SOME ASPECTS OF GENETIC PROGNOSTIC FACTORS FOR THE COURSE OF NONSPECIFIC ULCERATIVE COLITIS

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Abstract: An open case-control study involving 61 patients with ulcerative colitis examined the effect of the TNFα G-308A gene polymorphism on the prognosis of ulcerative colitis, the effectiveness of steroid therapy, and the formation of the need for cytostatic therapy.
Keywords: nonspecific ulcerative colitis, tumor necrosis factor alpha, gene polymorphism, steroids.

INTRODUCTION

Nonspecific ulcerative colitis (NUC) occupies one of the leading places in the structure of diseases of the digestive tract in terms of severity, frequency of complications and disability of the working population [3]. Determining the prognosis of UC is an important task at the stage of diagnosing the disease, choosing management tactics and treatment algorithm. Often, unsuccessful pathogenetic treatment leads to progression of the disease, the development of life-threatening complications such as intestinal bleeding, toxic dilatation and perforation of the colon, colorectal cancer, and the risk of surgical treatment with disability in young people [1].

MATERIALS AND METHODS

In the prognostic aspect, it is important to assess the course of NUC in the first 5 years from the moment of onset, when the nature and severity of the disease, the formation of resistance to basic treatment, and the development of life-threatening complications are determined [2]. In this regard, the issue of introducing “top-down” treatment tactics into practice is being actively discussed all over the world - “top-down” strategy, where anti-cytokine drugs are used first and foremost, and are not an alternative when salicylates, steroids, and immunosuppressants are ineffective with the classical strategy “step-up”, which has an ascending nature [3].

The research cohort consisted of 61 patients aged 18 to 60 years with an established diagnosis of NUC for 5 years or more before inclusion in the study, who signed an informed consent to participate in the study.

RESULTS AND DISCUSSION

In recent years, there has been an increased interest in the study of genetic determinants of disease development and progression and response to drug therapy. The most widely studied genetic factors include single nucleotide polymorphisms (SNP), which are associated with point substitutions or microdeletions and insertions in the genome [2, 4]. It is believed that the presence of single nucleotide substitutions is one of the factors that determines the individual characteristics of the course of the disease, and their identification can be used to determine the prognosis of the disease.

Currently, the study of “functional (responsible for altered production) gene polymorphism” of cytokines and their receptors is of great interest, since it is these mediators that make the greatest contribution to the regulation of immunity [1]. Cytokine gene expression begins in response to antigenic stimulation or tissue damage.

In NUC, there is increased production of cytokines - interleukin 1β (IL 1β), IL 5, IL 6, IL 8, IL 13, IL 17, IL 22, tumor necrosis factor α (TNFα), TL1A. Data on the influence of polymorphism in genes encoding the synthesis of cytokines and their receptors are constantly being updated; we will dwell on just one of them.

In most epidemiological studies on NUC, no difference in the incidence of the disease between men and women was found, or a slight predominance of men was observed [3], this feature was

also noted in our observations. Of those examined, 28/61 were men (45.9%) and 33/61 were women (54.1%). The average age of the patients was 28.96 years (18-60 years). The age of onset of the disease in 36/61 (59%) patients was 21-35 years, which corresponds to the global trend [3]. 11/61 (18%) patients are on disability due to their underlying disease. In our study, 3.2 years passed from the onset of the first symptoms to diagnosis. In Novosibirsk, this indicator for NUC was 2.7 years [1].

According to the length of the inflammatory process among 61 of the examined patients with NUC with total lesions of the colon were diagnosed in 19/61 patients, including one patient with total lesions with retrograde ileitis (31.2%), subtotal - in 29/61 (47.5%), distal colitis in 13/61 patients (21.3%).

A chronic continuous course with a disease duration of 5 years was observed most at the time of inclusion in the study in 38/61 examined patients (62.3%), recurrent in 23/61 patients (37.7%). Extraintestinal manifestations were detected in 29/61 patients (47.5%): aphthous stomatitis - in 2/61 (3.3%), erythema nodosum - 1/61 (1.6%), pyoderma gangrenosum - 1/61 (1 .6%). These systemic manifestations, according to the literature, are rare; the proportion of identified manifestations corresponds to global trends. Arthropathy was noted in 13/61 patients (21%), liver damage (autoimmune hepatitis, transient increase in transaminases, hepatomegaly) - 5/61 (8%), cholelithiasis - in 9/61 (14.8%), urolithiasis - in 4/61 (6.6%), which are, according to the literature, more frequent extraintestinal manifestations [3]

When genotyping this region of the TNFα gene polymorphism, taking into account the effect on the severity of the disease in patients with NUC with a developed need for steroids in the first 5 years of the disease, the genotypes were distributed as follows: a mild course was noted in 20/61 patients (32.8%), among whom homozygote G/G was detected in 13/20 (65%), heterozygote G/A – in 4/20 (20%), homozygote A/A – in 3/20 (15%); moderate severity – 29/61 (47.5%), among which homozygote G/G was detected in 18/29 (62%), heterozygote G/A – in 11/29 (38%), homozygote A/A – not detected ; severe course - 12/61 (19.7%), among which homozygote G/G was detected in 9/12 (75%), heterozygote G/A - in 3/12 (25%), homozygote A/A - not detected .

CONCLUSION

1. In the examined patients, the TNFα gene polymorphism G-308A is associated with the onset of the disease at a young age (20-35 years).
2. The influence of the TNFα G-308A gene polymorphism in the homozygous state for allele A on the severity of the disease was noted.
3. An association of the TNFα G-308A gene polymorphism with an increased risk of pseudopolyp formation in the first 5 years from the onset of the disease was revealed.
4. The likelihood of the influence of the TNFα G-308A gene polymorphism on the formation of steroid dependence and steroid resistance in the first 5 years from the onset of the disease in moderate and severe NUC has not been identified.
5. Considering the polygenic nature of NUC, it is necessary to study the influence of cytokine gene polymorphisms to assess the prognosis of the disease, the effectiveness of therapy and the development of a patient management algorithm taking into account genotyping results.

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