УДК: 616.72-002.77-097:616.71-007.24

Ibragimov Khasan

Head of simulation training department, PhD

Samarkand State Medical University

IMMUNOLOGIC PROFILING OF SYNOVIAL FLUID IN PATIENTS WITH RHEUMATOID ARTHRITIS

Abstract

A joint's synovial cavity contains clear, viscous, straw-colored fluid with biomechanical, metabolic, and regulatory activities. RA synovial fluid was greenish and turbid with reduced viscosity, elevated protein, and glucose levels, indicating active inflammation and altered joint metabolism. In RA joints, increased leukocytes and lymphocyte subpopulations (CD3+, CD8+, CD16+, CD20+, CD95+) indicate a strong immunological response and increased apoptosis.Humoral Immunity: Increased immunoglobulins (IgG, IgM, IgA) indicate B-cell activity, leading to RA's chronic inflammation. RA immunology changes with radiologic stage, with early immune activity increasing and advanced apoptosis increasing. These findings demonstrate the utility of synovial fluid analysis in RA diagnosis, progression monitoring, and therapy guiding, enabling customized therapies.

Keywords: *Rheumatoid arthritis, synovial fluid, biomarkers, cytokines*

Ибрагимов Хасан

Заведующий кафедрой симуляционного обучения, PhD

Самаркандский государственный медицинский университет

ИММУНОЛОГИЧЕСКОЕ ПРОФИЛИРОВАНИЕ СИНОВИАЛЬНОЙ ЖИДКОСТИ У ПАЦИЕНТОВ С РЕВМАТОИДНЫМ АРТРИТОМ

Аннотация

Синовиальная жидкость в норме прозрачная и вязкая, выполняет биомеханические и регуляторные функции. При ревматоидном артрите (РА) она становится мутной, менее вязкой, с повышенным содержанием

белка и глюкозы, что отражает активное воспаление и нарушение суставного метаболизма. Повышение числа лейкоцитов и субпопуляций лимфоцитов (CD3+, CD8+, CD16+, CD20+, CD95+) сопровождается активацией гуморального иммунитета (IgG, IgM, IgA), поддерживающего хроническое воспаление. Иммунологические изменения зависят от стадии заболевания: на ранних этапах преобладает активация иммунных клеток, на поздних — процессы апоптоза. Анализ синовиальной жидкости может служить ценным инструментом для диагностики, мониторинга прогрессирования и подбора терапии при РА.

Ключевые слова: *ревматоидный артрит, синовиальная жидкость, биомаркеры, цитокины*

Introduction. Synovial fluid (SF) is a clear, viscous fluid that maintains joint homeostasis, providing lubrication, nutrient transport, and metabolic regulation. Produced by synovial membrane cells and enriched with hyaluronic acid and low molecular weight proteins, SF reflects both normal physiology and joint pathology. In healthy joints, it supports cartilage remodeling, while in inflammatory conditions its volume and cellular content change, often increasing immune cells and inflammatory cytokines [2,5,6]. In musculoskeletal disorders such as RA and OA, SF contains inflammatory mediators and biomarkers of cartilage turnover; proteomic studies have identified numerous proteins involved in immunity and joint remodeling [3–7]. Thus, SF serves as a valuable diagnostic substrate for joint diseases [1,6]. In this study, we analyzed synovial fluid from RA patients to assess immunologic parameters and the intra-articular interleukin profile.

Materials and Methods. This observational study, approved by the Institutional Review Board of Samarkand State Medical University, compared physicochemical and immunological features of synovial fluid in patients with rheumatoid arthritis (RA; diagnosed by ACR/EULAR criteria) and controls with posttraumatic hemarthrosis. Synovial fluid was aspirated from knee joints,

centrifuged, and analyzed for color, viscosity, protein (Bradford), glucose (enzymatic assay), leukocyte and erythrocyte counts, and rhegocytes. Flow cytometry identified lymphocyte subpopulations (CD3+, CD4+, CD8+, CD16+, CD20+, CD25+, CD95+), while RF, CRP, and immunoglobulins (IgA, IgM, IgG) were quantified by ELISA. Radiographs assessed joint damage. Statistical analyses included descriptive statistics, mixed-effects models, Kaplan–Meier survival, Cox regression, subgroup analyses, and multiple imputation for missing data, all performed in R.

Results. In patients with rheumatoid arthritis (RA), synovial fluid showed distinct abnormalities compared to controls with posttraumatic hemarthrosis. Instead of being clear and straw-colored, it appeared slightly greenish and turbid. Viscosity was markedly reduced (3.51 ± 0.21 vs. 20.12 ± 0.78 mPa·s), indicating fundamental changes in fluid composition related to intra-articular inflammation. Total protein concentration was significantly elevated (24.50 ± 0.08 vs. 15.98 ± 0.83 g/L), reflecting enhanced inflammatory activity, while glucose levels were also higher (5.18 ± 0.14 vs. 4.33 ± 0.14 mmol/L), suggesting altered joint metabolism. Leukocyte counts were more than four times higher in RA (11.68 ± 0.71 vs. 2.69 ± 0.37 × 10^{10}/ml), whereas erythrocytes were reduced, likely due to trauma-related hemarthrosis in controls. Macrophage-like rhogocytes containing immunoglobulins and rheumatoid factor were consistently detected in RA, underscoring the autoimmune nature of the disease.

Markers of inflammation and autoimmunity were significantly increased. Rheumatoid factor levels reached 7.91 ± 1.13 MU/ml in RA patients, while being undetectable in controls. Similarly, CRP was elevated (5.30 ± 0.78 mg/L) in RA but absent in controls, indicating active inflammation and disease activity. Immunologic profiling of synovial fluid revealed a distinct lymphocyte pattern: CD3+ and CD8+ T cells were significantly increased, pointing to an activated T-cell response, while CD4+ helper T cells showed a slight, non-significant

decrease. Natural Killer cells (CD16+) and B cells (CD20+) were markedly elevated, indicating heightened innate immune activity and B-cell activation. CD25+ activated T cells showed a modest rise, whereas CD95+ apoptosis-related lymphocytes were strongly increased (10.1 ± 0.25), reflecting ongoing apoptotic processes within inflamed joints.

Humoral immunity was also altered, with all major immunoglobulin classes elevated in RA. IgG showed the most pronounced increase (13.36 ± 0.47 vs. 3.58 ± 1.54 g/L), followed by IgM (3.60 ± 0.27 vs. 0.62 ± 0.05 g/L) and IgA (2.83 ± 0.35 vs. 0.93 ± 0.10 g/L). These findings demonstrate robust B-cell activity and persistent antibody production within the joint, characteristic of chronic inflammation.

When analyzed by radiologic stage, immune changes showed distinct patterns. At early stages (Stage II), cellular and humoral immune activation was particularly strong, with significant increases in NK and B-cell populations. In advanced stages (III–IV), the total number of immune cells tended to decline, but CD25+ and CD95+ lymphocytes increased, indicating a shift toward T-cell activation and apoptosis. Immunoglobulin levels (IgG, IgA, IgM) remained elevated across all stages, peaking in early disease.

Conclusions. Our study of synovial fluid in rheumatoid arthritis (RA) revealed characteristic alterations, including greenish discoloration, turbidity, reduced viscosity, and elevated protein and glucose, reflecting active inflammation and altered metabolism. Leukocyte increases and the presence of rhogocytes indicated a strong immune response, while elevated CD3+, CD8+, CD16+, and CD20+ lymphocytes reflected heightened T-cell, NK-cell, and B-cell activity. Increased CD95+ lymphocytes pointed to enhanced apoptosis, a hallmark of RA pathogenesis. Immunoglobulin levels (IgG, IgM, IgA) were significantly elevated, underscoring active B-cell involvement in sustaining chronic inflammation. Stage-specific changes showed stronger immune activation in early disease and greater apoptotic activity in advanced stages.

These findings highlight the value of synovial fluid analysis for RA diagnosis, monitoring, and therapy guidance, with immunologic profiles serving as potential biomarkers of progression and treatment response..

References:

1. Altobelli E, Angeletti PM, Piccolo D, De Angelis R. Synovial fluid and serum concentrations of inflammatory markers in rheumatoid arthritis, psoriatic arthritis and osteoarthitis: a systematic review. Current rheumatology reviews. 2017;13(3):170–9.
2. Oliviero F, Galozzi P, Ramonda R, de Oliveira FL, Schiavon F, Scanu A, et al. Unusual findings in synovial fluid analysis: a review. Annals of Clinical & Laboratory Science. 2017;47(3):253–9.
3. Sohn D, Sokolove J, Sharpe O, Erhart JC, Chandra PE, Lahey LJ, et al. Plasma proteins present in osteoarthritic synovial fluid can stimulate cytokine production via Toll-like receptor 4. Arthritis Res Ther. 2012;14(1):R7.
4. Mok, S. W.-F., Law, B. Y.-K., Wong, V. K.-W., & Liu, L. (2018). Immunotherapeutic approaches of rheumatoid arthritis and the implication on novel interventions for refractoriness. In *Immunoregulatory aspects of immunotherapy*. IntechOpen. https://doi.org/10.5772/intechopen.80871
5. J. Huang, X. Fu, X. Chen, Z. Li, Y. Huang, and C. Liang, “Promising therapeutic targets for treatment of rheumatoid arthritis,” Frontiers in immunology, vol. 12, p. 686155, 2021.
6. WHO. “Rheumatoid arthritis.” https://www.who.int/news-room/fact-sheets/detail/rheumatoid-arthritis (accessed Sep. 05, 2023).
7. L. J. Crofford, “Use of NSAIDs in treating patients with arthritis,” Arthritis research & therapy, vol. 15, pp. 1–10, 2013.