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Influence of Inducing Factors on the Pathogenicity of Dysplastic Gastric Carcinoma

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Abstract: *Gastric cancer is a kind of gastric epithelial dysplasia and adenoma. At present, it is recognized that the formation process of gastric cancer is normal gastric mucosa chronic atrophic gastritis (Ag) - intestinal metaplasia (IM) - dysplasia gastric cancer. In addition to genetic factors, environmental factors such as microorganisms, nutrients and drugs in the stomach can affect the formation of dysplasia by changing the stomach. In this paper, the influence of inducing factors on the pathogenicity of dysplastic gastric cancer was discussed.*

Keywords: *Helicobacter pylori, endophytic mutant, MNNG*

1. Introduction

Gastric cancer is an adenoma with abnormally proliferating gastric epithelium, with abnormal cells and structures, and flat cells. Zeng Wenming et al. [1] shows that gastric cancer is atypical hyperplasia. The main manifestations of clinical observation are loss of appetite, weight loss, pain, fullness, high morbidity and mortality, and relatively poor prognosis, threatening human health. As a highly malignant tumor with multiple etiologies, gastric cancer is the result of a long-term interaction between environmental factors and genetic factors. Environmental factors that cause a high incidence of gastric cancer include Helicobacter pylori (H.pylori) infection, excessive salt and nitrification, food intake and tobacco exposure. One of the currently recognized gastric cancer models is the gastric cancer process proposed by Correa et al. [2]: Normal gastric mucosa-chronic atrophic gastritis (AG)-intestinal metaplasia (IM)-dysplasia-gastric cancer. According to statistics from the International Agency for Research on Cancer [3], in 2012, there were approximately 951,000 gastric cancer treatment cases and 723,000 deaths nationwide, ranking fifth in the incidence of malignant tumors and third in the mortality rate. Among the new cases of gastric cancer worldwide, the molecular biological factors of gastric cancer are complex and are related to many pathogenic factors. Therefore, revealing the mechanism of occurrence and development of gastric cancer is of great significance to the diagnosis and treatment of gastric cancer. It can be seen from the above that the research on the pathogenesis of gastric cancer and the diagnosis and treatment strategy has high theoretical and clinical significance in China. This article will review the influence of various pathogenic factors on the pathogenicity of proliferative gastric cancer.

2. Helicobacter pylori (HP) and gastric cancer

Helicobacter pylori (HP) is the only microorganism species known to survive in the human stomach. It is used by the World Health Organization (IARC) as an initiation factor for inducing precancerous diseases such as gastritis and gastric cancer among environmental factors. Listed as the first type of carcinogen for gastric cancer. Long-term presence of HP in the stomach can cause chronic gastric diseases such as chronic ulcers and gastritis, and eventually gastric cancer. There are also several possible mechanisms for HP infection to cause gastric cancer. Zhang Hailian et al. [4-5] pointed out the mechanism of HP causing gastric disease, such as: (1) Helicobacter pylori caused damage to gastric cells due to its toxic genes producing corresponding toxins. Under the action of HP virulence factor, cytotoxin-associated protein A (CagA gene) can damage the gastric mucosa, increase DNA damage and cause cell mutations, and eventually gastric cancer. (2) HP infection causes an immune response. T lymphocytes that play a leading role in the immune response will play a role. The positive and negative regulatory systems in cellular immunity induce each other and restrict the T cell network to maintain the balance of the immune system. After Hp infection Abnormal positive and negative regulation leads to immune system disorders, induces gastric diseases, and promotes the development of gastric cancer. (3) HP

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catalyzes the reduction of nitrate to nitrite and then becomes cancerous. (4) HP can cause cell cycle protein abnormalities, cell membrane abnormalities, cell cycle proliferation disorder and apoptosis balance imbalance, epithelial cell regulation imbalance, leading to gastric cancer. (5) The oxidative free radicals of cancer cells continue to stimulate the destruction of cell membranes after infection, and eventually lead to abnormal secretion in cancer. Causes gastric acid secretion disorders, causing mucosal damage. Treatment of Helicobacter pylori infection is the most important before the occurrence of atrophic gastritis and intestinal metaplasia. Once the patient develops atrophic gastritis and intestinal metaplasia, the treatment can eradicate Helicobacter pylori. The pathological changes that have occurred cannot be reversed and reduce the risk of gastric cancer. . Therefore, research on the pathogenicity of gastric cancer based on Helicobacter pylori is the basic starting point for gastric cancer prevention.

2.1 CagA and gastric cancer

Jiang Zhe [6] found that the Helicobacter pylori (HP) cytotoxin-related gene A (CagA) protein is the core pathogenic factor of gastric diseases, and it is encoded by the CagA gene on the Cag Pathogenic Island (Cag PAI) of HP. CagA (cytotoxin-associated protein) of gastric epithelial cells is continuously exposed to bacteria. It will bind to and damage DNA, resulting in the inability and independence of intracellular signaling molecules, etc., and the connection between cells will be destroyed. CagA protein secretes CagA into the host's gastric mucosal epidermal cytoplasm through type IV secretion system. It is the only protein that plays a biological role. After tyrosine phosphorylation, CagA protein specifically binds to the SH2 domain of SHP2 to form CagA- SHP2 complex, the complex formed can induce cell elongation and shape change, and ultimately induce the occurrence of gastric cancer and promote the development of gastric cancer.

2.2 Immune system disorders

When the stomach is infected by Helicobacter pylori, a large number of T cell infiltration can be seen in its mucosal tissue, mainly Th1 type cells, which are the functional subgroups of helper T and B cell responses. Th cells are differentiated from CD4+ T cells, and HP can specifically bind to the immunodominant epitopes of CD4+ T cells and make them active. Lee et al. [7] found that Hp infection caused T cell immune disorders, and Th1 and other immune disorders may be related to the balance between host defense and Hp setting. The most important role is the immune response mediated by Th17 cells. Th17 and Th17 the levels of IL-6, TGFβ, and IL-21 are positively correlated. Even if Helicobacter pylori is eradicated, the immune response activity mediated by Th17 cells still exists, and the interleukins produced by it still increase the risk of cancer.

2.3 Cell cycle disorders

The research on the abnormal regulation of apoptosis genes during the development of gastric cancer has shown that the Mye gene, P53 gene and cbl-2 gene mutations are important factors leading to the occurrence of gastric cancer. The results of Jain et al. [8] showed that the increase of AgNOR in the nucleolar tissue area, the increase of the mucosal epithelial proliferation index PCNA index, the Helicobacter pylori (HP) infection can accelerate the gastric mucosal hyperplasia, and have a higher canceration. Dangerous. HP infection aggravated the DNA damage of gastrointestinal mucosa, suggesting that HP infection can induce gastric cancer.

2.4 Endogenous injury

The proteases, proteases and phospholipids of Helicobacter pylori (HP) destroy the integrity of the gastric mucus layer, increase the solubility of gastric mucus, reduce its hydrophobicity, and reduce the protective effect of the mucus layer on epithelial cells. Zhao et al. [9] found that HP can make cell replication errors. Under the action of endogenous infection mutagens and exogenous food mutagens, it can cause cell proliferation and increase. The body's normal protective mechanism can repair most DNA damage. Unrepaired DNA damage will continue to increase with the continuous action of mutagens, etc. The longer the infection time, the more inappropriate DNA repair, which is more likely to lead to malignant gastric diseases.

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3. N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) and gastric cancer

N-nitroso complex (NOCs) infection is one of the main causes of gastric cancer. Methyl nitro nitrosoguanidine (MNNG) is a synthetic nitrosoguanidine compound. Su Qi [10] and other experimental studies are often used to replace nitrosoguanidine compounds in nature to simulate the body's exposure. Carcinogenesis of gastric mucosal cells caused by the introduction of nitroso compounds is often used as a model in experiments. Since MNNG's carcinogenic effect does not rely on enzymes but directly acts on the gastric mucosa, this makes local effects particularly important. MNNG can produce O^6-methylguanine when it reacts locally in the stomach. During repair, O^6-methylguanine and thymine are mispaired, causing point mutations, resulting in the loss of 5-methylcytosine and DNA hypomethylation. Eventually cause cell changes. Therefore, MNNG has a greater influence on the occurrence of gastric cancer.

4. Conclusion and Prospects

Gastric cancer is a heterogeneous tissue hyperplasia that occurs under the combined action of genetic and environmental factors. Susceptible people are more likely to develop tissue cancer under the action of pathogenic factors. Therefore, to find the pathogenicity and pathogenic mechanism of pathogenic factors is gastric cancer. The prevention and treatment of gastric cancer have an important role. This article mainly discusses the occurrence of gastric cancer from two main pathogenic factors. However, there are still many problems to be solved based on the pathological mechanism of gastric cancer. The establishment of a table of gastric cancer susceptibility factors and the construction of a ternary interaction model that combines genetic and environmental factors are key issues for gastric cancer prevention.

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