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Rheumotid Arthritis Associated with Inflammatory Diseases Gastrointestinal Tract

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Summary: *This review is intended to study topical issues of the pathogenesis of inflammatory diseases of the gastrointestinal tract and rheumatoid arthritis. In the pathogenesis of inflammatory diseases of the gastrointestinal tract and rheumatoid arthritis, there are many similar links: the commonality of immune participants in inflammation and the forms of their interaction, the cellular composition of the inflammatory infiltrate of the gastrointestinal tract and the synovial membrane of the joints, the hyper production of pro-inflammatory cytokines and antibodies, the commonality of clinical manifestations.*

Keywords: *rheumatoid arthritis, inflammatory diseases of the gastrointestinal tract, neutrophils, monocytes.*

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Considering the mechanisms of the development of an immunoinflammatory reaction, it is necessary to point out the leading role of neutrophils and blood monocytes. The study of the functional activity of neutrophils and monocytes, which are directly involved in the development of inflammatory reactions and are the main components of inflammatory infiltrates of the intestinal wall and synovial membrane in inflammatory diseases of the gastrointestinal tract and rheumatoid arthritis, will help to better reveal the issues of their pathogenesis.

Rheumatic diseases are the oldest human pathology, and are considered the most common disease of the XXI century. In recent decades, there has been some progress in the field of theoretical and clinical rheumatology. According to E.A. Galushko and E.L. Nasonov's rheumatic diseases include more than 80 diseases and syndromes [19].

Rheumatoid arthritis (RA) is a serious medical and social problem, characterized by a steadily progressive disorganization of the connective tissue, which is based on deep immunopathological changes with features of autoaggression. Rheumatoid arthritis (RA) is an autoimmune disease characterized by the development of chronic destructive polyarthritis with frequent involvement of other systems in the pathological process. Extra-articular systemic lesions in RA can have a serious impact on the prognosis of the disease [5, 36].

RA ranks first in prevalence among inflammatory diseases of the joints. The social significance of this disease is determined not only by its high prevalence, but also by the great material damage caused to society, the patient, his family due to high disability and early onset disability. The steady progression of the pathological process, despite the use of modern methods of therapy, causes not only a significant functional insufficiency of the musculoskeletal system, but also leads to a

reduction in the life expectancy of patients by 4-10 years, to an increase in mortality, which exceeds that of the general population.

The prognosis is especially unfavorable in patients with RA with systemic manifestations: generalized vasculitis, rheumatoid nodules, lymphadenopathy, damage to the lungs, heart, liver, kidneys and other organs and systems. Among the extra-articular manifestations of RA, lesions of the gastrointestinal tract (GIT) are the least studied, although the most severe process is well known - intestinal amyloidosis, which occurs in 11% of patients and is usually combined with amyloidosis of other internal organs [21,24,26,37].

Patients with RA were noted to have impaired motility and secretory function of the stomach [27, 30, and 40], the development of chronic atrophic gastritis [31], which is three times higher than its occurrence in the general population, as well as the frequent occurrence of mucosal ulcers [1].

A number of researchers considered the nature of these changes in the context of the systemic nature of rheumatoid inflammation, believing that immune disorders are the basis of atrophic gastritis [43,3]. So, A.I. Strukov [25] emphasized that cell infiltration of the gastric mucosa fits into the concept of immune inflammation. D. Malone noted that the occurrence of ulcers correlates more with the nature of the course of RA than with the anti-inflammatory drugs used by patients [2]. Nevertheless, the question of the specific gravity, on the one hand, of immune disorders in the stomach caused by the underlying disease, on the other hand, of the damaging effect of the mucous membrane of drugs that patients are forced to take constantly, is still debatable.

In the literature of recent years, the main emphasis in the development of gastric disorders is on drug-induced gastropathy [22, 38].

Gastroenterology and rheumatology are closely related disciplines [33]. The commonality of pathogenetic lines and immune "participants" in the development of a typical clinical picture of inflammatory bowel diseases (IBD), in particular Crohn's disease (CD) and ulcerative colitis (NUC), as well as rheumatoid arthritis (RA) in recent years has become increasingly noticeable.

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Currently, IBD is considered a polyetiological disease with a genetic predisposition. The idea of the autoimmune nature of IBD has received a new development due to the information that the commensal microflora and its metabolic products serve as autoantigens, and the development of inflammation occurs due to the loss of tolerance to substances of the normal intestinal flora, which are usually harmless [45]. The frequency of microbiota disorders in IBD reaches 66-93% [6, 46].

Autoimmunization, as well as a high concentration of circulating immune complexes (CIC), indicates a selective loss of immunological tolerance, which ultimately leads to an intense inflammatory process [42].

In the affected area of the alimentary canal in CD, transmural lymphocytic, neutrophilic, macrophage infiltration with focal lymphoid hyperplasia (follicles) and fibrosis of all layers of the intestinal wall is detected. Characteristic (30-60%) for CD is also the detection in the submucosal layer of epithelioid granulomas containing Pirogov-Langhans giant cells. Their presence is a reliable histological criterion for Crohn's disease [15, 28].

At that time, the mucosa (SO) of the colon of patients with UC and CD contains a significant amount of long-lived IgG-producing plasma cells, as well as polymorphonuclear leukocytes, which

produce a large number of metalloproteinases (MMPs), causing destruction of the extracellular matrix and basement membranes [18 , 44].

A characteristic histological sign of UC is the formation of microabscesses between the crypts of the mucous membrane, the so-called "crypt abscesses", which are an accumulation of polymorphonuclear leukocytes [29].

Macrophages are also one of the main cellular elements of the inflammatory infiltrate in IBD. The former originate from circulating monocytes, make up 30-40% of the macrophages present in the intestinal mucosa (CO), develop and maintain a chronic inflammatory process in the colon. [17].

The inflammatory infiltrate of the intestinal wall in UC and CD is represented by those cells (mainly neutrophils and monocytes) that migrated here from the peripheral blood flow. Inflammation of the mucous membrane leads to an imbalance of cytokines, which determines the course of IBD [11].

Changes in cytokine regulation consist in an increase in the production of inflammatory cytokines, primarily TNF-α, as well as interleukins-1, -6, -8, -12 with a decrease in anti-inflammatory interleukins-4, -10, -11, as well as a pronounced imbalance of regulatory cytokines IL -2, -5. One of the most active pro-inflammatory cytokines is TNF-α, which, together with IF-gamma and IL-1, mediates delayed hypersensitivity responses and macrophage activation, leading to the formation of granulomas in CD. [47,8].

During inflammation, this cytokine stimulates Th1 helpers and macrophages, induces systemic acute phase reactions with increased synthesis of IL-1, -2, -6, -8. If an increase in IL-2 provides autocrine stimulation of T-lymphocyte proliferation and stimulates the growth of B-lymphocytes, the functional activity of natural killers, leads to the activation of macrophages, and hence clonal proliferation and differentiation of lymphocytes [16], then IL-8 stimulates chemotaxis and causes activation of T -lymphocytes with the formation of oxygen radicals and the release of lysosomal enzymes [14, 20].

Rheumatoid arthritis (RA) belongs to a group of diseases characterized by polarization of the immune response by type 1 T-helper immune response, manifested by hyperproduction of pro-inflammatory cytokines such as IL-6 and TNF-α [41,7].

The earliest manifestations of RA are inflammation and occlusion of small vessels in the synovium. There is evidence of a role for asymptomatic Proteus urinary tract infection in RA. A number of foreign scientists, such as Rashid T., Ebringer A., McGuckin M.A. believe that in genetically predisposed individuals, the causative microbe can initiate the disease, followed by the production of antimicrobial and cross-over autoantibodies that bind to antigens and damage tissues by activating the complement system and producing cytotoxic products by inflammatory cells [9].

The essence of the pathological process in RA is systemic autoimmune inflammation, which affects the synovial membrane of the joints with maximum intensity [39].

In the synovial tissue, there is an increase in the number of type A synoviocytes (cells resembling macrophages) and B (cells resembling fibroblasts), infiltration by immune and inflammatory cells (macrophages, T- and B-lymphocytes, plasma and dendritic cells), the formation of follicles consisting of lymphoid cells, which resemble the growth centers of the lymphatic corners. An early sign of rheumatoid synovitis is the formation of new vessels (angiogenesis or neovascularization) [32].

The synovial fluid contains more neutrophils than lymphocytes. The immune complexes formed in it activate complement; at the same time, anaphylatoxins and chemotaxis factors are released, which

cause adhesion of leukocytes to the endothelium of postcapillary venules. Activate complement and IL-1, TNF-α and leukotriene B4 secreted by synovial macrophages.

Along with this, TNF-α, C5a, leukotriene B4 and IL-8, histamine and prostaglandin E2 contribute to the release of neutrophils from the vascular bed into the synovial fluid. Once in the synovial fluid, neutrophils absorb immune complexes, which lead to the release of oxygen free radicals and other substances that enhance the inflammatory response [4].

Cell interactions are considered an important factor in the development of RA. Intercellular interactions are regulated by cytokines, which are produced in particular by activated cells of the synovial membrane. It is likely that these cytokines stimulate the inflammatory response in the synovial membrane, the release of cells and inflammatory mediators into the synovial fluid, the proliferation of synoviocytes, and are involved in the destruction of cartilage and bone and the development of extra-articular manifestations of rheumatoid arthritis [34].

The group of cytokines with pro-inflammatory action is made up of interleukins (IL): IL-1, IL-2, IL-6, IL-8, etc., TNF-a, interferon-gamma (IF-g). Anti-inflammatory and regulatory cytokines include IL-10, IL-11, endogenous antagonists of IL-1 receptors (IL-1ra), transforming growth factor-b (TRF-b) [10].

Of all the variety of pro-inflammatory cytokines, TNF-α deserves special attention. In addition to macrophages, it is synthesized by various types of cells - type 1 T-helpers, endothelial cells, but monocytes / macrophages, of course, are its main source. No wonder it is considered one of the key in the process of inflammation in RA, Crohn's disease and other autoimmune diseases. TNF-α, on the other hand, determines the expression of adhesive molecules on endothelial cells, resulting in an increased influx of phagocytes into the inflammation site [35].

A significant percentage of RA patients, namely 80%, have antibodies (IgM and IgG), mostly identified as rheumatoid factor (RF). Antibodies accumulate in the synovium and activate complement in the synovial fluid. RF uptake by macrophages and neutrophils, which is cytologically defined as the presence of phagocytes, stimulates the production of cytokines and the release of proteolytic enzymes that increase inflammation. RF is one of the prognostic markers of destructive joint damage [23].

From all of the above it follows that in the pathogenesis of IBD and RA there are many similar links: the commonality of immune participants in inflammation and the forms of their interaction, the cellular composition of the inflammatory infiltrate of the intestinal wall and synovial membrane of the joints, hyperproduction of pro-inflammatory cytokines, in particular TNF-α, as well as hyperproduction of antibodies, namely IgG. Often, with IBD, there is also an articular syndrome, as well as with RA, there may be damage to the intestines.Sometimes intestinal manifestations of autoimmune processes come to the fore or, conversely, articular syndrome masks intestinal pathology, i.e. we are already talking about the commonality of the clinical manifestations of IBD and rheumatoid arthritis [13].

From the foregoing, it follows that further study of the functional activity of blood cells, in particular neutrophils and monocytes, which are directly involved in the development of inflammatory reactions and are the main components of inflammatory infiltrates of the intestinal wall and synovial membrane in IBD and rheumatoid arthritis, will help to further reveal the issues of their pathogenesis.

Literature:

1. Axmatovna M. S. et al. Peculiarities of the morphophenotype and characteristics of the physical performance of young football players and their relationship with the gaming amplitude

//Academicia: an international multidisciplinary research journal. – 2021. – Т. 11. – №. 2. – С. 1381-1388. 12

2. Axmatovna M. S. et al. Peculiarities of the morphophenotype and characteristics of the physical performance of young football players and their relationship with the gaming amplitude //Academicia: an international multidisciplinary research journal. – 2021. – Т. 11. – №. 2. – С. 1381-1388.16
3. Boltaeva M. M. Treatment of Arterial Hypertension in Elderly Patients and Senile Age Group..- Vol. 45. - P. 475-483.14
4. Helen L. Wright,Robert J. Moots, Roger C. Bucknall, Steven W. Edwards. Neutrophil function in inflammation and inflammatory diseases // Rheumatology. –2010. – V. 49(9). – P.1618-1631.42
5. Hickson LJ, Crowson CS, Gabriel SE, et al. Development of reduced kidney function in rheumatoid arthritis. *Am J Kidney Dis.* 2014;63:206-13. doi: 0.1053/j.ajkd.2013.08.010 2
6. Kholmurodovich U. F. Liver Fibrosis-Modern Methods of Diagnostics and Drug Correction //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2021. – Т. 2. – №. 2. – С. 158-167.22
7. MacDonald T.T. The cytokine network in IBD // Falk symposium. – 2006.– P. 24.38
8. McInnes I., Schett G. Cytokines in the pathogenesis of rheumatoid arthritis // Nat. Rev. Immunol. – 2007. – V. 7(6). – P. 429-42. 22. Rashid T., Ebringer A. Autoimmunity 33
9. Rashid T., Ebringer A. Autoimmunity in Rheumatic Diseases Is Induced by Microbial Infections via Cross reactivity or Molecular Mimicry // Autoimmune Dis. – 2013. – № 1.–P. 3-20.39
10. E., Panaccione R., Loftus E., Tremain W. Infliximab for Crohn's disease in clinical practice at the Mayo Clinic: the first 100 patients // Am. J. Gastroenterol. – 2001. – V. 96. – P. 722-729. 44
11. Sartor R.B., Hoentjen F. Proinflammatory cytokines and signaling pathways in intestinal innate immune cells // Mucosal Immunology. – 2005. – № 30.– P. 681-701.31
12. Travis S., Gert Van Assche, Axel Dignass et al. On the second ECCO Consensus on Crohn`s disease // Journal of Crohn`s and Colitis. – 2010. – V. 4. – P. 1-6. 20
13. Абдулганиева Д.И., Салихов И.Г. Гастроэнтерологические проблемы при ревматических заболеваниях // Практическая медицина. – 2011. – Т 1. – С. 89-95 47
14. Адлер Г. Болезнь Крона и язвенный колит. – М.: ГЭОТАР– Медиа, 2001. – 527 с.35
15. Аруин Л.И., Капуллер Л.Л., Исаков В.А. Морфологическая диагностикаболезней желудка и кишечника. – М.: Триада-Х, 1998. – 496 с.25
16. Белоусова Е.А. Язвенный колит и болезнь Крона. – Тверь: ООО «Издательство «Триада», 2002. – 128 с. 34
17. Воробьев Г.И., Халиф И.Л. Неспецифические воспалительные заболевания кишечника. – М.: Миклош, 2008. – 400 с. 30
18. Воробьев Г.И., Халиф И.Л. Неспецифические воспалительные заболевания кишечника. – М.: Миклош, 2008. – 400 с. 27
19. Галушко ЕА, Насонов ЕЛ. Распространенность ревматических заболеваний в России. Альманах клинической медицины. 2018;46(1):32–39.doi:10.18786/2072-0505-2018-46- 1-32-39.3 1

20. Гребенев А.Л., Мягкова Л.П. Болезни кишечника (современные достижения в диагностике и терапии). – М.: Медицина, 1994. – 400 с.36
21. Гребнев, А.Л. Клинико-морфологическая характеристика изменений желудка при ревматоидном артрите / А.Л. Гребнев, В.Б. Золотаревский, Т.И. Сотникова // Сов. Медицина. – 1990. - № 10. - С. 85-88. 4
22. Григорьев, П.Я. Гастро- и дуоденопатии, обусловленные НПВП. Лечение и профилактика / П.Я. Григорьев, Э.П. Яковенко // Врач. – 1997. - №11. - С. 11-12. 17
23. Гусева И.А., Демидова Н.В., Сорока Н.Е. и др. Иммуногенетические аспекты раннего ревматоидного артрита // Вестник Российской академии медицинск их наук. – 2013. – № 4. –С. 36-43. 46
24. Гусева, Н.Г. Патогенетические механизмы нарушений микроциркуляции при ревматических заболеваниях / Н.Г. Гусева, Н.Н. Грицман, В.Ф. Сысоев // Тер. архив. – 1983. - № 7. - С. 7-11. 5
25. Джаббарова М. Б. и др. Сравнительная характеристика лекарственых средств, используемых для лечения хронических гепатитов и цирроза печени //Новый день в медицине. – 2019. – №. 4. – С. 151-154.15
26. Джаббарова М. Б., Раджабова Г. Б. ДИАГНОСТИКА НАРУШЕНИЙ ДЫХАНИЯ В НОЧНЫЕ ЧАСЫ И РЕСПИРАТОРНАЯ ТЕРАПИЯ ПАЦИЕНТОВ С ХОБЛ //Биология и интегративная медицина. – 2022. – №. 2 (55). – С. 84-94.6
27. Джаббарова М. Б. Распространенность и клинические проявления бронхиальной астмы //Биология и интегративная медицина. – 2021. – №. 1 (48). – С. 160-171.8
28. Капуллер Л.Л., Маринушкин Т.Л., Костенко Н.В. Морфологические особенности раковых опухолей, возникающих на фоне хронического неспецифического язвенного колита//Российский журнал гастроэнтерологии, гепатологии, колопроктологии. – 2003. – № 4. – С. 58-64.26
29. Кветной И.М., Комаров Ф.И., Осадчук А.М., Осадчук М.А. Неспецифический язвенный колит. – М.: МИА, 2008. – 256 с. 29
30. Кравченко, Л.Ф. Состояние желудка при инфекционном неспецифическом (ревматоидном) полиартрите / Л.Ф. Кравченко, А.В. Курганская // Вопросы ревматологии. – 1972. - № 12. - С. 71-76. 9
31. Кравченко, Л.Ф. Состояние желудка при инфекционном неспецифическом (ревматоидном) полиартрите / Л.Ф. Кравченко, А.В. Курганская // Вопросы ревматологии. – 1972. - № 12. - С. 71-76 11
32. Марченко Ж. С., Лукина Г. В. Роль сосудистого эндотелиального фактора роста в патогенезе ревматоидного артрита // Научно-практическая ревматология. – 2005. – № 1. – С.57-60 41
33. Насонов Е.Л. Сегодня в изучении патогенеза ревматических болезней на первый план выходят исследования механизмов хронического воспаления // Фарматека. – 2005. – № 7. –С. 4-7.19
34. Насонов Е.Л. Сегодня в изучении патогенеза ревматических болезней на первый план выходят исследования механизмов хронического воспаления // Фарматека. – 2005. – № 7. – С. 4-7. 43

35. Насонов Е.Л. Сегодня в изучении патогенеза ревматических болезней на первый план выходят исследования механизмов хронического воспаления // Фарматека. – 2005. – № 7. – С. 4-7. 45

36. Насонов Е.Л., Каратеев Д.Е., Балабанова Р.М. Ревматоидный артрит. В кн.: Ревматология. Национальное руководство. Под. ред.Е.Л. Насонова, В.А. Насоновой. М.: ГЭОТАР-Медиа, 2008; с. 290-331 [Nasonov EL, Karateev DE, Balabanova RM. Rheumatoid arthritis.In: Rheumatology. National Guide. Nasonov EL, Nasonova VA, ed.Moscow: GEOTAR-Media, 2008; p. 290-331 (In Russ.) 3

37. Насонова, В.А. Гастропатии, связанные с приемом НПВП / В.А. Насонова // Росс. журнал гастроэнтерологии. – 1994. - № 1. - С. 7-10 7

38. Насонова, В.А. Гастропатии, связанные с приемом НПВП / В.А. Насонова // Росс. журнал гастроэнтерологии. – 1994. - № 1. - С. 7-10.18

39. Никулина С.Ю., Чернова А.А., Большакова Т.Ю. и др. // Сибирское медицинское обозрение.– 2014. – N. 3.– С.11-18. 40

40. Осколкова, А.В. Состояние желудка при инфекционном неспецифическом (ревматоидном) артрите: Автореф. дис. … канд. мед. наук / А.В. Осколкова. - Владивосток, 1972 10

41. Ревматология: Национальное руководство / Под ред. Е.Л. Насонова, В.А. Насоновой. – М.: ГЭОТАР-Медиа, 2010. – 72 0 с.37

42. Румянцев В.Г. Язвенный колит: Руководство для врачей. – М.: Медицинское информационное агентство, 2009. – 424 с.24

43. Саидова М. М. ОЦЕНКА ПАРАМЕТРОВ ТОЛЩИНЫ ИНТИМА-МЕДИА СОННЫХ АРТЕРИЙ КАК РАННЕГО ПРЕДИКТОРА РАЗВИТИЯ АТЕРОСКЛЕРОЗА У БОЛЬНЫХ РЕВМАТОИДНЫМ АРТРИТОМ //Журнал кардиореспираторных исследований. – 2022. – Т. 3. – №. 1.13

44. Ткачёв А.В., Мкртчян Л.С., Никитина К.Е., Волынская Е.И. Воспалительные заболевания кишечника: на перекрёстке проблем // Практическая медицина. – 2012. – № 58. – С. 17-2228

45. Фарелл Р., Пепперкорн М. Язвенный колит // Международный медицинский журнал. – 2003. – Т. 6. – № 1. –[Электронный ресурс]. Режим доступа http://medi.ru/doc/773012.htm/ (дата обращения: 11.03.2015). 21

46. Халиф И.Л., Лоранская И.Д. Воспалительные заболевания кишечника (неспецифический язвенный колит и болезнь Крона): клиника, диагностика, лечение. – М.: Миклош, 2004. – 88с. 23

47. Царегородцева Т.М., Серова Т.И., Ильченко Л.Ю. и др. Цитокины и цитокинотерапия при заболеваниях органов пищеварения // Терапевтический архив. – 2004. – № 4. – С. 69-72.32