THU0069 RELATIONSHIPS BETWEEN SYNOVIAL FLUID METALLOPROTEINASES AND INTERLEUKIN-1B, AND SERUM CRP IN OSTEOARTHRITIS OF THE KNEE

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Background Interleukin (IL)-1 and metalloproteinases (MMP) are thought to play a crucial role in the cartilage degradation of osteoarthritis (OA). Recently it has been proposed that CRP may be useful index of OA activity and severity.

Objectives We studied the relationships between synovial fluid (SF) IL-1b, MMP1 and MMP3, and serum levels of CRP in patients with OA of the knee (KOA) to investigate the role of CRP in KOA.

Methods In the SF from 25 patients with KOA (Altman criteria, Kellgren and Lawrence score of 2 or greater on X-ray plan films) we determined the levels of IL-1b, MMP-1 and MMP-3 (ELISA), along with WBC number. In the same patients serum concentration of CRP was analysed by ultrasensitive rate nephelometry. No patients were taking NSAIDs or other antirheumatic drugs.

Results In SF, MMP1 was correlated with MMP3 ($r = 0.61$, $p = 0.0009$), and MMP3 with IL-1b ($r = 0.67$, $p = 0.0002$). In turn, serum CRP was correlated with MMP3 ($r = 0.76$, $p < 0.0001$) and, at lower level, with MMP1 ($r = 0.49$, $p = 0.01$) and IL-1b ($r = 0.49$, $p = 0.01$).

Conclusion The correlations found between serum CRP and SF levels of substances believed to be crucial in OA cartilage degradation, such as MMPs and IL-1, confirm the role of marker of disease severity recently proposed for this acute phase protein.

THU0070 IMMUNOHISTOLOGICAL AND LECTIN HISTOCHEMICAL STUDIES OF STERNOCLAVICULAR AMYLOIDOSIS

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Background In a prospective necropsy study of the sternoclavicular joints of 31 unselected subjects (15 female, 16 male; mean age 71 years, range 23–92) to ascertain the prevalence of the features of osteoarthrosis, 29 (93.5%) showed bilateral localised amyloidosis as detected by alkaline Congo red with apple-green dichroism in polarised light. These amyloid deposits were characterised by immunohistological and lectin histochemical techniques.

Objectives

Methods Amyloid deposits were noted in synovial stroma, in the intra-articular fibrocartilaginous disc and in hyaline articular cartilage (usually superficial and middle zones). In synovial stroma only, there were related accumulations of CD68 positive mono- and multinucleated cells (37% of cases). All amyloid deposits stained with anti P-component antibody. None stained with anti AA monoclonal antibody. Ninety per cent of deposits stained with anti Beta2 microglobulin antibody, 74% with anti lambda antibody and 61% with anti kappa antibody (all monoclonal antibodies). Mixed patterns of immunoreactivity were noted.

Results For lectin histochemical studies sections were probed with a panel of 14 biotinylated lectins using techniques standardised in our laboratory. Chondrocytes (including clones) in all layers of articular cartilage and in disc cartilage showed positive

cytoplasmic reactions with HHA (Hippeastrum hybrid agglutinin). In addition PSA (Pisum sativum agglutinin) stained particularly the territorial and interterritorial matrices of hyaline articular cartilage in relatively normal and osteoarthrotic cases. E-PHA (Phaseolus vulgaris erythroagglutinin) selectively stained the neomatrix in osteoarthrotic cases.

Conclusion These results showed a high prevalence of localised amyloidosis in the sternoclavicular joint which is not only an age-related phenomenon but is also related to osteoarthrosis, being particularly marked in fibrillated cartilage. A large number of deposits contained Beta2-microglobulin mixed with lambda and kappa light chains and the ubiquitous P-component. Beta2-microglobulin amyloidosis is a feature of dialysis amyloid arthropathy. None of the cases in this series were on any form of dialysis and none had impairment of renal function of clinical significance. Light chain amyloidosis usually shows a clonal restriction related to plasma cell dyscrasia/proliferation; the polyclonality and the mixed chemical nature of the amyloidosis reported here is unusual. The lectin profiling showed clear cytoplasmic and matrical differences indicating the presence of non-reducing terminal alpha-mannosyl residues in the former and bi/tri antennary non-bisected complex N-linked glycans in the latter. Cartilage neomatrix expressed bi/tri antennary bisected complex N-linked glycans. There was no particular relationship between glycan expression and the amyloid deposits. It has been suggested¹ that the presence of particular glycosaminoglycans in cartilage favours localised amyloidosis either by playing a role in the folding of amyloidogenic proteins in fibril formation or protecting established amyloid deposits from proteolytic degradation. The present results would not support this hypothesis.

REFERENCE

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THU0071 THE ROLE OF TRANSFORMING GROWTH FACTOR B (TGFB) IN BONE METABOLISM IN RHEUMATOID ARTHRITIS

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Background TGFb can be found in high concentrations in bone matrix. It is produced by osteoclasts and osteoblasts and is considered as a local regulator of bone metabolism. TGFb is an important factor in the coupling of bone resorption and formation. TGFb induces synthesis of matrix proteins and inhibits matrix degradation by downregulation of MMPs and may thereby counteract pro-resorptive cytokines such as IL-1, IL-6 and TNFa. The role of the different isoforms of TGFb is not yet fully understood. In rheumatoid arthritis elevated plasma levels of TGFb1 and TGFb2 have been described.

Objectives It was the aim of this study to determine the role of TGFb for bone metabolism in RA.

Methods 36 RA patients and 55 patients with osteoarthritis (OA) were included in this study. Total TGFbs in plasma samples and bone extracts were determined after transient acidification applying three isoform specific ELISAs.

Bone mineral density was measured by dextra-scan (Hologic QDR 4500W) at the lumbar spine and femoral neck. Diagnosis of osteoporosis and osteopenia, respectively, was defined according to the WHO osteoporosis criteria from 1994.