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Review of Immunotherapy for Ulcerative Colitis

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Abstract: ***Ulcerative colitis (UC) is a variety of factors, such as genetic background, environmental and luminal factors and mucosal immunity, disorders, and other unknown etiology, chronic and inflammatory typical gastrointestinal chronic diseases, given the high incidence of UC in developed countries and greatly increased incidence in developing countries, UC has evolved into a global burden. Therefore, further studies on the underlying pathogenesis of UC force the emergence of new therapies. This article discusses recent immunotherapies for ulcerative colitis.***

Keywords: Ulcerative colitis, Chronic inflammation, Immunotherapy**.**

1. Introduction

1.1 Introduction to Ulcerative Colitis

Ulcerative digestive colitis (UC, Ulcerative Colitis) is an inflammatory gastrointestinal disease (IBD)[1]. The pathological features of UC is spread from the colon to the proximal rectum in a continuous manner[2-6]. Inflammation in the UC is generally confined to the mucosal layer leading to surface damage to the intestinal wall. The cause of UC and its mechanisms remain unknown. Abdominal pain, mucinous bloody diarrhea are the most common symptoms of UC[5]. The introduction of biologics targeting cytokines and adhesion molecules has enabled a significant improvement in long-term efficacy, including achieving corticosteroid-free remission[6,7]. However, many patients still need surgical treatment due to treatment failure or dysplasia[8].

The annual incidence and prevalence of UC are increasing throughout the world. UC is now considered a progressive disease because of the risk of proximal dilation, stricture, bowel dysmotility, anorectal dysfunction, the need for colectomy, hospitalization, colorectal cancer, disability, and impaired quality of life. Given its potentially progressive and debilitating disease process, the therapeutic goals of UC have changed over the past decade, from treating symptoms to mucosal healing, with the aim to alter the natural history of the disease and improve long-term outcomes[9,10]. Indeed, histologic remission is associated with a lower risk of hospitalization, colectomy, and colorectal cancer as compared to endoscopic treatment[11-20]. The histopathological features of UC mainly include changes in mucosal structure (including colon crypt morphology and reduced crypt density), altered lamina propria cell architecture, immune cell infiltration (crypt abscess and basal plasmactosis), and epithelial abnormalities (including metaplasia and goblet cell loss) [14].

1.2 General Treatment Methods for Ulcerative Colitis

The treatment of UC mainly depends on the severity of the disease, the degree of inflammation, and its evolution over time. However, the treatment goals of all patients should be very similar, namely, achieving endoscopic resolution of rectal bleeding and diarrhea, and of mucosal fragility and ulceration within 3 months of initiation of treatment[15]. Patients with acute severe colitis require timely admission [16]. The multidisciplinary discussion approach is the basis, and it is recommended to contact the colorectal surgeon on admission. Sometimes, emergency surgery may be required early, if a toxic megacolon, perforation, or major bleeding occurs. Although treatment should not be initiated afterwards in severe cases, excluding the differential diagnosis (including bacterial infection) is critical[16]. Most patients should receive aggressive medication, first with intravenous corticosteroids. Due to an increased risk of thromboembolism (i. e., blood clots), anticoagulants, such as low molecular weight heparin, calcium, and vitamin D supplements, should be started in addition to appropriate fluid and electrolyte replacement. Inpatients should undergo regular multidisciplinary reevaluation, including physicians, surgeons, radiologists, specialist nurses, pharmacists, and dietitians. Failure of intravenous corticosteroids on days 3-5 should be immediately salvage treated with cyclosporine, infliximumab, or surgery [17-20].

2. Research Progress in Immunotherapy for Ulcerative Colitis

Since the early 2000s, many new treatments have been introduced into the treatment of UC. By applying oral small-molecule or gut-selective therapies, the new therapies have potential advantages, including higher efficacy, safety, and patient acceptability. However, even the latest drugs have a 50% response rate, and many drugs experience a secondary response loss in the initially responding patients; therefore, more advanced therapies are still needed[21-31].

2.1 Cell Factor

Intracellular immunometabolic factors mainly participate as an important immune transmission signal between immune cells conduction important cell molecules through traffic function, and specific autologous immune cell receptor interaction on the immune cell unit, the immune cell neutral immune receptor metabolism and metabolic response and inhibit cell immune inflammation, it can also play an important role in immune conduction suppression[32-36]. Two of the neutral tumor cell immune factors endocrine in Th1 cell membrane receptor are protein mesin-2 (IL-2), IL-12,

interferon- (IFN-) and TNF-), and the cytokines produced by Th2 cells are IL-4, IL-5, IL-10 and IL-13.The former is mainly responsible for the participation of the tissues in guiding the metabolic suppression response of the neutral immune cells in the immune cells of the body, while the latter is mainly responsible for guiding the neutral immune metabolism activation of the neutral tumor type b leukocyte cells and their cells, and in regulating the immune metabolism response in the Th1 cells[32-40].

2.2 Cellular Proinflammatory Factor

The protein serum IL-1 produced in the diseased mucosa tissue of active UC patients and the single nuclei and mitochondrial cell nucleus extracted from the isolated intermediate cell nucleus and isolated cells was significantly increased. In addition, some clinical research staff in China early found that the significant concentration of serum IL-6 concentration was only found in only chronic patients with UC medical diseases, and was related to the formation of normal changes in the severity range of early intestinal mucosal lesions and the severity degree of early intestinal mucosal lesions, And only found in the disease activity period only in UC early patients with chronic disease of chronic intestinal mucosa patients with serum IL-6 type A positive MRCA and a b positive protein blood expression compared with abnormal intestinal lesions of chronic intestinal mucosa, the nature and symptoms of the intestinal lining mucosa chronic inflammatory disease patients with normal control and normal lesion tissue of blood control concentration significantly increased, It is also related to the normal severity of severe grade in patients with early intestinal mucosal inflammation[34-36]. IL-8 is a potent cellular chemokine and activation factor[33]. According to the research results, someone found that IL-8 can be widely used in diagnosis as one of the important leading indicators of early diagnosis detection of early disease diagnosis efficacy and as an important leading indicator of early treatment disease diagnosis for the prevention of continuous recurrence of early disease recurrence in UC[34].

2.3 Cellular Anti-inflammatory Factors

Anti-inflammatory cell antibacterial immune cell receptor immunosuppressive factor also has direct inhibition and indirect regulation of the normal immune system function in mice, and can be considered to effectively inhibit the secretion of IL-1, IL-6 and IL-8, and increase the receptor combination cell ratio of IL-1 / IL-1r.IL-10 can be considered to inhibit the anti-inflammatory antibacterial cells, a number of clinical studies experimental results show that knocking out an IL-10 gene in a viral worm mouse cells may not directly effectively lead to the experimental acute intestinal colitis, and IL-10 in viral mice in clinical treatment of UC liver virus patients, is considered to improve the gastrointestinal tract and skin mucosa bacterial inflammation in viral mice[35]. IL-4 is able to downregulate TNF-, IL-1, which is used to produce other mediators of inflammatory response, reduce its own tissue damage when inflammation occurs, and effectively promote tissue repair[15-23]. Specific active antibody binding occurs and can promote the transcription of the related antibody genome, participate in and coordinate the normal expression of various intestinal inflammation and autologous immune cell genes, and promote the normal release of its immune cell immune factors, which can in turn further activate it to form N f-b, thus forming a normal feedback immune regulation and expanding its inflammation range. N f-b uric acid is an important marker of bacterial infection in the human intestinal and gastric mucosa. Its level of uric acid level can not only directly reflect the severity of its disease, but also can be used as an important evaluation of the clinical treatment of disease effect[31-40].

2.4 Adhesion Molecules

Cell adhesion molecules are a large group of glycoprotein molecules located on the surface of the cell membrane, which play an important role in the process of immune response and inflammatory response. Three classes of adhesion molecule receptors are known to be involved in complex interactions between lymphocytes and the surrounding stroma or cells. They include selectins, integrins, and immunoglobulin, as well as molecules that have not been classified. P-selectin and ICAM-1 are now widely studied in the adhesion molecules. Some people found that the peripheral blood adhesion molecule P-selectin and ICAM-1 were significantly higher in active UC patients, and their expression was also increased in the intestinal tissue, and they were positively correlated with the severity of the disease. P-selectin is mainly expressed on the surface of activated platelets and endothelial cells, mediating the initiating adhesion of leukocytes to vascular endothelial cells. ICAM-1 is mainly expressed on the surface of endothelial cells and other immune cells, and can mediate the swimming out of monocytes and neutrophils into blood vessels. P-selectin and I-CAM-1 are mainly involved in the damage of intestinal tissue[35,36].

2.5 Anti-neutroloplasmic Antibodies

ANCA antibodies generally refer to a group of specific serum antibodies against neutrooidal cells and granule binding proteins in mononuclear neutrophils. New ANCA antibodies are regarded as an important serum biological signature of activity in UC patients, and it has been suggested that they may play an important indicator in both the history and mechanism of UC patients. General immunofluorescence method to detect ANCA antibody can be divided into three kinds of leukocyte plasma, paronuclear and atypical serum paronuclear type, paronuclear type is closely related to UC, because all ANCA antibodies in patients against UC death presents familial and aggregation phenomenon, so new ANCA antibodies may hope to develop against UC specific typical serum antibody markers[42-47].

2.6 Nitric Oxide

At present the relationship between NO and inhibition of UC more and more, NO type has two main types of science, namely cell structure (cNOS) and cell induced type (iNOS), in the inhibition of UC positive colon in the mucosal epithelial layer mainly to inhibit iNOS cells, the researchers found that these iNOS positive cell expression products are mainly found in granulocytes distributed in the adenular colon epithelium [40], iNOS produces NO, NO through catalytic enzyme binding to arginine, which has both cytoprotective effects in inhibiting UC neutral inflammatory immunity, and has dual

anti-toxic and pro-inflammatory protective effects of cell killing[41-50]. IL-4 and inhibition of IL-13 can also be used to delay and inhibit the production of neutral peroxidase, respectively, and regulate the cellular generation of NO by inhibiting reducing the cellular expression and activity of iNOS[50].

3. Summary

The main etiology of UC and the pathogenesis of drugs are complex, which are related to various medical problems in secretology, immunology, science, genetics and in vivo environmental factors. With the further medical research on the etiology of UC, it will be the future development trend of medicine to clarify the main etiology mechanism of U C, and it is also necessary to continuously find more and more effective therapeutic drugs.

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