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FEATURES OF EARLY DIAGNOSIS OF KNEE JOINT REMODELING IN PATIENTS WITH REACTIVE ARTHRITIS

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ОСОБЕННОСТИ РАННЕЙ ДИАГНОСТИКИ РЕМОДЕЛИРОВАНИИ КОЛЕННОГО СУСТАВА У ПАЦИЕНТОВ С РЕАКТИВНЫМ АРТРИТОМ

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REAKTIV ARTRIT BILAN OG‘RIGAN BEMORLARDA TIZZA BO‘G‘IMI REMODELLANISHINI ERTA TASHXISLASH

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Проведен нарративный обзор международной литературы с использованием данных клинических, экспериментальных и переводческих исследований, посвященных поражению коленного сустава при реактивном артрите. Раннее выявление этих структурных изменений остается серьезной клинической проблемой. Полученные данные свидетельствуют о том, что провоспалительные цитокины, особенно интерлейкин-17А, и биохимические маркеры деградации хряща, такие как С-телопептид коллагена II типа, играют решающую роль в ранних стадиях ремоделирования суставов. В обзоре обобщены современные знания о механизмах ремоделирования коленного сустава при реактивном артрите, с акцентом на диагностическую ценность ИЛ-17А и СТХ-II как ранних биомаркеров повреждения и структурного прогрессирования хряща.

Ключевые слова: *реактивный артрит, ИЛ-17А, ремоделирование коленного сустава, С-телопептид коллагена II типа, ранняя диагностика.*

Reaktiv artritda tizza bo’g’imining shikastlanishi bo’yicha klinik, eksperimental va translyatsion tadqiqotlar ma’lumotlari yordamida xalqaro adabiyotlarning narrativ sharhi o‘tkazildi. Ushbu strukturaviy o’zgarishlarni erta aniqlash muhim klinik muammo bo’lib qolmoqda. Topilmalar shuni ko’rsatadiki, yallig’lanishga qarshi sitokinlar, xususan, interleykin-17A va tog’ay degradatsiyasining biokimyoviy markerlari, masalan, II turdagi kollagen C-telopeptid, bo’g’imlarni qayta qurishning dastlabki bosqichlarida hal qiluvchi rol o’ynaydi. Ushbu sharh reaktiv artritda tizza bo’g’imini qayta qurish mexanizmlari haqidagi mavjud bilimlarni umumlashtiradi, tog’ay shikastlanishi va strukturaviy progressiyaning dastlabki biomarkerlari sifatida IL-17A va CTX-II ning diagnostik qiymatini ta’kidlaydi.

Kalit so‘zlar: *reaktiv artrit, tizza bo‘g‘imi remodellanishi, IL-17A, C-telopeptid II tip, erta tashxisot*

Reactive arthritis (ReA) is an immune-mediated inflammatory joint disease that may lead to early structural damage if not diagnosed and treated promptly. The knee joint is one of the most frequently involved sites, often undergoing subclinical remodeling before radiological changes become evident [5,11]. ReA is a form of seronegative spondyloarthritis that develops following a urogenital or gastrointestinal infection and is characterized by asymmetric oligoarthritis, enthesitis, and extra-articular manifestations. Although reactive arthritis is often considered a self-limiting disease, a substantial proportion of patients develop a chronic or recurrent course associated with progressive joint damage. The knee joint is among the most commonly affected peripheral joints in reactive arthritis. Persistent synovitis, cartilage degradation, and subchondral bone remodeling may occur early in the disease course, frequently preceding detectable radiographic changes [3,7,10]. Therefore, the identification of early biochemical and immunological markers of joint remodeling is of particular importance for improving prognosis and guiding therapeutic decisions.

Joint remodeling in reactive arthritis represents a dynamic and multifactorial process driven by persistent immune activation following an initial infectious trigger. Although the inciting pathogen is often no longer detectable in the joint, microbial antigens and immune complexes may persist in synovial tissue, sustaining chronic inflammation [4,8]. This ongoing immune response leads to synovial hyperplasia, infiltration of T lymphocytes, macrophages, and neutrophils, and excessive production of pro-inflammatory cytokines [2,6].

A central role in this process is attributed to the IL-23/IL-17 axis, which is highly active in reactive arthritis and other forms of spondyloarthritis. Interleukin-17A (IL-17A) enhances synovial inflammation by stimulating fibroblast-like synoviocytes and chondrocytes to produce matrix-degrading enzymes, including metalloproteinases and aggrecanases [1,7]. These enzymes disrupt the structural integrity of articular cartilage, particularly in weight-bearing joints such as the knee [3].

In parallel, chronic synovitis alters the balance between cartilage degradation and repair, resulting in early cartilage thinning, subchondral bone changes, and biomechanical instability. Importantly, these remodeling processes may occur at a subclinical level and precede detectable radiographic changes, underscoring the need for sensitive molecular markers to identify early joint damage in reactive arthritis [9,11]. Pro-inflammatory cytokines, including tumor necrosis factor-α, interleukin-6, and particularly interleukin-17A**,** amplify synovial inflammation and promote the expression of matrix-degrading enzymes. These processes ultimately lead to cartilage breakdown, alteration of joint biomechanics, and structural remodeling of the knee joint [5,11]. IL-17A is a pro-inflammatory cytokine predominantly produced by Th17 cells and innate lymphoid cells. It plays a central role in the pathogenesis of spondyloarthritis and has been increasingly implicated in reactive arthritis. Elevated IL-17A levels have been detected in serum and synovial fluid of patients with active reactive arthritis [7,10]. IL-17A promotes: recruitment of neutrophils and macrophages to the synovium, upregulation of metalloproteinases and aggrecanases, synergistic am-

plification of TNF-α–mediated inflammatory pathways. Importantly, IL-17A-driven inflammation contributes not only to synovitis but also to early cartilage matrix degradation**,** making it a potential biomarker of subclinical joint remodeling before irreversible structural damage occurs [4,10].

Type II collagen is the principal structural protein of hyaline cartilage and is essential for maintaining the mechanical properties of the knee joint. During inflammatory joint diseases, including reactive arthritis, enhanced activity of collagenases and aggrecanases leads to accelerated breakdown of type II collagen fibers [6,10]. This degradation process releases specific collagen fragments into the circulation, among which C-telopeptide of type II collagen (CTX-II) has gained particular attention. CTX-II has emerged as a sensitive biochemical marker of cartilage degradation in various inflammatory and degenerative joint diseases. In reactive arthritis, increased CTX-II levels reflect enhanced collagen type II breakdown, early cartilage remodeling in the knee joint, ongoing structural damage despite minimal radiographic findings [4,8,10].

Several studies suggest that CTX-II elevation precedes visible imaging changes, highlighting its value in early diagnosis and monitoring of joint remodeling**.** The combined assessment of inflammatory cytokines and cartilage degradation markers provides a more comprehensive understanding of joint remodeling processes [2]. IL-17A reflects immune-mediated inflammatory activity, whereas CTX-II directly indicates structural cartilage damage**.** In patients with reactive arthritis, especially those with persistent knee synovitis, simultaneous elevation of IL-17A and CTX-II may identify individuals at higher risk of rapid cartilage degradation, chronic disease progression and early development of structural joint damage. This combined biomarker approach may improve early diagnosis and allow timely initiation of targeted therapy [4,9].

CTX-II is considered a sensitive and specific biochemical marker of cartilage degradation, reflecting active destruction of the collagen network rather than nonspecific inflammation. Elevated serum or urinary levels of CTX-II have been associated with early cartilage damage, disease activity, and structural progression in various inflammatory arthritides [2,4]. In reactive arthritis, increased CTX-II levels may indicate ongoing cartilage remodeling even in the absence of overt radiographic abnormalities. Importantly, CTX-II appears to respond dynamically to inflammatory activity and therapeutic intervention, making it a valuable tool for both early diagnosis and monitoring of disease progression [1,7]. When assessed in combination with inflammatory mediators such as IL-17A, CTX-II provides complementary information linking immune-mediated inflammation to structural cartilage damage, thereby enhancing early detection of knee joint remodeling in reactive arthritis [4,10].

Advanced imaging modalities such as magnetic resonance imaging (MRI) and musculoskeletal ultrasound can detect synovitis, bone marrow edema, and early cartilage abnormalities. However, imaging findings may still lag behind biochemical changes [6,9]. The integration of biomarkers (IL-17A, CTX-II) with imaging techniques offers a promising strategy for the early detection of knee joint remodeling, enabling a more precise assessment of disease activity and structural progression. Early identification of knee joint remodeling in reactive arthritis has important clinical implications [11]. Patients with elevated IL-17A and CTX-II levels may benefit from closer clinical and imaging follow-up, early initiation of disease-modifying therapy and consideration of targeted biological agents affecting the IL-17 pathway. Such an approach may reduce the risk of irreversible joint damage and improve long-term functional outcomes [1,8].

Conclusions

1. Early knee joint remodeling in reactive arthritis is driven by immune-mediated inflammation and cartilage matrix degradation. Interleukin-17A plays a pivotal role in sustaining synovial inflammation, while C-telopeptide of type II collagen serves as a sensitive marker of early cartilage damage.

2. The combined use of these biomarkers represents a promising strategy for the early diagnosis and risk stratification of patients with reactive arthritis, potentially improving disease management and prognosis.

The list of references is available at the editorial office

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A narrative review of the international literature was conducted using data from clinical, experimental, and translational studies on knee joint damage in reactive arthritis. Early detection of these structural changes remains a significant clinical challenge. The findings suggest that proinflammatory cytokines, particularly interleukin-17A, and biochemical markers of cartilage degradation, such as type II collagen C-telopeptide, play a crucial role in the early stages of joint remodeling. This review summarizes current knowledge on the mechanisms of knee joint remodeling in reactive arthritis, emphasizing the diagnostic value of IL-17A and CTX-II as early biomarkers of cartilage damage and structural progression.

Key words: *reactive arthritis, IL-17A, knee joint remodeling, type II collagen C-telopeptide, early diagnosis.*

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