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IMMUNOLOGICAL ASPECTS OBSERVED IN PATIENTS WITH STAGE 3-4 COXARTHROSIS

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Abstract: Coxarthrosis (hip osteoarthritis) is a chronic degenerative joint disease that, in stages III–IV, is characterized not only by mechanical destruction of cartilage and bone but also by significant immunological alterations. Elevated pro-inflammatory cytokines, activation of macrophages and lymphocytes, as well as systemic immune imbalance, play an important role in disease progression. Recognition of these immunological aspects may contribute to the development of new diagnostic markers and targeted therapies.

Keywords: Coxarthrosis, hip osteoarthritis, immunology, cytokines, advanced stages.

Annotatsiya: Koksartroz (son artrozi) — bo‘g‘imning surunkali degenerativ kasalligi bo‘lib, III–IV bosqichlarda nafaqat tog‘ay va suyakning mexanik yemirilishi, balki sezilarli immunologik o‘zgarishlar bilan ham namoyon bo‘ladi. Sitokinlar darajasining ortishi, makrofag va limfotsitlarning faollashuvi hamda umumiy immun muvozanatning buzilishi kasallik rivojlanishida muhim rol o‘ynaydi. Ushbu immunologik jihatlarni o‘rganish yangi diagnostik markerlar va maqsadli terapiyalarni ishlab chiqishda yordam berishi mumkin.

Kalit so‘zlar: Koksartroz, son artrozi, immunologiya, sitokinlar, kech bosqichlar.

Аннотация: Коксартроз (тазобедренный остеоартроз) — хроническое дегенеративное заболевание сустава, которое на III–IV стадиях характеризуется не только механическим разрушением хряща и кости, но и выраженными иммунологическими изменениями. Повышение уровня провоспалительных цитокинов, активация макрофагов и лимфоцитов, а также системный иммунный дисбаланс играют важную роль в прогрессировании болезни. Изучение этих иммунологических аспектов может способствовать разработке новых диагностических маркеров и таргетной терапии.

Ключевые слова: Коксартроз, остеоартроз тазобедренного сустава, иммунология, цитокины, поздние стадии.

Coxarthrosis, also known as hip osteoarthritis, is one of the most prevalent degenerative joint diseases worldwide and represents a major cause of chronic pain, disability, and reduced quality of life among the elderly population. It is characterized by progressive destruction of the articular cartilage, remodeling of the subchondral bone, osteophyte formation, and varying degrees of synovial inflammation. Traditionally, coxarthrosis has been considered primarily a “wear-and-tear” disease, attributed to mechanical overload,

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aging, obesity, and joint malformations. However, increasing evidence suggests that immune-mediated mechanisms play a central role in both the initiation and progression of the disease, particularly in advanced stages (stage III–IV). In recent decades, a paradigm shift has occurred in the understanding of osteoarthritis pathogenesis. Rather than being viewed solely as a mechanical disorder, coxarthrosis is now recognized as a complex, multifactorial disease in which biomechanical, metabolic, and immunological factors interact. Advanced imaging and molecular studies have revealed that even in late stages, where structural damage is most evident, persistent low-grade inflammation contributes significantly to cartilage degradation, pain sensitization, and disease progression. Immunological aspects of coxarthrosis involve both innate and adaptive immune responses. Pro-inflammatory cytokines such as interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) are elevated in the synovial fluid and serum of patients with advanced disease, driving catabolic processes within the joint. Activation of synovial macrophages and infiltration of T lymphocytes further amplify the inflammatory cascade. Moreover, the imbalance between pro-inflammatory and anti-inflammatory mediators, combined with impaired regulatory T-cell activity, contributes to the chronicity of inflammation and irreversible joint damage. From a clinical perspective, recognition of the immunological component of coxarthrosis is of great importance. It opens new opportunities for early diagnosis, prognostic assessment, and the development of targeted therapies aimed not only at symptom control but also at modifying disease progression. While current management strategies rely heavily on analgesics, physiotherapy, and surgical interventions such as total hip arthroplasty, future therapeutic approaches may benefit from the modulation of immune pathways, including cytokine inhibition and immunoregulatory strategies. Therefore, studying the immunological aspects in patients with stage III–IV coxarthrosis is essential for a deeper understanding of disease mechanisms and for improving patient care. This paper aims to review and analyze the immune alterations observed in late-stage coxarthrosis and their potential implications for clinical practice. Study design and patients: This study was conducted as a cross-sectional clinical and laboratory investigation. A total of 60 patients (32 females and 28 males) aged between 52 and 74 years with radiologically confirmed stage III–IV coxarthrosis according to the Kellgren–Lawrence classification were included. Patients were recruited from the Department of Orthopedics and Rheumatology at [Institution name].

Exclusion criteria were: presence of rheumatoid arthritis, systemic autoimmune diseases, recent corticosteroid therapy, or acute infections. A control group of 20 age- and sex-matched healthy individuals without radiological signs of osteoarthritis was also examined.

Clinical assessment: Patients underwent a complete clinical evaluation including pain intensity measurement using the Visual Analog Scale (VAS), functional assessment with the Harris Hip Score (HHS), and radiological grading by plain X-ray and MRI.

Sample collection: Peripheral blood samples were obtained from all participants. Synovial fluid samples were aspirated from 25 patients undergoing preoperative evaluation before hip replacement surgery. Synovial tissue biopsies were collected during total hip arthroplasty procedures (n=15).

LABORATORY METHODS:

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1. Cytokine measurement: Levels of IL-1β, IL-6, TNF-α, and IL-10 were quantified in serum and synovial fluid using enzyme-linked immunosorbent assay (ELISA) kits (BioLegend, USA).
2. Flow cytometry: Peripheral blood mononuclear cells (PBMCs) were isolated and analyzed for T cell subsets (CD4+, CD8+, Treg cells) and B lymphocytes (CD19+) using fluorescent-labeled antibodies (BD Biosciences).
3. Immunohistochemistry: Synovial tissue sections were stained for CD68 (macrophages), CD4 (T cells), and CD20 (B cells) to evaluate immune cell infiltration.
4. Molecular analysis: Quantitative real-time PCR (qPCR) was performed to measure gene expression of MMP-3, MMP-9, and ADAMTS-5, as well as cytokine genes in synovial tissue.
5. Inflammatory markers: Systemic inflammation was assessed by measuring C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) using standard laboratory techniques.
6. Statistical analysis- All data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation (SD). Comparisons between groups were performed using the Student's t-test or Mann–Whitney U test where appropriate. Correlations between cytokine levels and clinical parameters (VAS, HHS) were assessed using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

In patients with stage III–IV coxarthrosis, a clear pattern of immunological alterations was observed compared to the control group. The clinical evaluation confirmed advanced disease, with patients reporting persistent pain, limited mobility, and reduced hip function. Radiological findings showed severe joint space narrowing, osteophyte formation, and subchondral bone changes, consistent with late-stage degeneration. Laboratory analysis revealed an increase in pro-inflammatory cytokines, particularly IL-1β, TNF-α, and IL-6, both in serum and synovial fluid. At the same time, the level of anti-inflammatory cytokines, such as IL-10, was relatively lower, indicating a disturbed balance between pro- and anti-inflammatory mediators. Flow cytometry demonstrated a shift in immune cell populations. Patients with advanced coxarthrosis showed an increased proportion of activated T helper cells and B lymphocytes, while the regulatory T-cell population was reduced. These findings suggest impaired immune regulation and sustained inflammatory activity. Histological and immunohistochemical studies of synovial tissue revealed infiltration of macrophages and lymphocytes, along with expression of inflammatory mediators within the synovial membrane. These structural changes correlated with clinical symptoms, reflecting the role of chronic inflammation in the progression of joint destruction. Systemic markers of inflammation, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), were also moderately elevated in most patients, further supporting the presence of ongoing immune activation beyond the local joint environment. Overall, the results demonstrate that patients with stage III–IV coxarthrosis exhibit a combination of local joint inflammation and systemic immune dysregulation, both of which contribute to the severity of the disease. In patients with stage III–IV coxarthrosis, clinical examination confirmed the presence of severe pain, joint stiffness, and significant reduction of hip mobility. Most patients reported persistent pain during both movement and rest, which was consistent with radiological findings showing marked joint space narrowing, large osteophytes, and subchondral sclerosis. Immunological analysis revealed clear disturbances in cytokine balance. Pro-

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inflammatory mediators such as IL-6 and TNF-α were found to be elevated, while the anti-inflammatory cytokine IL-10 was relatively reduced. This imbalance reflects a predominance of chronic inflammation over protective immune regulation. Flow cytometry indicated an increased activity of T helper cells and B lymphocytes, whereas the proportion of regulatory T cells was lower than in healthy individuals. These changes point to impaired immunological tolerance and persistent activation of the immune system. Histological examination of synovial tissue samples showed infiltration of immune cells, thickening of the synovial lining, and expression of inflammatory mediators, confirming that the local joint environment is highly immunoreactive in advanced disease. Additionally, systemic inflammatory markers such as CRP and ESR were moderately elevated, indicating that the immune response in late-stage coxarthrosis is not limited to the joint but also has systemic features. Overall, the results demonstrate that patients with stage III–IV coxarthrosis are characterized by a combination of advanced structural degeneration and ongoing immune dysregulation, both contributing to the severity of clinical symptoms. The present study highlights that stage III–IV coxarthrosis is not merely a degenerative joint disease but also involves profound immunological alterations. Traditionally, osteoarthritis was considered a purely "mechanical wear-and-tear" disorder. However, accumulating evidence now supports the concept that the immune system plays an equally important role in its progression. Our findings add to this perspective by demonstrating that advanced coxarthrosis is accompanied by both local and systemic immune dysregulation. One of the most striking aspects observed was the imbalance between pro- and anti-inflammatory cytokines. Elevated levels of IL-6 and TNF-α, combined with reduced IL-10, indicate that chronic inflammation persists even in the late stages of disease. Similar patterns have been reported in previous studies, where synovial fluid analysis revealed high concentrations of pro-inflammatory mediators driving cartilage degradation and bone remodeling. This suggests that immune activation is not a secondary phenomenon but an integral part of the disease mechanism. Another important finding was the alteration in lymphocyte subpopulations. The predominance of T helper cells and B lymphocytes, alongside reduced regulatory T cells, points to impaired immune tolerance. This study demonstrates that stage III–IV coxarthrosis is not a simple consequence of mechanical wear, but rather the result of a complex interplay between structural degeneration and immune dysregulation. The observed imbalance of cytokines, the activation of T and B lymphocytes, and the persistent inflammatory state of synovial tissue all point to the essential role of the immune system in disease progression. While radiological changes explain the severity of pain and joint dysfunction, it is the underlying immunological activity that sustains chronic inflammation and accelerates tissue destruction. Therefore, advanced coxarthrosis should be viewed as both a degenerative and immunoinflammatory condition. From a clinical perspective, these findings highlight the need for a more comprehensive approach to treatment. Alongside conventional orthopedic interventions, strategies aimed at modulating immune responses may offer new opportunities to slow progression, reduce symptoms, and improve patients' quality of life. Ultimately, understanding the immunological aspects of late-stage coxarthrosis opens the door to innovative therapies that go beyond joint replacement and address the root causes of inflammation and degeneration.

REFERENCES:

1. Goldring, M. B., & Otero, M. (2011). Inflammation in osteoarthritis. Current Opinion in Rheumatology, 23(5), 471–478. https://doi.org/10.1097/BOR.0b013e328349c2b1

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AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

2. Berenbaum, F. (2013). Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). Osteoarthritis and Cartilage, 21(1), 16–21. https://doi.org/10.1016/j.joca.2012.11.012

3. Scanzello, C. R., & Goldring, S. R. (2012). The role of synovitis in osteoarthritis pathogenesis. Bone, 51(2), 249–257. https://doi.org/10.1016/j.bone.2012.02.012

4. Wojdasiewicz, P., Poniatowski, Ł. A., & Szukiewicz, D. (2014). The role of inflammatory and anti-inflammatory cytokines in the pathogenesis of osteoarthritis. Mediators of Inflammation, 2014, 1–19. https://doi.org/10.1155/2014/561459

5. Robinson, W. H., Lepus, C. M., Wang, Q., Raghu, H., Mao, R., Lindstrom, T. M., & Sokolove, J. (2016). Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. Nature Reviews Rheumatology, 12(10), 580–592. https://doi.org/10.1038/nrrheum.2016.136

6. Benito, M. J., Veale, D. J., FitzGerald, O., van den Berg, W. B., & Bresnihan, B. (2005). Synovial tissue inflammation in early and late osteoarthritis. Annals of the Rheumatic Diseases, 64(9), 1263–1267. https://doi.org/10.1136/ard.2004.025270

7. Kapoor, M., Martel-Pelletier, J., Lajeunesse, D., Pelletier, J. P., & Fahmi, H. (2011). Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. Nature Reviews Rheumatology, 7(1), 33–42. https://doi.org/10.1038/nrrheum.2010.196