Repetitive Physiologic Stresses Create Osteochondral Lesions in Juvenile Rabbits

Introduction: Juvenile osteochondritis dissecans (JOCD) is an increasingly common source of knee pain in young patients and can predispose patients to osteoarthritis. JOCD involves subchondral bone injury that may not be visible on arthroscopy. The precise etiology of JOCD remains elusive, but it may involve repetitive stress on the joint [6]. Previous animal studies created articular cartilage damage and subchondral fractures through repetitive stress in adult rabbits [3] or generated lesions through drilling [1]; however, no model using repetitive stress in immature rabbits exists. We sought to determine if repetitive physiologic loads produced subchondral lesions in skeletally immature rabbits without gross articular surface involvement.

Materials and Methods: Six 4-week-old New Zealand White rabbits were subjected to repetitive submaximal compressive loading forces of the right femorotibial joint 5 times per week for 5 weeks for 45 minutes. Protocol was IACUC approved. Rabbit mounting and loading followed previously published reports [3]. Each right hind limb was cyclically loaded with 1.5-2.5 x body weight with a 170 ms impulse at 1Hz. Non-loaded left hind limbs served as internal controls. Weekly radiographs were obtained until euthanization after five weeks.

Following euthanasia, hind limbs were disarticulated and immediately scanned using µCT (MicoCAT-II, InTek, Knoxville, TN). The femur and tibia were carefully dissected to remove overlying soft tissues and the articular surfaces were photographed. Cartilaginous defects were graded from the photographs using the International Cartilage Repair Society Classification (ICRSC) of OCD lesions. Intact knee joints were decalcified (EDTA), sagittally cut into 4 µm sections, and stained with hematoxylin and eosin (H&E). The femur and tibia were carefully dissected to remove overlying soft tissues and the articular surfaces were photographed. Cartilaginous defects were graded from the photographs using the International Cartilage Repair Society Classification (ICRSC) of OCD lesions. Intact knee joints were decalcified (EDTA), sagittally cut into 4 µm sections, and stained with hematoxylin and eosin (H&E).

Results: Four of six rabbits completed all 5 weeks of testing (two completed 4 weeks). All rabbits grew at a similar rate to weights on 0.5 mm, Fig. 2a). Joint surface irregularities included horizontal cracks or vertical fissure-like clefts in two animals (Fig 2c,d), and focal depressions or elevations in most animals (Fig. 2c,f). Geographic nuclear drop-out was also present in those areas, wherein nuclei lost their normal basophilic (blue) staining pattern (Fig. 2e). Chondrocyte cloning was identified in all cases, wherein nests of chondrocytes cluster abnormally in ball-like formations (Fig. 2f).

One rabbit was found to have a fracture prior to loading and was immediately euthanized. The rabbit was not photographed and was not graded. In the 5th week of testing, one rabbit developed a Salter-Harris II physeal fracture and was withheld from testing for 2 days and euthanized. Three rabbits had evidence of physeal widening and healing callus formation by µCT.

Discussion: Osteochondral lesions were induced in skeletally immature rabbits by a particular mechanical loading regimen. Repetitive stress in juvenile athletes is considered to be one of the most likely etiologies of human JOCD. Prior animal models of JOCD involved surgical drilling or biopsy of the articular surface, a mechanism that is not an etiology of human JOCD.

Lesions generated in this study were similar in location to JOCD lesions found in humans [4]. Early human JOCD lesions frequently have no gross articular cartilage changes on arthroscopy despite extensive subchondral bone involvement [4]. Histologic changes detected in all loaded limbs included areas of thickened cartilage, up to twice that of normal, and the abundant appearance of chondrocyte cloning (Fig 2). These findings are similar to those in a recent study of surgical biopsies of articular cartilage in patients with JOCD that found increased cartilage thickness with frequent chondrocyte cloning [6]. Sites of frank separation and micro-fractures at the deep layer of articular reported in adolescent patients [6] were not detected in the loaded rabbit limbs. Our loading regime also created mild articular surface lesions, which are not commonly seen in early JOCD. Chondrocyte clones are also present in other conditions of the knee, such as osteoarthritis [5]. The results suggest that consistent pediatric knee injuries may be produced using these methods, and that adjustments to the loading regimen may produce osteochondral lesions with qualities similar to human JOCD.

Fig 1: Representative gross pathology (R1,L1) and corresponding µCT reconstructions (R2,L2) and slices (R3,L3) from a single rabbit. Arrows point to the osteochondral lesions. R: loaded; L: contralateral control; m: medial, la: lateral.

Fig 2: Representative histopathology stained with H&E.


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