High Plasma and Synovial Fluid Levels of Osteopontin Correlate with Severity of Primary Knee Osteoarthritis

INTRODUCTION:
Osteoarthritis (OA) is a chronic degenerative joint disease that is characterized by the progressive destruction of articular cartilage. Diagnosis is relied on symptoms and signs in conjunction with radiography. Although clinical research on OA has been extensively investigated, the etiology of this disease remains poorly elucidated. Several biochemical and biomechanical factors are considered for the pathogenesis. Osteopontin is a highly phosphorylated and sulfated glycoprotein with cell binding and matrix binding properties (1). In addition, osteopontin is one of the major noncollagenous bone matrix proteins produced by various cell types, including activated T cells, macrophages, osteoblasts and chondrocytes (2). Osteopontin expression during chondrocyte maturation is one of the important events involved in cartilage-to-bone transitions in fracture repair (3). There is evidence suggesting that OPN functions as a proinflammatory cytokine and play a critical role in the regulation of tissue repair and remodeling (4). The purpose of the present study was to investigate the levels of osteopontin in both plasma and synovial fluid (SF) of patients with primary knee OA, and evaluate the possible correlations with severity of the disease.

MATERIALS AND METHODS:
The study was approved by the Ethical Committee on Human Research of our university and was conducted under the guidelines of the Declaration of Helsinki.

Thirty-two patients with primary knee OA (28 females and 4 males; mean age 70.5±1.3 years) according to the criteria of the American College of Rheumatology and 15 healthy controls (10 females and 5 males; mean age 65.5±0.7 years) were enrolled in the study. The severity of the disease was determined using plain radiography of the affected knee, according to the Kellgren and Lawrence classification (5). SF was aspirated from the affected knee during surgery, when a total knee arthroplasty was performed, and stored immediately at -80°C until used. Plasma and SF were assessed with commercial enzyme-linked immunosorbent assay (ELISA) for osteopontin (Quantikine, R&D Systems, Minneapolis, MN, USA) according to the manufacturers’ instructions.

Statistical analysis was carried out with SPSS 16.0 for Windows. Comparisons between the groups were performed using Student’s t-test for unpaired data. Pearson's correlation coefficient (r) was used to determine correlation between variables. Data were expressed as a mean ± SEM. P values < 0.05 were considered significant.

RESULTS:
Plasma and SF levels of knee OA patients and plasma of controls are demonstrated in Figure 1. OA patients had higher plasma osteopontin concentrations compared to healthy controls (168.8±15.6 vs 67.2±7.7 ng/ml, P<0.0001). Osteopontin levels in SF were significantly higher with respect to paired plasma samples (272.1±15.0 vs 168.8±15.6 ng/ml, P<0.001). Interestingly, plasma osteopontin levels showed a positive correlation with SF osteopontin levels (r=0.373, P=0.035). According to the Kellgren and Lawrence (KL) grading scale, 8 patients were KL grade 2, whereas 12 patients were KL grade 3 and 12 patients were KL grade 4 osteoarthritus. The plasma and SF levels of osteopontin were analyzed and compared in relation to radiological KL grading of OA. The plasma osteopontin levels from KL grade 2 were 69.8±23.1 ng/ml; those from KL grade 3 were 193.8±17.9 ng/ml; and those from KL grade 4 were 209.8±21.8 ng/ml. The data revealed that SF osteopontin levels in KL grade 3 and 4 were significantly elevated compared with those of KL grade 2 (P<0.001). Although the mean plasma levels of osteopontin in KL grade 4 were greater than those in KL grade 3, the difference was not statistically significant (P=0.835). Additionally, the SF levels of osteopontin from KL grade 2 were 191.9±36.7 ng/ml; those from KL grade 3 were 300.5±10.2 ng/ml; and those from KL grade 4 were 497.1±22.3 ng/ml. The data revealed that SF osteopontin levels in KL grade 3 and 4 were significantly elevated compared with those of KL grade 2 (P<0.001). We further analyzed the correlation between the plasma and SF levels of osteopontin and the severity of knee OA. The plasma osteopontin levels significantly correlated with severity of disease (r=0.592, P<0.001) (Figure 2). The SF levels of osteopontin also correlated with disease severity (r=0.451, P=0.01) (Figure 3).

DISCUSSION:
The present study revealed a marked increase of osteopontin levels in both plasma and SF of patients with primary knee OA compared to the control plasma levels. It is of interest to note that osteopontin levels of SF were significantly higher than those seen in paired plasma samples. Elevated levels of osteopontin in SF are possibly caused by either the release of osteopontin residing in extracellular matrix, or the increase in its production, or both processes. Our findings suggest increased local and systemic production of osteopontin in the primary knee OA. These results indicate that plasma and SF levels of osteopontin may play a significant role in the pathogenesis of OA. Measurements of plasma and/or SF levels of osteopontin could possibly serve as a biochemical parameter for determining disease severity and may be predictive of prognosis with respect to the progression of osteoarthritic disease process.

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REFERENCES: