was assessed subjectively. An occasionally found aggregate of lymphocytes, especially in the deep mucosa, may occur normally in children and was so regarded. Lymphoid follicles with active-appearing germinal centers were regarded as pathologic. When only occasionally encountered, hyperplasia was recorded as moderate; when frequently noted, the designation was marked. Acute duodenitis was diagnosed when neutrophilic invasion of epithelium and lamina propria was present.

All antral biopsies had gastritis scores assigned according to the following scoring system: extent of gastritis—none 0, focal 1, superficial diffuse 2, panmucosal diffuse 3; type of inflammation—none 0, chronic 1, chronic active 2; lymphoid nodularity—none 0, moderate 1, marked 2. Using this system, a maximum score of 7 denotes the most active and extensive gastritis, while 0 indicates no gastritis is present. In our experience no significant gastritis is present if the score is 2 or less and lymphoid nodularity is absent.

**RESULTS**

During the six-year period studied, only four patients were encountered with duodenal ulcer unassociated with the presence of *H. pylori* (group 3). No cases of primary chronic gastric ulcer were seen; gastric ulcers encountered were invariably associated with the use of aspirin, other nonsteroidal antiinflammatory drugs, or hypoxemia-acidosis-sepsis ("stress" ulcers).

The 37 patients with *H. pylori*-positive biopsies were divided into two groups. Group 1 patients had duodenal ulcer disease; group 2 patients did not. Group 3 comprised four patients with duodenal ulcer and no *H. pylori* present. Tables 1 and 2 give further details on each group.

**Clinical Features**

**Group 1.** Of the 23 patients in the duodenal ulcer disease group, 10 were Native Indian, six were Chinese, one Japanese, one East Indian, one Vietnamese, one Chilean, and three Caucasian. There were 20 males and three females, of average age 11.5 years. Seven presented with abdominal pain alone, seven with abdominal pain and gastrointestinal bleeding, eight had bleeding but no pain, and one presented with acute severe pain and perforation of a duodenal ulcer.

**Group 2.** Of the 14 patients in the nonulcer group, seven were males and seven females, of average age 11.9 years. All 13 were Caucasian. Patients 24-34 had presented with abdominal pain and/or nausea. Patients 35-37 were found to have *H. pylori* antritis as an incidental finding on routine antral biopsies taken at endoscopy performed for celiac disease or reflux (Table 1). None of the 14 had gastrointestinal bleeding or perforation.