Articular Cartilage and Intervertebral Disc Degeneration in Ovariectomized Mice
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Introduction: There are larger increases in women than in men in the incidence and prevalence of osteoarthritis as well as disc degeneration after 50 years of age. Furthermore, hormone replacement therapy for the menopause seems to be associated with a decrease in the prevalence of symptoms and radiological alterations related to hip and knee osteoarthritis. There has been no satisfactory explanation for these actions, nor are there many details on the effects of estrogen in articular cartilage and intervertebral discs (IVDs). Previous studies have shown the presence of estrogen receptors in articular cartilage and IVDs, indicating that these tissues can respond to estrogens [1,2]. The aim of this study was to evaluate the developmental changes in mouse articular cartilage and IVDs under estrogen deficiency.

Materials and Methods: Experimental animals - Experimental studies used 6- to 7-month-old adult female wild-type (+/+) C57Bl/6. Mice underwent bilateral ovariectomy from a posterior approach. All animals were sacrificed at the same age interval (8- to 9-months). Mice were immediately frozen and stored at -20°C.

Histological preparation and staining - Prior to dissection posterior-anterior and lateral X-rays of whole mice were done. The mice were then dissected carefully, removing the right knee joint and cervical to lumbar spine. These specimens were immediately placed in neutral-buffered 10% formalin. These fixed samples were then decalcified, dehydrated, embedded in paraffin and cut into 4 μm sections. One section from each specimen was stained with the following: Hematoxylin-Eosin (H&E), Safranin-O/Fast green, and Weigert’s hematoxylin/alcan blue/picrosirius red. The slides were examined under light microscopy and digital pictures were taken for appropriate comparison.

Bone mineral density (BMD) analysis - Mice were sacrificed and imaged using a PIXImus Bone Densitometer System #56069 (GE Lunar corporation), which measures bone densitometry using dual-energy x-ray absorptiometry. The femur and lumbar vertebrae were selected and analyzed using a Windows 98 Based Software.

Micro computed tomography (CT) - Micro CT data were acquired on a SkyScan T1072 X-ray Microscope-Microtomograph (Skyscan, Aartselaar, Belgium). CTan Software (from SkyScan) was used to analyze the sample.

Results: Histological findings in IVD: We observed numerous changes in the IVD of ovariectomized (Ovx) mice. Namely, the degeneration of the nucleus pulposus (NP) including the loss of notochordal cells in the NP. The annulus fibrosus (AF) showed marked thinning as compared to the wild type (Fig. 1). Furthermore, the ovariectomized group as a whole showed decreased IVD heights to 0.44 ± 0.03 mm (mean ± SD) compared to 0.59 ± 0.06 mm in the wild type. In addition, there was an observable trend of endplate ossification in the ovariectomized group.

Histological findings in knee joint: Knee joints of ovariectomized mice showed a trend towards having more gross degenerative changes, like areas of cartilage erosion. A decrease in articular cartilage thickness could be measured, yielding a thickness of 66 ± 9 μm (mean ± SD) compared to 93 ± 6 μm in the wild type (Fig. 2). Certain layers of cartilage were more affected than others, possibly indicating a specific role of estrogen in the developing cartilage.

Discussion: In the present study, we demonstrated the effects of lacking estrogens on both the articular cartilage and IVD. Observations were made on AF thinning, decreased IVD height, NP degeneration, and loss of cellular components in the NP. Likewise, the articular cartilage revealed more degenerative changes including a decrease in articular thickness. Our results suggest that estrogen plays a role in maintaining healthy cartilage and IVDs.


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