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A Current Clinical Overview of Atrophic Gastritis

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Abstract: *Chronic atrophic gastritis(CAG), as a subtype of chronic gastritis, refers to the loss of gastric gland function in the inflammatory background caused by Helicobacter pylori (H.pylori) infection or autoimmune factors, with or without intestinal metaplasia(IM) , and is a precancerous disease. The main clinical manifestations of CAG are upper abdominal distension, early satiety, belching, decreased appetite, and irregular dull pain in the upper abdomen. As a clinically common and refractory disease, CAG can go on a long time. Traditional Chinese and western medicine in CAG are cut both ways, and this article provides a detailed description of the research progress on CAG to and provide some reference for clinic.*

Keywords: *Chronic atrophic gastritis; H. pylori; Diagnostics; Treatment; TCM*

1. Introduction

Chronic atrophic gastritis(CAG) , as a subtype of chronic gastritis, refers to the loss of gastric gland function in the inflammatory background caused by Helicobacter pylori (H. pylori) infection or autoimmune factors, with or without intestinal metaplasia(IM) , and is a precancerous disease [1]. The main clinical manifestations of CAG are upper abdominal distension, early satiety, belching, decreased appetite, and irregular dull pain in the upper abdomen. It is a common digestive disease, and its symptoms are prone to recurrence and difficult to cure in clinical practice. Correa [2] proposed that normal gastric mucosa, chronic superficial gastritis, atrophic gastritis, intestinal metaplasia, intraepithelial neoplasia, and gastric cancer are the occurrence patterns of intestinal type gastric cancer (Figure 1). Research has shown that CAG patients have a higher risk of developing intestinal and type I gastric cancer [3].

2. Epidemiology

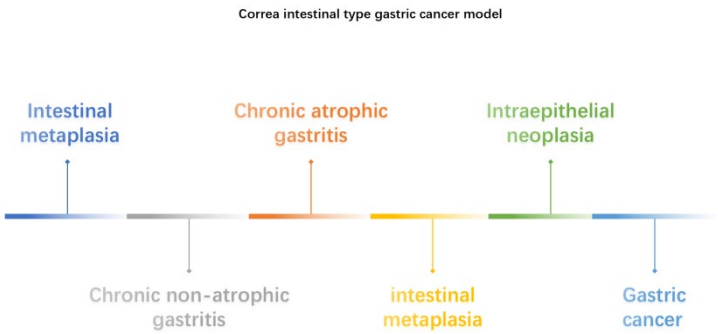

Figure 1: Correa intestinal type gastric cancer model

Epidemiological investigation shows that the incidence rate of CAG increases with people's age [4]. The survey statistics show that the incidence rate of CAG in China is 17.7% [5]. Wang Nuanfeng randomly selected 2532 patients who underwent gastroscopy and gastric mucosal pathology in a hospital in Heilongjiang Province, and carried out CAG analysis on their clinical data. The results showed that the incidence rate of CAG was 7.83% among patients before the age of 30, which rose linearly after the age

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of 30, reached its peak at the age of 51 to 60, and gradually declined after the age of 60 [6].

3. Etiology and Pathogenesis

At present, the pathogenesis of CAG in Western medicine is not yet clear. It is generally believed that the occurrence of CAG is related to H. pylori infection, autoimmune disease, bile reflux, and Non-H. pylori bacteria in the stomach [7].

3.1. H. pylori infection

H. pylori mainly depends on interpersonal transmission, especially among family members. Its incidence rate is lower among people with better economic development or higher education level, and there is no significant difference in incidence rate between men and women [8,9].

H. pylori can cause chronic inflammation of the gastric mucosa, leading to the development of CAG and even gastric cancer. After H. pylori enters the gastric cavity, in order to avoid the harsh low pH environment, it will move to the protective mucus layer of the surface of the gastric mucosa through flagella, adhere to the host cells through the interaction of pili and adhesin receptor, and release toxin factors to cause tissue damage. On the one hand, gastric acid exposure will activate H. pylori flagellin and enhance the motility of H. pylori flagella. On the other hand, under the extremely acidic environment in the stomach, H. pylori will produce urease to induce inflammation and release ammonia. Ammonia plays an important role in neutralizing gastric acid and destroying the integrity of cells to cause gastric mucosal damage. H. pylori flagella can also induce the secretion of proinflammatory cytokines and enhance the inflammatory response at the site of infection. There are adhesins such as adhesin A, blood group antigen binding adhesin (BabA), sialic acid binding adhesin (SabA), and related adhesins (AlpA, AlpB) on the surface of H. pylori flagella and cell, which lead to the occurrence of persistent inflammatory response. In addition, H. pylori can form water-insoluble biofilms during its growth. The stronger its ability to form biofilms, the stronger the adhesion of the bacterial surface (Figure 2). The formation of biofilms gives H. pylori protection, allowing it to survive in the gastric environment for a long time and avoid the removal of gastric acid disinfection and sterilization. Long term inflammatory stimulation causes the stomach to lose normal mucosal glands, leading to the occurrence of CAG. The mucosal glands lost by CAG are replaced by immature new glands and epithelial cells similar to colon or small intestine, which in turn lead to IM and even gastric cancer [10-13].

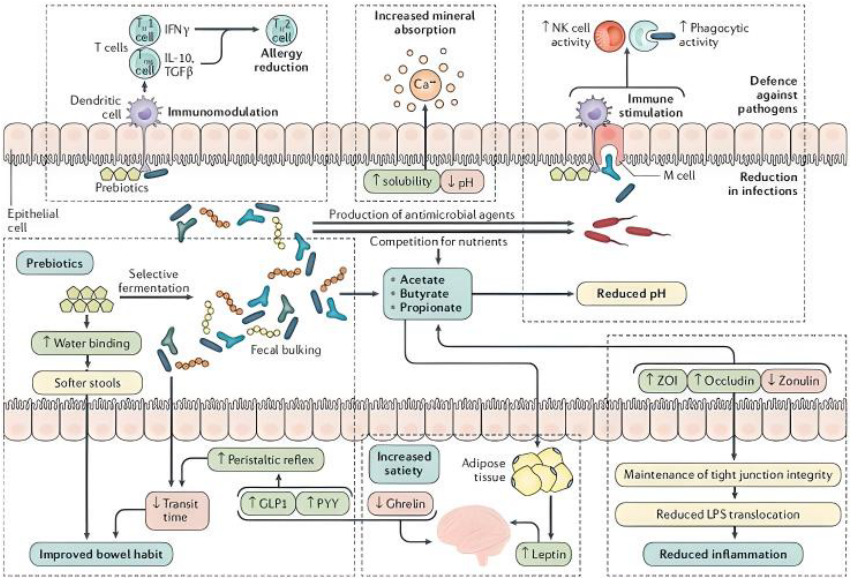

Figure 2: The pathogenic process of H. pylori

3.2. Autoimmune

The mechanism of the initial event of autoimmune mediated CAG is not clear now. Currently, it is believed that Cd4+ T lymphocytes combine the proton pump of gastric arm cells as antigen with autoantibodies, which leads to the inflammatory reaction of gastric mucosa. Some studies proposed that

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previous H. pylori infection caused the loss of autoimmune tolerance. This may be related to autoimmune atrophic gastritis. In addition, some primary autoimmune diseases, such as autoimmune thyroid disease and type 1 diabetes mellitus, have also become hypotheses related to the autoimmune pathogenesis of CAG [14-16].

3.3. Bile reflux

Animal model studies have found that intragastric bile reflux can lead to a significant increase in gastric juice pH, total bile acids, serum gastrin, and a significant decrease in gastric mucosal prostaglandin E2 (PGE2). Anatomic pathology showed obvious inflammation of gastric mucosa and atrophy of glands. IM and atypical hyperplasia were partially present [17]. The bile acid in bile is alkaline, which neutralizes gastric acid and increases the pH in the stomach. With the aggravation of bile reflux, the probability of IM caused by high concentrations of bile acids increases. Bile reflux may participate in the occurrence and development of IM by affecting the expression of CDX2, Sox2 and TGR5 [18,19].

3.4. Non-H. pylor flora

The diversity of Non- H. pylori flora in the stomach gradually decreased in the gastric juice of CAG patients, which may be related to the occurrence of CAG. Compared with normal people, Butyrivibrio disappeared in the stomach of CAG patients. Butyrivibrio metabolizes butyrate, and butyrate is a major nutrient for the regeneration and repair of gastrointestinal epithelial cells, it participates in inhibiting atrophy of gastric mucosa [20]. The study found that the abundance of pathogenic microorganisms such as Acinetobacter lwoffii, Streptococcus anginosus, Ralstonia, Erwinia and Prevotella in the stomach of CAG patients increased. Acinetobacter lwoffii induces gastrin production, proliferation of gastric G cells and gastric parietal cells, and the occurrence of inflammatory responses [21].

4. Diagnosis

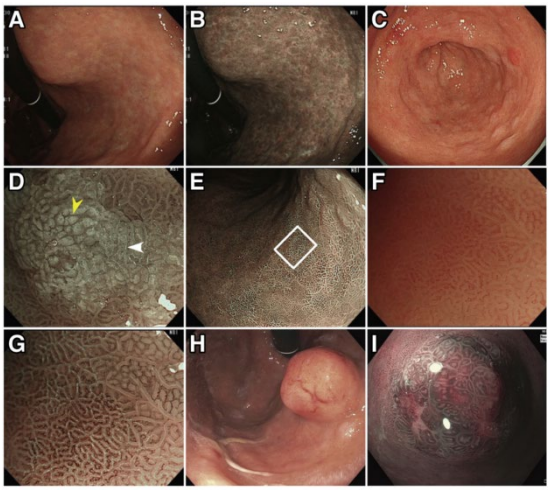

Figure 3: Atrophic gastritis(A, B) ; Mild nodular appearance of IM gastric mucosa(C) ; LBC sign(D-G); Gastric neuroendocrine tumor(H, I) .

The clinical manifestations of CAG are nonspecific, so the diagnosis of CAG mainly depends on gastroscopy and histological examination [22]. CAG gastroscopy showed that the atrophic mucosa was pale and thin, the gastric folds disappeared, and the submucosal blood vessels were exposed(Figure 3A, B). Mild nodular, ridged or tubular villous mucosa is the typical microscopic manifestation of IM(Figure 3C) . LBC (light blue crest) sign is another feature of IM(Figure 3D-G), which refers to the blue white thin line on the ridge of visible epithelial surface [1]. Generally, the symptoms of CAG patients are independent of the severity of pathology [23]. Some patients may have no obvious symptoms, and some patients also show symptoms such as upper abdominal fullness, early satiety, belching, anorexia, irregular dull pain in the upper abdomen, etc. Patients with gastroesophageal reflux disease may have acid reflux and heartburn. Patients with bile reflux may have bitter mouth. Patients with autoimmune gastritis mainly present with pernicious anemia [22].

Studies have shown that Pepsinogen, gastrin-17 and H. pylori antibody combined with serological

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detection are reliable in the diagnosis of CAG [24]. It is suggested to detect serum gastrin, vitamin B12, anti-mural cell antibody, anti-internal factor antibody, etc. in CAG caused by suspected autoimmunity [22].

Due to the significant differences in clinical manifestations among patients with clinical CAG, the choice of examination method mainly depends on the individual's clinical symptoms and clinical suspicion of CAG, as well as its use for differential diagnosis (Figure 4).

Figure 4: Unified fonts make reading more fluent

5. Treatment

5.1. Western medicine treatment

Up till the present moment, there is no clear treatment method in western medicine to reverse the occurrence of atrophy. In treatment, it is often taken to improve gastric motility, protect gastric mucosa, and supplement folic acid and B vitamins.

For HP positive patients, eradication therapy is the basic treatment of CAG. The expert consensus on the collaborative diagnosis and treatment of Chinese and Western medicine for gastritis caused by Helicobacter pylori in adults (2020, Beijing) pointed out that the HP infected population aged 18-70 years old should recommend quadruple therapy to eradicate H. pylori in the absence of liver and kidney dysfunction or other intolerable multisystem diseases [25]. It is recommended to use bismuth quadruple for 14 days in the initial scheme, and two antibiotics, bismuth and proton pump inhibitors (PPIs) are selected for quadruple drugs. The anti- H. pylori quadruple antibiotic groups recommended by the fifth national consensus report on the treatment of H. pylori infection are: Amoxicillin and Clarithromycin; Tetracycline, Metronidazole; Amoxicillin, Metronidazole; Amoxicillin, Tetracycline; According to the local drug resistance situation, the antibiotic combination with low drug resistance rate is preferred. Regimens containing Levofloxacin and Furazolidone are not recommended for initial treatment [26].

Because CAG is difficult to be cured by western medicine, and the clinical symptoms are recurrent, there is a risk of progression to gastric cancer, so patients often have anxiety and depression [27]. It is also important to carry out science popularization and education for patients to correctly understand the risk of CAG canceration and maintain a positive attitude. If necessary, anti anxiety and depression treatment can be carried out.

5.2. Traditional Chinese medicine treatment

In recent years, traditional Chinese medicine has shown its unique advantages in the treatment of CAG with its overall concept and characteristics of syndrome differentiation and treatment. Traditional Chinese medicine decoction, Chinese patent medicine, acupuncture and moxibustion are widely used in the treatment of CAG. Traditional Chinese medicine has a clear effect on the reversal of CAG. Traditional Chinese medicines such as Coptis chinensis, Scutellaria baicalensis and honeysuckle can inhibit atypical hyperplasia and proliferation of gastric cells and kill H. pylori [28]. Decoction of Four Noble Drugs, a traditional Chinese medicine decoction, can reverse gastric mucosal atrophy by anti-inflammatory, regulating cell proliferation, apoptosis and energy metabolism [29]. Banxia Xiexin Decoction can treat CAG through biological pathways such as Interleukin, Cyclooxygenase-2, MAPK cascade activation, ERK protein phosphorylation, etc [30]. Chinese patent medicine Morodan can inhibit neutrophil

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proliferation, reduce the level of inflammation, promote apoptosis and differentiation, and promote lipid accumulation [31]. Jixu et al. [32] selected Shangwan, Zhongwan, Xiawan, Qihai, Tianshu, Neiguan and Zusanli acupoints for fire needle fast needling to treat CAG. After several weeks of treatment, the expression levels of serum G17, PGI and PGR increased, and the clinical curative effect was clear.

6. Conclusions

CAG, as a common and difficult to treat disease in clinical practice, has a lingering course and is considered a high-risk factor for cancer transformation. Although Western medicine has a rapid therapeutic effect on CAG, it has significant side effects and is difficult to maintain long-term efficacy, resulting in poor patient compliance. Traditional Chinese medicine has a clear therapeutic effect on CAG, which can fundamentally reverse the occurrence of atrophy. However, the subjectivity of traditional Chinese medicine syndrome differentiation and the differences in the origin of traditional Chinese medicine make the efficacy reactions of traditional Chinese medicine decoctions uneven. Looking forward to further exploring the mechanism of traditional Chinese medicine in treating this disease, learning from each other's strengths and weaknesses, and combining traditional Chinese and Western medicine to achieve better therapeutic effects in the future.

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