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The Value of *Helicobacter pylori* IgG Antibody in Estimating the Severity of Gastritis in Children

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A serologic test for antibodies is useful for diagnosis of Helicobacter pylori(H.pylori) infection in children. We evaluated the reliability of H.pylori IgG antibody titer in grading the severity of infection in children. We surveyed the sero-prevalence of H.pylori infection in 300 healthy school children(13 to 15 years old). Thirty-four percent(102 of 300 children) were sero-positive for H.pylori. Of the 102 sero-positive children, 70 underwent gastroscopic examination. Ninety percent of sero-positive children(63 of 70 children) were proven to be H.pylori infected. All children with H.pylori infection had histologically proven gastritis, and its severity did not correlate with the IgG antibody titer. Although a serologic test is useful to identify H.pylori infection in children, it can not predict the severity of H.pylori associated gastritis.

Key Words : *Helicobacter pylori, Gastritis, IgG*

INTRODUCTION

Primary gastritis in children is known to be associated with *Helicobacter pylori(H.pylori)* infection (Giacomo et al., 1990). *H.pylori* infection induces a humoral immune response and therefore can be diagnosed by serologic test with high reproducibility in children (Barthel and Everett, 1990 ; Giacomo et al., 1990 ; Glassman et al., 1990). It is not recommended to treat *H.pylori* infection without disease such as duodenal ulcer. However the presence of gastritis warns the physician of possible complications. Gastritis can be diagnosed by means of gastrofiberscopy, but this is not available for most pediatricians.

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It is known that clusters of the *H.pylori* are associated with infiltrations of inflammatory cells and the extent of gastritis (Karttunen et al., 1991). There is a positive correlation between the number of *H.pylori* and the severity of polymorphonuclear leukocyte infiltration (Satoh et al., 1991). A serologic titer of antibody often reflects the severity of a certain disease (Barthel and Everett, 1990). Yet, there have been no reports that have studied specifically the relationship between the severity of gastritis and the titer of antibody in children. With the hypothesis that systemic humoral immune response to *H.pylori* infection reflects the degree of gastric mucosa inflammation, we investigated whether antibody titer can indicate the degree of *H.pylori* associated gastritis in children without the help of gastroscopic examination.

At first, it is important to establish the presence of *H.pylori* infection and gastritis in asymptomatic children. Therefore we investigated the correlation between antibody titer and the degree of gastritis in healthy normal children.

MATERIALS AND METHODS

Subjects

Serologic examinations for *H.pylori* were performed in three hundred randomly sampled healthy children between ages 13 to 15 years. All lived in the suburbs of Seoul. All children were healthy without abdominal discomfort or pain. They received no medication at the time of blood sampling and gastrofiberscopy.

All children voluntarily participated in this study. Parents gave written, informed consent for endoscopic examination prior to participation.

Serologic examination

We took blood samples and separated sera immediately (less than six hours). The sera were stored at −40℃ till antibodies were measured.

The Cobas Core Anti-*H.pylori* EIA (IgG) (Roche Pharmaceuticals & Chemicals Ltd. Hong Kong) was used for serologic examination. The procedures and calibration were performed according to the instruction manual. Antibody levels greater than 40 U/ml were considered positive.

Endoscopic examination

Gastrofiberscopic examinations were undertaken in seventy children out of one hundred and two sero-positive children. None of these children complained of abdominal discomfort or pain before or on the day of endoscopy. All endoscopies were performed by one pediatric endoscopist. The mucosal status and presence of mucosal nodularity were recorded. Three pieces of biopsy were taken from the gastric antrum within 1 to 2 cm of the pylorus.

Specimens were allotted to 1) rapid urease test (CLO test of Delta West Pty Ltd., Bentley, Western Australia), 2) culture for *H.pylori*, and 3) histologic examination.

Histology

The biopsies were fixed in 10 % neutral formalin and were routinely processed. All sections were stained with hematoxylin and eosin, and were interpreted by one pathologist who was unaware of the serologic and endoscopic results.

Sections were evaluated for the histological grading of gastritis according to the following classification: Grade 0; normal histology, Grade 1; slight increase of mononuclear cells in the lamina propria of the gastric mucosa, but within normal limits, Grade 2; increase of mononuclear and polymorphonuclear cells in the lamina propria of the gastric mucosa; Grade 3 ; increase of mononuclear and polymorphonuclear cells in the lamina propria of the gastric mucosa, presence of intraepithelial polymorphonuclear cells (Whitehead, 1985). The biopsies having features consistent with grades 2 and 3 were regarded as histologic gastritis, whereas grades 0 and 1 were regarded as morphologically normal.

The presence of *H.pylori* were studied from sections stained with modified Giemsa. Whole biopsy specimens were examined for the presence of typical rod-like organisms in the mucus overlying the mucosa.

Microbiology

One biopsy specimen was put in sterile saline 0.9 % and then transported to the microbiology department for culture. The culture was regarded as positive when typical colonies of the *H.pylori* were seen and the colonies were positive in urease, catalase and oxidase. If the culture did not show growth after seven days it was regarded as negative.

Statistics

Logistic regression was applied to evaluate the correlation between *H.pylori* IgG titer and the grade of gastritis.

RESULTS

One hundred and two children were positive for *H.pylori* in serologic studies(Table 1). The mean of antibody titer in positive children was 96.39 U/ml (Standard deviation : 57.84, Range : 41-275 U/ml).

Table 1. Number of children tested.

Age	Number	Serology positive	Endoscopy performed
13	100	29	18
14	100	33	22
15	100	40	30
All	300	102	70

Table 2. Histologic gastritis in endoscoped children.

Grade of gastritis*	No. of children Endoscoped	*H. pylori* positive**	*H. pylori* negative
0	1	0	1
1	4	2	2
2	10	6	4
3	55	55	0
No. of children	70	63	7

*Gastritis (+) : Grade 2 and 3.
Gastritis (−) : Grade 0 and 1.
** *H. pylori* positive : 1. *H. pylori* was cultured from biopsy tissue, or
2. CLO test was positive and *H. pylori* was seen in the tissue

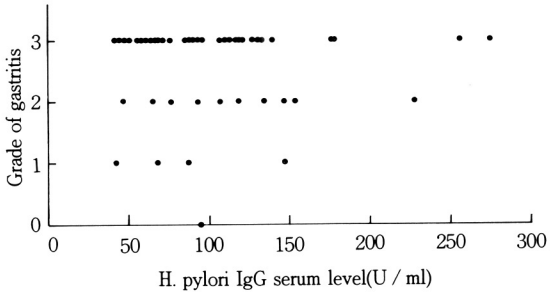

Fig. 1. Lack of correlation between *H.pylori* IgG serum level and severity of gastritis.

Among 102 serology positive children, 70 children underwent endoscopies with tissue biopsy.

The criteria for positive *H.pylori* infection were : 1) *H.pylori* was cultured from tissue ; or 2) CLO test was positive and *H.pylori* was simultaneously seen in modified Giemsa stained tissue. Among 70 children who received endoscopic examination, 63 (90 %) were positive for *H.pylori* infection and seven children were negative.

On histologic examination, sixty-one children had gastritis among sixty-three *H.pylori* positive children (96.8 %). Of note is that four children with gastritis were among seven *H.pylori* negative children (57.1 %)(Table 2).

Nodularities were noted in fifty-five children (78.6 %). Of those fifty children were *H.pylori* infected and five were not.

The *H.pylori* IgG antibody titers did not correlate with the grade of gastritis (Fig. 1). Also, the neutrophil counts in the gastric mocusa did not correlate with antibody titer. Therefore, it appears that *H.pylori* antibody corresponds to gastric infection, but does not necessarily indicate the severity of gastritis.

DISCUSSION

There have been some reports that serologic examination is useful to diagnose *H.pylori* infection in children (Evans et al., 1989 ; Giacomo et al., 1990 ; Thomas et al., 1990 ; Blecker et al., 1993). Several serologic test kits are commercially available to diagnose *H.pylori* infection (Taha et al., 1993). Their excellent sensitivity, specificity, low cost, and acceptability support their clinical use to distinguish individuals who have been exposed to the organism from the general population (Evans et al., 1989 ; Pena et al., 1989 ; Mertz et al., 1991 ; Sobala et al., 1991 ; Rocha et al., 1993).

Does the serology reflect the severity of gastritis? The serum level of antibody may reflect the local immunity of the gastric mucosa. In general, there is no good correlation between endoscopic mucosal appearance and the presence of *H.pylori* in children (Drumm et al., 1987a ; Loffeld et al., 1988).

Some studies reveal that there is not a quantitative association between *H.pylori* and gastritis (Drumm et al., 1987b ; Loffeld et al., 1988 ; Bayerdorffer et al., 1989 ; Villako et al., 1990). It is known that histologic gastritis is common in healthy asymptomatic individuals and is strongly associated with the presence of *H.pylori* (Jones et al., 1984 ; Barthel et al., 1988 ; Dooley et al., 1989 ; Hassall and Dimmick, 1991). However, the subjects in our study were asymptomatic healthy children. We noticed that the presence of gastritis was relatively common and was associated with *H.pylori* infection even in asymptomatic healthy children. However, we found that the *H.pylori* IgG titer did not correlate with the histologic grade of gastritis.

The gastric mucosa underlying collections of *H.pylori* almost always shows a combination of inflammation and epithelial changes. *H.pylori* gastritis elicits both a local and a systemic immune response as a chronic infection. These responses are the bases for serologic diagnosis of gastric *H.pylori* infection. Bacterial load is not the only potential determinant of mucosal injury ; others may include host response and strain differences. Factors related to the host (age, state of immune competence) and the host-organism interaction (duration of infection, bacterial load) may also influence antibody formation. This

means that humoral immune response does not necessarily reflect the degree of local mucosal response. Therefore the serologic examination is useful for diagnosis of *H.pylori* infection, and for the presence of gastritis. But the severity of gastritis may not be assessed by the level of IgG titer against *H.pylori*.

The dominant mucosal immunoglobulin is IgA. Serum IgA to *H.pylori* is also known to be useful for diagnosis (Veenendaal et al., 1991 ; Kosunen et al., 1992). Therefore serum IgA may be a better indicator for the severity of gastritis than IgG. So far, there have been no studies that answer this question.

Interestingly, we noted histologic gastritis, though mild, in *H.pylori* negative children. Generally it is considered that primary gastritis is usually associated with *H.pylori* in children. Since in this study we used rigid criteria for *H.pylori* infection, a *H.pylori* negative child may have had *H.pylori*. This could have produced the above finding.

The gastric nodularities, some documented to be characteristic in child *H.pylori* infection, were also noted in *H.pylori* negative children in this study (Bujanover et al., 1990 ; Hassall and Dimmick, 1991). It is not easy to perform gastric endoscopy in healthy children, and again the criteria for *H.pylori* infection in this study were strict. Thus, the above *H.pylori* negative children might have been *H.pylori* positive. Certainly, more studies of *H.pylori* infection in children will be needed to interpret gastric nodularity in *H.pylori* negative children.

Our results suggest that serum *H.pylori* IgG titer does not indicate the severity of *H.pylori* related gastritis. Gastroscopy and tissue biopsy are still the best methods to grade *H.pylori* gastritis with accuracy.

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REFERENCES

Barthel JS, Everett ED. *Diagnosis of Campylobacter pylori infections : the "gold standard" and the alternatives. Rev Infect Dis 1990 ;12(suppl 1) : s107-14.*

Barthel JS, Westblom TU, Havey AD, Gonzalez F, Everett ED. *Gastritis and Campylobacter-pylori in healthy, asymptomatic volunteers. Arch Intern Med 1988 ;148 : 1149-51.*

Bayerdorffer E, Oertel H, Lehn N, Kasper G, Mannes GA, Sauerbruch T, Stolte M. *Topographic association between active gastritis and Campylobacter pylori colonisation. J Clin Pathol 1989 ;42 : 834-9.*

Blecker U, Hauser B, Lanciers S, Peeters S, Suys B, Vandenplas Y. *The prevalence of Helicobacter pylori-positive serology in asymptomatic children. J Pediatr Gastroenterol Nutr 1993 ;16 : 252-6.*

Bujanover Y, Konikoff F, Baratz M. *Nodular gastritis and Helicobacter pylori. J Pediatr Gastroenterol Nutr 1990 ;11 : 41-4.*

Dooley CP, Cohen H, Fitzgibbons PL, Bauer M, Appleman MD, Perez Perez GI, Blaser MJ. *Prevalence of Helicobacter pylori infection and histologic gastritis in asymptomatic persons. N Engl J Med 1989 ;321 : 1562-6.*

Drumm B, O' Brien A, Cutz E, Sherman P. *Campylobacter pyloridis-associated primary gastritis in children. Pediatrics 1987 ;80 : 192-5. a.*

Drumm B, Sherman P, Cutz E, Karmali M. *Association of Campylobacter pylori on the gastric mucosa with antral gastritis in children. N Engl J Med 1987 ;316 : 1557-61. b.*

Evans DJ Jr, Evans DG, Graham DY, Klein PD. *A sensitive and specific serologic test for detection of Campylobacter pylori infection. Gastroenterology 1989 ;96 : 1004-8.*

Giacomo CD, Fiocca R, Villani L, Lisato L, Licardi G, Diegoli N, Donadini A, Maggiore G. *Helicobacter pylori infection and chronic gastritis : clinical, serological, and histologic correlations in children treated with amoxicillin and colloidal bismuth subcitrate. J Pediatr Gastroenterol Nutr 1990 ;11 : 310-6.*

Glassman MS, Dallal S, Berezin SH, Bostwick HE, Newman LJ, Perez Perez GI, Blaser MJ. *Helicobacter pylori-related gastroduodenal disease in children diagnostic utility of enzyme-linked immunosorbent assay. Dig Dis Sci 1990 ;35 : 993-7.*

Hassall E, Dimmick JE. *Unique features of Helicobacter pylori disease in children. Dig Dis Sci 1991 ;36 : 417-23.*

Jones DM, Lessells AM, Eldridge J. *Campylobacter like organisms on the gastric mucosa : culture, histological, and serological studies. J Clin Pathol 1984 ;37 : 1002-6.*

Karttunen T, Niemela S, Lehtola J. *Helicobacter pylori in dyspeptic patients : quantitative association with severity of gastritis, intragastric pH, and serum gastrin concentration. Scand J Gastroenterol 1991 ;26(suppl 186) : 124-34.*

Kosunen TU, Seppala K, Sarna S, Sipponen P. *Diagnostic value of decreasing IgG, IgA, and IgM antibody titers after eradication of Helicobacter pylori. Lancet 1992 ;339 : 893-5.*

Loffeld RJLF, Potters HVPJ, Arends JW, Stobberingh E, Flendrig JA, van Spreeuwel JP. *Campylobacter associated gastritis in patients with non-ulcer dyspepsia. J Clin Pathol 1988 ;41 : 85-8.*

Mertz H, Lafrance N, Kafonek D, Yardley J, Hendrix T. *Diagnosis of Campylobacter pylori gastritis. Dig Dis Sci 1991 ;36 : 1-4.*

Pena AS, Endtz HP, Offerhaus GJ, Hoogenboom Verdegaal A, Duijn W, Vargas N, Hartog G, Kreuning J, Reyden J, Mouton RP. *Value of serology (ELISA and immunoblotting) for the diagnosis of Campylobacter pylori infection. Digestion 1989 ;44 : 131-41.*

Rocha GA, Queiroz DMDM, Mendes EN, Carvalho ASTD, Oliveira AMRD, Moura SBD. *Serodiagnosis of Helicobacter pylori infection in children by an indirect immunofluorescence test. J Pediatr Gastroenterol Nutr 1993 ;16 : 247-51.*

Satoh K, Kimura K, Yoshida Y, Kasano T, Kihira K, Taniguchi Y. *A topographical relationship between Helicobacter pylori and gastritis : quantitative assessment of Helicobacter pylori in the gastric mucosa. Am J Gastroenterol 1991 ;86 : 285-91.*

Sobala GM, Crabtree JE, Pentith JA, Rathbone BJ, Shallcross TM, Wyatt JI, Dixon MF, Heatley RV, Axon AT. *Screening dyspepsia by serology to Helicobacter pylori. Lancet 1991 ;338 : 94-6.*

Taha AS, Reid J, Boothmann P, Gemmell CG, Lee FD, Sturrock RD, Russell RI. *Serological diagnosis of Helicobacter pylori - evaluation of four tests in the presence or absence of non-steroidal anti-inflammatory drugs. Gut 1993 ;34 : 461-5.*

Thomas JE, Whatmore AM, Barer MR, Eastham EJ, Kehoe MA. *Serodiagnosis of Helicobacter pylori infection in childhood. J Clin Microbiol 1990 ;28 : 2641-6.*

Veenendaal RA, Pena AS, Meijer JL, Endtz HP, Est MM, Duijn W, Eulderink F, Kreuning J, Lamers CB. *Long term serological surveillance after treatment of Helicobacter pylori infection. Gut 1991 ;32 : 1291-4.*

Villako K, Maards H, Tammur R, Keevallik R, Peetsalu M, Sipponen P, Kekki M, Siurala M. *Helicobacter (Campylobacter) pylori infestation and the development and progression of chronic gastritis : results of long-term follow-up examinations of a random sample. Endoscopy 1990 ;22 : 114-7.*

Whitehead R. *Mucosal biopsy of the gastrointestinal tract. In Bennington JL, ed. Major Problems in Pathology. Philadelphia : WB Saunders, 1985.*