IP58. WHAT IS OSTEARTHROIS? NOVEL CONCEPTS
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Much research has been performed over the last few decades into the aetiology and treatment of osteoarthritis. The vast majority of this research has used structural change on imaging or histology to define the disease. The main concern of patients however, is of pain and reduced function and substantially less research has been performed using these outcomes. Although there is a statistically significant association between structural change and symptoms, there is a major discrepancy between structural change on x-ray and joint pain; with up to 50% of subjects with radiographic OA not reporting regular symptoms. It was hoped that MRI imaging, by visualizing cartilage directly in addition to peri-articular soft tissues would reduce this discordancy, unfortunately this has not proved to be the case.

How should we move forward? We should take a lead from the field of osteoporosis, which experienced similar issues with BMD and fracture. They have abandoned a structure based diagnosis of osteoporosis using bone density and moved to assessing a patient’s absolute risk of fracture using all known risk factors, of which bone density and moved to assessing a patient's risk of osteoporosis, which experienced similar issues with BMD and differentiates of follicular dendritic cells (FDC) networks. Evidence in patients with and animal models of SS demonstrated that the formation and maintenance of ELS in the SG is critically dependent on the ectopic expression of lymphotaxis (LT) and lymphoid chemokines CXCL13, CCL19, CCL21 and CXCL12. Together with inflammatory infiltrates in the exocrine glands, the other hallmark of SS is the presence of an antigen-driven activation and proliferation of B lymphocytes. In SS, this process leads to the production of SS-associated autoantibodies such as RF, anti-Ro/SSA and anti-La/SSB that can be detected in the serum of most SS patients. In addition, autoantibodies such as anti-muscarinic M3 receptor have been demonstrated to mediate glandular dysfunction by blocking parasympathetic stimulation of epithelial cells. A critical question which arises is whether the development of immune cell infiltrates in the glands and the activation of autoreactive B cells are closely associated events and which are the cellular and molecular mechanisms underlying these processes. Recent data from our and other groups support the conclusion that ELS in SS represent functional niches whereby autoreactive B cells undergo affinity maturation, clonal selection and differentiation into autoantibody producing cells, contributing to autoimmunity over and above secondary lymphoid organs. In addition, recent evidence suggested that higher levels of immunological organization and B cell function within ELS in the SG can identify subsets of SS patients with more severe clinical phenotypes and increased risk of evolution towards B cell lymphoma. Thus, it is increasingly clear that the investigation of the cellular and molecular mechanisms leading to B cell activation in the SG of SS patients can allow us to identify biomarkers of disease evolution and will provide guidance for the use of novel biological therapies targeting B cell-related pathways.

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has demonstrated much more abundant pathology than we previously considered. Importantly, synovitis is found extremely commonly, with detection reflecting the sensitivity of the imaging tool employed. Poor detection by clinical examination has made us think inflammation is uncommon in OA, though subclinical synovitis in RA is now a widely accepted concept. Although generally less in volume and vascularity than in RA, this imaging-detected synovitis has been associated with the pain of OA, and also with (independently) progression to knee joint replacement.

This imaging data reflects older data on synovitis in OA, with biopsy studies demonstrating synovitis is present from the earliest chondral changes. In terms of cellular make up, there is cellular infiltration with macrophages, activated T and B cells and vascular proliferation. Though cytokine levels are often less than in RA, they are still elevated compared with normals, with a similar pattern to RA.

It is noteworthy that of our current pharmacological agents, the 2 with the most consistent modest effect sizes are NSAIDs and intra-articular corticosteroids - both of which have significant anti-inflammatory or anti-synovitis actions.

Why then not consider the use of RA DMARDs as anti-synovial agents in OA, not primarily to achieve structure modification, but to provide new symptomatic therapies? Anecdotally clinicians have used these agents for years in what they considered inflammatory OA. There are small studies, often with poor design, using either hydroxychloroquine or methotrexate in hand and knee OA. Data are now emerging from recent trials on the use of traditional anti-inflammatory RA therapies as analgesics in OA.

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