Comparative evaluation of gastric mucosa morphological changes in children and adults with positive IgG antibodies to Helicobacter pylori

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Abstract

Purpose: Helicobacter pylori colonization of gastric epithelium causes a local and systemic, cellular and humoral immune response. Despite this immune response involvement in the infection, its elimination from the organism does not take place and the process usually becomes chronic.

The purpose of the study was to establish the prevalence of gastric mucosa inflammation in children and adults with serum positive anti-Helicobacter pylori antibodies IgG.

Material and methods: The study included 171 patients comprising 109 (63.7%) children and 62 (36.3%) adults with IgG positive titre against Helicobacter pylori, who were qualified to the study basing on epidemiological examinations estimating the prevalence of Helicobacter pylori infection in the population of north-eastern Poland living in the country, town and city. All patients reported dyspeptic symptoms. The evaluation was performed basing on the morphological (endoscopy) and histopathological examinations estimating the changes in gastric mucosa of these patients.

Results: The evaluation of antrum and corpus gastric mucosa proved normal gastric mucosa in 34 children (31.1%) and 10 adults (16.1%) with positive IgG antibodies against Helicobacter pylori. The evaluation of the severity showed the predominance of moderate inflammation within corpus in children (37.6%) and marked inflammation in adults (45.1%).

Conclusions: The concentration of IgG antibodies against Helicobacter pylori in both groups was highest in patients with marked antrum gastric mucosa inflammation.

Key words: Helicobacter pylori, gastric mucosa inflammation, children, adults.

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Introduction

Helicobacter pylori infection causes gastric mucosa inflammation in both children and adults. Neutrophilic activation is an important feature of this inflammation [1,2]. Leukocytes are found in the pyloric part and the corpus of the stomach. They are located in the lamina propria of the mucosa, within the epithelium (especially at the neck of the nodules) and in the lumen of foveoli, where "foveolus abscesses" can be formed. The density of neutrophils within the epithelium is correlated with the extent of mucosa damage and the intensification of Helicobacter pylori infection [3]. Neutrophils are very sensitive indicator of the presence or absence of Helicobacter pylori and disappear in few days after its eradication. If the infiltrates are still found in the sample obtained after treatment and no bacteria are discovered, special staining should be applied to detect the bacteria [4,5].

However, lymphocyte aggregates are the most characteristic histological feature of gastric mucosa inflammation caused by this strain of bacterium. They are found in 100% of Helicobacter pylori infection cases. Their equivalent in a macroscopic picture is nodularity of the antral mucosa. Moreover, less or more diffused chronic infiltrate, which can differ (even by two grades) between the antrum and corpus, is observed in most of gastric mucosa samples in the histopathological examination [6].

The purpose of the study was to establish the prevalence of gastric mucosa inflammation in children and adults with serum positive IgG titre against Helicobacter pylori basing on the morphological (endoscopy) and histopathological examinations of changes in gastric mucosa of these patients [7].

Table 1. Macroscopic picture of changes in gastric mucosa, the results of urease test and the level of IgG antibodies against Helicobacter pylori in the patients examined.

Children							Adults					
	Present		IgG	Absent		IgG	Present		IgG	Absent		IgG
	N	%	U/ml	N	%	U/ml	N	%	U/ml	N	%	U/ml
Macroscopic picture	43	39.4	164.8	66	60.5	125.8	27	43.5	136.9	33	53.2	95.7
Urease test	65	59.6	157.4	44	40.3	117.3	39	62.9	132.0	23	37.0	85.7
Lymphatic follicles	65	59.6	186.3	44	40.3	132.9	19	30.6	157.5	40	64.4	110.0

Material and methods

The study was performed in 171 patients including 109 (63.7%) children and 62 (36.3%) adults with positive anti-Helicobacter pylori antibodies IgG chosen in epidemiological examinations estimating the prevalence of Helicobacter pylori in the population of north-eastern Poland in the country, town and city. After having established serum positive IgG, all patients underwent endoscopy. They also reported dyspeptic symptoms.

The evaluation of specific IgG antibody concentration was carried out by means of the screening quantitative test of Recom Well Helicobacter IgG of MIKROGEN GmbH firm to detect and identify directly serum IgG against Helicobacter pylori. The antigens used in this test are obtained by genetic engineering; they are optimal antigens without any impurities and proteins causing cross reactions. The use of CagA recombinant antigen enhances a diagnostic value of the test. The titre above 24 U/ml is regarded as positive.

The endoscopic and histological estimation of gastric mucosa was performed according to the Sydney Classification [8]. The urease test was made during endoscopy (CLO--test = H. pylori).

The rapid urease test for Helicobacter pylori detection in gastric bioptates was made using the kits produced and distributed by The Institute of Food and Nutrition in Warsaw.

The biopsy specimens of gastric mucosa obtained from the antepyloric area were placed on the blotting – paper dripped with distilled water from the firm kit. The change of color from yellow to amaranth was considered as the result indicating explicitly Helicobacter pylori infection.

The histological examination of antrum and corpus gastric mucosa was performed according to the Sydney System, evaluating the severity of Helicobacter pylori infection and for grading the gastritis (staining with hematoxylin and eosin (H-E) and modified Giemsa).

The endoscopic examinations of the upper part of the alimentary tract in children and adults, who due to clinical indications and with positive IgG against Helicobacter pylori agreed to gastroscopy, were carried out in the Endoscopic Laboratory of the III Department of Children's Diseases of the Medical University of Białystok.

Statistical analysis was performed using The Statistica 6 package. Student-t test for paris, Student-t for two mean values, median test were used. The tests were selected depending on conditions determined by the obtained values of the parameters.

Results

In our study, the analysis of the endoscopic picture of children with positive IgG showed macroscopic changes in 39.4% of children. A similar percentage was observed in adults (43.5%).

Positive urease test was found in 59.6% of children and 62.9% of adults. Lymphatic follicles were observed in 59.6% of children and 30.6 % of adults (*Tab. 1*).

Normal gastric mucosa of antrum and corpus was found in 34 children (31.1%) and 10 adults (16.1%) with positive IgG antibodies in serum.

The estimation of the severity of the inflammation (according to the Sydney System) in corpus showed the predominance of moderate degree – in children (37.6%) and marked degree – in adults (45.1%).

The estimation of the severity of the inflammation in antrum revealed the predominance of marked degree both in adults and children (*Tab. 2*).

The marked inflammation in antrum was found in both children (44.9%) and adults (36.7%). The moderate inflammation in corpus was higher in children than in adults, in whom the marked mucosa inflammation predominated – 45% of all examined (*Tab. 3*).

Discussion

Gastric mucosa inflammation (gastritis) is an acute condition of Helicobacter pylori infection both in children and adults [9]. In adults, the infection may be accompanied by primary peptic ulcer and very rarely by MALT lymphoma [10,11]. In children, there are no such disorders in the course of Helicobacter pylori infection, frequently, despite the infection, no clinical symptoms are reported.

Helicobacter pylori infection causes initially an acute inflammatory process in gastric mucosa, which after 3-4 weeks changes into a chronic process. In the acute stage of the infection, infiltrates of polymorphonuclear cells in the lamina propria, degenerative changes and intensified epithelium shedding can be observed. The spontaneous eradication of bacteria and the regression of inflammatory symptoms can take place exceptionally. However, in most cases, gastric mucosa inflammation continues and becomes chronic.

In the endoscopic examinations, that accompany Helicobacter pylori infection, are found normal gastric mucosa, or with eryhtema, erosions, ulceration, and antrum gastric mucosa

Table 2. The incidence of histopathological changes of corpus and antrum gastric mucosa in the patients examined.

CORPUS								
Children					Adults			
Hist-path changes	inflammation		activity		inflammation		activity	
	N	%	N	%	N	%	N	%
No changes	34	31.2	34	31.2	10	16.2	10	16.2
Mild	47	43.1	5	4.6	28	45.1	4	6.4
Moderate	26	23.8	41	37.6	19	30.0	20	32.3
Marked	2	1.8	29	26.6	5	8.0	28	45.1
ANTRUM								
Children					Adults			
Hist-path changes	inflammation		activity		inflammation		activity	
	N	%	N	%	N	%	N	%
No changes	34	31.2	34	31.2	9	14.5	9	14.5
Mild	6	5.5	4	3.7	6	9.6	4	6.4
Moderate	38	34.8	22	20.2	26	41.9	9	14.5
Marked	31	28.4	49	44.9	21	33.8	40	64.5

Table 3. Severity of corpus and antrum gastric mucosa inflammation and the level of IgG against Helicobacter pylori in the groups examined*.

Hist-path changes	CORPUS					
	Children			Adults		
	N	%	IgG U/ml	N	%	IgG U/ml
No Changes	34	31.2	110.5	10	16.1	52.4
Mild	5	4.6	139.3	4	6.4	37.2
Moderate	41	37.6	148.6	20	32.2	131.2
Marked	29	26.6	167.2	28	45.1	131.7
Hist-path changes	ANTRUM					
	Children			Adults		
	N	%	IgG U/ml	N	%	IgG U/ml
No changes	34	31.2	110.5	9	14.5	53.8
Mild	4	3.6	129.4	4	6.4	39.3
Moderate	22	20.1	141.6	9	14.5	118.3
Marked	49	44.9	163.4	40	36.7	132.0

* according to Sydney Classification

nodularity, especially in children [9,12,13]. If Helicobacter pylori infection is accompanied by duodenal ulcer in children, disseminated nodularity in antrum is observed. However, when Helicobacter pylori causes only primary gastric mucosa inflammation, nodularity is observed only in 50-60% of cases [14]. The authors quoted, observed no nodularity in the case of duodenal ulcer without co-existing Helicobacter pylori infection and in none of cases without ulceration and Helicobacter pylori infection. They based their observation on the material of 5000 children. In our earlier studies, nodularity of antrum occurred in 61.1% of children with Helicobacter pylori-connected gastric mucosa inflammation [7]. When nodularity is not visible during the endoscopic examination, blood exuding during biopsy seems to be helpful. It fuses with mucosa into 'a carpet of nodules'. This method is called hematochromendoscopy [14].

In the physiological conditions, the lymphoid tissue (lymphoid follicles) are not found in gastric mucosa [8].

The elements of the lymphoid tissue are produced by an inflammatory reaction associated with Helicobacter pylori infection. It was proved that in these follicles, Helicobacter pylori activated T lymphocytes, which stimulated B cell proliferation. Lymphoid follicles were no found in any other gastric mucosa inflammation [8].

Gastric mucosa stimulation by Helicobacter pylori antigens leads to its inflammation, which is characterized by the infiltration of neutrophils with lymphocytes and plasma cells comprising epithelium and mucosal membranes in the initial stage of the inflammation. Later lymphoidal cells form the follicle structures. The absence of M cells in gastric mucosa proves that there is no direct intake of antigens (including Helicobacter pylori antigens) in the stomach [15].

On the other hand, the epithelial cells in the inflamed mucosa express the antigens of MHC class II and the antigens of B7-1 and B7-2 taking part in the antigen presentation

[15,16]. Thus, local lymphoidal cells of mucosa take part in the effector activity of the immune response producing antibodies and cytokines. The presence of lymphoid follicles is a proof of this phenomenon and they are present in 60% of children and 30% of adults infected with Helicobacter pylori in our material. Lymphoid follicles were found in patients with moderate and marked antrum gastric mucosa inflammation.

Nodularity of antrum seen in the endoscopic examination can be observed for months and years after Helicobacter pylori eradication and ulcer healing. The absence of endoscopic changes in about 50% of children with Helicobacter pylori infection resulting from a focal mucosa inflammation indicates that the biopsies must be taken from the antrum, cardia and corpus as an integral part of an examination [17-19].

In our study, the analysis of the endoscopic picture of children and adults examined showed macroscopic changes in a similar percentage in both children and adults. A significant difference was found in the prevalence of antrum nodularity in children and adults (*Tab. 1*). Nodularity of antrum was accompanied by an increase in the serum concentration of IgG against Helicobacter pylori in children and adults examined. The highest mean serum concentration of specific IgG was observed in children (*Tab. 1*).

The density of inflammatory infiltrate was proved to correlate with the intensification and extent of bacterium colonization. Helicobacter pylori invades mainly the surface of gastric epithelium and is found in the highest quantity in the epithelium of the opening of gastric nodules. The generative cell exposure of the isthmus of gastric nodules to an inflammatory infiltrate may cause cell damage and result in intestinal metaplasia and /or nodule atrophy. The presence of neutrophils always indicates active chronic gastritis.

The localization and intensification of gastric mucosa inflammation in the course of Helicobacter pylori infection are changeable and always affects antrum, next cardia, and later corpus [17].

In our study, normal gastric mucosa of antrum and corpus was found in 34 children (31.1%) and 10 adults (16.1%) with positive IgG antibodies in serum.

The estimation of the severity of the inflammation (according to the Sydney System) in corpus showed the predominance of moderate degree – in children (37.6%) and marked degree – in adults (45.1%).

The estimation of the severity of the inflammation in antrum revealed the predominance of marked degree both in adults and children (*Tab. 2*).

Antigen-specific and nonspecific response of the immune system of gastric mucosa due to Helicobacter pylori infection determines the development of its inflammation. Both types of an immune response may take part in controlling the infection and at the same time they may contribute to gastric mucosa damage.

The serum concentration of specific IgG for Helicobacter pylori was highest in patients with marked antrum inflammation. The medium value of IgG against Helicobacter pylori in children (163 U/ml) was higher than its medium values in adults (132 U/ml) with marked antrum inflammation. The mean value of IgG in children with normal mucosa was 110.5 U/ml; in adults – it was lower and equaled 53.8 U/ml.

These mean values of IgG seem to indicate that generalized humoral response of the developmental age in Helicobacter pylori infection is more potent than in adults. In spite of the higher antibody production in Helicobacter pylori infections, it can often become chronic. The access of antibodies to infectious foci formed by Helicobacter pylori rods penetrating mucosal membrane may be hindered [20].

A generalized humoral response is a systemic response to superficial Helicobacter pylori antigens and cannot be a reliable indicator of active Helicobacter pylori infection. Tests for determining serum IgG concentration cannot be used to estimate the effectiveness of bacterium eradication, either, since the level of these specific antibodies is maintained for a long time after eradication.

The histological evaluation of mucosa inflammation activity of antrum and corpus in children and adults is presented in *Tab. 3*.

The marked inflammation in antrum was found in both children (44.9%) and adults (36.7%). The moderate inflammation in corpus was higher in children than in adults, in whom the marked mucosa inflammation predominated (45% of all examined).

A higher increase in both serum IgG level and in a quantity of follicles in percentages in children seems to indicate a stronger immune response to Helicobacter pylori infection in children than in adults.

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