Comparison of gene expressions in subchondral bone osteoblasts from hip osteoarthritis, rapidly destructive coxarthrosis and rheumatoid arthritis

Introduction:
The representative hip joint diseases include osteoarthritis (OA), rapidly destructive coxarthrosis (RDC) and rheumatoid arthritis (RA). They have different clinical courses and progression of joint destruction. OA is characterized by chronic degeneration of joint cartilage and periarticular bone formation, whereas RDC and RA result in rapid and intensive joint deterioration. Recent studies suggest that an abnormal subchondral bone metabolism may be involved in the progression of joint destruction [1-4]. However, the etiology of this difference remains mostly unknown. Various inflammatory cytokines and proteases and factors are reportedly involved in the initiation and progression of cartilage degeneration, while few studies have investigated the subchondral bone adjacent to the articular cartilage. In this study, we examined the gene expression of biochemical factors such as inflammatory cytokines, proteases and factors related to bone metabolism in the subchondral bone of OA, RDC and RA.

Material and Methods:
The subjects were 7 OA patients aged 48-71 years (mean: 59.6 years), 3 RDC patients aged 63-84 years (mean: 75.3 years), 3 RA patients aged 73-74 (mean: 73.3 years) who received total hip arthroplasty (THA). Four patients aged 72-90 (mean: 77.5 years) who were diagnosed with femoral neck fracture (FNF) and had received femoral head prosthetic replacement, were used as controls. Patients who received steroids or bisphosphonate, which influence bone metabolism, were excluded from this study. Subchondral bone tissues were harvested from the loaded area in the femoral head at the time of arthroplasty. The subchondral bone osteoblasts (SBOs) were isolated and total RNA was extracted from the isolated SBOs. Quantitative real-time RT-PCR was performed by monitoring the increase of the reporter fluorescence of each TaqMan probe for interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), matrix metalloproteinase-13 (MMP-13), ADAMTS-5, receptor activator of NF-kappaB ligand (RANKL), receptor activator of NF-kappaB (RANK) and osteoprotegerin (OPG) during PCR. Statistical significance was assessed by Student’s t-test, and p values of less than 0.05 were considered significant.

Results:
The expression levels of IL-1β, IL-6, ADAMTS-5 and MMP-13 in the SBOs from OA patients were 5.0, 11.4, 13.9 and 6.1 times higher than in the SBOs from FNF patients. RANKL/OPG ratio of these two groups had no significant difference [Fig 1]. Comparing RDC with OA, IL-8 gene expression and RANKL/OPG ratio in the RDC-derived SBOs were 4.5 and 4.9 times higher than OA, respectively [Fig 2]. The gene expression levels of proteases in the RDC-derived SBOs tended to be higher than OA, but not significant. With comparison of RA and OA, the mRNA level of ADAMTS-5 in the RA-derived SBOs was 1.8 times higher than OA, but the level of OPG was half of that in the OA-derived SBOs [Fig 3]. RANKL/OPG ratio of the RDC-derived SBOs was 3.0 times of that in the OA-derived SBOs.

Discussion
Recent researches suggested that subchondral bone might play an important role in the pathogenesis of joint destruction. In the OA patients, subchondral bone turnover has shown to be much increased compared to that of normal bone turnover [1], and a research using spontaneous OA model animal indicated that subchondral changes preceded the changes in the cartilage [2]. Regarding to the joint destruction of RDC, vulnerability of subchondral bone has been described and discussed [3]. In RA, activities of osteoclasts have been shown to play an important role in the joint destruction [4]. Among these diseases, the clinical courses were quite different, but the details regarding their pathophysiology have not been clarified yet. In the present study, we investigated the gene expression of biochemical factors related to bone remodeling in the subchondral bone of destructive hip joint diseases. As a result, the gene expression of inflammatory cytokines and proteases increased in the SBOs from OA compared to those from FNF. However, bone resorptive factors did not change. On the other hand, not only inflammatory cytokine or protease but bone resorptive factors in the SBOs from RDC and RA were higher than those in OA. These finding suggested that the production of inflammatory cytokines and proteases around the subchondral bone area might have an influence on the bone metabolism, which might contribute to the progression of cartilage degeneration in OA. In RDC and RA, in addition to the highly expression of inflammatory cytokines and proteases, upregulated osteoclastic activities might accelerate the joint destruction and resulted in the rapid clinical course.

Reference:

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