Commentary

Autoimmune response in cartilage-delivered peptides in a patient with osteoarthritis

Kusuki Nishioka

Arthritis Research Centre, Institute of Medicine, St Marianna University, Kawasaki, Japan

Corresponding author: Kusuki Nishioka (e-mail: k4nishi@marianna-u.ac.jp)

Received: 7 Jul 2003 Accepted: 22 Oct 2003 Published: 5 Dec 2003

Arthritis Res Ther 2004, **6**:6-7 (DOI 10.1186/ar1025)

Abstract

Whatever the initiating factor of osteoarthritis (OA), the process ultimately unmasks the immunogenic determinants of chondrocytes, proteoglycans and collagens, which then triggers autoimmune reactions. Although the precise mechanism of the immune responses in the pathogenesis of OA requires further investigation, here I postulate that the presence of autoimmunity to cartilage components has an important role in the process of cartilage degradation in OA. Current studies strongly suggest that a immunoregulatory therapeutic strategy should be established.

Keywords: cartilage, chemokines, components, immunological intervention, osteoarthritis

Introduction

My colleagues and I have recently reported several lines of evidence for a potential role of immunological intervention in the pathogenic process of osteoarthritis (OA). In particular, we have focused on the role of activated T cells [1] after an immunological response to the cartilage component [2–4] with activation by chemokines [5,6]. The background of this concept comes from a pathological feature of OA synovium. Although OA is generally accepted as one of the commonest degenerative joint disorders caused by biomechanical stress or aging, instances of inflammatory features such as synovial effusion or swelling of affected joints have been reported. The accumulation of mononuclear cells in synovial fluid, an increasing concentration of immunoglobulin and pathological findings of OA synovial tissue such as hyperplasia of synovial lining cells and infiltration of inflammatory cells into the sublining layer strongly suggest chronic inflammatory features of OA. These findings resemble the early stage of rheumatoid arthritis [7–9]. We were therefore interested in the immune response to cartilage components such as cartilage intermediate layer protein (CILP) and YKL39 [10,11]. In particular, endogenous articular cartilage components have been found to provide a rich source of antigenic determinants in OA.

We previously detected CD3 T cells in the synovium tissue and $CD4^+CD8^+$ cells in the sublining layer in OA. Moreover, the number of interferon-γ-bearing T cells was fivefold that of IL-4-positive cells. In addition, we identified clonal diversity in the infiltrated T cells [1]. These findings of oligoclonal T cell expansion in OA synovium and the presence of T cell aggregates undergoing *in situ* activation in a rather specific manner indicate that a Th1 cell-mediated specific immune response might be taking place in OA synovium, driven by local antigens.

Why should T cells have a potential role in the pathogenic process of cartilage destruction in OA? Current work suggests that extracellular matrix-filling material hyaluronan can modulate the function of antigen-presenting cells in monocytes. Recent studies show that dendritic cells and T cells constitutionally express genes involved in hyaluronan synthesis (*HAS1* and *HAS3*) and encoding hyaluronidase, *Hyal3* [12]. After the secretion of hyaluron-degrading enzymes, dendritic cells and T cells need to detach from the extracellular matrix to migrate from or to lymph nodes. Either way, an involvement of the T cell activation process in joints is strongly associated with turnover of extracellular hyaluronan.

OA = osteoarthritis.

In conclusion, I would like to emphasize that examining the potential role of T cells and autoantibody against cartilage components in OA has been instrumental in developing not only new insights into the pathogenesis of OA but also novel strategies for the treatment of OA, such as the application of an immunomodulative agent.

Competing interests

None declared.

References

1. Nakamura H, Yoshino S, Kato T, Tsuruha J, Nishioka K: **T-cell mediated inflammatory pathway in osteoarthritis.** *Osteoarthritis Cartilage* 1999, **7:**401-402.
2. Tsuruha J, Masuko-Hongo K, Kato T, Sakata M, Nakamura H, Nishioka K: **Implication of cartilage intermediate layer protein in cartilage destruction in subsets of patients with osteoarthritis and rheumatoid arthritis.** *Arthritis Rheum* 2001, **44:**838-845.
3. Sekine T, Masuko-Hongo K, Matsui T, Asahara H, Takigawa M, Nishioka K, Kato T: **Recognition of YKL-39, a human cartilage related protein, as a target antigen in patients with rheumatoid arthritis.** *Ann Rheum Dis* 2001, **60:**49-54.
4. Sakata M, Tsuruha JI, Masuko-Hongo K, Nakamura H, Matsui T, Sudo A, Nishioka K, Kato T: **Autoantibodies to osteopontin in patients with osteoarthritis and rheumatoid arthritis.** *J Rheumatol* 2001, **28:**1492-1495.
5. Yuan GH, Masuko-Hongo, Nishioka K: **Role of chemokines/ chemokine receptor systems in cartilage degradation.** *Drug News Perspect* 2001, **14:**591-600.
6. Yuan GH, Masuko-Hongo K, Sakata M, Tsuruha J, Onuma H, Nakamura H, Aoki H, Kato T, Nishioka K: **The role of C-C chemokines and their receptors in osteoarthritis.** *Arthritis Rheum* 2001, **44:**1056-1070.
7. Peyron J: **Inflammation of osteoarthritis (OA): review of its role in clinical picture, disease progress, subsets and pathophysiology.** *Semin Arthritis Rheum* 1980, **Suppl 1:**115-116.
8. Pelletier JP, Martel-Pelletier J, Abramson SB: **Osteoarthritis, an inflammatory disease: potential implication for the selection of new therapeutic targets.** *Arthritis Rheum* 2001, **44:**1237-1247.
9. Golderg DL, Egan MS, Cohen AS: **Inflammatory synovitis in degenerative joint disease.** *J Rheumatol* 1982, **9:**204-209.
10. Poole AR: **Immunology of cartilage.** In: *Osteoarthritis: Diagnosis and Medical/Surgical Management.* 2nd edition. Edited by Moskowitz RW, Howell DS, Goldberg VM, Mankin HJ. Philadelphia: WB Saunders; 1992:155-189.
11. Banerjee S, Poole AR: **Immunity to cartilage proteoglycans.** *J Rheumatol* 1992, **33 (Suppl):**36-39.
12. Christian T, Jonathan PS, Jan CS: **Hyaluronan – magic glue for the regulation of the immune response?** *Trends Immunol* 2003, **24:**112-114.

Correspondence

Kusuki Nishioka, MD, Arthritis Research Centre, Institute of Medicine, St Marianna University, 2-16-1 Sugao Miyamae-ku, Kawasaki 216-8512, Japan. Tel: +81 44 977 8111; fax: +81 44 977 9165; e-mail: k4nishi@marianna-u.ac.jp