Original article

Nodular gastritis and Helicobacter pylori infection in childhood

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SUMMARY

Helicobacter pylori (HP) associated gastritis and peptic ulcer have been initially reported in adult patients. Recently, this association has also been demonstrated in children. We investigated 18 children (8-14 years old) with recurrent abdominal pain. In 7 patients gastroduodenoscopy revealed gastritis and HP was identified. Giemsa stain was more sensitive than urease testing in identifying the bacteria. In 5 of the 7, a nodular appearance of the antral mucosa was observed. The histological examination suggests lymphoid hyperplasia as the cause of the nodularity. All 7 patients became symptomless after a triple therapy with omeprazole, clarithromycin and amoxycillin for 2 weeks.

We conclude that nodular gastritis is a peculiar type of gastritis in children. It is frequently found in association with HP infection. Two weeks triple therapy is an effective treatment in children with HP infection.

Key words: Helicobacter pylori, nodular gastritis, peptic ulcer disease, childhood

INTRODUCTION

Many studies have been published to elucidate the prevalence of Helicobacter pylori (HP) infection and the related symptomatology in childhood.[1-4] The prevalence of HP in children living in developed countries is low (15-25%) compared to the prevalence in children living in developing countries (40-60%).[5] Earlier studies have elucidated a prevalence of HP gastritis of 30-60% in children with recurrent abdominal pain (RAP)[2,6] and HP was therefore assumed to play a role in this symptom complex. In children, epigastric pain, haematemesis and vomiting have been reported as symptoms that correlate to the HP infection,[7-9] while other authors have not found any specific symptoms related to this infection.[4,10-12] Since the successful culture of HP by Marshall in 1983 many reports have demonstrated a consistent association of this bacterium with gastritis and peptic ulcer in adult patients.[13] A similar association was also demonstrated in the pediatric age group.[14-15] Typically, the inflammatory process in the gastric mucosa of infected individuals is a chronic type B gastritis, which is characterized by crypt atrophy and chronic inflammatory cell infiltrate.[16,17] In the infected duodenal mucosa, gastric metaplasia can often be seen.[17] The macroscopic appearance of nodular gastritis is a phenomenon typically and frequently found in children infected by HP and is characterized by the appearance of Lymphonodular hyperplasia of the antral mucosa.[18-20]

We report our yearly experience of 18 children with RAP, our endoscopical findings and the results of 2 weeks of treatment with omeprazole, clarithromycin and amoxicillin.

PATIENTS AND METHODS

During a 12 month period, 18 children (11 males and 7 females, aged 8-14 years) underwent endoscopy for evaluation of RAP according to Apley's criteria (more than three attacks of diffuse or localized abdominal pain in a period of >3 months affecting the daily living activities of the child),[21] and no other obvious causes of RAP. RAP disturbed the patient's activities and sleep, and often accompanied by nausea and vomiting.

All children were screened for the presence of serum specific IgG antibodies against HP antigens using an

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Acknowledgments: RAP: recurrent abdominal pain, HP: Helicobacter pylori, CLO: tissue urease test

ELISA quantitative immunoassay method. Gastroduodenoscopy was done since routine laboratory examinations and abdominal ultrasonography was negative. The gastroduodenoscopy was performed using an Olympus Qx20 endoscope. During endoscopy, two biopsies were taken from gastric antrum and body, and duodenal bulb for histology, using Giemsa stains, as well as two antral biopsies for urease testing (CLO-test). Histological examination of all paediatric samples was performed by the same paediatric histopathologist and the infection was diagnosed by three positive identification test of HP.

RESULTS

HP gastritis was diagnosed in 7 (38,8%) patients of the 18 investigated. In two of the seven duodenitis was also observed. The endoscopic appearance in five patients of the seven (71%) was characterized by multiple small nodules covering most of the antral area 4 and part of the distal area of the fundus. In addition, several superficial erosions were observed. The nodular appearance was confined to the gastric mucosa and was not seen in the duodenum. In the other two patients, only antral erosions were observed. The histological picture of the nodular gastric mucosa was characterized by a heavy inflammatory cell infiltrate consisting mainly of monocytes and an increased number of lymphoid follicles. The inflammatory process in the cases without the nodularity was significantly milder.

HP was identified by urease test in five, and by Giemsa stain in all seven cases. Nine patients had high serum IgG antibody titers against HP. All patients became symptomless after a period of two weeks of treatment that consisted of a proton pump inhibitor (omeprazole: 0,7 mg/kg/d), clarithromycin (25 mg/kg/d) and amoxycillin (50 mg/kg/d). None has relapsed for 6-8 months following treatment.

Three of the patients who underwent a second endoscopy, 3 months after the end of the treatment, had very mild antral nodularity (significantly less than initially observed), almost complete disappearance of the inflammatory process, and HP could not be identified.

DISCUSSION

Inflammation of the gastric and duodenal mucosa is the end result of an imbalance between mucosal defensive and aggressive factors. The degree of the inflammation and imbalance between defensive and aggressive factors can then results in varying degrees of gastritis and/or frank mucosal ulceration.[22] The fact that HP is demonstrated in 80-90% of gastritis cases in adults and has a worldwide distribution suggests a major role for HP in the etiology of peptic disease.

The reports of HP-associated gastritis or ulcer are fewer in pediatric patients than in adults and include a smaller percentage of patients infected by the bacteria. The intrafamiliar spread of HP infection from person to person with common environmental (a common contaminated source with HP within the household) or genetic factors and this could possibly even explain the high incidence of infection in paediatric population. Fecal-oral, oro-oral and gastro-oral (contact with vomits or gastric secretions) routes, are the most likely mode of transmission.[23] The incidence of HP among children undergoing endoscopy for upper gastrointestinal symptoms ranges between 11% and 24%.[24-27] However, previous descriptions of the prevalence of HP among children with gastrointestinal complaints have been impaired by imprecise definitions of the population investigated according to ethnicity and selection of patients.[2,3,6,28] In our study, HP was identified in 38,8% of the patients undergoing endoscopy for RAP. The prevalence of HP infection in children diagnosed as having primary gastritis, however, is higher and varies between 70-80%.[15,24,26]

Several direct/invasive and indirect/non-invasive diagnostic tests are available for the diagnosis of HP infection. Invasive tests require biopsy sampling of the gastric mucosa and include rapid urease test, histology, bacterial culture and polymerase chain reaction technique. Noninvasive tests include the urea breath test and serological assays.[29] We based the diagnosis of HP infection in our study on three methods- Giemsa staining, urease test and serum antibody titers (ELISA). There is no diagnostic gold standard in general clinical practice. Accurate interpretation of specially stained slides is a learned activity with a tendency towards overdiagnosis early on. Urea breath testing is likely to be the diagnostic method of choice for untreated patients in general clinical practice although antibody testing is almost as accurate.30 The use of a positive serological test as a single method before starting treatment of a hp infection in children cannot be used.[26,27]

Our report as well as those of other authors,[18-20] describe a peculiar frequent endoscopic picture of the antral mucosa of children infected with HP. Nodular gastritis was observed in 66-90% of the cases reported by other authors. In our study the percentage was 71%. Histologic examination in nodular gastritis consisting mainly of mononuclear cells and eosinophils and an increased number of lymphoid follicles. These macroscopic

and microscopic findings closely resemble benign lymphoid hyperplasia, which is frequently seen in small and large bowel mucosa of children. It seems that the inflammatory process in the gastrointestinal tract in children has its own specific characteristics differing from those seen in the adult. Although three cases were reexamined by endoscopy, the findings of these cases suggest that disappearance of HP precedes the complete resolution of the inflammatory process. Despite biopsies were taken from antral body of the stomach and the duodenal bulb we have 9 seropositive children but 7 with positive Giemsa stain test and 5 with positive CLO test. The reasons may be (i) localization of HP outside the antrum-corpus region; (ii) previous broadspectrum antibiotic treatment (ex, amoxicillin or cotrimoxazole) for other infectious diseases; (iii) spontaneous eradication of HP and (iv) a small number of bacteria.[27] The remaining 2 children who were seropositives for anti-HP IgG but negatives for the other two assays; might have recovered from HP infection, and the positive antibody test result might have been attributable to the presence of convalescent antibodies. It is also possible that these were false-positive antibody test results.[26] These patients were not considered positive for HP infection.

Serial or parallel IgG titers offer equivalent diagnostic accuracy for confirming HP eradication after therapy. When a decline of > or = 25% in titer 6 months after therapy is a sensitive and specific marker for eradication of the infection.[31]

We close to treat our patients with omeprazole, amoxicillin and clarithromycin for 2 weeks. This treatment resulted in the disappearance of symptoms in our patients and the improvement of histological findings on the 2nd endoscopy which was performed on 3 children. Tiren et al and Oderda et al[32,33] showed that 2 weeks of treatment with omeprazole, clarithromycin and amoxicillin in children with RAP and HP gastritis yielded an eradication rate of 75-78%. Recent studies[34,35] showed that one-week therapy with omeprazole, clarithromycin and metronidazole or amoxicillin is an effective treatment in children with HP infection.

It can be concluded that from our reported experience as well as those of others, it is suggested that HP play a role in childhood peptic ulcer disease. the endoscopic is suggested that HP play a role in childhood peptic ulcer disease. the endoscopic observation of nodular gastritis may serve as a clue to the diagnosis of HP infection. The confirmation of this bacterial infection can direct the pediatrician in the choice of treatment.

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