mechanism (Fig. 2). Food and microbial antigens in the portal circulation have been shown to induce specific unresponsiveness (1). This indicates that the liver is an important factor in oral tolerance.

Conclusion

The mucosal immune system is characterized by the secretory antibody response and gut-associated lymphoid tissue. Contact between antigens and the mucosal immunologic apparatus called GALT initiates a diverse series of immunologic reactions including the production of IgA, which is transported through the intestinal epithelium to the external surface of the intestinal mucosa as sIgA. The liver plays an important role in immune responses or regulation of the mucosal immune system. I emphasized in this article that the mucosal immune system plays a central role in the maintenance of homeostasis in the immuno-inflammatory responses in the intestine.

References


2. The Immunological Aspects of Chronic Gastritis

Toshiro Sugiyama and Akira Yachi

Key words: parietal cell antibody, H⁺,K⁺-ATPase, Helicobacter pylori

Strickland and Mackay (1) classified chronic atrophic gastritis as two types, type A gastritis and type B gastritis from an immunopathological standpoint. Type A gastritis is closely associated with an immunopathological mechanism (autoimmune gastritis) and pernicious anemia is representative of it. Type B gastritis is non-autoimmune and a major type of chronic atrophic gastritis in Japan. Until recently the etiology of type B gastritis had not been elucidated. Helicobacter pylori (H. pylori), which was discovered and identified from human gastric mucosa in 1983 by Warren and Marshall (2), is now considered as a potential etiological agent in chronic atrophic gastritis (3, 4). A new classification of gastritis (5), the Sydney system, which was proposed at the World Congress of Gastroenterology in Sydney in 1990, recognized the major cause of chronic gastritis in humans. Here, we present the immunological aspects of chronic gastritis, autoimmune gastritis and H. pylori gastritis.

In autoimmune gastritis (Type A gastritis), auto-antibodies against the stomach, parietal cell antibody (PCA) and intrinsic factor antibody (IFA) are frequently detected in the serum. Karlsson et al (6) recently reported that PCA in serum inhibited the H⁺,K⁺-ATPase activity in vitro. As H⁺,K⁺-ATPase (proton pump) is a key enzyme which plays an important role in acid secretion, PCA may have a pathophysiological implication in the occurrence of hypo- or achlorhydria, hypergastrinemia and gland atrophy in autoimmune gastritis.

In order to elucidate a target epitope on the H⁺,K⁺-ATPase recognized by serum PCA, a recombinant fusion protein containing H⁺,K⁺-ATPase α subunit catalytic domain was produced and analyzed. In 30 PCA positive sera, 20 sera (66.7%) clearly reacted with the recombinant catalytic domain protein. In type A gastritis, 6 of 9 sera (66.7%) reacted with the recombinant protein. However, there was no reactive serum in 11 patients with type B gastritis positive for H. pylori. These observations suggest that H⁺,K⁺-ATPase α subunit catalytic domain itself is the primary target epitope recognized by PCA in serum of the type A gastritis patients.

The histological features of type B gastritis positive for H. pylori are characterized by the numerous infiltrations of mononuclear cells and neutrophils in the lamina propria. These inflammatory cells appear to implicate an immune response against H. pylori infection in gastric mucosa. We observed that secretory IgA antibody specific for H. pylori is frequently detected in gastric juice of the H. pylori-positive patients. By enzyme-linked immunospot assay (ELISPOT) using gastric mononuclear cells, H. pylori-specific antibody-producing cells

The Department of Internal Medicine (Section 1), Sapporo Medical University School of Medicine, S-1, W-16, Chuoh-ku, Sapporo 060

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in gastric mucosa can be determined (8). Mononuclear cells of H. pylori-positive gastric mucosa were found to actively produce H. pylori-specific antibodies (IgA ELISPOT; 838 cells/10^6 MNC, IgG ELISPOT; 366 cells/10^6 MNC, n=34). These ELISPOT numbers correlate with the histological grade of gastritis. Thus, the inflammatory infiltrate is considered to be a specific response against H. pylori infection.

Next, we investigated whether these H. pylori-specific antibodies in gastric mucosa and/or neutrophils are responsible for cytotoxicity to epithelial cells. Soluble H. pylori antigen, IgG type H. pylori antibody and neutrophils are the three factors which were required to induce the cytotoxicity, the vacuolation of cultured Vero cells in vitro. Immune complex formed with H. pylori antigen and the antibody induced the superoxide production of neutrophils. The addition of human recombinant superoxide dismutase (SOD) to the culture inhibited the vacuolation of Vero cells induced by the above three factors. These observations suggest that superoxide, produced from the neutrophils stimulated with H. pylori antigen and antibody immune complex, might be the final cytotoxic agent to epithelial cells. We emphasize that the immunological interactions may be associated with the pathophysiology of type B gastritis positive for H. pylori.

References


3. Inflammatory Bowel Disease and Immunology

Kenzo KOBAYASHI

Key words: inflammatory bowel disease, ulcerative colitis, Crohn's disease

Inflammatory bowel disease and immunology

Ulcerative colitis (UC) and Crohn’s disease (CD) are collectively called (idiopathic) inflammatory bowel disease (IBD), and treated as a single group in practice. However, in recent years, detailed analysis of the clinical pictures of the diseases and immunological studies of their pathogenesis suggested that UC and CD are different from each other both clinically and pathophysiologically. Recent advances in immunology and molecular biology have greatly contributed to this renewed understanding of the diseases (1, 2).

UC is a diffuse, chronic, non-specific inflammatory disease which mainly affects the mucosa and forms erosion and ulcers. It is intractable with alternating phases of remission and relapse. The colonic mucosal lesions are markedly infiltrated with lymphocytes, plasma cells, macrophages and other immunocompetent cells, suggesting that an immunological mechanism is involved in the development of the disease as well as in its persistence and progress to a chronic state.

One recent topic is the finding that HLA-DR antigen, a class II MHC which is not expressed in the colonic mucosal epithelium of healthy people, was detected in epithelial cells of the colonic mucosa of patients with UC. Activated T cells, B cells, macrophages and neutrophils were found in the lesions. It is also known that adhesion molecules, accessory molecules which appear when macrophages present antigens, are expressed.

The pathogenic mechanism of the mucosal lesions in UC is believed to be mediated by IL-1, other cytokines, oxygen radicals, PAF, LTB4 and other chemical mediators.

CD mainly affects young adults. It presents granulomatous inflammatory lesions with accompanying fibrosis and ulceration, and its clinical picture is very diverse. Attention has been directed to functional abnormalities of macrophages in CD in relation to the immunological modifications. CD differs immunologically from UC in antigen proteins corresponding to blood antibodies and in IgG subclasses of antibody producing cells.

From these results, the etiology of inflammatory bowel...