OARSI 2024

View Abstract

CONTROL ID: 4034186

TITLE: THE RAT OSTEOARTHRITIS BONE SCORE: A NEW HISTOLOGICAL SYSTEM FOR SCORING SUBCHONDRAL PATHOLOGY IN RAT KNEES ANALOGOUS TO HISTOLOGICAL CORRELATES OF HUMAN OA BONE MARROW LESIONS

PRESENTATION TYPE: Either Podium or Poster

CURRENT CATEGORY: Mechanistic Studies of OA (Metabolism, Cell Signaling, Ageing, Inflammation, Cytokines, Matrix Biology, Cell-Cell Interactions, Mechanobiology, etc.)

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Purpose (the aim of the study): Bone marrow lesions (BMLs) are detected by MRI in the in human osteoarthritis (OA) subchondral bone and associated with pain. We previously described 7 histological features associated with BMLs from which we developed the Osteoarthritis Bone Score (OABS) for human subchondral bone. We now describe parallel histopathological features in rat OA, and validate a rat version of the OABS (rOABS).

Methods: Histological features contributing to the human OABS system were identified knees from rats with OA induced by intra-articular injection with sodium monoiodoacetate (MIA, n=10), or by meniscal transection (MNX, n=10). Controls were vehicle injected (n=10) injected, or sham-operated (n=8). Pain behaviour (weightbearing asymmetry and paw withdrawal threshold) were analysed from during the final 7 days of each model before sample collection (MIA: 28 days, MNX 42 days after model induction). Coronal knee sections were stained using haemotoxylin and eosin, or safranin-O, fast green and haemotoxylin. Scoring criteria from human OABS were adapted for rat knees. Optimal numbers of sections were determined by comparing the variances of averages from 1, 2 or 3 sections. Reliability of rOABS was assessed between observers using intraclass correlation coefficients. rOABS was compared between OA models and their respective controls (MIA vs vehicle; MNX vs sham operation) using Mann-Whitney U-tests. Associations of rOABS with pain behaviour, and with histological scores for cartilage involvement, synovitis or osteophytes, were evaluated using Spearman's rho.

Results: Features of human OABS were found in rat models of OA. The MNX and MIA models displayed similar rOABS features. One section per knee permitted reliable assessment of rOABS. The rOABS scores were higher in each model than their controls; MIA vs vehicle 4 (2 to 4) vs 0 (0 to 0) respectively, and MNX vs sham 4 (2 to 5) vs 0 (0 to 0) respectively. Reliability from 2 raters for rOABS was good with intra-class correlation coefficient = 0.79 (0.63 to 0.88), p<0.001. The rOABS was positively associated with OA scores for cartilage involvement (rho = 0.77, p <0.001), synovial inflammation (rho = 0.80, p<0.001) and osteophyte (rho = 0.60, p <0.001). Moderate associations were detected between rOABS and pain behaviour (weight-bearing asymmetry: rho = 0.32, p=0.05, paw withdraw threshold: rho = -0.30, p=0.07).

Conclusions: The rOABS is a reliable measure of subchondral pathology in two rat models of knee which reflects changes associated with bone marrow lesions in humans. Significant associations with cartilage involvement, synovitis and osteophytes underline the nature of OA as a `whole joint' disease. Although subchondral pathology may contribute to OA pain, other factors likely also contribute to pain behaviour in rat OA models. Scoring of subchondral pathology by rOABS opens the door to preclinical testing of interventions aiming to reduce pain or joint damage by targeting bone marrow lesions.

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KEYWORDS: bone marrow lesions, rat, histology.

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