Review Article

Rheumatoid Arthritis in Temporo-Mandibular Joint: A Review

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Abstract

This article summarizes the temporomandibular joint (TMJ) rheumatoid arthritis (RA). In particular, TMJ-RAs are collected in a short summary by examining every aspect of RA; the treatment of TMJ-RA is also briefly mentioned. TMJ-RA is usually characterized by bilateral pain, tenderness and swelling, and limitation of jaw movements. Due to these symptoms, patients may experience limitations in their daily activities, such as eating, speaking, and swallowing. MEDLINE and Scopus databases were searched electronically using the terms "temporomandibular joint" and "rheumatoid arthritis." The electronic search includes articles or books published in English and December 2017. A search of the reference lists of selected articles was also carried out.

Keywords: *Biochemistry, histopathology, rheumatoid arthritis, temporomandibular joint*

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Introduction

Temporomandibular joint (TMJ) play important roles in crucial processes, such as chewing and speaking and swallowing. Diseases of the TMJ affect every part of the society.[1,2] Because of the symptoms of temporomandibular origin, patients usually refer to a dentist where solutions to some problems are tried. Apart from these attempts, many patients with TMJ problems refer to or are directed to other specialists. However, different disciplines can differ between terminology, etiology, and treatment modalities.[3]

Inflammatory disease of the jaw joint and understanding how it happens is of great importance. These are divided into four main groups as synovitis, capsulitis, retrodiscite, and arthritis. Arthritis refers to the inflammation of articular surfaces of the joint. Various types of arthritis affect the TMJ. The most common of these are osteoarthritis and polyarthritis. Polyarthritis is a systemic condition that affects all joints. Inflammation in the TMJ and tenderness in other joints manifests itself as rheumatoid arthritis (RA) characterized by pain.

RA is a varied, chronic, systemic, autoimmune, and inflammatory disease that focuses on erosive symmetrical joint disease and is sometimes distinctly accompanied by extra-articular involvement. The inflammation of the synovial membranes characterizes it. This inflammation also affects the connective tissue and articular surfaces in the environment causing these surfaces to thicken and become more sensitive. TMJ involvement usually includes bilateral pain, tenderness, and swelling, as well as restriction of jaw movements. In the late phase of the disease, ankylosis is more likely to occur.[4,5] RA in other joints, including the TMJ, requires medical and dental treatment.

Search strategy

The MEDLINE and Scopus databases were searched electronically taking into consideration only English articles and published until December 2017. In addition, relevant journals and books of TMJ were searched along with reference lists of primary studies to identify additional results.

Epidemiology and etiology

Worldwide, the overall prevalence of RA has been reported as 0.1%–2%. It is 2–3 times more commonly seen in females and elders. Although it may be seen in all ages, the onset of the disease is mostly between the ages of 40 and 60 years.[6]

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The most comprehensive prevalence studies have been carried out by Wolfe *et al*.[7] using questionnaires from 17,683 RA patients. They found there was jaw pain in 19% of the respondents. However, neither the diagnostic criteria nor the complaint duration was reported. In another prevalence study conducted by Sem *et al*., the prevalence of TMJ pain was found to be 10.6% in the first year and 3.6% at the end of the first year after diagnosis.[8]

The etiology of RA is not fully known. Numerous factors, either alone or in a multifactorial fashion, can lead to the development of this disease. Factors such as genetics, smoking, autoimmune causes, and microbial infections may increase the incidence of RA.[9]

Histopathology and biochemistry

In epidemiology, several autoimmune conditions are gender-related with rheumatic diseases being more common in women. Immune systems of women have an enhanced reactivity by increasing antibody generation, interferon (IFN) response, monocytes with high antigen presenting activity, and greater homograft rejection rates. However, men are more susceptible to infections of their hormonal system.

In women, low doses of estradiol seem to induce pro-inflammatory cytokines, such as tumor necrosis factor (TNF) or interleukin (IL-) 1 beta. Although during pregnancy, estradiol doses are high, which can decrease the signaling of pro-inflammatory cytokines.[10]

Degenerative changes are seen in joints affected by RA from inflammatory cells present in synovial fluid. Macrophages, granulocytes, and plasma cells infiltrate the synovial tissues in RA.[11] In this case, synovium becomes thicker and is called "pannus." Pannus is the damage resulting from the invasion of the bone, cartilage, and tendons by inflammatory synovial tissue mass. The pannus grows towards the joint space and forms protruding folds. This creates pain by disrupting joint functions and causing soft tissue to stretch.[12] Lysosomal enzymes released from granulocytes and macrophages in the synovium cause destruction and erosion in the condyle head and temporal bone. These degenerative changes may result in disruption of joint functions, fibrous and bone ankyloses, occlusal-facial deformities, and occlusal discrepancies.[13]

RA triggers oxidative stress. It has been observed that mitochondrial reactive oxygen species (ROS) are generated five times more in the blood and monocytes of RA patients compared to healthy individuals. This result is one of the pathogenic hallmarks of RA. Free radicals cause joint damage as they contribute to inflammatory and immunological cellular response in RA as secondary messengers. Free radicals attack cartilage proteoglycan and halt its synthesis and can degrade the joint cartilage.[14] Oxidative damage caused by hyaluronic acid and lipoperoxidation products, oxidation of low-density lipoproteins, and increased carbonyl generated from protein oxidation has been both observed in RA and as DNA damage. The p53 protein mutation occurred in RA-derived fibroblast-like synoviocytes has a connection with genotoxic aspects triggered by ROS.[15] Also, it has been indicated that the antioxidant system, regardless of being enzymatic or not, is disrupted in RA. The chronic oxidative stress in the RA synovium occurs due to the increased articular pressure in RA joints and leads to elevated ROS production in the cellular oxidative phosphorylation that promotes repetitive cycles of hypoxia/reoxygenation. Hypoxia occurs in RA joints and is produced as a result of rapid cellular proliferation, which is induced by the inflammatory response. The effect of oxidative stress on the synoviocytes in RA can then occur. As a result of these events, phagocytic cells get activated and can increase the oxidative damage. Environmental factors, such smoking, drugs, and ultraviolet light may also contribute to this.[16]

Inflammatory mediators that are released from inflammatory cells cause joint destruction. TNF-α and IL-1β are associated with the pathogenesis of arthritis and cause an increase in the secretion of proteolytic enzymes such as matrix metalloproteinase-2 (MMP-2) and matrix metalloproteinase-9 (MMP-9) in synovium stromal cells.[17,18] These enzymes are responsible for the expression of inflammatory cells by altering the specific peptide bonds of extracellular matrix proteins [Figure 1].

Stress kinase involved in intracellular communication in the pathogenesis of RA, mitogen-activated protein kinase (MAPK) along with the route signal transducer, and activator of transcription 3 (STAT3) also contributes to RA pathogenesis. These pathways result in intermediate products acting in oxidation, apoptosis, and differentiation.[19]

Synovial mesenchymal stem cells (MSC) inhibit the MAPK signaling pathway that plays a role in RA pathogenesis. This suggests that MAPK pathway plays a role in differentiation, immunoregulation and apoptosis. Also, this pathway releases the pro-inflammatory cytokines, which causes severe damage all over the tissue. It is also known that IL-6 is related to RA pathogenesis. It has been determined that the placement of MSCs from the outside of the joint tissue causes downregulation of the MAPK pathway by the cooperation of the MSCs present in the tissue.[20,21]

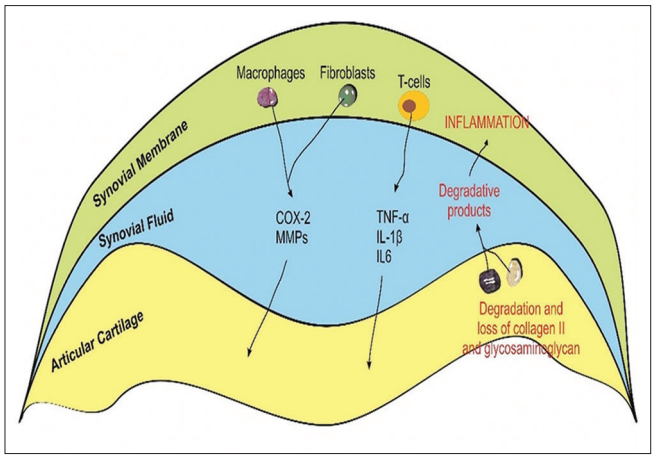

Figure 1: Demonstration of the effect of inflammatory mechanism in rheumatoid arthritis on TMJ

Cyclooxygenase (COX) is a multifunctional enzyme that catalyzes the conversion of arachidonic acid to prostaglandin. Two isoforms of the enzyme cyclooxygenase have been identified. Cyclooxygenase-1 (COX-1) is structurally expressed in many cells. In synovial tissues, especially at the synovial boundary layer, there is no difference in the COX-1 level, even if tissue inflammation occurs. On the other hand, under normal conditions, cyclooxygenase-2 (COX-2) release is extremely low, but its release is increased during inflammation. In both clinical and experimental studies, it has been shown that COX-2 increases in RA.[22,23]

In RA, localization of vascular endothelial cells in the joint region and infiltration of mononuclear inflammatory cells and fibroblast-like cells (synoviocytes) were observed.[24]

Temporomandibular joint rheumatoid arthritis: Clinical findings

Bilateral pain, tenderness, swelling, and limitation of jaw movements are distinct characteristics of in RA of the TMJ. There may be no radiological findings in the early stages, but in later stages, the condylar articular surface is degenerated, the joint gap is narrowed, and anterior open bite can be seen. In children, this degeneration can lead to growth retardation and facial deformity in the mandible. In adults, it varies from hardening of the joint to occlusal facial deformities. There is a high likelihood of ankyloses in all patients.[5,25]

In 1874, Garrod reported RA in TMJ involvement for the first time. The TMJ may have unilateral involvement as well as symmetric involvement.[26] The most common clinical symptom is deep preauricular pain during function. Joints are sensitive to palpation, and joint stiffness is present in the morning. There is also a decrease in click, creep, and bite strength.[27] Moen *et al*.[28] reported pain and dysfunction from TMJ in 77% of RA patients with the most common deformity being anterior open bite. Lin *et al*.[29] reported that, in their study of 56 patients with RA, fibrous and bone ankyloses accompanied anterior open bite in 3 patients.

Patients with TMJ-RA have clinical findings such as joint sounds, myalgia-related musculature, and limited mandibular movement. TMJ condylar destruction is observed in early RA disease and can be investigated 6 months after the first diagnosis. Also, after long-term follow-up, radiographic findings, such as erosion, flattening, and resorption of the condyle was most commonly observed.[30]

Initial symptoms of oropharyngeal dysphagia (OD) can be seen as a consequence of joint deformation. A decrease in the mandibular movement, including fatigue, pain, masticatory difficulties, and improvement in chewing and swallowing duration has a link to several oral preliminary and oral stage OD signs and symptoms, which leads to weight loss. These signs and symptoms of OD can decline the quality of life in the RA population.[31]

Temporomandibular joints: Imaging and findings

Magnetic resonance imaging (MRI) is the best option to assess intra-articular processes and, as it provides a high definition of the soft tissue, it is now the best and the preferred technique to diagnose disc disorders. Computed tomography (CT) is the best technique used to assess osseous components. Cone-beam computed tomography (CBCT) has a similar capability to image osseous tissue with CT. CBCT is more advantageous than CT regarding low radiation doses used while its drawbacks include elevated noise, motion artifacts, and lack of assessment of the soft tissue. Using MRI, soft tissue can be visualized; however, it is hard to distinguish between capsule and synovium. The synovium has been subjected to changes in inflammatory arthritis. RA occurs both in osseous and soft tissue (synovial-pannus). Basically, severe bone changes in the condylar and enlarged synovium show a difference in RA from degenerative osteoarthritis. In severe degenerative osteoarthritis, erosive bone changes do not occur together with enlarged synovium.[32]

Conclusions and Future Directions

RA is known to be an autoimmune and systemic disease. Because of the destructive power of the disease, it is important that maxillofacial surgeons work with rheumatologists. Prescribing drugs or symptomatic treatments, such as arthrocentesis, are being used, but this is not a one-time application and should be compulsory and continuous.

Symptoms of TMJ due to osteoarthritis or degeneration may worsen because of trauma. However, in diseases such as RA, pain may increase, and movement may disappear in the event of loss of function due to destruction even in remission, which maintains the continuity of inflammation.

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Conflicts of interest

There are no conflicts of interest.

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