

Gastric Diseases by H. Pylori and the Role of Mast Cells



Healthcare

Keywords: Helicobacter pylori, mast cell, gastritis.

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Abstract

H. Pylori deemed as one of the causes of gastric pathologies (mainly chronic superficial gastritis, chronic atrophic gastritis, gastroduodenal ulcer, etc.) which can progress to gastric atrophy and cancer of the stomach. Although still not well known pathogenesis and Physiopathology of damage by H. Pylori, has recently attracted attention histological framework of these diseases. In particular, mast cells are found frequently and in a number of pathologies such increased at a significant correlation what makes think that mast cells have a manifestly impact in pathogenesis of these pathologies. We wanted to verify whether any correlations exist between HP positivity, type of gastritis and presence of mast cells. We examined 90 bioptic fragments of gastric mucosa obtained by diagnostic oesophagogastroduodenoscopy. The study population consisted of 22 patients with chronic superficial gastritis and 8 with chronic atrophic gastritis (20 males and 10 females). HP detection was performed on Giemsa-stained preparations. Mast cell detection was performed on Giemsa- and PAS-stained preparations. Sixty-eight percent of chronic superficial gastritis cases were found to be HP-positive and mast cell were present in 87% of these and absent in 13%. In chronic atrophic gastritis cases 50% were HP-positive and mast cell were present in 50% and absent in the rest. On the basis of our data a significant correlation was found (86%) between HP-positivity and presence of mast cells in the inflammatory gastric mucosa.

Introduction

Since 1983 when Warren and Marshall showed presence of gastric antral mucosa HP in patients with type B antral gastritis and / or peptic ulcer, literature data for such correlation have been risen.

Observations according to Giemsa-stained preparations for the HP research has long shown in infiltration of chronic gastritis, variable presence of mast cells (MTC).

Mast cells eosine-hematoxiline-stained present several characteristics: they have a diameter about 8-15 μ and a central densely nucleus, round or oval, cytoplasm filled with anfofil granules that many mediators of inflammation such as histamine, leukocyte chemiotactic factors, PAF, heparin, hyaluronic acid and mucopolisacaride, nonsulphide acid, whose role is not yet clearly defined. Mast cells can interfere with enzymes in the inflammation single complex mechanism of gastric mucosa caused by HP.

Materials and methods

We have examined 300 fragments of gastric mucosa biopsy obtained through oesophagogastroduodenoscopy Diagnostic Center Hospital "Dr. Xhaferr Kongoli "Elbasan in dyspeptic patients. Histological examination was conducted at the Service of Pathology of the University Hospital Center "Mother Theresa". The study population comprised 22 cases with chronic gastritis surface (GCS) and chronic atrophic gastritis 8 with (GCA), of which 20 males and 10 females. Age average growth rate is 55, of which 57 for males (with age limits from 30 to 76) and 52 for females (with age limits from 20 to 85).

	N. of cases	Age average	Age limits
Males	20	57	30-76
Females	10	52	20-85
Total	3	55	

The distribution of cases by sex and age

The incidence of pathology shows a first peak growth in the fifth decade of life (29.5%) and a second peak in the seventh decade of life (27%) unrelated to sex. Search for HP took in stained preparations by Giemsa and were examined. Search of mast cells was conducted in stained preparations by Giemsa and PAS.

Results

In the case of GCS 68% (15 cases) resulted positive in the search for HP, in which mast cells were present (HP⁺/MTC⁺) in 87% of cases (13 cases) and missing (HP⁺/MTC⁻) in 13% of cases (2 cases). At 32% (7 cases) resulted negative in the search for HP and mast cells were present (HP⁻/MTC⁺) in 14% of cases (1 case) and missing (HP⁻/MTC⁻) at 86% (6 cases). Also in the case of GCS is present the mast cells infiltration (HP⁺/MTC⁺ and HP⁻/MTC⁺) in 64% of cases (14 cases) and misses (HP⁺/MTC⁻ and HP⁻/MTC⁻) to 36% (8 cases).

In the case of GCA 50% (4 cases) resulted positive in the search for HP and mast cells were present (HP⁺/MCT⁺) in 50% of cases (2 cases) and missing (HP⁺/MCT⁻) in the remaining 50%. In 4 cases with negative GCA match HP mast cells were present (HP⁻/MCT⁺) in only one case (25%) and missing (HP⁻/MCT⁻) in 3 other cases (75%). GCA has therefore matching (HP⁺/MCT⁺ and HP⁻/MCT⁻) to 63% (5 cases) and doesn't match to 37% (3 cases). In the entire population as a whole is seen a matching in 86% of cases and no matching in 14% of cases.

	HP ⁺				HP ⁻					
	HP ⁺ /MCT ⁺		HP ⁺ /MCT ⁻		HP ⁻ /MCT ⁺		HP ⁻ /MCT ⁻		%	
	N. of cases	%	N. of cases	%	N. of cases	%	N. of cases	%	N. of cases	%
GCS	13	87	2	13	1	14			6	86
N° total			15				7			
%			68				32			
GCA	2	50	2	50	1	25			3	75
N°total			4				4			
%			50				50			

Percentage and distribution of positivity for HP and mast cells

Discussion

Helicobacter pylori was discovered by Warren and Marshall in 1982. They showed that this bacterium (then called Campylobacter Pylori) was able to live at acid pH of stomach and cause gastritis. Subsequent studies showed that the bacterium, later called Helicobacter pylori (H. pylori) is the main agent of gastric pathological manifestations. H. pylori is a gram-negative flagella bacterium, with dimensions of 3.5-0.5 nm, ribosomal subunit RNA consisting of a specific nucleotide sequence, which infects about half of the world population, whose main deposit is the human stomach. Gastric colonization by H. pylori usually occurs during the first decade of life, and in the absence of antibiotic treatment the infection continues for a lifetime.

H. pylori has unique microbiological features that allows it to survive in conditions such as stomach acid environment. Transmission of infection occurs mainly through oro-fecal route and oro-oral, particularly through contaminated food and water. Once penetrating the stomach, H. pylori turns gastric urea fluid in NH₃ and CO₂ thanks to ureasa. NH₃ produced from urea lysis actively pumped into extracellular space contributing to the creation of an alkaline pH which allows the survival of bacteria in the acidic environment of gastric juice. After colonization in the stomach, H. pylori contributes to the induction of an inflammatory response, profound changes in gastric homeostasis regarding the regulation of acid secretion and regulation of cell cycle and programmed death (apoptosis) of gastric epithelial cells. These changes will then be partly responsible for the evolution of the infection.

Regulation of gastric secretion mainly achieved in gastric antrum level where D cells which produce somatostatin restrain gastric G-manufacturing cells, gastrointestinal hormone which stimulates the secretion of hydrochloric acid by the stomach. In the case of H. pylori infection, antrum inflammation is associated with a reduction and ban D cells production. For this reason, G cells, not inhibited by D cell somatostatin, produce more gastrin.

In general, all H. pylori positive subjects are hypergastrinemic. Gastrin secreted by G cells enters the circulation and reaches the end of the gastric corpus region, rich in parietal cells, whose surface are located the main receptors responsible for the regulation of gastric secretion, including those for gastrin. Gastric interaction and its receptor activate HK- ATP-dependent pump (proton pump) and the production of hydrochloric acid. If the mucosa of the region is intact, hypergastrinemia forced by infection will cause in susceptible subjects, or by increasing the amount of parietal cells, or the presence of parietal cells more sensitive to stimulus gastrinemic, an acid hyper secretion which can later lead to the development of duodenal peptic ulcers. In subjects where H. pylori infection has caused the inflammation in gastric corpus terminus region, with atrophy of acid-secreting mucosa, the hypergastrinemia will be associated with hypo-aklorhidria, a prerequisite for gastric cancer. H. pylori infection diagnosis is based on invasive tests (oesophagogastrroduodenoscopy, endoscopy, and biopsys) and non-invasive tests.

Invasive tests are:

- 1 Quick ureasa test, which consists in placing a sample taken for biopsy stomach, containing urea and a pH indicator which changes color from yellow to red in the case of alkaline from forming bacterial ureasa CO₂ and NH₃. The test has a sensitivity of 90%;
2. Histological examination of stomach material biopsy after coloring with eosine -hematoxiline or Giemsa. Histological

examination is the gold standard in the diagnosis of *H. pylori* infection with a specific sensitivity around 99%. (Our study reference refers to this method)

3. Bacterial culture that allows, when positive, to test the sensitivity of bacteria isolated to specific antibiotics commonly used to eradicate them. The test has high specificity (100%), but the sensitivity ranging from 77% - 92%.

Non-invasive tests that do not require the execution of endoscopy are:

1. Serology, by examining the anti *H. pylori* IgG antibodies.

This test, although it has high sensitivity and specificity, does not distinguish between active infections from healed infection spontaneously or due to therapy.

2. ¹³C-Urea Breath Test (UBT ¹³C). This test, which uses ureasa bacterial activity, based on oral administration of ¹³C labeled urea and evaluation by the amount of ¹³C spectrometry present in exhaled breath.

Sensitivity and specificity of this test is approximately 98%.

3. HPSA (*H. pylori* Stool antigen). The test consists in the identification of an antigen ELISA *H. pylori* in faeces.

Sensitivity and specificity are similar to those of UBT ¹³C.

A recent survey, conducted by Gianni Marone and Amato de Paulis, has identified another cell that interferes in the action mechanism of *Helicobacter pylori*, which opens the possibility to understand and block the mechanism that causes chronic gastritis and ulcers, a disease that can degenerate into cancer of the stomach. Identified cell is an immune cell, unnoticed up to now, that results to be a valuable ally of *Helicobacter pylori*. According to them the bacterium doesn't penetrate deeply into the tissues of the stomach, but remains localized in the surface layer of mucous. In its place, what penetrates deeply is a protein secreted by bacteria called Hp (2.20). Once placed in stomach tissue, protein affects basophiles, which are identified as involved in the ulcer and gastritis. In basophiles were identified two receptors (FPRL1 and FPRL2) related to protein produced by *H. pylori*. So, there is another immune system cell involved in the diseases that lead to the appearance of tumors of the stomach. According to this data, blocking receptors in the cell becomes possible to prevent the progression of gastric cancer. It also paves the way for a new treatment of gastritis and peptic ulcer. From the analysis of our population shows a significant correlation (86%) between HP positivity research and mast cells presence of inflammatory infiltrate in the gastric mucosa. At 14% of the corresponding cases can't not be explained by changes subsequent to the environment such as hypochlorhidria gastric, intestinal metaplasia, overlapping competitive bacterial flora or by taking medication that has not been possible to verify. In conclusion, the registered results of the correlation HP / MTC suggest a major role of mast cells within gastric disease HP correlates. Literature data seem to confirm this.

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