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Clinical and Immunological Aspects of Prognosis of Purulent-Inflammatory Complications of Ulcerative Colitis

A.F. Ollokov[1]

ABSTRACT

Background. *Ulcerative colitis is the main form of inflammatory bowel disease. The exact cause of ulcerative colitis is unknown. However, genetically susceptible individuals appear to have an unregulated mucosal immune response to the commensal intestinal flora, resulting in intestinal inflammation.*

Material and methods. *The object of the study was to analyze the results of the examination and treatment of 92 patients with ulcerative colitis who were examined and treated at the clinical bases of the Tashkent Medical Academy and the Bukhara State Medical Institute from 2015 to 2024. We conducted a comparative analysis of the effectiveness of methods for diagnosing and predicting the development of purulent inflammatory complications in patients with ulcerative colitis. General clinical, immunological, biochemical, endoscopic, imaging and statistical research methods were used.*

Results. *It has been established that purulent-inflammatory complications of ulcerative colitis most often develop in patients with an acute form of the disease. In contrast, in the postoperative period, purulent-inflammatory complications develop in 45.7% of cases and become the leading cause of death in 29.3% of patients with ulcerative colitis. It was revealed that the degree of severity of clinical manifestations of ulcerative colitis is accompanied by anaemia, hypoproteinemia, electrolyte imbalance, as well as laboratory signs of generalization of the inflammatory process in the form of an increase in the leukocyte index and haematological index of intoxication.*

Conclusion. *In nonspecific ulcerative colitis, cellular immunity indicators are characterized by progressive imbalances of the main subpopulations of T- and B-lymphocytes and a decrease in the immunoregulatory index in the case of a chronic continuous and acute course of the disease. It has been proved that during the period of a constant and acute course of ulcerative colitis, there is an increase in the level of pro-inflammatory cytokines IL-1, IL-6, IL-8 and TNF-α, which in terms of the intensity of formation exceed the values of patients with a chronic relapsing course of the disease.*

Keywords: *ulcerative colitis, purulent-inflammatory complications, cellular and humoral immunity*

[1] ***Corresponding author:*** *Bukhara State Medical Institute, Bukhara Branch of the Republican Scientific and Practical Medical Center for Emergency Medical Care, Bukhara, Uzbekistan, e-mail: ollokovasliddin@mail.ru*

INTRODUCTION

Inflammation in ulcerative colitis is usually limited to the surface of the mucous membrane. The disease begins in the rectum and spreads proximally continuously through the entire colon. However, some patients with proctitis or left-sided colitis may have cecum inflammation. The spread of the disease is stratified by the degree of colon involvement, from proctitis to left-sided colitis, extensive colitis, or pancolitis [1].

Ulcerative colitis is the most common disease among inflammatory pathologies of the large intestine. Countries in the northern and western hemispheres have the highest ulcerative colitis rates. It ranges from 9 to 20 cases per 100,000 people, and the prevalence rate ranges from 156 to 291 cases per 100,000. In contrast, low values of ulcerative colitis are found in the southern hemisphere and eastern regions. It is interesting that in countries switching to an industrial lifestyle, there is an increase in the incidence of ulcerative colitis. This indicates environmental factors that may be decisive in ulcerative colitis [2].

Improved sanitation in industrialized countries can reduce susceptibility to enteric infections in childhood, thereby limiting the maturation of the mucous membrane immune system, which can lead to an inadequate immune response when exposed to infectious microorganisms later in life [3].

Episodes of prior gastrointestinal infection (e.g., Salmonella spp., Shigella spp., and Campylobacter spp.) double the risk of subsequent ulcerative colitis development, suggesting that acute intestinal infection may lead to changes in the intestinal flora, hence the onset of a chronic inflammatory process in genetically predisposed individuals [4].

There are weak epidemiological data on the association between exposure to non-selective, nonsteroidal anti-inflammatory drugs and the onset or recurrence of ulcerative colitis [5].

The most effective in terms of radicality today are surgical methods of treating ulcerative colitis - proctocolectomy using ilio-anal anastomosis. However, the presence of underlying disorders of a systemic immunological nature, among which the most common is the development of a pelvic abscess [6].

There are results of empirical observations on the increase in postoperative complications from the formed sac from the ileal stump with long-term use of corticosteroids and Infliximab in the preoperative period. Clinicians observed a significant increase in postoperative septic complications [7]. Clinicians associate this circumstance with a suppressive effect on the immune system.

The development of such complications in the early postoperative period, in the future from 15% to 30% of cases, leads to the development of anastomosis stricture and intestinal obstruction, chronic flatulence, sexual dysfunction, impaired urination, and female infertility, with a threefold increase in risk after the use of ilio-anal anastomosis [8].

Thus, the high proportion of postoperative complications in patients with ulcerative colitis, despite the use of radical interventions, still creates an increased risk of their development. Given such high values of unsatisfactory treatment results, scientists focus on studying the features of immunological disorders leading to the development of postoperative complications.

The study aimed to improve the results of predicting the development of purulent-inflammatory complications of ulcerative colitis by developing and substantiating the effectiveness of clinical and immunological monitoring methods in patients with this disease.

MATERIAL AND METHODS

The study was conducted in 92 patients with ulcerative colitis who were under our observation from 2015 to 2024. According to the WHO criteria, male patients prevailed, mainly young (43.4%) and middle-aged (35.8%). The ratio of male and female patients was 1.39 units, and the control group consisted of 20 volunteers recognized by the medical commission as healthy. We accepted the results of the immunological studies of the control group as reference values.

The criteria for inclusion of patients in the study were the presence of confirmed (endoscopically and morphologically) nonspecific ulcerative colitis; mandatory written consent of the patient to conduct the study; the age of patients over 18 years; absence of pregnancy and lactation period at the time of treatment and examination; absence of complications of nonspecific ulcerative colitis in the form of malignant neoplasm of the intestine, upon detection of which patients were excluded from the cohort; the presence of activity of ulcerative colitis; absence of severe extraintestinal somatic and mental pathology; absence of drug and alcohol dependence, as well as confirmed pathologies of the immune system, including HIV infection; consent to additional laboratory and instrumental research methods—any discrepancy with the above determined the criteria for excluding patients from the study.

The extent of lesions with ulcerative colitis was identified according to the Montreal classification (2005). The severity of the attack of ulcerative colitis was determined according to the criteria of S.P. Travis and L. Dinesen [9]. The activity of the course of ulcerative colitis was carried out using an endoscopic picture.

Concomitant diseases, together with extraintestinal lesions of ulcerative colitis, were found in 231 names according to the medical history records; on average, there were 2.5 names of diseases per 1 patient. The most common lesions (84.8% and 82.6% of cases) were noted from the musculoskeletal system and the skin surface.

For immunological studies, blood was taken from the ulnar vein into a centrifuge tube treated with heparin in 5.0 ml. We selected 10 μl for counting leukocytes and lymphocytes in Goryaev's chamber using paint by Zadorozhny S.I. and Dozmorov I.M. (1987). Mononuclear cells from peripheral blood were obtained by isolating at the density gradient ficoll-verographin with a density of 1.077 g/l according to Boyum (1968). The number of cells in Goryaev's chamber was counted by the conventional method under a microscope, and the concentration of lymphocytes was brought to 2x106 per 1 ml; the viability of lymphocytes was determined in a test with 0.1% trypan blue.

The state of the patient's immune system was assessed by the expression of CD-differentiation and activation antigens. The following markers of immunocompetent cells were determined: CD3+-, CD4+, CD8+-, and CD119+-lymphocytes. Expression of CD receptors was carried out in the rosette formation reaction using monoclonal antibodies of the LT series, manufactured by Sorbent LLC (Russia) according to the method of Garib F.Y. et al. (1995).

According to Manchani (1963), the concentration of the examined immunoglobulins of the three main classes, M, A, and G g/l, in the blood serum was determined by radial immunodiffusion.

Interleukins (cytokines) were determined in the blood serum of patients examined by enzyme-linked immunosorbent assay. To implement this option, two monoclonal antibodies with different etiotropic specificity to interleukins IL-1α, IL-1b, IL-6, IL-8, TNF-α were used using special kits for enzyme-linked immunosorbent assay according to the standard procedure.

In accordance with the goals and objectives of the study, the calculation of elementary statistical indicators (mean values, errors of means, standard deviations, range of data dispersion), construction and visual analysis of data dispersion diagrams were carried out. The indicators were compared using signs of nonparametric criteria. The significance of the differences between the samples, which were close to the norm in terms of the nature of the distribution, was established according to the parametric Student's test with a 95% reliable probability interval. The criterion for the statistical reliability of the conclusions obtained was considered to be the generally accepted in medicine value $p<0.05$.

RESULTS

When assessing the nature of the clinical and laboratory manifestations of ulcerative colitis, it was revealed that the most characteristic clinical signs of ulcerative colitis are diarrhoea (81.5%), abdominal pain (67.4%) and bloody stools (60.9%). At the same time, the frequency of clinical manifestations in ulcerative colitis is determined by the activity and severity of the disease, which directly affect their growth. The degree of severity of clinical manifestations of ulcerative colitis is accompanied by anaemia, hypoproteinemia, electrolyte imbalance, as well as laboratory signs of generalization of the inflammatory process in the form of an increase in the leukocyte index and a haematological indicator of intoxication.

When assessing the nature of changes in cellular immunity indices in patients with various forms of ulcerative colitis, high CD3+CD19- values up to 84.25±0.32% ($p<0.05$) were found relative in patients with chronic recurrent ulcerative colitis, with a decrease in patients with chronic continuous (up to 55.17±0.92%) and acute course of the disease (up to 44.16±1.64%). However, when analyzing the absolute values, we revealed a progressive growth of B-lymphocytes. At the same time, the reverse nature of changes was noted about the dynamics of changes in CD19+CD3- in patients with various forms of the course of ulcerative colitis.

The nature of changes in CD3+CD4+ in patients with various forms of ulcerative colitis showed a decrease in relative values both about reference (from 43.15±0.37%) and in relation to the chronic relapsing form of the disease (from 57.13±0.32%) to 36.24±1.56%. As for the absolute values, it is possible to note an increase in values in the acute course of the disease (from 0.65±0.05 $x10^9$/l to 0.82±0.09 $x10^9$/l). The nature of changes in the relative and absolute values of CD3+CD8+ in patients with various forms of the course of ulcerative colitis showed an increase in the values of 22.14±0.33% to 38.95±1.37% and from 0.31±0.01 $x10^9$/l to 0.78±0.02 $x10^9$/l.

Thus, in ulcerative colitis, cellular immunity indicators are characterized by a progressive imbalance of the main subpopulations of T- and B-lymphocytes, manifested by a decrease in the immunoregulatory index in the case of a chronic continuous and acute course of the disease. The multidirectional changes in the relative and absolute values of T- and B-lymphocytes indicate the presence of tension in the immune system in patients with ulcerative colitis. The range of changes in the relative number of T-helper cells with the development of more severe forms of the disease indicates a decrease in the induction of this link of immunity. Against this background, there is an increase in the suppressor-cytotoxic link of T-lymphocytes. In patients with acute ulcerative colitis, there is a significant increase in CD3+CD8+ cells, which may indicate a tendency to increase apoptosis of T-lymphocytes.

The results obtained in impaired cellular immunity in patients with various forms of ulcerative colitis can be considered as immunological diagnostic markers reflecting the presence and activity of the inflammatory process, on the one hand, as well as the possible development of purulent-inflammatory complications, impaired immunoregulation and activation of the autoimmune component, on the other.

The nature and analysis of changes in the indicators of humoral immunity in patients with various forms of the course of ulcerative colitis showed that the intensity of immunoglobulin formation in the blood of patients with ulcerative colitis depends entirely on the form of the course of the disease. High values of all forms of the studied immunoglobulins are characterized by the development of remission of ulcerative colitis. At the same time, a decrease in immunoglobulins in the blood leads to an exacerbation of the disease up to the acute form of the disease. This nature of changes corresponds to the dynamics of IgM and IgG concentrations in the blood. However, the nature of IgA changes in all phases and forms of ulcerative colitis remained higher than the reference values, the decrease of which occurred in relation to patients with a chronic relapsing course of ulcerative colitis.

In patients with ulcerative colitis, significant changes in the system of pro-inflammatory cytokines were revealed. In the period of continuous and acute course of the disease, there is an increase in the level of cytokines IL-1, IL-6, IL-8 and TNF-α, which in terms of the intensity of formation exceed the values of patients with a chronic recurrent course of ulcerative colitis by an average of 4.5 times. A separate analysis of IL-1 fractions revealed a relatively more significant formation of IL-1b, the proportion of which was equal to 74%, which indicates the pronounced importance of this marker of the inflammatory process in conditions of exacerbation of ulcerative colitis and the possible development of its purulent-inflammatory complications.

The distribution of preoperative complications of ulcerative colitis showed that in patients with a chronic recurrent course of the disease, intestinal bleeding was observed in 1 (3%) patient, perforation of the large intestine in 5 (15.2%) patients, and toxic megacolon in 9 (27.3%) patients. In the analysis of clinical data of ulcerative colitis in patients with chronic continuous disease, intestinal bleeding was observed in 3 (7.9%) patients, intestinal perforation in 6 (15.8%) patients, and toxic megacolon in 12 (31.6%) patients. Patients with the acute form of ulcerative colitis in 2 (9.5%) cases were characterized by the presence of intestinal bleeding, in 8 (38.1%) cases – by intestinal perforation and in 3 (14.3%) cases – by toxic megacolon.

All patients with ulcerative colitis were operated on, and in the case of purulent-inflammatory complications of the disease in the preoperative period, they were of an emergency or urgent nature, which determined such a large proportion of unsatisfactory results of operations.

Thus, postoperative complications after hemicolectomy developed in 21.4% of cases, after colproctomies – in 19% of cases, after subtotal colectomy – in 16.7% of cases, after colectomy – in 11.9% of cases, and various resections of the large intestine – also in 11.9% of cases. Separately, I would like to note the high frequency of postoperative complications performed as reconstructive or repeated (relaparotomy) operations (19%).

Thus, surgical operations in patients with ulcerative colitis against the background of the development of purulent-inflammatory complications in 45.7% of cases end with the development of postoperative complications.

Twenty-seven patients died in the postoperative period, who had complications, including purulent-inflammatory ones. Among them, we diagnosed an abscess of the abdominal cavity, which formed in 15 (11.3%) patients; peritonitis in the postoperative period, which developed in 7 (5.3%) patients; suppuration of the postoperative wound, which developed in 41 (30.8%) patients, which subsequently led to inconsistency of sutures with eventration of internal organs in 38 (28.6%) patients; Another 32 (24.1%) patients developed parastomal phlegmons of the anterior abdominal wall in the postoperative period.

Purulent-inflammatory complications in the postoperative period caused mortality in 14.3% of cases after hemicolectomies, in 16.7% of cases after colproctomies, in 14.3% of cases after relaparotomies, in 7.1% of cases after colectomies and various resections of the colon, as well as in 4.8% of cases after subtotal colectomy.

Thus, purulent-inflammatory complications of ulcerative colitis in patients with various forms of the course of the disease develop in 46.7% of cases, requiring the use of surgical methods of treatment in an emergency or urgent manner. Most often, purulent-inflammatory complications of ulcerative colitis develop in patients with an acute form (52.4%) of the course of the disease. In the postoperative period, purulent-inflammatory complications develop in 45.7% of cases and become the main cause of death in 29.3% of patients with ulcerative colitis. Such a high incidence of purulent-inflammatory complications and mortality among patients with ulcerative colitis indicates the need for early diagnosis and prognosis of their development at the stage of conservative treatment of this disease.

In order to substantiate the role and place of the clinical and immunological relationship in the pathogenesis of the development of purulent-inflammatory complications of ulcerative colitis at the first stage, we made numerical designations of the forms of the course of ulcerative colitis, which increased with the deterioration of the form of the course of the disease, the possibility of complications and the onset of death. At the same time, the point randomization of the forms of the disease, complications and mortality of ulcerative colitis was of an increasing nature, the type of the operation performed according to the severity of its performance (radicality) or the repeated nature of the intervention due to the development of purulent-inflammatory complications in the postoperative period.

It was also possible to identify the administrative curve of cloud cover in the classification of forms of clinical manifestation of ulcerative colitis and the forms of its course. At the next stage, we constructed a comparative graphic curve of cloud coverage of the classification forms of clinical manifestation of ulcerative colitis and the form of its course.

Thus, the linear correlation analysis allowed us to identify the maximum dependence of the regularity of the manifestation of clinical forms, variants of the course and degree of lesions of the large intestine in patients with ulcerative colitis. It may reflect the basis of a platform for building a relative correlation between the clinical forms of manifestation of ulcerative colitis and changes in cellular and humoral immunity indicators.

The studied forms of the disease had gradations from 1 to 3 points, while the zero position was attributed to the standard (reference) value of the studied indicators of cellular humoral immunity. The construction of a point gradation of various forms of the course and development of purulent-inflammatory complications of ulcerative colitis made it possible to identify a close coincidence of the chronic recurrent form of the course of the disease with a mild degree of attack severity, with minimal endoscopic activity and a limited extent of the lesion at the level of proctitis. The chronic continuous course of ulcerative colitis was closely correlated with a moderate attack, moderate endoscopic activity, and the extent of the lesion at the level of the left half of the large intestine. The acute form of the disease was often characterized by a severe attack, pronounced endoscopic activity and a total length of the process. Such labelling of clinical signs of the disease allowed us to identify a correlation between the absolute and relative values of cellular immunity in patients with ulcerative colitis, depending on the form of the disease.

Already when assessing the correlation between the absolute and relative values of cellular immunity indicators in patients with various forms of the course of ulcerative colitis, an ambiguous picture of changes was revealed.

The correlation coefficient of the CD3+CD8+ relative values had a direct correlation with all the studied absolute indicators of cellular immunity (CD3+CD19- R=0.983; CD19+CD3- R=0,322; CD3+CD4+ R=0,877; CD3+CD8+ R=0,989). For the rest of the indicators, the correlation was inverse. The maximum inverse correlation was observed between the absolute and relative values of CD3+CD19- and CD19+CD3 (R=-0.952), as well as CD3+CD4+ and CD19+CD3- (R=-0.838).

The correlation between the indicators of humoral immunity in patients with different forms of the course of ulcerative colitis showed that IgM and IgG had a negative correlation with all the studied cytokines, while IgA had a positive relationship in most cases except for IL-6 (R = -0.058). The values of circulating immune complexes were interesting, the correlation significance of which turned out to be in a direct correlation with all pro-inflammatory cytokines in the blood studied (from R=0.911 to R=0.995).

The construction of a correlation curve of the significance of immunological markers of the development of purulent-inflammatory complications of ulcerative colitis

made it possible to identify a specific sequence of growth or decrease in indicators in the cloud cover. According to this figure, it is possible to clearly trace the significance of changes in the marker of the immunological system in the development of purulent-inflammatory complications (Figure 1).

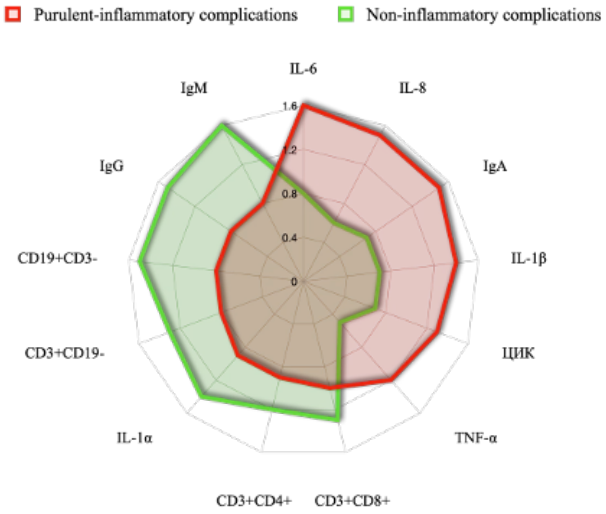

Figure 1. Comparative graphical curve of cloud coverage of changes in the level of cellular and humoral immunity among patients depending on the form of complications of ulcerative colitis

According to generally accepted data on the role of the immune system in the pathogenesis of the development of ulcerative colitis, the mechanisms of participation of both cellular and humoral system indicators are known. Such a mechanism is based on the primary action of an antigen, which is considered to be an unclassified antigen of epithelial cells of the intestinal mucosa. Later, the cells of the lamina proper begin to act as an antigen (Figure 2).

The primary contact of these antigens with lymphocytes at an early stage of the development of ulcerative colitis leads to the activation and growth of the number of T-helper cells and macrophages. At this stage, the production of pro-inflammatory cytokines of the IL-1 group contributes to the production of appropriate cell growth and proliferation factors aimed at repairing damage and achieving recovery of the affected part of the intestine. However, at this level, there is an imbalance of IL-1α and IL-1β in favour of the growth of the latter, which leads to the activation of the Th2 lymphocyte system, which in turn activates B-lymphocytes. They also act as co-factors in the activation of B-lymphocytes. At this stage of the immunological reaction, immunoglobulins are produced, a sufficient concentration of which can transform the inflammatory process in the intestine into chronic recurrent nonspecific ulcerative colitis with prolonged stages of remission.

However, in the case of a low cellular immune response, there is an increase in the production and release of pro-inflammatory cytokines such as IL-6, IL-8 and TNF-α into the systemic circulation.

Local (local) release of pro-inflammatory cytokines into the bloodstream should contribute to the activation of macrophages and neutrophil chemotaxis. Also, due to this production, metabolic processes associated with the growth of connective tissue are activated, and the proliferation of fibroblasts and epithelial cells is stimulated. This mechanism also contributes to the healing, damage and restoration of the integrity of the mucous membrane of the large intestine.

Unfortunately, however, as a result of an insufficient response to cellular immunity, there is an unregulated release of pro-inflammatory cytokines into the systemic circulation, which is accompanied by systemic inflammatory disorders. It is the insufficiency of Th1 lymphocytes at an early stage of the development of the above mechanisms that lead to the development of purulent-inflammatory complications of ulcerative colitis, acquiring the opposite direction of regenerative processes.

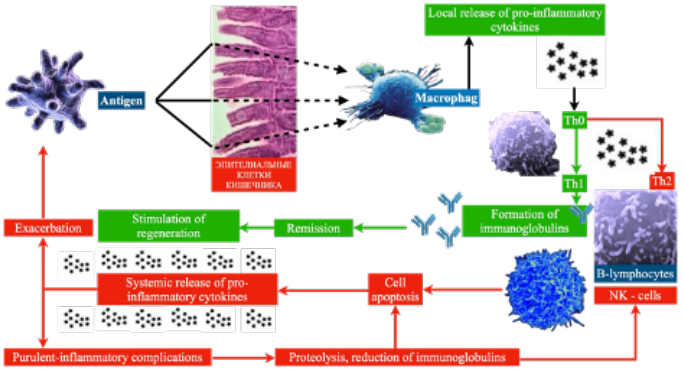

Figure 2. Scheme of immunological imbalance in the pathogenesis of the development of purulent-inflammatory complications of ulcerative colitis

The release of cytokines into the systemic circulation is manifested by fever, an increase in body temperature, adapting to a decrease in the ability of a number of bacteria to reproduce and stimulate processes associated with the proliferation of lymphocytes. Dysproteinemia develops, an increase in the number of leukocytes, the formation of nitrogenous components in the liver and proteins of the acute phase, components of the complement system. This is also accompanied by a decrease in

albumin synthesis and an imbalance of electrolytes in the blood.

In general, it can be summarized that hypercytokinemia is essentially a system for organizing the body's protective reaction. However, such an effect of cytokines is possible only in the balance of activation of Th1 lymphocytes with the production of a sufficient amount of immunoglobulins that reduce the aggressive impact of antigens and the development of purulent-inflammatory complications of ulcerative colitis.

Thus, in the pathogenesis of the development of purulent-inflammatory complications of ulcerative colitis at different stages of therapeutic measures, there is a significant violation in the immune system, which is characterized by a decrease in the expression of T-helper cells against the background of IgA formation and early immunosuppression, leading to increased apoptosis of lymphocytes. There is an increased production and release of pro-inflammatory cytokines IL-6, IL-8, IL-1β and TNF-α into the systemic circulation, which is accompanied by an increase in the number of circulating immune complexes. A vicious circle is formed, in which an increase in the activity of the Th2-cell pathway acquires the leading link in the immunological reaction, leading to the development of an acute or continuous form of the course of ulcerative colitis and its purulent-inflammatory complications both in the preoperative and postoperative periods.

The distribution parameters revealed a high sensitivity of IL-6 and IL-1β, moderate sensitivity of TNF-α and the level of circulating immune complexes, and a relatively low sensitivity of IL-8. At the same time, the confidence interval of the selected values in all cases has a significant value ($p<0.001$).

The choice of the above parameters allowed us to build a logarithmic program "PCNUC" with carefully selected parameters for predicting the development of purulent-inflammatory complications of ulcerative colitis based on a combination of the relationship between the form, severity of the attack, activity and extent of the disease, the level of IL-6, IL-1β, TNF-α, IL-8 and circulating immune complexes in the blood at the time of the comprehensive examination of the patient (Table).

As our studies have shown, a low probability of developing purulent-inflammatory complications of ulcerative colitis is possible in patients with a recurrent form of the disease with a mild attack, with minimal activity in a limited affected area (proctitis), with blood levels: IL-6 ≤10 ng/ml, IL-1β ≤121 ng/ml, TNF-α ≤40 ng/ml; IL-8 ≤50 ng/mL; circulating immune complexes ≤50 units.

In the presence of a continuous form of the disease with a moderate attack, with moderate activity in a limited affected area (left-sided lesion of the large intestine), with blood levels: IL-6 11-39 ng/ml, IL-1β 120-199 ng/ml, TNF-α 41-79 ng/ml; IL-8 51-149 ng/mL; circulating immune complexes are 51-79 units.

Table

Point gradation of various prognostic prognostics of the development of purulent-inflammatory complications of ulcerative colitis

MARKERS	PREDICTIVE PROBABILITY		
	LOW	HIGH	CRITICAL
Form	Recurrent	Continuous	Acute
The severity of the attack	Easy	Moderate	Grind
Activity	Minimum	Moderate	Expressed
Extent	Proctitis	Left-handed	Total
IL-6 (ng/ml)	≤10	11-39	≥40
IL-1β (ng/ml)	≤121	120-199	≥200
TNF-α (ng/ml)	≤40	41-79	≥80
IL-8 (ng/ml)	≤50	51-149	≥150
Circulating immune complexes (units)	≤50	51-79	≥80

At the same time, in the presence of an acute form of the disease with a severe attack, with pronounced activity with total damage to the large intestine, with blood levels: IL-6 ≥40 ng/ml, IL-1β ≥200 ng/ml, TNF-α ≥80 ng/ml; IL-8 ≥150 ng/mL; circulating immune complexes ≥80 units, the prognostic probability of the development of purulent-inflammatory complications of ulcerative colitis acquires a critical degree.

A comparative assessment of the effectiveness of the value of the developed method for predicting purulent-inflammatory complications of ulcerative colitis showed that accurate positive prognostic results by the traditional method were noted in 35.9% of cases, while when carried out under the PCNUC program - in 44.6% of cases. Accurate negative prognostic results were reported in 20.7% of cases with the traditional method, while with the PCNUC program - in 48.9% of cases. False-positive prognostic results were noted in 32.6% of cases, while in 4.3% of cases, when carried out according to the PCNUC program. False-negative prognostic results were noted in 10.9% of cases when carried out according to the traditional method, while in 2.2% of cases when carried out according to the "PCNUC" program.

Thus, a comparative assessment of the effectiveness of the PCNUC prognostic program developed by us in patients with ulcerative colitis showed that in comparison with the traditional method of predicting purulent-inflammatory complications, an increase in true-positive and true-negative results was achieved by an average of 1.9 times, and the reliability of predicting the development of purulent-inflammatory complications was in-

creased by an average of 1.8 times. This made it possible to reduce the number of false results of predicting purulent-inflammatory complications of ulcerative colitis by 2 times. All this indicates a significant increase in the reliability of predicting the development of purulent-inflammatory complications of ulcerative colitis both in the preoperative and postoperative periods of treatment.

DISCUSSION

To date, it has already been proven that the epithelial barrier coated with the mucinous layer is the first line of defence of the mucosal immune system, as it provides physical separation between the host's immune cells and luminal microbes and synthesizes antimicrobial peptides. B.J. Van Klinken et al. [10] found that ulcerative colitis reduces the synthesis and sulfation of some subtypes of colon mucin, i.e. mucin-2.

Damage to the epithelial barrier, according to F. Heller et al. [11] leads to increased permeability, possibly due to defective regulation of tight joints. This loss of the barrier ensures increased absorption of luminal antigens. However, it is unclear whether such dysfunction precedes ulcerative colitis or is the result of chronic inflammation.

According to A. Rahman et al. [12] In addition to creating a physical barrier, the intestinal epithelium contributes to the host's defence by producing antimicrobial peptides, thereby limiting bacterial invasion. However, after several years of similar studies, it remains not fully understood whether this increase in the production of antimicrobial peptides is induced by a response to microorganisms, inflammatory cytokines, or both.

Usually, the intestinal immune system maintains a balance between tolerance to commensal flora and food antigens and an adequate response to intestinal pathogens. Data from genetically modified animal models that develop chronic intestinal inflammation after colonization by commensal gut bacteria but remain disease-free under bacteria-free conditions suggest a predominant role for non-pathogenic gut bacteria in the pathogenesis of ulcerative colitis.

Human studies also confirm the importance of the intestinal microbiota not only in the pathogenesis of the disease. But also potentially in terms of the severity of intestinal inflammation and the phenotype of the disease [13, 14].

Thus, ulcerative colitis appears to result from an imbalance in the homeostatic balance between host mucosal immunity and the intestinal microbiota, resulting in an aberrant immune response against commensal non-pathogenic bacteria. Immunological disorders causing inflammation in ulcerative colitis include an exaggerated T-cell (modified atypical Th2) response that causes mucosal hypersensitivity to commensal bacteria in genetically predisposed hosts. The development of knowledge about the immunological mechanisms of the progression of the inflammatory process and the development of complications of the disease, including surgical ones, is crucial for the development of new strategies for the treatment of patients with this pathology. However, as the analysis of the literature has shown, such studies have not actually been conducted.

CONCLUSION

The most characteristic clinical signs of ulcerative colitis are diarrhoea (81.5%), abdominal pain (67.4%) and bloody stools (60.9%). At the same time, the frequency of clinical manifestations in ulcerative colitis is determined by the activity and severity of the disease, which directly affect their growth. The degree of severity of clinical manifestations of ulcerative colitis is accompanied by anaemia, hypoproteinemia, electrolyte imbalance, as well as laboratory signs of generalization of the inflammatory process in the form of an increase in the leukocyte index and a haematological indicator of intoxication.

In ulcerative colitis, cellular immunity indicators are characterized by a progressive imbalance of the main subpopulations of T- and B-lymphocytes, manifested by a decrease in the immunoregulatory index in the case of a chronic, continuous and acute course of the disease. The multidirectional changes in the relative and absolute values of T- and B-lymphocytes indicate the presence of tension in the immune system in patients with ulcerative colitis. The range of changes in the relative number of T-helper cells with the development of more severe forms of the disease indicates a decrease in the induction of this link of immunity. Against this background, there is an increase in the suppressor-cytotoxic link of T-lymphocytes. In patients with acute ulcerative colitis, a significant rise in CD3+CD8+ cells is noted, which may indirectly indicate the presence of a tendency to increase apoptosis of T-lymphocytes.

The nature and analysis of changes in the parameters of humoral immunity in patients with various forms of ulcerative colitis showed an increase in immunoglobulins M, G and A in patients with the phase of remission of the disease. In patients with the phase of exacerbation and development of purulent-inflammatory complica-

tions of ulcerative colitis, a decrease in immunoglobulins below the reference value is accompanied by an increase in the proportion of circulating immune complexes of the blood. In patients with ulcerative colitis, significant changes in the system of pro-inflammatory cytokines were revealed. In the period of continuous and acute course of the disease, there is an increase in the level of cytokines IL-1, IL-6, IL-8 and TNF-α, which in terms of the intensity of formation exceed the values of patients with a chronic recurrent course of ulcerative colitis by an average of 4.5 times. A separate analysis of IL-1 fractions revealed a relatively more significant formation of IL-1b, the proportion of which was equal to 74%, which indicates the pronounced importance of this marker of the inflammatory process in conditions of exacerbation of ulcerative colitis and the possible development of its purulent-inflammatory complications.

Purulent-inflammatory complications of ulcerative colitis in patients with various forms of the course of the disease develop in 46.7% of cases requiring the use of surgical methods of treatment in an emergency or urgent manner. Most often, purulent-inflammatory complications of ulcerative colitis develop in patients with an acute form (52.4%) of the course of the disease. In the postoperative period, purulent-inflammatory complications develop in 45.7% of cases and become the leading cause of death in 29.3% of patients with ulcerative colitis. Such a high incidence of purulent-inflammatory complications and mortality among patients with ulcerative colitis indicates the need to develop methods for early diagnosis and prognosis of their development at the stage of drug treatment of this disease.

In the pathogenesis of the development of purulent-inflammatory complications of ulcerative colitis at different stages of therapeutic measures, significant disorders in the immune system are noted, which are characterized by a decrease in the expression of T-helper cells against the background of IgA formation and early immunosuppression, leading to increased apoptosis of lymphocytes. There is an increased production and release of pro-inflammatory cytokines IL-6, IL-8, IL-1β and TNF-α into the systemic circulation, which is accompanied by an increase in the number of circulating immune complexes. A vicious circle is formed, in which an increase in the activity of the Th2-cell pathway acquires the leading link in the immunological reaction, leading to the development of an acute or continuous form of the course of ulcerative colitis and its purulent-inflammatory complications both in the preoperative and postoperative periods.

The primary method for predicting purulent-inflammatory complications of ulcerative colitis is the corresponding program "PCNUC" developed by us, which is based on a combination of the form, severity of the attack, activity and extent of the disease, the level of IL-6, IL-1β, TNF-α, IL-8 and circulating immune complexes in the blood at the time of the comprehensive examination of the patient. A comparative assessment of the effectiveness of the PCNUC prognostic program developed by us in patients with ulcerative colitis showed that in comparison with the traditional method of predicting purulent-inflammatory complications, an increase in true-positive and true-negative results was achieved by an average of 1.9 times, and the reliability of predicting the development of purulent-inflammatory complications was increased by an average of 1.8 times. This made it possible to reduce the number of false results of predicting purulent-inflammatory complications of ulcerative colitis by 2 times. All this indicates a significant increase in the reliability of predicting the development of purulent-inflammatory complications of ulcerative colitis both in the preoperative and postoperative periods of treatment.

Conflict of interest – the authors have not claimed any conflicts of interest.

Ethical aspects – during this study, all ethical standards were observed in accordance with the protocol approved by the Ministry of Health of the Republic of Uzbekistan.

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YARALI KOLITNING YIRINGLI-YALLIG'LANISH ASORATLARI BASHORAT QILISH KLINIK VA IMMUNOLOGIK JIHATLARI

Ollokov A.F.

Buxoro davlat tibbiyot instituti

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Buxoro, O'zbekiston.

ABSTRAKT

Dolzarblik. Yarali kolit ichak kasalligining asosiy yallig'lanish shaklidir. Yarali kolitning aniq sababi noma'lum. Biroq, genetik jihatdan moyil shaxslar kommensal ichak florasiga tartibga solinmagan immunitetga ega bo'lib, ichak yallig'lanishiga olib keladi.

Materiallar va tadqiqotlar. Tadqiqot ob'ekti 2015 yildan 2024 yilgacha Toshkent tibbiyot akademiyasi va Buxoro davlat tibbiyot institutining klinik bazalarida yarali kolit bilan 92 nafar bemorning ko'rikdan o'tishi va davolash natijalarini tahlil qilish edi.

Natijalar. Ma'lum bo'lishicha, yarali kolitning yiringli-yallig'lanish asoratlari ko'pincha kasallikning o'tkir shakli bo'lgan bemorlarda rivojlanadi, operatsiyadan keyingi davrda yiringli-yallig'lanish asoratlari 45,7% hollarda rivojlanadi va yarali kolit bilan og'rigan bemorlarning 29,3% da o'limning asosiy sababi hisoblanadi. Yarali kolitning klinik ko'rinishlarining og'irlik darajasi anemiya, gipoteinemiya, elektrolitlar muvozanati, shuningdek leykotsitlar indeksi va intoksikatsiyaning gematologik indeksi ko'payishi natijasida yallig'lanish jarayonining umumiylashuvining laboratoriya belgilari bilan birga bo'ladi.

Xulosa. Nospesifik yarali kolitda hujayrali immunitet ko'rsatkichlari T- va B-limfotsitlarning asosiy pastki populyatsiyalarining progressiv muvozanati va kasallikning surunkali doimiy va o'tkir davrida immunoregulyatoriya indeksining pasayishi bilan tavsiflanadi. Yarali kolitning uzluksiz va o'tkir davrida yallig'lanishga qarshi IL-1, IL-6, IL-8 va TNF-α sitokinlarning ko'tarilishi kuzatiladi, bu esa shakllanish intensivligi jiddiyligi jikmesidan kasallikning surunkali yo'li bo'lgan bemorlarning ko'rsatkichlaridan oshib ketadi.

Kalit so'zlar: yarali kolit, yiringli-yallig'lanish asoratlari, hujayra va gumoral immunitet

КЛИНИКО-ИММУНОЛОГИЧЕСКИЕ АСПЕКТЫ ПРОГНОЗИРОВАНИЯ ГНОЙНО-ВОСПАЛИТЕЛЬНЫХ ОСЛОЖНЕНИЙ ЯЗВЕННОГО КОЛИТА

Оллоков А.Ф.

Бухарский медицинский институт

Бухарский филиал республиканского научно-практического медицинского центра экстренной медицинской помощи

Бухара, Узбекистан.

АБСТРАКТ

Актуальность. Неспецифический язвенный колит является основной формой воспалительных заболеваний кишечника. Точная причина неспецифического язвенного колита неизвестна.

Материал и методы. Объектом исследования явился анализ результатов обследования и лечения 92 больных с неспецифическим язвенным колитом находившиеся на обследовании и лечении в клинических базах Ташкентской медицинской академии и Бухарского государственного медицинского института за период с 2015 по 2024 годы.

Результаты. Установлено, что наиболее часто гнойно-воспалительные осложнения неспецифического язвенного колита развиваются у больным с острой формой течения заболевания, тогда как в послеоперационном периоде гнойно-воспалительные осложнения развиваются в 45,7% случаев и становятся основными причинами летального исхода у 29,3% больных с неспецифическим язвенным колитом.

Заключение. При неспецифическом язвенном колите показатели клеточного иммунитета характеризуются прогрессирующим нарушения баланса основных субпопуляций Т- и В-лимфоцитов и снижением иммунорегуляторного индекса в случае хронического непрерывного и острого течения заболевания.

Ключевые слова: неспецифический язвенный колит, гнойно-воспалительные осложнения, клеточный и гуморальный иммунитет