

Rheumatoid arthritis (RA) and osteoarthritis (OA) represent the most common forms of musculoskeletal disorders that affect diarthrodial joints, lead to joint damage and disability. Extra-articular manifestations accompanied the joint disease only in RA. Diagnosis of both conditions most commonly bears on the conventional radiography. Mostly in OA, radiographic changes often occur late in the disease and are largely irreversible. Molecular markers could reflect joint damage, inflammation, or immune response. Current investigation revealed potential uses of molecular markers, ranging from understanding pathogenesis of the diseases to predicting and monitoring the outcome of the treatment.

The aim of the thesis was to analyze several biochemical markers in serum, synovial fluid and synovial tissue samples from patients with RA and OA. and to evaluate their diagnostic and predictive values as well as their contribution to the pathogenesis of the diseases.

We found increased serum pentosidine concentrations in OA patients that were of a predictive value of the joint space narrowing in OA of the knee joint and correlation between pentosidine and cartilage oligomeric matrix protein (COMP) in synovial fluid that make pentosidine one of the new potential biomarkers of the OA. Serum level of COMP was similar among patients with OA and RA as well as healthy individuals. In our study, COMP in serum was not predictive for further progression of OA and did not correlate with any marker of inflammation both in OA and RA. On the other side, COMP was significantly elevated in OA synovial fluid in contrast to RA synovial fluid, which may reflect distinct pathogenic feature of cartilage loss in OA process. Relationship between modulator of bone metabolism osteoprotegerin (OPG) and marker of bone turnover deoxypyridinolin in serum from OA patients could represent a balance between bone-protective role of OPG and bone resorption.

In RA patients significantly elevated levels of pentosidine were associated neither with disease activity nor with CRP. One can thus speculate about pentosidine as a surrogate marker of disease activity in RA. Relationships between COMP and anti-CCP antibodies in serum and COMP and OP*C*_i in synovial fluid may reflect the association of systemic cartilage turnover and immune activity, and local cartilage destruction and bone metabolism in RA. Decreased levels of OPG in RA can be responsible for the periarticular osteoporosis and bone destruction observed in RA, and predicate of an insufficient bone-protective role of OP*C*_i in inflammatory diseases. Moreover, we found the expression of metastasis-inducing protein - S100A4 at sites of invasion in RA synovium. In addition, exogenous S100A4 modulated expression and production of several matrix metalloproteinases (MMP) by RA synovial fibroblasts. Since several phenomena are similar between RA and malignant tumors, it can be hypothesized that S100A4 contributes to the aggressive, invasive, and tumor-like behavior of RA synovium.

In conclusion, pentosidine may represent new biochemical marker of OA progression. Increased COMP in synovial fluid from OA patients can be a result of a different pathogenic feature of cartilage destruction in OA compared to RA. A relationship between several cartilage, bone, and immunological markers in RA could show a complexity of the disease. S100A4 could represent a new molecule that might be implicated in the pathogenesis of RA.