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Abstract

Background & Aim:

Recently, we created a novel surgical drilling model of post-traumatic osteoarthritis (PTOA) in the Yucatan minipig, which allowed us to investigate the isolated effects of inflammation on PTOA development, while eliminating potential confounding mechanical instability. The purpose of this study was to investigate the therapeutic effects of anti-inflammatory protein Alpha 2-macroglobulin (A2M) on PTOA development in our minipig model.

Methods:

48 Yucatan minipigs (age 15–16 months old, weight 58–70kg) were divided into 4 groups (n=12): sham, surgery-induced PTOA, surgery-induced PTOA/one intra-articular injection of A2M (A2M-1), and surgery-induced PTOA/three intra-articular injections of A2M (A2M-3). The knee joints were harvested 15 weeks post-surgery. Frozen synovium sections were prepared for hematoxylin & eosin (H&E) staining and synovium feature were evaluated using microscopic scoring systems. The macroscopic cartilage scoring was used to assess the severity of the cartilage after India ink staining. Secondary outcomes of IL-1 β , NF- κ B, MMP13, and TNF- α expression levels were evaluated using RT-PCR.

Results:

We compared morphological changes of the synovium and the cartilage from the same anatomical location amongst the four groups. Surgery-induced PTOA animals exhibited severe synovitis and cartilage damage in comparison to all the other groups. The A2M groups displayed a mild to moderate synovitis and cartilage damage than the sham group as well as the contralateral knee of the surgery-induced PTOA group. No difference was found between the A2M-1 and A2M-3 groups. The synovium in the A2M groups presented significantly lower mRNA expression levels of IL-1 β , NF- κ B, MMP13, TNF- α than the surgery-induced PTOA group.

Conclusion:

This porcine model allows us to evaluate the anti-inflammatory effects of A2M as a potential PTOA treatment. The results of this study indicate that A2M reduces both synovitis and levels of inflammatory factors associated with cartilage damage in PTOA in our fit-for-purpose model. This study also advances our understanding of treating synovium inflammation to attenuate the complex pathogenesis of osteoarthritis.

Clinical Implications:

The results of this study indicate that A2M reduces both synovitis and levels of inflammatory factors associated with cartilage damage in PTOA in our fit-for-purpose model. This study also advances our understanding of treating synovium inflammation to attenuate the complex pathogenesis of osteoarthritis.