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PATHOGENESIS OF ULCEROGENESIS IN THE STOMACH AND DUODENUM

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Annotation: *As is known, the formation and formation of the immune system is a process that is determined by the interaction of the gene regulation of development with environmental factors (antigens). Peptic ulcer of the stomach and duodenum is a chronic recurrent disease that occurs with alternating periods of exacerbation and remission, the main morphological feature of which is the formation of ulcers in the stomach and / or duodenum. The ulcerative defect penetrates through the muscle plate of the mucous membrane into the submucosal base or deeper. Under normal conditions, aggressive and protective factors are balanced, and therefore damage to stomach cells does not occur, however, in case of violation of this balance, damage to the mucosa in the form of erosions and / or ulcers may occur. Protective factors are represented by three components: preepithelial, epithelial, and postepithelial. The preepithelial mucus includes mucin, bicarbonates and surfactant phospholipids. The epithelial component includes surface cells, their apical dense contacts and membrane transporters.*

Keywords: *children, gastroduodenitis, peptic ulcer, Helicobacter pylori, immunology, genetics.*

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INTRODUCTION

Peptic ulcer of the stomach and duodenum is a chronic recurrent disease that occurs with alternating periods of exacerbation and remission, the main morphological feature of which is the formation of ulcers in the stomach and/or duodenum [1]. The ulcerative defect penetrates through the muscle plate of the mucous membrane into the submucosal base or deeper. Under normal conditions, aggressive and protective factors are balanced, and therefore damage to stomach cells does not occur, however, in case of violation of this balance, damage to the mucosa in the form of erosions and / or ulcers may occur. Protective factors are represented by three components: preepithelial, epithelial, and postepithelial. The preepithelial mucus includes mucin, bicarbonates and surfactant phospholipids. The epithelial component includes surface cells, their apical dense contacts and membrane transporters. Postepithelial protection is provided by mucosal blood flow, which is also important for repair [2]. Aggressive factors include hyperacidity of gastric juice, pepsin, duodenogastric reflux, ischemia of the gastric wall, violation of motor evacuation function, helicobacter microbial contamination of the gastric mucosa, nervous and humoral regulation disorder, local digestive disorders, destruction of the gastric mucosa, constitutional and hereditary factors, as well as taking nonsteroidal 2

Ivanova K. A. Traditional views on ulcerogenesis in the stomach and duodenum. anti-inflammatory drugs, the presence of bad habits (smoking, alcohol abuse) [3]. Main part: I. HP Helicobacter pylori (H. pylori) is a pathogenic, extracellular bacterium that colonizes the stomach of approximately 50% of the world population. This microorganism interacts with the epithelium of the stomach and mainly causes asymptomatic gastritis. It is believed that colonization of H. pylori leads to the development of ulcers in approximately 20% of infected patients, which can progress to stomach cancer or lymphoma of the mucous membranes in 1%. Researchers associate H. pylori with stomach cancer and the World Health Organization classifies it as a class I carcinogen [4]. After the bacterium enters the stomach, unlike other bacteria, it does not die under the influence of gastric juice, but begins to secrete enzymes, in particular, urease, which decomposes urea in the gastric contents into carbon dioxide and ammonia. They form a shell around the bacterium with an optimal pH, so that the bacterium can exist. Through its flagella, the bacterium moves to the stomach cells through a layer of mucus away from the acid. There it attaches itself to the cells and inhabits significant spaces. The products secreted by the bacterium Helicobacter pylori as a result of vital activity significantly weaken the protection factors, and the aggression factors can manifest themselves to a greater extent. The mucosal layer is destroyed and the gastric juice rushes to the cells. There is an inflammation of the stomach – gastritis. The stomach reacts to an increase in pH, although local, by a total decrease in pH and an increase in its motor activity. As a result, acidic contents and bacteria are thrown into the duodenum. To protect against the aggressive environment in the intestine, the epithelium begins to regenerate and becomes the same as in the stomach. Bacteria populate the duodenum, which ultimately leads to the destruction of the protective layer and its inflammation – duodenitis. In places that are least protected by mucus, where damaged cells recover the worst and are poorly supplied with blood, an ulcer forms. However, it is still not clear why in some cases, even in the presence of the bacterium Helicobacter pylori and risk factors, the disease may not develop, and, conversely, in the absence of risk factors, it develops. It is not yet possible to explain what causes the cyclical course and different rhythms of recurrence of the disease [5]. II. Stress, nervous system. For the first time, the link between stress and peptic ulcer disease was observed in men working in the operational dispatch service, among whom there was a much higher spread of ulcers than in people holding managerial positions or workers. Cobb S., Rose R.M. It was found that air traffic controllers are almost twice as likely as civilian second pilots to have ulcers, and especially those who have a higher level of stress in their workplace [6]. Duodenal ulcers were much more common in prisoners of war than in non-captured Vietnam War veterans. In 30 examined children with peptic ulcer disease, compared with the selected control group of 30 people, there were more frequent nervous disorders and tragic life events preceding the onset of the disease in the anamnesis. Feldman et al. we noticed that patients with peptic ulcer disease reacted to some difficult life events more negatively than others. Alp M.H. and Ellard K. found that chronic stress and acute life-threatening events were closely related to the onset and recurrence of duodenal ulcers [7, 8]. Stress affecting society as a whole allows us to indirectly determine the relationship between the nervous system and ulcerogenesis. It is assumed that stress of this kind should increase the number of people with peptic ulcer disease. Riley I.D.

He found that the incidence of peptic ulcer disease increased during periods of mass resettlement of the population in the early urbanization of society and during wartime, the number of people with perforated ulcers increased during the bombing of Great Britain by Nazi Germany, during the Second World War [9]. Later, a group of Japanese scientists noticed an increased incidence of bleeding ulcers after the Great Hanshin-Awaji Earthquake in southern Hyogo, Japan, which killed more than 6,000 people. The comparison was made between a group of 10,831 patients who underwent endoscopy within 2 months after the earthquake and a group of 16,100 patients who underwent endoscopy in the same hospitals during the same time period in the previous year. In the area most affected by the disaster, an increase in the number of patients with stomach ulcers was noticed. In particular, a noticeable increase in the number of bleeding ulcers was found, which gives reason to believe that such a powerful stress factor not only caused peptic ulcer disease, but also provoked the development of its complications. Stress as an etiological factor could help explain the increasing trend towards the development of peptic ulcer disease and its complications, seasonal exacerbation of this disease and the presence of a significant proportion of patients with non-HPV-associated, non-HP-associated ulcers. III. The immune system. In patients with peptic ulcer of the stomach and duodenum, both non-immunological and immunological mechanisms of protection of the gastrointestinal tract are violated, which, in turn, determines the occurrence of this disease, the severity of clinical manifestations, the possibility of complications. For the first time, it was revealed that in patients with acute UD, an increase in spontaneous apoptosis of lymphocytes and activation apoptosis of T cells is detected. Programmed death of circulating lymphocytes in patients with UD is one of the mechanisms of immunosuppression, since it is associated with inhibition of proliferative activity of T-lymphocytes and a decrease in the number of lymphocytes in peripheral blood. At the same time, the relationship between increased apoptosis and the unfavorable nature of the course of the disease was revealed. It was found that impaired functional activity of lymphocytes in patients with UD is associated with changes in the production of pro-inflammatory and anti-inflammatory cytokines. On the other hand, elevated levels of LPS-stimulated IL-10 production were found in patients with UD, which is accompanied by a sharp decrease in the TNF-a/IL-10 ratio index, which characterizes the balance of pro- and anti-inflammatory cytokines. The data obtained on the presence of immune dysfunctions in UD, their conjugation with the severity of the disease, the possibility of correcting immune disorders with cytokines and achieving a clinical effect in general indicate the importance of immune disorders in the pathogenesis of gastric ulcer and duodenal ulcer in patients with helicobacter infection. The revealed development of secondary immune insufficiency in patients with prolonged and complicated course of UD indicates the need for immunocorrective therapy. Cytokines, having a pleiotropic effect, are able to directly and indirectly participate in the ulcerogenesis of the mucous membrane of the gastroduodenal zone. The realization of their pro and anti-inflammatory effects is determined by the activity of mediators, receptors, receptor antagonists, components of the regulatory cytokine network, neuroimmunoendocrine effects, quantitative and qualitative composition of the microbiocenosis of the body. Changes in serum and tissue concentrations of cytokines reflect the dynamics of ulcerative and reparative processes. Determination of the cytokine status of

patients with gastric and duodenal ulcer disease allows predicting the course of the disease, the effectiveness of basic and eradication therapy, and correction of treatment. Immunogenetic examination of patients and their family members with targeted determination of the presence of polymorphisms of the IL1B, IL1RN, IL4, IL6, IL8, IL18 genes, taking into account the geographical and ethnic prevalence of mutant alleles, can serve not only to identify a predisposition to ulceration, an indication for immunomodulation of treatment, but also to predict cancer risk. With the formation of an ulcer defect, a decrease in the level of PgE2, I2 and an increase in the content of PgE1, PGF2a and TxA2 in the gastric mucosa were detected. Ulcer healing is accompanied by an increase in the level of COX-2, PgE2, E1, F2a, I2 and TxA2, which allows us to conclude that the formation and healing of experimental gastric ulcer proceeds under the control of a local tissue defense mechanism implemented by prostaglandins. Along with changes in the general immunity in patients with peptic ulcer disease, shifts in the system of local immunity were revealed. Lymphoid-plasma infiltration of the gastric mucosa, considered as an expression of immune inflammation, was detected not only in the area of the ulcer, but also in the stroma of the stomach, as well as in the liver. In patients with gastric ulcer, the number of interepithelial lymphocytes is increased three times, the number of cells producing IgA increases in the mucosa of the edges of the ulcer. Changes in the indicators of nonspecific protection (decrease in the titer of complement and lysozyme, phagocytic activity of micro- and macrophages), shifts in the immune system (decrease in the content of T-lymphocytes, T helper cells) lead to a violation of non-immunological and immunological mechanisms of gastrointestinal protection and increased permeability of mucocellular and non-cellular barriers. The appearance of lymphoid-plasma infiltration, an increase in immune processes in the lymphocytes of the gastric mucosa and lymphatic regional nodes, an increase in the content of IgG, IgA and B lymphocytes indicates the activation of both the general and local links of the immune system in patients with peptic ulcer disease, an increase in the permeability of protective barriers leads to the entry into the body of protein molecules and polypeptides (the so-called medium molecules) carrying an antigenic structure. Their circulation in the blood can cause various immunological reactions, including allergic ones.

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