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COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract
The analysis of the clinical, morphological and immunological significance of small intestine pathology in rheumatoid arthritis (RA) was carried out. The study included 120 patients with RA. The patients were assigned according to the DAS index 28. All received basic anti-inflammatory therapy. Symptoms of intestinal dysfunction, the presence of dysbiotic disorders, neuroendocrine imbalance were taken into account, endoscopic and morphological features of colonobies in patients with RA were studied. RA is associated with functional and structural changes in the intestinal mucosa. Pronounced disorders of the intestinal microecology are recorded with a high degree of RA activity. Intestinal dysfunction in RA with a DAS index of 28 > 5.1 is associated with significant changes in mast cells and apudocytes producing substance P and vasointestinal peptide.

Keywords: Rheumatoid arthritis, intestine, dysbacteriosis, diffuse endocrine system (DES).

Introduction

Rheumatoid arthritis (RA) is a chronic systemic connective tissue disease with progressive damage to mainly peripheral joints of the type of erosive-destructive polyarthritis with the possible development of multiple organ damage and severe complications.

The development of multiple systemic manifestations determines the severity and unfavorable prognosis of the disease [3]. Pathology of the gastrointestinal tract (GIT) is detected in 13–62% of patients suffering from RA [12] and occupies an important place among the extra-articular manifestations of this disease [3]. Many works have been devoted to the study of gastroduodenal lesions in RA [1, 2, 11]. Intestinal pathology in RA is considered in the literature in terms of side effects of basic therapy [5, 8]. Morphological and endoscopic activity of the disease are distinguished. For example, the presence of clinical symptoms in combination with erosions and ulcers, crypt abscesses, and pseudopolyps detected endoscopically are highly likely to indicate UC [5]. Morphological criteria for UC activity include neutrophilic infiltration of the colon mucosal stroma (TMT), intraepithelial microabscesses, cryptitis. The search for biological markers of IBD is high, many markers have been extensively studied and applied in everyday practice. The main goal of further study of IBD biomarkers is to avoid repeated endoscopic examination to assess the course, activity of the disease, or ascertain remission. Below are biological markers that are used in routine practice, as well as some parameters that have been proposed relatively recently. However, due to the massive radiation exposure during the procedure, the complexity and high cost of the study, this method is more often used for scientific research than in routine practice [9]. C-reactive protein (CRP) is a plasma protein that is produced by the liver in response to any

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inflammatory reaction occurring in the body [10]. J.Y. Yoon et al. (2014) studied the correlation between CRP and ESR in comparison with endoscopic activity in patients with UC. Half of the patients had a relapse of the disease within a year. Was
it has been established that there are no differences between the analyzed parameters in the detection of endoscopic remission of UC [15]. Lactoferrin is a multifunctional protein from the transferrin group, which is one of the components of the immune system, takes part in the system of non-specific humoral immunity, regulates the functions of immunocompetent cells, and is a protein of the acute phase of inflammation [16]. It is found in breast milk, blood plasma, in almost all exocrine secretions and neutrophils. It is released during their degranulation and may indirectly reflect the intensity of the inflammatory response in IBD [17]. Lactoferrin is relatively stable in the environment and can remain unchanged in the feces for up to five days [18].

Functional and structural features of different disease activity remain less studied, and their role in maintaining autoimmune systemic inflammation has not been established. The role of biogenic amines and peptide hormones produced by the diffuse endocrine system (DES) in the regulation of motility, absorption in the gastrointestinal tract, nociception, tissue trophism and induction of the inflammatory process is widely discussed. Several studies have been devoted to the study of the concentration of neuropeptides in RA in the synovial membrane and blood plasma [7, 10], the quantitative density of DES components of the intestinal mucosa in RA and the relationship with the activity of the autoimmune process have not been studied.

The role of intestinal pathology in RA remains unstudied. Changes in the intestine can be a consequence of the development and manifestation of immune inflammation and can be an inducer of a pathological process during which the body is sensitized to the components of the autoflora. Intestinal microecology has a significant impact on homeostasis, taking a direct part in the formation of the immune response. There are published data that patients with RA have defective circulating T cells (Treg) [13], an increased titer of Th17 cells in plasma and synovial fluid [9, 14], the role and significance of which are being studied. It is possible that dysregulatory and dysbiotic disorders of the intestine can lead to impaired immune tolerance, being one of the triggers of the systemic response. Criteria for inclusion of patients in the study: persons of both sexes aged 18-60 years, suffering from RA in the stage of progression; informed consent of the patient to participate in the study and compliance with the doctor's instructions regarding the prescribed therapy. Exclusion criteria: severe concomitant pathology of internal organs with functional insufficiency, the presence of which may affect the results of the study (high risk of cardiac complications - CHD (> III FC), heart failure (> 2 degrees), myocardial infarction or stroke in anamnesis during the previous year of life, diabetes mellitus, tumors of any localization); the presence of inflammatory bowel diseases, diverticular disease; parasitic invasions and infections of the gastrointestinal tract; history of anticytokine therapy; the fact of taking antibiotics and anticytokinin drugs within the next 3 months; the patient's refusal to be examined. The diagnosis of RA was established in accordance with the ACR/EULAR criteria (2010) [6]. The total RA activity and functional class (FC) were recorded in accordance with the RA classification adopted at the plenum of the Association of Rheumatologists of Russia in 2007. Intestinal dysfunction in RA with systemic manifestations of a progressive course is associated with hyperplasia of sigmoid colon cells immunopositive for melatonin, substance P and VIP. The most pronounced changes on

the part of cells producing substance P and VIP, in the absence of a reaction from the cells, are at DAS 28 > 5.1 (see figure). In RA with systemic manifestations, hypoplasia and a decrease in the optical density of mast cells in the mucous membrane of the small intestine are observed, which indicates functional depletion of the mast cell population. A decrease in the number and degranulation of mast cells of the small intestinal mucosa in relapsed RA may be associated with the release of large amounts of histamine and other biological amines involved in immune responses.

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