Spondyloarthropathies: Current Insights

Written by Maria Vinall

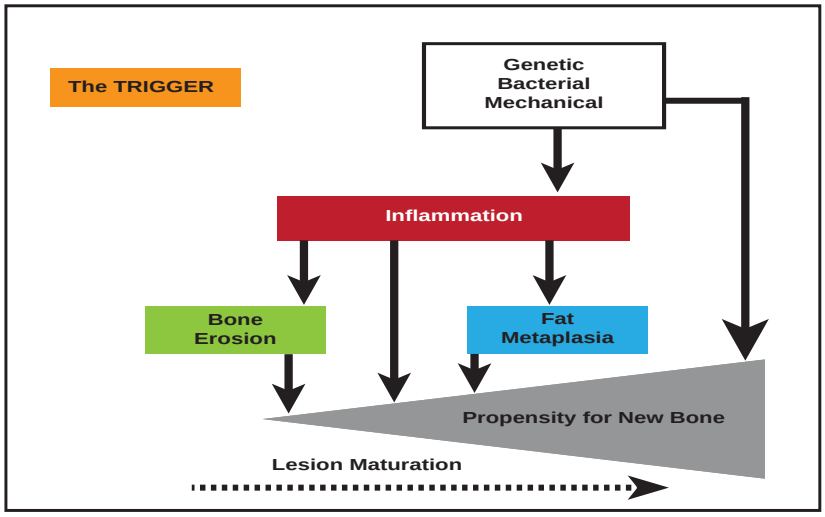
TNF Inhibition and Structural Damage Progression in Ankylosing Spondylitis

Walter P. Maksymowych, MD, University of Alberta, Edmonton, Alberta, Canada, discussed the relationship between anti-TNF agents, inflammation, and lesions that demonstrate fat metaplasia in the structural progression of ankylosing spondylitis (AS).

Anti-TNF agents safely and effectively treat signs and symptoms of AS and improve health-related quality of life [Davis JC et al. *Arthritis Rheum* 2005; Lambert RG et al. *Arthritis Rheum* 2007]. Nonetheless, structural progression in AS has not been shown to be impacted by anti-TNF agents, despite the role of TNF-induced inflammation in the disease [van der Heijde D et al. *Arthritis Rheum* 2008]. This question has not been fully answered because of limitations in study design.

Questions persist over which MRI lesions predict the progression of AS. There is evidence that inflammatory lesions predict new bone formation, although the majority of new syndesmophytes develop at sites without active inflammation [Maksymowych et al. *Arthritis Rheum* 2009]. It has now been shown that inflammatory lesions that resolve undergo fat metaplasia and that this is associated with new bone formation. Fat metaplasia, therefore, appears to be an important intermediary in the pathway from inflammation to new bone (Figure 1) [*Ann Rheum Dis* 2011].

Figure 1. Pathogenesis of New Bone is Ankylosing Spondylitis.



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PsA: Is Methotrexate a Disease-Modifying Agent?

Methotrexate (MTX) is often used as the primary treatment for psoriatic arthritis (PsA). However, there are limited data to demonstrate its clinical benefit, especially for axial disease [Gottlieb A et al. *J Am Acad Dermatol* 2008; Ritchlin CT et al. *Ann Rheum Dis* 2009; Gossec L et al. *Ann Rheum Dis* 2011]. Gabrielle H. Kingsley, MB, PhD, FRCP, Kings College, London, United Kingdom, discussed the role of MTX in the treatment of PsA, with a focus

on whether MTX can be considered a disease-modifying antirheumatic drug (DMARD).

According to Prof. Kingsley, the aim of DMARD therapy is to improve long-term outcomes, not just symptoms. However, definitive demonstration of DMARD efficacy is difficult to confirm outside of placebo-controlled, randomized, controlled trials.

The MTX in Psoriatic Arthritis (MIPA) Trial [Kingsley et al. *Rheumatology*. In Press 2011] was a 6-month RCT that compared MTX with placebo to test the hypothesis that the drug improves disease activity and function in PsA. Key findings from the study indicate that MTX improves self-reported symptoms but has no effect on objective joint counts or acute phase reactants, which classifies it as a "symptom-modifying agent" rather than a DMARD. Prof. Kingsley recommends a reconsideration of current guidelines, based on new data [Baranauskaite A et al. *Ann Rheum Dis* 2011; Lie E et al. *Ann Rheum Dis* 2009; Kingsley GH et al. *Rheumatology*. In press 2011].

Reactive Arthritis: Clinical Insights and Treatment Options

Reactive arthritis (ReA) occurs 1 to 6 weeks after exposure to a causative organism, either postdysentery or postvenereal. John D. Carter, MD, University of South Florida, Tampa, Florida, USA, discussed the epidemiology of ReA and the pathophysiology, treatments, and outcomes of *Chlamydia trachomatis*-induced ReA (CiReA) [Carter JD et al. *Arthritis Rheum* 2009].

In the United States, the incidence of ReA is underestimated and underdiagnosed. Dr. Carter concluded that *Chlamydia* might be a common cause of undifferentiated spondyloarthropathies; that ocular serovars appear to be uniquely capable of causing ReA [Gerard HC et al. *Microb Pathog* 2010]; that ReA is a Th2-predominant disease; and that combination antibiotics show promise in the amelioration of CiReA symptoms and the elimination of the persistent state of *Chlamydia*.

Pain, the Brain, and Osteoarthritis

Written by Maria Vinall

Data that were presented by Apkar Vania Apkarian, PhD, Northwestern University, Chicago, Illinois, USA, appear to demonstrate that chronic pain imparts a specific signature on the brain that is associated with functional, behavioral, and chemical changes in the cerebral cortex. The specificity of this pain signature for different clinical conditions may provide the opportunity to develop targeted therapies for osteoarthritis and other chronic painful conditions.

Dr. Apkarian reviewed a study that was conducted at Northwestern University in which painful pressure stimuli were applied to the knee of osteoarthritis (OA) patients and healthy controls and ratings of evoked pain and related brain activity were subsequently examined. In this study, the psychophysical pressure pain ratings and brain activation patterns of evoked pain were essentially the same between OA patients and healthy subjects and between knees with better and worse OA. In addition, the location of brain activity for evoked pain did not overlap the areas that were associated with continuous pain. However, brain activity that was related to pain scoring systems, such as the Western Ontario and McMaster Universities Osteoarthritis Index and the McGill Pain Questionnaire, mainly overlapped areas that were identified for chronic pain [Parks EL et al. *Eur J Pain* 2011].

Regional gray matter density studies indicate decreases in grey matter in specific regions of brain that are associated with chronic OA pain. There was also evidence for reversibility, whereby treatment may potentially undo grey matter decreases. In a recent, yet-to-be published study, Dr. Apkarian's group also examined brain anatomical changes in healthy patients compared with those who have chronic back pain, complex regional pain syndrome, or OA. Using Voxel-wise Voxel-based morphometry, the group examined how the brain reorganizes regionally in response to pain. They identified unique morphological signatures that are associated with the different types of chronic pain. Areas of brain interaction increased in chronic pain subjects, destroying spatial relationships. This was not apparent in healthy subjects. Whether pain was chronic versus acute determined the amount of time the brain required to reorganize into its new anatomical state.

Specificity of this signature for each clinical condition provides the opportunity to develop targeted therapies. In a double-blind, placebo-controlled brain imaging study in which chronic back pain subjects were treated with a 5% lidocaine patch or placebo, no difference in pain perception or brain activity was noted between the two groups at 2 weeks. However, when the subjects were regrouped into persisting pain (nonresponders) and decreasing pain (responders), it was possible to identify at baseline two functional connections in the brain that distinguish between persisting and decreasing chronic