A93 COMPLEMENT ACTIVATION AND REGULATION IN EARLY AND ADVANCED STAGE OSTEOARTHRITIS

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10.1136/ard.2010.129627f

Objective Although not considered a classical inflammatory arthropathy, osteoarthritis (OA) is often associated with low-grade synovitis. The stimuli required to establish inflammation in OA synovium are as yet unclear, but there is emerging evidence to suggest activation of the complement pathway may have a role in this process. The aim of this study is to better describe the role that complement activation may play in the establishment or perpetuation of synovial inflammation in early and advanced OA.

Methods Gene expression of complement regulatory proteins was determined in RNA extracted from the synovium of 14 early and 28 advanced stage OA patients using real-time PCR. Immunohistochemistry was used to assess the level of C3 and membrane attack complex (MAC) C5b-9 protein deposition as well as expression of the MAC inhibitor CD59 in early and advanced stage OA synovium. In order to investigate the effect of oxidative stress, OA fibroblast-like synoviocytes (FLS) were treated with H_2O_2 and subsequently exposed to normal human serum. CD59 expression was then assessed by fluorescent immunocytochemistry and the level of intact C3 in the supernatant determined by western blot.

Results The expression of properdin, a positive regulator of the alternative complement pathway, and CD59, an inhibitor of MAC formation, were significantly upregulated in early OA synovium compared with advanced stage OA synovium by 2.2-fold ($p=0.03$) and 2.1-fold ($p=0.02$), respectively. Evidence of C3 and C5b-9 deposition and CD59 protein expression was observed in both early and advanced stage OA, predominantly localised to the synovial membrane. Treatment of OA FLS with H_2O_2 led to decreased CD59 expression on the cell surface and a reduction in the amount of intact C3 present in the supernatant.

Conclusions Increased synovial expression of properdin mRNA and C3 and C5b-9 protein deposition suggests local activation of the alternative complement pathway in early OA. While increased CD59 gene expression at an early stage of disease may protect the tissue from associated damage, the authors hypothesise that complement activation in the setting of oxidative stress might contribute to impaired expression of complement regulatory proteins and uncontrolled inflammation, resulting in progression to chronic joint damage. Characterisation of the regulation of CD59 and other complement regulatory proteins in the OA synovial membrane may suggest novel approaches to interrupt OA progression and reduce joint damage.