

Pain-Related Cytokines in Osteochondral Lesions of the Talus: A Role for Prognosis and Risk Factors for Arthritis?

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Summary:

Our research demonstrates elevation of pain-related cytokines in painful ankles with osteoarthritis and not in osteochondral lesions of the talus.

Abstract:

Background:

Osteochondral lesions of the talus (OLTs) can cause pain and activity limitations in both competitive and recreational athletes. Surgical treatment is frequently required for these athletes to reduce pain and mitigate the development to degenerative changes, which were historically reported to occur in up to half of patients with OLTs (1,2). The presence of pain-related and inflammatory cytokines in synovial fluid has been associated with several painful joint conditions. For example, Interferon gamma (IFN-g), interleukins 1 and 6 (IL-1, IL-6) and macrophage inflammatory protein-1 beta (MIP-1b) have been demonstrated to be elevated in fluid samples from painful knees with meniscal tears³. IL-6 and monocyte chemoattractant protein 1 (MCP-1) have also been shown to be elevated in synovial fluid in arthritic ankles, and tumor necrosis factor (TNF-alpha) is known to be elevated in the synovial fluid of inflammatory arthritides. However, it is currently unknown whether pain-related intra-articular cytokines are elevated in patients with symptomatic OLTs, and whether similar cytokines are elevated in arthritic ankles. We hypothesize that there will be greater concentrations of inflammatory cytokines in painful ankles with OLTs compared to controls, and that greater concentrations of cytokines will be present in ankles with endstage arthritis compared with those with OLTs.

Methods:

We enrolled 50 consecutive patients undergoing arthroscopic or open surgical treatment for painful ankle synovitis, symptomatic OLTs, or ankle arthritis. Synovial fluid was obtained from each ankle using a lavage technique at the beginning of the indicated surgical procedure. Samples were also obtained from 14 asymptomatic control ankles. Visual analog pain scale (VAS) and AOFAS ankle scores were obtained for each patient pre-operatively. Patient radiographs and magnetic resonance images (MRIs) were classified by a musculoskeletal radiologist using Kellgren-Lawrence and Hepple scoring systems, respectively. Outerbridge scores were recorded for intra-operative findings. Synovial fluid samples were assessed for concentrations of several pain-related cytokines, including TNF-alpha, matrix metalloproteinases (MMP-3 and MMP-9), IL-1, IL-6, MIP-1, MCP-1 and vascular endothelial growth factor (VEGF). Statistical analysis was performed by the Mann-Whitney t test and multiple group comparisons using ANOVA and post-hoc analysis. Pearson correlations were calculated comparing cytokine levels with clinical and radiographic variables.

Results:

There were 64 patients total: 21 with OLTs, 29 with ankle arthritis, and 14 controls. Compared to controls, specimens from ankles with osteoarthritis had significantly greater concentrations of IL-1, MCP-1, TNF-alpha and VEGF. There was no difference between OLT and control specimens in concentrations of any of the tested cytokines. Radiographs

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demonstrating grade 4 arthritic changes (Kellgren-Lawrence) were associated with significantly increased levels of IL-1, IL-6, MCP-1, and VEGF compared to grades 0-3. MRIs classified as grade 3 (Hepple) were associated with significantly increased levels of IL-1, MCP-1, and TNF-alpha compared to other grades (0-2 and 4). Patients with Outerbridge IV articular changes had higher levels of MMP-1, MMP-3, IL-1, MCP-1, and MIP-1. Correlation analysis demonstrated a low positive correlation between patient-reported pain scores and concentrations of IL-1, IL-6, MIP-1 and MCP-1.

Discussion:

Inflammatory cytokines have been shown to be predictive of intra-articular pathology in painful joint conditions and to correlate with pain. Our results demonstrated elevated levels of pain-related cytokines in arthritic ankles, but not in symptomatic OLTs, compared to controls. The findings were consistent for arthritic changes noted both intra-operatively and radiographically. We also found some correlation between patient-reported pain scores and concentrations of cytokines. These findings suggest that inflammatory and pain-related cytokines are associated with osteoarthritis in the ankle, but do not appear to be elevated in OLTs. Interestingly, we found increased cytokine levels in Hepple 3 OLTs (detached but nondisplaced fragment), but not grade 4 (completely displaced fragment). It is possible that pain associated with OLTs may be secondary to a mechanical component or stimulation of the nerve endings in the subchondral bone beneath the cartilage defect, rather than a degenerative or inflammatory process as seen in ankle arthritis (3). The identification of a biomarker that correlates with pain and chronic chondral inflammation in patients with ankle pathology may ultimately optimize diagnostic, treatment, and prognostic algorithms. The cytokines that play a dominant role in the development of osteoarthritis could be isolated as therapeutic targets for specific therapeutic and preventive interventions in the future.

References:

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