Transforming growth factor-β1, interleukin-1β and collagenase activity in subchondral bone of the femur and the severity of osteoarthritis of the hip

Sirs,

Factors and mechanisms determining the development of osteoarthritis are not yet defined. Apart from interleukins or metalloproteinases, growth factors such as transforming growth factor-β1 (TGF-β1) or bone morphogenetic proteins (BMPs) are often listed as compounds which can be involved in the pathogenesis of osteoarthritis (1).

The activation of repair processes are responsible for increased osteosynthesis and production of osteophytes. In the literature available there is little data assessing the content of growth factors that could participate directly in the development of osteoarthritis of the hip joint.

The aim of the study was to determine the relationship between the content of TGF-β1, IL-1β and the activity of collagenase in subchondral bone of the femoral head and the severity of osteoarthritic changes of the hip joint.

32 samples of subchondral bone were collected from patients with hip osteoarthritis during total hip replacement. There were 21 women and 11 men enrolled. The mean age was 66 (range from 37 to 80 yrs.). For the evaluation of the severity of osteoarthritis of the hip, the Kellgren and Lawrence classification was used (2). It is a five-degree scale classifying osteoarthritic changes on the basis of the hip X-ray in AP view. Along with an evaluation of these changes, a joint is placed into a higher class. Ten joints (31.2%) were classified as group 1, 11 as group 2 according to Kellgren-Lawrence classification. Eleven joints (34.4%) and 11 joints (34.4%) were classified as group 3 and group 4 (34.4%), respectively.

The content of total protein in bone samples was measured with the use of BCA-Protein Assay Reagent (Pierce, Beijerland, Hollland) (3). The concentration of TGF-β1 and IL-1β was determined with the use of the enzyme-linked immunosassay (ELISA) Quantikine Human Immunoassay Test (R & D Systems, Minneapolis, USA) (4, 5). Col- lagenase activity was assessed theoreti- cally (Baschem, Biochemical GmbH Heidel- berg, Germany) (6). For quantity data, the variability range, dispersions and means, as well as normal distribution errors, have been marked. Results presented in this paper involve the data-cleansing procedure. Correlation coefficients between the quantities analysed were measured. The data from the analysed subgroups were compared with the use of the t-Student test. The data was statistically significant at the level below 0.05.

We found direct proportional correlation between the content of TGF-β1 converted into total protein and the severity of osteoarthritic changes (p < 0.05) (Fig. 1). The mean content of TGF-β1 in patients with minimal osteoarthritic changes of the hip joint classified to group II according to Kellgren-Lawrence classification was 0.86 pg/µg. In patients with moderate hip osteoarthritis (group III) the mean content of TGF-β1 was 1.24 pg/µg. The highest mean content of TGF-β1 (1.72 pg/µg) was observed in patients with the most severe osteoarthritic changes (classified as group IV). Similar correlation but with no statistical significance was observed for IL-1β. We found no correlation between the activity of collagenase and the severity of osteoarthritis.

Our results confirm the vital role of TGF-β1 in the pathogenesis of bone formation in osteoarthritis of the hip joint. In patients with more severe osteoarthritic changes of the hip joint, the content of TGF-β1 in subchondral bone layer was higher. This observation is also confirmed in animal studies by Scharstuhl et al. (7). In experimental- ly induced knee osteoarthritic changes in mice, adding proteins such as mLAP-1, SMAD6 and SMAD7 as intracellular TGF-β1 and BMP inhibitors, caused a decrease in osteophyte formation in the joint. The role of TGF-β1 in osteophyte formation during osteoarthritis in the experimental model was also postulated by Van der Berg (8).

Further examination of the role of TGF-β1 and other cytokines in the development of osteoarthritis can lead to their application in treatment or prevention of this particular illness.

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References


Successful treatment of necrotizing vasculitic lesions after infusion of iloprost in a patient with cryoglobulinemia and chronic HCV infection

Sirs,

We report a case of a patient with cryoglobulinemia and chronic HCV infection who presented necrotizing vasculitic lesions treated with iloprost who positively responded to this treatment. Cryoglobuline- mic vasculitis (CV) is an immune-complex mediated systemic vasculitis involving small and medium sized vessels, in which a causative role of HCV in 80-90% of pa- tients has been definitely established. Purpura and rheumatic complaints are the most common symptoms found in HCV associat- ed CV (1). HCV genomic sequences cannot be integrated into the host genome, since the HCV is a single-stranded RNA virus without a DNA intermediate, not directly cytopathic (2) but it can trigger the immuno- logical alterations indirectly by exerting a chronic stimulus to the immune system. New insights on the pathogenetic mechanisms of HCV-related immunological disorders include the evidence that the HCV envelop protein E2, interacting with CD81 molecule expressed on B-lymphocytes, may increase the frequency of VDJ rearrangement in antigen-reactive B-cell. One possible consequence may be the activation of anti-apoptotic Bcl-2 protooncogene that leads to extended B-cell survival. The B- lymphocyte expansion is responsible for a