The molecular biology of the rotator cuff tear: Significance of synovitis in the subacromial bursa and glenohumeral joint

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The rotator cuff diseases frequently occur in the middle aged and the elderly, and pose a significant problem.

Interests have been exclusively paid in the subacromial bursa, since it has been considered to be responsible for shoulder pain.

However, recent arthroscopic studies have demonstrated that, in addition to the subacromial synovitis, concurrent glenohumeral synovitis occurs in the rotator cuff disease. Few studies have addressed the glenohumeral synovitis in rotator cuff diseases. We measured the inflammatory intensity in the subacromial bursa and glenohumeral joint and tried to disclose the significance of these inflammations.

In this presentation, the diseases were divided into two categories. Non-perforating tear group includes subaromial bursitis and partial-thickness tear. Perforating tear group contains full-thickness tear.

[Cases] Synovial tissue specimens of the subacromial bursa and glenohumeral joint were obtained from 39 patients during surgery. The non-perforating tear group comprising 10 subacromial bursitis and 9 partial-thickness tears, and perforating tear group comprising 20 full-thickness tears. Ten specimens were obtained as normal

controls. The shoulder joint fluid could be obtained from 7 partial-thickness tears, 15 supraspinatus tears and 10 massive tears before opening the joint. Degree of shoulder pain was evaluated before the operation in each patient using Visual Analogue Scale. The subacromial bursa specimens were harvested from the surrounding tissue of the greater tuberosity. The specimens of the glenohumeral joint were obtained from the rotator interval and the subscapularis bursa. These specimens were stored at -80 degrees Celsius for total cellular RNA isolation. Specimens were also fixed in 4% paraformaldehyde or in Zammboni solution and embedded in paraffin. In order to evaluate quantity and localization of cytokine-mRNAs, semi-quantitative RT-PCR, in situ RT-PCR were performed. Immunohistochemical staining was performed for localization of cytokine-proteins, and Western blot analysis was quantifying the amount of cytokine-proteins. SpearmanÆs rank correlation test and Mann-Whitney U test were applied for statistical analysis.

[Result 1] The shoulder pain in non-perforating tear group was significantly higher than that of perforating tear group. The expression levels of IL-1β mRNA in the synovium of the subacromial bursa and glenohumeral joint of rotator cuff diseases were significantly higher than the control group. IL-1β mRNA in subacromial bursa was significantly higher in the non-perforating tear group, but those of glenohumeral joint were significantly higher in the perforating cuff group than in the opposite group.

The mRNA expression levels of IL-1β in the subacromial bursa synovium were correlated with the degree of shoulder pain.

The mRNA expressions of two different IL-1 receptor antagonists in the subacromial bursa and glenohumeral joint showed the same results to that of IL-1β mRNA.

The mRNA expression levels of two different IL-1 receptor antagonists showed the same results to that of IL-1β mRNA. In situ RT-PCR revealed that synovial lining cells, infiltrating mononuclear cells and synovial fibroblasts were shown to express IL-1β mRNA in the glenohumeral joint of the perforating tears.

In the subacromial bursa of non-perforating tears, the vessels, infiltrating mononuclear cells and synovial fibroblasts were shown to express cytokine-mRNAs. The sublining cells expressed secretedIL-1 receptor antagonist mRNA in particular, while the synovial lining cells preferentially expressed intra-cellular IL-1 receptor antagonist mRNA. Immunohistochemical analysis demonstrated positive staining identical to the results of in situ RT-PCR. Western blot analysis revealed that mature IL-1β was produced at higher levels in subacromial bursa of non-perforating tears and in glenohumeral joint of perforating tears than those of the opposite group.

IL-1 β production in subacromial bursa could explain shoulder pain, while that in glenohumeral joint could not.

substance P in the subacromial bursa

Substance P was increased in primary afferent nerves during chronic pain. Previous reports mentioned the presence of neuropeptide-immunoreactive nerve fibers in the subacromial bursa of rotator cuff tear, but gave only a rough estimate of quantitative changes. Sensitive and specific radioimmunoassay and immunohistochemistry were performed in our study.

[Result 2] The concentration of substance P in the subacromial bursa synovium was significantly higher in the non-perforating tear group than in the perforating tear group. Both groups showed significant difference compared with control.

Substance P was observed in the thin neurons around the vessels and inside and immediately beneath the synovial lining. An increase in the number of immunoreactive nerve fibers was observed in both groups, but fewer was observed in the controls.

These results suggest that increased substance P in the subacromial bursa reflects painful situation in rotator cuff diseases.

Some of rotator cuff tears develop degenerative changes of articular cartilage of shoulder.

McCarty and Neer reported degenerative arthritis after rotator cuff tear, and Hamada has reported that roentgenographic findings of massive cuff tears develop as time passed. Therefore, it is suggested that joint destruction activity is accelerated, especially after massive tears.

Cartilage degradative enzyme, cartilage degradation and collagen

type II synthesis in the joint fluid

In our study, the levels of MMP-1, -3 and TIMP-1, GAG and carboxy-terminal type II procollagen peptide were measured.

[Result 3] Compared with partial-thickness tears, synovial fluid in full-thickness tears showed higher levels of cartilage degradative enzyme (MMP-1,-3) and molecule of cartilage degradation (GAG) but, collagen type II synthesis (pCOLII-C) did not increase, which means accelerated enzymatic digestion of cartilage or prompt turn-over of cartilage matrix. Moreover, if compared with isolated SSp tear, synovial fluid in massive tear showed higher levels of cartilage degradative enzyme and molecule of cartilage degradation but, collagen type II synthesis did not increase, which means accelerated enzymatic digestion of cartilage or prompt turn-over of cartilage matrix. Our results may indicate the potentials for accelerated cartilage-degrading activity in the glenohumeral joint in full-thickness tears, especially massive tears.

Itæs well known that the synthesis of MMPs and TIMP is elevated by treating the cells with IL-1. So, IL-1 β in glenohumeral joint could contribute to elevating the levels of MMP-1 and -3 in the synovial fluid of perforating tear group.

In conclusion, IL-1β production in subacromial bursa was higher in non-perforating tears than in perforating tears, which could explain shoulder pain. IL-1β production in glenohumeral joint was higher in perforating tears than in non-perforating tears, which could explain

development of glenohumeral arthropathy.

References

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