A Hypothesis of the Possible Immunological Mechanisms Behind the Chronic Gastritis and Peptic Ulcerations Associated with the Campylobacter pylori Infection

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A short review of the data regarding the presence of Campylobacter pylori in the peptic ulcer patients and those with chronic gastritis has been presented together with the data regarding the presence and functions of the gastric mucosal mast cells and IgE molecules at their surface.

A speculation is made that the physiological role of the IgE/mast cell system in the gastric mucosa, beside bringing the immunocompetent cells to the place of infection, consists also in producing a local tide in the gastric acid secretion that would facilitate pathogen elimination. Chronic infection with C. pylori and other pathogens could lead to the permanent activation of this system resulting in the chronic gastritis or spots of hyperacidity that might turn into ulcers.

Findings of the humoral response to C. pylori in ulcer patients support the presented hypothesis. Further studies of the total and specific IgE content in the gastric mucosa of ulcer patients and experimental animals are required to test its validity.

Key words: Campylobacter pylori, gastritis, IgE, infection, peptic ulcer

Since the first papers by Marshall and Warren on finding Campylobacter-like organism in the gastric mucosa of the patients with gastritis and peptic ulcerations, numerous studies have confirmed that there is a more or less significant association between the presence of Campylobacter pylori and the conditions of the type B chronic gastritis or gastric and duodenal ulcerations. Possible pathological mechanisms behind this association are often left unclear. The source of infection and its transmission routes still remain undefined.

This association can help us to speculate about the physiological role of histamine in the regulation of the gastric acid secretion. Since the idea of histamine as a final gas- tric parietal cell stimulator has been abandoned, no other hypothesis has been replaced it. Therapeutical use of H2 blockers has proved that histamine liberation occurs continuously in the normal gastric mucosa.

Mast cells have been recognised as the main source of histamine in the gastric mucosa and it is believed that they are of the same kind as elsewhere. IgE molecules have been detected on their surface, which allows us to presume that the specific IgE mediated mast cell degranulation could be the main mode of histamine liberation in the gastric mucosa. Some histamine can also be liberated after some other nonspecific stimulations, as it has been observed on mast cells elsewhere in the body.

The real importance of IgE — mast cell system in the body is often left unclear. It seems very unlikely that a whole class of Ig molecules and the cells with receptors for it have been developed in numerous species just to be used in parasite infestations and potentially harmful atopic reactions. Each organ or system has to improve the survival chances of the individual organism continuously, or it has to be modified or even lost during evolution. This basic principle of evolution emphasizes the suggested importance of IgE as a gatekeeper.

IgE and mast cells might have developed as a specific changeable and tuneable alarm system of the extravasal tissue space that cannot be fully and permanently controlled by the immunocompetent cells. In this case the system of IgE and mast cells is being used to gather immunocytes where necessary. Under normal conditions, only a few of the mast cells would recognise the specific antigen and degranulate simultaneously, affecting only the neighbouring vessels.

This kind of allarm system can be temporarily sensitized and tuned up by the idiotypes of circulating IgE covering the mast cell surface. Since the half-life of IgE attached to the surface of mast cells ranges from one to two weeks, changes in the available IgE idiotypes can cause very slow changes and modifications in the sensitivity of the whole system.

Gastric acid and pepsin play an important role in our defense against mycobacteria. Still better efficacy would be achieved if the gastric acid secretion could be deliberately increased in the presence of pathogens. The parietal cells would have to be able to recognise the mast cell degranulation, caused by the encountering the specific antigen.

It is possible to speculate that under physiological conditions pathogens are being closely followed on their stomach route by a local tide in the gastric acid secretion. The tide is promoted by the specific, IgE mediated, histamine liberation from the mucosal mast cells (as shown in Fig. 1).

This histamine action on the parietal cells is mediated through the H2 receptors. The same type 1 reaction in the lower parts of the digestive tube might be responsible for the changes in the gut motility and secretion, often provoked by parasytes.

C. pylori, as a specific pathogen able to survive in stomach, can easily produce chronic infections of the gastric mucosa and submucosa. Numerous mast cell degranulation would lead to the chronic inflammatory response, as seen in the chronic gastritis, probably mediated by the vasal H2 receptors. On the other hand, liberated histamine would strongly stimulate the neighbouring parietal cells producing the spots of chronic focal hyperacidity with good chances of turning into ulcers.

Arguments in favour of the presented hypothesis are as follows. C. pylori is able to survive in stomach and even pe-
Specific IgG serum antibodies against *C. pylori* have been significantly (p<0.001) more common in the group of 37 ulcer patients compared to the control group of 50 laboratory staff and 31 children under the age of 10. Distribution of these specific IgG antibodies varies among different populations, which is probably connected with the sources of infection and other factors. High incidence of IgG positive sera against *C. pylori* have been studied in a group of 347 persons. It showed that the levels of specific IgG and IgA detected in the sera of the gastritis and ulcer patients and infected experimental animals are higher than among healthy individuals. Low titers of specific IgG and IgA detected in the sera of the gastritis and ulcer patients and infected experimental animals. The next step would be to study specific mast cell degranulation in the presence of *C. pylori*.

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**REFERENCES**

Sažetak

HIPOTEZA O MOGUĆIM IMUNOLOŠKIM MEHANIZMIMA NASTANKA KRONIČNOG GASTRITISA I PEPTIČKOG ULKUSA POVEZANIH S INFEKCIJOM CAMPYLOBACTER PYLORIDIS

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Učinjen je kratki pregled podataka o povezanosti prisustva Campylobacter pylori u bolesnika s kroničnim gastritisom i peptičkim ulceracijama, zajedno s podacima o prisustvu i funkciji mastocita i IgE u sluznici želuća.

Ukratko je objašnjeno shvaćanje da se IgE/mastocit sustav razvio tijekom evolucije kao sustav za uzbunjivanje i dovođenje imunokompetentnih stanica u dijelove tijela koji su nedostupniji cirkulirajućim stanicama imunog sustava. Tu spadaju sva rubna tkiva, u što spada i probavna cijev, te interstanični tkivni prostori. Specifičnost i osjetljivost takvog sustava za uzbunjivanje je u direktnoj vezi sa spektrom idio-tipova IgE antitijela u cirkulaciji.

U želučanoj sluznici je dokazano postojanje mastocita prekrivenih antitijelima klase IgE, te se smatra da su oni glavni izvori oslobađanja histamina unutar sluznice. Uz mogućnost liberalizacije histamina iz mastocita na nespecifične podražaje, ne može biti isključena mogućnost da je specifična imunološka reakcija IgE/mastocit sistema, nakon susreta sa specifičnim antigenom, glavni izvor oslobodenog histamina u želučanoj sluznici.

Učinjena je hipoteza da je posebna fiziološka uloga IgE/mastocit sustava u želučanoj mukozi, uz pozivanje imunokompetentnih stanica na mjesto infekcije, također i stvaranje lokalne plime u lučenju želučane kiseline koja olakšava eliminaciju patogena. Kronična infekcija sluznice s C. pylori i sličnim patogenim mogla bi dovesti do permanentne aktivacije ovog sistema, što bi moglo doprinijeti razvoju kroničnog gastritisa ili nastanku točaka stalne hiperacidnosti pogodnih za nastanak ulkusa.

U prilog hipotezi govore nalazi specifičnog humoralnog odgovora na C. pylori u bolesnika s ulkusnom bolešću. Pravu provjeru bi pružile studije sveukupnog i specifičnog IgE u želučanoj sluznici duodenalnih bolesnika i inficiranih eksperimentalnih životinja.

Ključne riječi: Campylobacter pylori, gastritis, IgE, infekcija, peptički ulkus