

Ankylosing spondylitis: a multidisciplinary approach

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Can we stop progression of ankylosing spondylitis?

Ankylosing spondylitis (AS) is characterized by inflammation of the spine and the entheses, followed by bone formation. Excessive bone formation in AS leads to the formation of bone spurs, such as syndesmophytes and enthesiophytes, which contribute towards ankylosis of joints and poor physical function [1].

Whether and how spondylitis and syndesmophyte formation are linked are unclear.

Tumour necrosis factor (TNF) is a key proinflammatory cytokine in AS, but is a potent inhibitor of bone formation, and so is unlikely to explain the formation of osteophytes in AS. This is also suggested by recent clinical data showing that TNF-blockade seems not to affect structural remodelling of the spinal skeleton in AS. Thus, molecular concepts of structural remodelling in AS need revision, and new pathways involved in bone formation need to be defined [2,3].

Molecular and cellular biology of new bone formation: insights into the ankylosis of ankylosing spondylitis

One of the most distinctive features of the spondyloarthropathies is the tendency for new bone formation at sites of chronic inflammation. This is important diagnostically because radiographic evidence of ankylosis is often stated as one of the classification criteria, and it is important clinically because loss of spinal mobility over time is a major contributor to disability in this disease. The mechanisms underlying this tendency for ankylosis have not yet been defined.

This process is based on increased differentiation of osteoblasts from their mesenchymal precursors, which allows to rapidly build up new bone. Prostaglandins, bone morphogenic proteins and Wnt proteins play an essential role in this process.

Wnt proteins have recently been identified as contributing to new bone formation in inflammatory arthritis. Therefore, fostering of the Wnt signalling pathway by blocking its natural inhibitor dickkopf-1 (Dkk1) leads

to the excessive growth of peripheral osteophytes as well as fusion of the sacroiliac joints. These observations suggested that Wnt signalling is of key importance in osteophyte formation and that Wnt activity may represent a biomarker for ankylosis. In support of this concept, low serum levels of the Wnt inhibitor sclerostin are predictive of progressive syndesmophyte formation in AS patients. Moreover, high serum levels of sclerostin as well as Dkk1 are linked to erosive bone diseases, such as rheumatoid arthritis (RA) or multiple myeloma [4].

Osteoporosis: a paradox in ankylosing spondylitis

AS is a chronic and severe inflammatory disease of the axial skeleton and the joints. Inflammation is associated with trabecular bone loss leading to osteoporosis but also with cortical new bone formation leading to progressive ankylosis of the spine and sacroiliac joints. This results in an apparent paradox of bone formation and loss taking place at sites located close to each other. Osteoporosis can be explained by the impact of inflammation of the bone remodelling cycle. In contrast, new bone formation has been linked to aberrant activation of bone morphogenic protein and Wnt signalling [5].

Treatment of ankylosing spondylitis and other spondyloarthritides

The management of AS and other spondyloarthritides such as psoriatic arthritis (PsA) is becoming increasingly more complex because of major advances, especially in the pharmacological therapy of these diseases. Biologics such as anti-TNF agents have the potential to improve almost all outcome parameters assessed usually.

There is increasing knowledge about the short-term and long-term efficacy of anti-TNF agents. As it stands now, radiographic progression of AS patients is not decelerated, in contrast to PsA. One major difference between the two spondyloarthritides is that AS is more an osteoproliferative disease, whereas PsA is more osteodestructive (although it certainly has both elements). Methotrexate offers no additional benefit for the axial symptoms in AS [6].

Thus, prevention of bony overgrowth can be considered as a therapeutic goal in the treatment of AS. Rapid and effective control of inflammation appears to be the best preventive strategy to protect from bony overgrowth and also, specific drug therapy that selectively targets the anabolic pathways involved in bony spur formation may be useful. However, targets allowing dissecting physiological bone formation from bony spur formation remain to be identified [1].

A systematic comparison of rheumatoid arthritis and ankylosing spondylitis: structural outcomes

Both RA and AS are chronic diseases with inflammation as a hallmark. Both diseases are characterized by structural abnormalities of the peripheral joints (RA) or the spine (AS) that can be visualized on conventional radiographs. RA is associated with destruction (erosions, joint space narrowing) whereas AS is dominated by bone formation (syndesmophytes). The causative relationship between inflammation and structural damage in RA is well established, whereas this relation is largely unknown but certainly less strong in AS. Progression of structural damage in RA is inhibited by disease-modifying anti-rheumatic drugs and especially by TNF-blockade, whereas progression of structural damage in AS seems to be insensitive to TNF-blockade, but sensitive to nonsteroidal inflammatory drugs [7].

Coexistence of ankylosing spondylitis and rheumatoid arthritis in a female patient

AS and RA are two distinguished representatives of inflammatory rheumatic diseases. The two diseases differ

significantly in their aetiology, pathology, clinical signs and the nature of articular manifestations. Their association has been a rarity in the literature. Here, the authors describe a case of a 55-year-old female patient with AS associated with RA. Her spinal symptoms started in 1979, and the diagnosis of AS was established on the basis of the typical clinical picture and radiograph. She developed severe spinal deformity during the next decades. In 2005, peripheral polyarthritis developed, although neither the diagnosis nor the treatment was modified. In 2007, authors diagnosed seropositive RA. Therapy included anti-inflammatory therapy and traditional disease-modifying agents, eventually followed by biological therapy [8].

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Conflicts of interest

There are no conflicts of interest.

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