Introduction: Successful treatment of osteoarthritis (OA) following partial meniscectomy depends on an understanding of progressive degradation of meniscus as well as articular cartilage. The present study demonstrates that the central region of meniscus produces high level of nitric oxide (NO) following partial meniscectomy, which may be the cause for the early development of OA. Following partial meniscectomy, degenerative changes of articular cartilage occur on the tibial plateau. It has been shown that NO plays an important role in cartilage degeneration and that NO induces chondrocyte apoptosis (1). Recently it has been demonstrated that meniscus has the capability to produce a large amount of NO and that chondrocyte-like cells in the meniscus are responsible for NO production (2). It was also suggested that the cell populations in meniscus differed in their morphology, with the peripheral cells being more fibroblastic than the more chondrocytic cells in the central region (3). These previous findings led us to hypothesize that the central part of the meniscus could synthesize high level of NO which has the capability to induce chondrocyte apoptosis following partial meniscectomy. In the present study, we examined the regional (central compared to peripheral) differential response of NO production in meniscus following partial meniscectomy. NO synthesis and cell apoptosis in tibial articular cartilage during the early stage of OA were also investigated.

Methods: Fourteen mature rabbits underwent bilateral partial meniscectomies on the medial menisci. One third of the inner region of each medial meniscus was excised. Sixteen animals were used for untreated or sham operated controls. All the operated rabbits were sacrificed at 12 wks postsurgery. At sacrifice, medial menisci (MM), lateral menisci (LM), and articular cartilage from medial tibial plateau were harvested. The MM and LM were divided into peripheral parts (MM-p and LM-p) and central parts (MM-c and LM-c). The tissues were cultured in DMEM for 48 hrs and the culture supernatants were collected for nitrites measurements by Griess reaction. The data were standardized by the DNA content of the tissues. Gene expression of inducible NO synthetase (iNOS) in the tissues was analyzed by RT-PCR. Localization of nitrotyrosine, in vivo evidence for NO synthesis, in medial meniscus and tibial articular cartilage was determined by the immunohistochemistry. In situ detection of chondrocyte apoptosis in the tibial articular cartilage was performed using the Apo Tag kit.

Results: NO production by explants: Following partial medial meniscectomy, MM-c produced a significantly higher amount of NO than that in the untreated and sham controls (p = 0.05). We also observed trends that the NO synthesis from the tibial articular cartilage following partial meniscectomy was larger than that from the untreated (p = 0.07) and sham (p = 0.15) control groups (Figure 1).

Gene expression of iNOS: Strong expression of iNOS gene was detected in MM-c, LM-c and tibial articular cartilage following partial meniscectomy. We also noted that the gene expression was present in MM-p and LM-p, but at a lower level than in the MM-c and LM-c (Figure 2).

Localization of nitrotyrosine: Medial menisci and tibial articular cartilage from the control groups showed only a few nitrotyrosine-positive cells. Strong expression of nitrotyrosine immunoreactivity was demonstrated in the central region of the medial menisci following partial meniscectomy. Nitrotyrosine-positive cells were present in the superficial and middle zone of the tibial articular cartilage from the meniscectomized animals.

In situ detection of apoptosis: The tibial articular cartilage from the controls contained very low numbers of apoptotic cells that were almost exclusively located in the surface layer. Following partial meniscectomy, apoptotic chondrocytes were demonstrated in the superficial zone of the tibial articular cartilage.

Discussion: The present study demonstrates the upregulation of NO production in the central region of menisci following partial meniscectomy. The cells in the central region of menisci as well as tibial articular cartilage may be responsible for NO production which has the potential to induce chondrocyte apoptosis during the early stage of OA following partial meniscectomy.


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