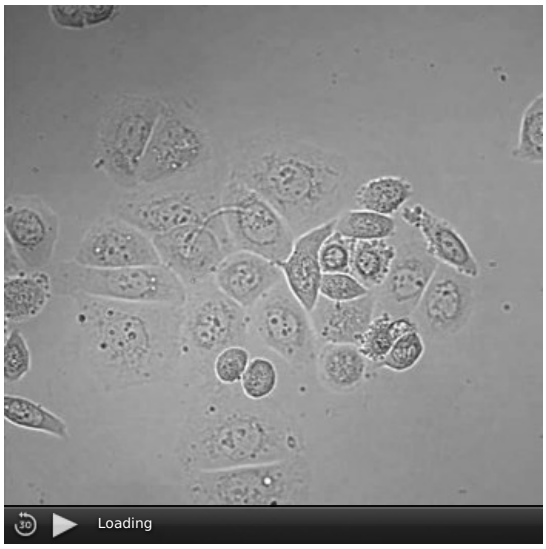
Role of Helicobacter Pylori in pathogenesis of stomach cancer

Gastric lumen infection Gram negative curved rod *Helicobacter pylori* is the most important factor in the development of inflammation, atrophic gastritis and histological development adenocarcinoma of stomach.

Various factors [[Pathogenicity of virulence] of this bacterium are involved in the pathogenesis of the disease. The natural course of infection can vary depending on the "genetic predisposition" of the bacterium and the host and the environment.



Růst Helicobacter pylori

Virulence factor

thumb|Prozánětlivé působení H. pylori (upraveno podle Fox, 2007). S **faktory virulence** *Helicobacter pylori* jsou spjaty čtyři genetické lokusy:

- ***cag PAI*** (cag Pathogenicity Island) – is a pathogenetic locus encoding several proteins. One encodes a secretory system capable of translocating CagA (a protein also encoded within "cag PAI") into gastric epithelial cells. Tyrosinové residues of internalized CagA protein are phosphorylated by SRC family kinases. Phosphorylated CagA subsequently activates ERK and tyrosine phosphotase-2 containing the SH2 domain (SRC-homologous 2 domain). This process is manifested by morphological transformation of the gastric epithelium. Tribes *H. Pylori containing a functional "cag PAI" can induce the production of proinflammatory modulators (eg IL-8).*

- 'vacA gene' - this gene encodes vacuolating cytotoxin. The cytotoxin acts as a voltage-gated channel for bicarbonate and organic anions. It induces vacuole formation in eukaryotic cells and stimulates apoptosis of epithelium.
- 'babA gene' - encodes the BabA outer membrane protein, which binds to the Lewis B antigen-blood group present on gastric cell membranes. It thus mediates the tight and firm adhesion of Helicobacter pylori to the gastric wall.
- 'iceA gene' - is a gene probably associated with virulence factors. Its function is not completely known. The expression of this gene is induced by the contact of the bacterium with the stomach wall and in some people it is associated with a higher risk peptic ulcer.

Proinflammatory action of H. pylori

H. pylori with its virulence factors stimulates an inflammatory response on the stomach wall.

One of the routes of action of the bacterium is through the secretory system created by genes *cag-PAI* . The created channel (T4SS - Type 4 secretion system) allows to transfer the CagA protein across the membrane epithelial cells of the stomach. Following its phosphorylation, the mitogen-activating protein kinase cascade is subsequently activated, leading to the activation of "NF & kappa; B" (nuclear factor & kappa; B) and "AP1" (" activator protein 1), leading to the production of proinflammatory factors. Likewise, the proteoglycan (*'PG'*) walls of a gram-negative bacterium can pass through T4SS, which via NOD1 (nuclotide-binding oligomerization domain-1) and *'RICK'* (receptor- interacting serine-threonine kinase (RIP2) also activates "NF & kappa; B" and thus the production of cytokines and other inflammatory mediators.

However, H. pylori can also act with its lipopolysaccharide through the "TLR4" (Toll-like receptor 4), which also stimulates an inflammatory response via NFβ kappa; B.

The role of the immune system

In the pathogenesis of gastric cancer, the mechanisms of the host's immune response to damage, e.g., H, also play an important role. pylori *. Experimental infection of mice without T and B lymphocytes with Helicobacter bacteria did not lead to changes in the gastric mucosa. Helicobacter spp. Infection in mice without B cells but capable of a normal T-cell response, severe atrophy and metaplasia mucosa. Further experiments have shown that "Th1 cells" are specifically involved in the pathogenesis of atrophic gastritis.*

Experiments in mice have also suggested that during chronic inflammation, hematopoietic cells may be recruited from bone marrow, stem cells, endothelial or epithelial progenitors, or myofibroblasts. These cells settle in the inflammatory tissue and are most likely involved in the *progression of the disease* .

The presence of "inflammatory mediators" represents a non-physiological environment for stem cells, in which [[Metaplasia | "metaplasia" "] to " dysplasia can occur. '. Further increased production of *IL-1β* ; causes decreased gastric acid secretion. Elevated pH is favorable for bacterial growth. Few species of bacteria can survive in the stomach with normal secretion of stomach acids. In contrast, at pH> 4, a wide range of species is able to grow.

Although it would appear that the administration of proton pump inhibitors (PPIs) in Reflux Esophagitis may dramatically increase the risk of atrophic gastritis by increasing pH, previous studies on this topic are contradictory and generally show no link.

We must also not forget the increased production of free radicals due to inflammation. Formation of ROS (reactive oxygen species, eg in natural neutrophilic immune response) and RNS (reactive nitrogen species, eg due to iNOS stimulation - inducible NO synthase - via "NF-κB") leads to further damage to tissue, cell structures and also to numerous mutations DNA.

Molecular mechanisms

Molecular mechanisms of gastric cancer include disorders and mutations of protooncogenes (*c-met* , *c-erbB2*), tumor suppressor genes (*TP53* , "APC", "RAR & beta" family, "RUNX" family), cell adhesion molecules (E-cadherin, CD44) and cell cycle control molecules (cyclin E, p27, E2F). Other genetic abnormalities may relate to instability of microsatellite sequences (associated with mutations in mismatch-repair genes), growth factors and cytokines. These factors may be involved in carcinogenesis either by increased cell proliferation, disruption of cell DNA repair mechanisms, uncontrolled growth or stimulation of the growth of surrounding cells. The effect of food is also described here, as nitrates present in food (eg sausages, but also vegetables) can be reduced to nitrites and possibly to nitrosamines, which have mutagenic effects.

Bacterial, genetic, immune and molecular factors are involved in the etiology and pathogenesis of gastric cancer. The key stimulus is probably the presence of *H. pylori* in the stomach. Eradication *H. Pylori* can not only stop pathological changes in the stomach wall, but can even reverse atrophy and restore the normal architecture of the stomach wall. The development of the disease ranges from inflammation through atrophic gastritis, intestinal metaplasia and dysplasia to adenocarcinoma. It depends on the genetic makeup of both the bacterium and the host, whether disease progression or infection. pylori *will be asymptomatic.* Template:Doplňte zdroj

Odkazy

Související články

- Viry
- Virulence
- Žaludek
- Karcinom žaludku
- Helicobacter pylori

Externí odkazy

- Rakovina žaludku (https://nemoci.vitalion.cz/rakovina-zaludku/%7C)
- Helicobacter pylori (http://www.rehabilitace.info/zdravotni/helicobacter-pylori-priznaky-lecba-a-jak-se-testuje/%7C)

Převzato z

Použitá literatura

Reference

Kategorie:Gastroenterologie Kategorie:Onkologie