COMMENTARY & PERSPECTIVE

Inflammatory Events in Cartilage in Early Stages of Femoroacetabular Impingement

Commentary on an article by Shingo Hashimoto, MD, PhD, et al.: "Molecular Characterization of Articular Cartilage from Young Adults with Femoroacetabular Impingement"

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Femoroacetabular impingement was recognized decades ago and has gained recognition as a distinct set of anatomic morphologies resulting in localized chronic damage to the hip joint. This abnormality typically manifests in younger patients and is thought to lead to secondary osteoarthritis¹. The two most commonly described subcategories are the "cam" and "pincer" morphotypes. In the cam type, abnormalities in the proximal aspect of the femur such as an aspherical head or insufficient femoral head-neck offset result in impingement at the anterior rim of the acetabulum, especially in flexion and internal rotation. The pincer type is commonly the result of a deep or malrotated acetabulum, which increases the risk of femoroacetabular impingement in deep flexion. The two abnormalities can coexist, thus compounding the impingement and presenting with mixed pathology².

Chronic mechanical injury of articular cartilage and/or labral tissue has been shown to induce matrix damage, an inflammatory response, and even cell death. However, there is very little clinically relevant evidence of the cellular response during the early stages of femoroacetabular impingement and of its relevance to joint degeneration and eventual osteoarthritis.

The study design involved two experimental groups and one control group. In the primary study group, twenty-five patients underwent femoral head-neck osteochondroplasty for femoroacetabular impingement. This group represented the early stage of femoroacetabular impingement before the appearance of apparent radiographic changes of osteoarthritis. The secondary study group consisted of seven patients with femoroacetabular impingement who were undergoing hip arthroplasty (total or resurfacing) for end-stage osteoarthritis. The experimental groups were compared with three age-matched controls (all female) undergoing hip surgery for developmental dysplasia of the hip.

Despite the small size of the control group, there were significant differences in the expression of genes for several chemokines (CXCL6, CXCL3, CCL3L1) and enzymes involved in matrix degradation (MMP-13, ADAMTS-4) as well as major matrix constituents (ACAN, COL2A1). This response was striking given the absence of apparent radiographic evidence of osteoarthritis in the primary study group. The upregulation of anabolic genes (COL2A1, ACAN) is reminiscent of an early stage of osteoarthritis with increased anabolism and catabolism, and it is also consistent with the younger age (thirteen to thirty-seven years) of these patients with impingement.

Femoroacetabular impingement is a very compelling model for studying the etiology and progression of secondary osteoarthritis due to chronic injury, as a specific cause can be identified by clinical examination and imaging, and in vivo tissue samples can be obtained at the time of surgical treatment. Ethical concerns limit the tissue analysis to the site of femoral osteochondroplasty. However, the extent of the molecular response beyond the site of impingement is an important concern from both scientific and clinical perspectives. A more generalized response in tissues beyond the site of impingement would indicate a greater likelihood of secondary osteoarthritis and would support earlier intervention. Clinically, the acetabular labrum and articular cartilage typically experience greater damage, also indicating that other tissues in the hip joint are likely to generate a similar response.

The data support a link between chronic impingement and an inflammatory response at the site of impingement. However, the lack of increased expression of the interleukin-1 (IL-1) gene despite the increased expression of genes that have been shown to be upregulated by IL-1 suggests a more indirect mechanism. As the authors correctly point out, further studies focusing on mechanisms of osteoarthritis are needed. Analysis of the synovial fluid and the synovial membrane is therefore also required to rule out whole-joint involvement, at least in the early stages.

Cell death in response to acute and chronic injury is being actively studied by several groups²⁻⁵. Various mechanisms including caspase-activated apoptosis, oxidative damage, dysregulation of autophagy, and an abnormal unfolded protein response have been identified. The relevance of cell death and its consequences in leading to further degeneration after femoroacetabular impingement are also of great interest.

In summary, the authors have conducted what appears to be the first study of local gene expression in the context of femoroacetabular impingement in a clinically relevant setting. A remaining question that is worthy of future study is specific to femoroacetabular impingement: Is there a difference in the tissue response to cam-type compared with pincer-type impingement? Answers to this question might reveal valuable insights into disease progression and support differential therapies.

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