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CONFLICT OF INTEREST: NONE DECLARED

ORIGINAL PAPER

Childhood and Coress Model of Carcinogenesis

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Introduction: In the last fifty years the incidence of gastric cancer in developed countries is a constant trend, but mortality in all countries remains at the same level and ranks second behind lung cancer. In the case of gastric cancer has a far more important the role the early diagnosis compared to prevention. Material and methods: The sample included 200 subjects aged 7-18 years treated at the Pediatric Clinic, University Clinic Tuzla and Pediatric Clinic and the Clinic for Child Surgery of Clinical Center of Sarajevo University who had endoscopic and histologically verified gastritis. The method of processing the tissue preparations of histologic sections of paraffin-fixed and paraffin tissue by hematoxylin-eosin method and Helicobacter pylori, using Giemsa. Results and discussion: Pathological analysis of the sample of patients with gastritis found that in 91% of patients had chronic superficial gastritis, while in 9% of patients were found atrophic changes, with or without intestinal metaplasia. Atrophic changes with or without intestinal metaplasia was found in 10.2% of H. pylori-positive patients with gastritis. The same analysis in a significant percentage of 5.7% of H. pylori-negative patients was atrophic changes, with or without intestinal metaplasia. Analysis of activity of the inflammatory process, we have found that the symptoms matched a statistically significant percentage (86.5%) with the active phase of the disease, which speaks against thinking that H. pylori infection is asymptomatic condition, which is often cited in the literature. Conclusion: Gastric mucosal lesion caused H. pylori infection is a reversible process and the eradication of this infection not only stops the activity of the inflammatory process, but also restores the mucous membranes. Eradication leads to a significant drop in the incidence of recurrence of gastritis and peptic ulcer disease, and can lead to prevention of malignant disease in 70-80% of cases, even, and perhaps more. Key words: childhood, Coress model, carcinogenesis.

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1. INTRODUCTION

In the last fifty years the incidence of gastric cancer in developed countries is a constant trend, but mortality in all countries remains at the same level and ranks second behind lung cancer. In the case of gastric cancer has a far more important the role the early diagnosis compared to prevention. Gastric cancer is localized at the antrum, corpus and cardia. While the incidence of cancer in the antrum and corpus continued to decline in developed countries, at the same time cardia cancer has continue with slow increasing trend.

Numerous articles show the importance of Helicobacter pylori in the etiology of gastric cancer (1). Gastric cancer (GC) is the most common malignant neoplasm of the gastrointestinal tract. The first hints of a connection between H. pylori infection and GC gave Marshall in 1983. The International Group for the study of cancer has indicated an increased risk of GC in patients with H. pylori infection and the World Health Organization in 1994 classified this microorganism was as the carcinogen (2). Younger people with H. pylori infection have a higher risk of GC then elderly (3). It is now recognized that chronic atrophic gastritis with intestinal metaplasia represents susceptibility to intestinal type of GC (4). It is possible that chronic inflammation caused by H. pylori leads to genetic changes and the development of diffuse-type GC, without developing severe atrophic changes and intestinal metaplasia (5,6).

Proper eradication of Helicobacter pylori was proposed by Maastricht study group (7). In this way, further changes in the gastric mucosa can be stopped, and prevent cancer. H. pylori infection occurs exclusively also in childhood and if left untreated lasts for decades and possibly lifetime, leading to increasing damage to the stomach lining.

According Coress model of carcinogenesis (8) it is necessary to pass 2-3 decades from initial gastric mucosal epithelial lesions to cancer. The sequence of events in the gastric mucosa is as follows: acute gastritis, chronic atrophic

gastritis, intestinal metaplasia, epithelial dysplasia, carcinoma of the stomach. Intestinal metaplasia is a change in the gastric mucosa, which have characteristics of small bowel mucosa. It represents most prominent change in the course of chronic atrophic gastritis and is modeled according to the model of carcinogenesis change as of utmost importance. It follows that the era when childhood Helicobacter pylori infection can be prevented or diagnosed and treated (9) and that eradication of this organism in adults will not be particularly effective, because the inflammation is already present for decades and probably passed most of Coress path of chronic gastritis through mucosal atrophy to intestinal metaplasia and dysplasia (10).

Association between Helicobacter pylori infection and gastric cancer located in the event of changes in the gastric antrum and corpus, and cardia cancer this association has not been proven.

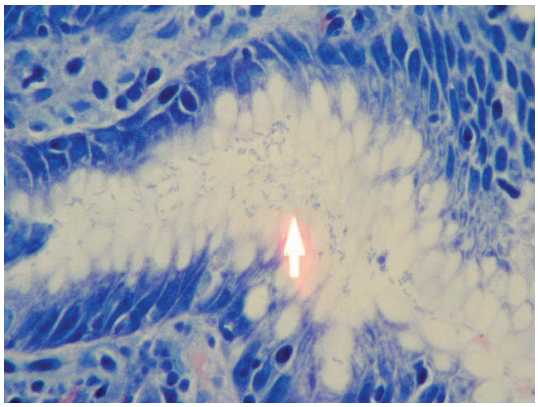

Figure 1. H. pylori positive chronic gastritis (modified Giemsa, 400x)

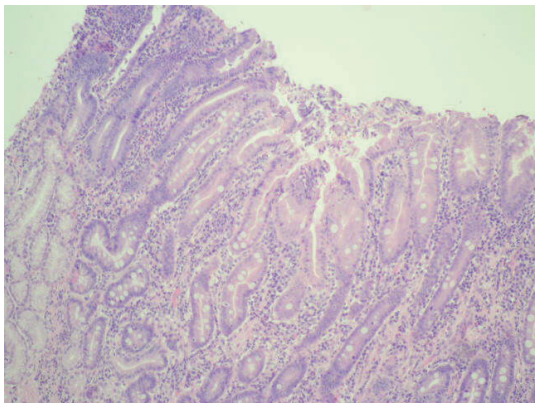

Figure 2. Chronic gastritis with intestinal metaplasia (active phase), (HE, 250X)

We must resolve two important questions. Does eradication of Helicobacter pylori infection can, as with peptic ulcer disease, which is also a multifactorial disease, prevent gastric cancer? Does eradication of this organism can lead to a significant drop in the incidence of gastric cancer?

Eradication leads to a significant drop in the incidence of and it can lead to the prevention in 70-80% of cases and possibly more.

All this leads us to the further testing and even better noninvasive diagnosis and treatment of Helicobacter pylori infection in early age, which can lead to even more significant success.

2. GOALS

- Analyze the histopathological findings and the degree of activity of the inflammatory process.
- Conduct an analysis of the age of the sample.
- Analyze the type of gastritis in children under Coress model of carcinogenesis.
- Identify epidemiologic analysis of H. pylori infection prevalence in the study group patients.

3. MATERIAL AND METHODS

The sample included 200 subjects aged 7-18 years treated at the Gastroenterology Department and Department of Child Surgery of Pediatric Clinic, University Clinic Tuzla, Pediatric Clinic and the Clinic for Child Surgery, Clinical Center of Sarajevo University who had endoscopic and histologically verified gastritis. All patients with signs of dyspeptic syndrome according to the diagnostic algorithm the gastroscopy and biopsy was taken on gastric mucosal pH and Giemsa for H. pylori.

The method of processing the tissue preparations of histologic sections of paraffin-fixed and paraffin tissue by hematoxylin-eosin method and Helicobacter pylori, using Giemsa.

Assessment of the activity of the inflammatory process has been carried out on the basis of the Sydney classification parameters that gave the interpretation of histopathological findings.

4. RESULTS

Histopathological analysis of the sample of patients with gastritis found that 182 (91%) patients had a chronic superficial gastritis and in 18 (9%) patients had atrophic changes with or without intestinal metaplasia.

Histopathological analysis of the sample found that H. pylori-positive patients with gastritis are present in 132 (89.8%) cases patients had a chronic superficial gastritis, and in 15 (10.2%) patients had atrophic changes with or without intestinal metaplasia.

Histopathological analysis of the sample H. pylori-negative patients with gastritis in 50 (94.3%) patients there were chronic superficial gastritis and 3 (5.7%) patients had atrophic changes with or without intestinal metaplasia.

Also there is a statistically significant lower number of patients with atrophic changes to the pattern of H. pylori-positive patients $\chi 2=112.358$; $p=0.0001$.

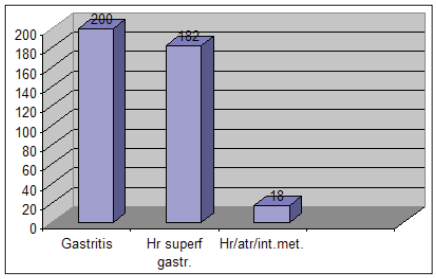

Figure 3. Histopathologic analysis of the sample

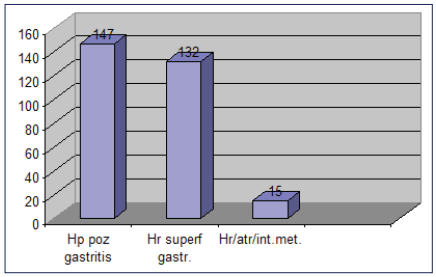

Figure 4. Histopathologic analysis of the H. pylori positive gastritis

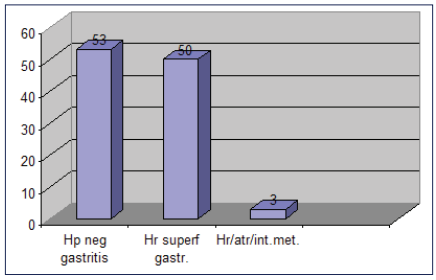

Figure 5. Histopathologic analysis of the H. pylori negative gastritis

Received: September 18th 2012 • ORIGINAL PAPER

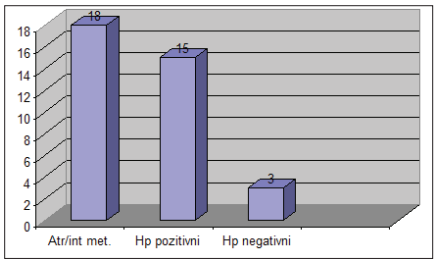

Figure 6. Etiological analysis of atrophic gastritis and gastric intestinal metaplasia

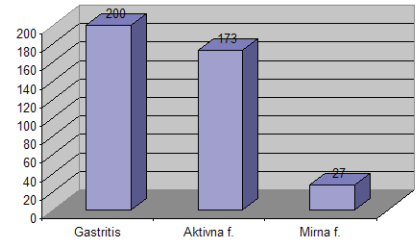

Figure 7. Analysis of the activity of the inflammatory process in patients

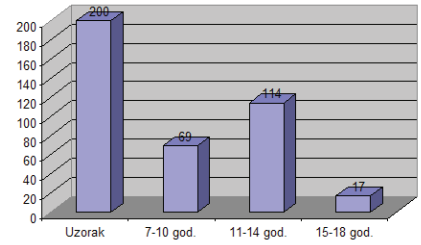

Figure 8. Analysis of the age distribution of the sample

Since atrophic gastritis and intestinal metaplasia are deeper lesions or mucosal route of carcinogenesis, that these lesions present in children as well as the fact that in most cases of H. pylori-positive patients confirms the fact that H. pylori infection is the cause of chronicity.

Of the 18 patients with atrophic gastritis with or without intestinal metaplasia were 15 (83.3%) H. pylori-positive and three (16.7%) H. pylori negative patients.

This suggests that Helicobacter pylori infection cause deep lesions in the gastric mucosa, precancerous in this case.

Of the 200 patients who had endoscopic and histologic gastritis diagnosed in 173 (86.5%) patients and was active and in only 27 (13.5%) patients were in the quiet phase, suggesting that the patient's symptoms coincide with phase of activity of inflammatory processes.

Analysis of age distribution of patients with gastritis found that in age between 7 and 10 years was 69 (24.5%) children, aged between 11 and 14–114 (57%) of children and between 15 and 18 years 17 (8.5%) children. $\chi 2=52.368$; $p=0.001$.

It can be concluded that a statistically significant predisposed from gastritis and proportional with age up to puberty, noting a sharp drop toward adolescence.

5. CONCLUSIONS

Pathological analysis of the sample of patients with gastritis found that in 91% of patients had chronic superficial gastritis, while in 9% of patients were found atrophic changes, with or without intestinal metaplasia.

Given that this is a pre-cancerous lesions in children are bound to further intensive monitoring to prevent gastric cancer. Coress carcinogenesis model should begin in childhood.

Atrophic changes with or without intestinal metaplasia was found in 10.2% of H. pylori-positive patients with gastritis. The same analysis in a significant percentage of 5.7% of H. pylori-negative patients was atrophic changes, with or without intestinal metaplasia. Which does not exclude the possibility that these lesions are preceded by H. pylori infection, which is explained by the previous loss of the conditions for further survival?

Analysis of activity of the inflammatory process, we have found that the symptoms matched a statistically significant percentage (86.5%) with the active phase of the disease, which speaks against thinking that H. pylori infection is asymptomatic condition, which is often cited in the literature.

Gastric mucosal lesion caused H. pylori infection is a reversible process and the eradication of this infection not only stops the activity of the inflammatory process, but also restores the mucous membranes. Eradication leads to a significant drop in the incidence of recurrence of gastritis and peptic ulcer disease, and can lead to prevention of malignant disease in 70-80% of cases, even, and perhaps more.

All this leads us to the necessity of further research and finding a better noninvasive diagnosis and treatment of H. pylori infection during childhood.

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