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Potential role of the posterior cruciate ligament synovio-entheseal complex in joint effusion in early osteoarthritis: a magnetic resonance imaging and histological evaluation of cadaveric tissue and data from the Osteoarthritis Initiative

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SUMMARY

Objective: This study explored posterior cruciate ligament (PCL) synovio-entheseal complex (SEC) microanatomy to determine whether it may participate in the early osteoarthritis (OA) disease process.
Methods: SEC microanatomy and OA features were evaluated in 14 non-arthritic cadaveric knees (mean age = 69.9) using magnetic resonance imaging (MRI) and histology. MRI images of 49 subjects selected from the progression cohort of the Osteoarthritis Initiative (OAI) were evaluated by a musculoskeletal radiologist using an original semi-quantitative method for features associated with OA at the PCL tibial enthesis. Statistical analysis was performed using chi-square and Wilcoxon signed-rank tests to evaluate associations between SEC configuration and OA features.
Results: The PCL formed a SEC-like structure encompassing bone- and ligament-lining intra-articular cartilages to which the posterior root of the medial meniscus contributed. Degenerative features at the PCL-SEC included: neovascularisation (44%), enthesis chondrocyte clustering (44%), collagen matrix fissuring at the enthesis (56%) and in the PCL itself (67%), tidemark duplication (44%), bone remodelling (44%) and microscopic inflammatory changes (33%). In the OAI cohort, SEC-related pathology included bone marrow lesions (BMLs) (69%) and osteophytosis (94%) at locations that corresponded to SEC-related cartilages. Posterior joint recess effusion (49%) was linked to MRI abnormalities at PCL-SEC cartilages ($\chi 2 = 7.27$, $P = 0.007$).
Conclusions: The PCL has a prominent SEC configuration that is associated with microscopic OA changes in aged clinically non-diseased joints. MRI determined knee OA commonly exhibited pathological features at this site which was associated with adjacent joint effusion. Thus, the PCL-SEC could play a hitherto unappreciated role in the early OA disease process.

Introduction

The pathogenesis of joint inflammation in osteoarthritis (OA) has consistently been conceptualised in relationship to articular cartilage damage with secondary synovitis[1,2]. The importance of synovitis in OA is underscored by the fact that its presence is associated with both pain and more rapidly progressive joint destruction[3] as assessed by arthroscopy[4], magnetic resonance imaging (MRI)[5–9] and C-reactive protein measurement[10].

Synovitis and associated joint effusion in OA may have a localised distribution influenced by concomitant intra-articular pathology

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originating in adjacent structures such as the posterior horn of the medial meniscus[11]. To better explain the pathophysiological phenotypes of OA, we have used conventional and high resolution MRI and histological assessment of joints and have provided data relating to the importance of ligaments and tendons and their entheses as potential drivers in the pathogenesis of OA[12]. Combined high-resolution MRI and histological studies have previously demonstrated the involvement of ligaments and tendons in the early stages of hand OA[13,14]. Other groups have shown evidence of anterior cruciate ligament (ACL) degradation and observed evidence of early histological changes in the ligament at various stages of macroscopic cartilage damage[15].

It is now known that ligament attachments often form a complex anatomical functional unit involving the ligament itself as well as adjacent synovium and bony tuberosities[16]. It has also been noted that ligament and tendon insertions are not simply focal attachments that have fibrocartilage at the point of bony insertion, but the fibrocartilages extend into the immediately adjacent joint cavities to minimise stressing, forming structures termed synovioentheseal complexes (SECs)[1,17]. The SEC formed by the posterior cruciate ligament (PCL) at its tibial insertion includes the posterior horn of the medial meniscus which acts as a sesamoid fibrocartilage, and has been described briefly in the context of spondyloarthritis[16].

The PCL is a strong structure that rarely ruptures and is not considered to be an important factor in the pathogenesis of knee OA in comparison to the ACL[18]. Recently, the anatomical distribution of synovitis and joint effusion associated with knee OA has been reported as being more common adjacent to the PCL[19]. A possible role for the PCL-SEC as an unappreciated contributor or driver of joint inflammation in this location has not been studied and remains unknown. The purpose of this study was to explore the PCL-SEC in non-arthritic cadaveric tissue and on MRI in OA subjects to determine whether it could contribute to the pathophysiology of OA. Here we use 3T MRI and correlative histology to show the involvement of the PCL-SEC in the early OA disease process.

Methods

Combined high-resolution MRI and histopathology of cadaveric tissue

Whole human knee joints were obtained from the Leeds GIFT Tissue Bank for the purpose of obtaining high-resolution MRI images of the tibial insertion of the PCL and comparative histopathology. The study was approved by the Local Research Ethics Committee and all donors had given their informed consent. Samples were collected from donors none of whom had an antemortem history of knee arthritis. A macroscopic assessment of tibial and femoral cartilage surfaces was made during dissection and no evidence of severe chondropathy was observed in any samples. For the purpose of the current study it is important to clarify what this might mean for disease pathogenesis. In this study our cadaveric specimens were taken from patients with no documented history of OA, but we did not obtain specimens from any young donors. Our specimens are therefore representative of normal, mature adults prior to clinical presentation, i.e., groups 1 and 2 depicted in Fig. 1.

21 knees were examined in total, from 18 donors (8 male, 10 female, mean age = 70.2 years). Whole joint MRI was performed on 14 cadaveric knees (6 male, 8 female, mean age = 69.9). Histopathologic analysis was performed on nine specimens (4 male, 5 female, mean age = 65.2), including two samples which had also undergone the whole joint MRI protocol. In summary, 12 samples underwent MRI analysis alone, seven samples underwent histological analysis alone and two samples underwent both histological and MRI analysis (Fig. 2). MRI images were acquired using a 3.0 T Siemens Verio system. The examination protocol implemented was based on that of the National Institute for Health (NIH) Osteoarthritis Initiative (OAI) MRI procedure for knee examination[20], and has been reported previously[21]. Coronal intermediate-weighted (IW), 2-D turbo spin-echo (TSE) without fat-saturation, TR = 3700 ms, TE = 29 ms, FOV = 140 mm, matrix = 310 × 384; sagittal IW 2-D TSE with fat-saturation (FS), TR = 3200 ms, TE = 30 ms, FOV = 160 mm, matrix = 314 × 448; coronal T1-weighted, 3-D fast low-angle shot (FLASH) with water excitation, TR = 20 ms, TE = 7.57 ms, FOV = 160 mm, matrix = 512 × 512; sagittal 3-D dual-echo in steady state (DESS) with water excitation, TR = 16.3 ms, TE = 4.7 ms, FOV = 140 mm, matrix = 307 × 384 and; sagittal 2-D multi-echo spin-echo (MESE), TR = 2700 ms, TE = 10, 20,30,40, 50, 60, 70 ms, FOV = 120 mm, matrix = 269 × 384 sequences were performed. Coronal IW 2-D TSE (TR = 3850 ms, TE = 28 ms, FOV = 100 mm, matrix = 384 × 384, 8 signal averages) and sagittal IW 2-D TSE FS (TR = 3200 ms, TE = 36 ms, FOV = 160 mm, matrix = 512 × 512, 8 signal averages) were also performed with increased resolution.

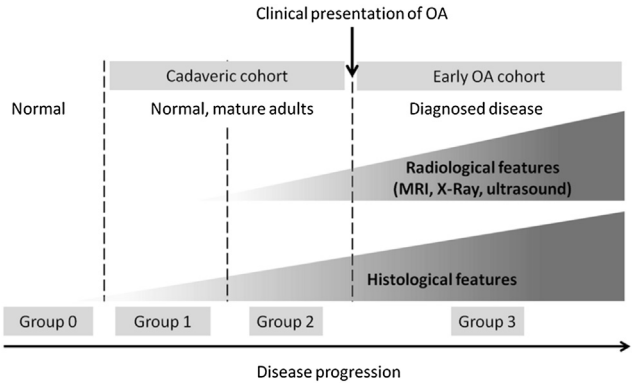

Fig. 1. Categorisation of study cohorts with respect to clinical presentation of OA, radiological and histological features of disease. The cadaveric cohort in this study consists of samples taken from non-arthritic donors but in which some age related pre-clinical histological and radiological features were present (group 1 and group 2). Completely normal tissue is defined as that which lacks both histological and radiological features of disease (group 0) of which none were included in this study. The OAI cohort had clinically defined OA and is representative of group 3. This study focused on groups 1 and 2 (preclinical disease) and group 3 (clinically demonstrable disease). Accordingly there may be some overlap between these groups. Adapted from Binks *et al.* Ann Rheum Dis Published Online First: 4 October 2013 http://dx.doi.org/10.1136/annrheumdis-2013-203972.

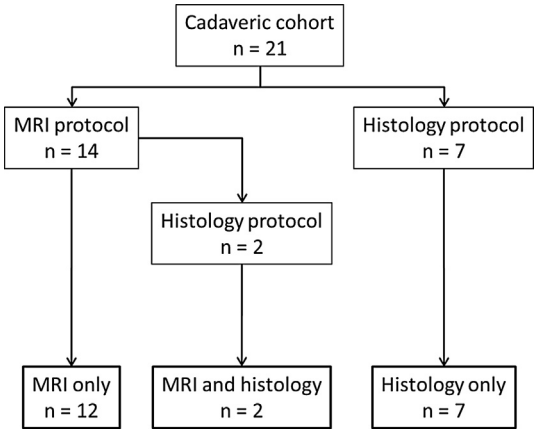

Fig. 2. Flow diagram showing the protocols performed on the 21 knee joints comprising the cadaveric cohort.