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Infliximab in Ankylosing Spondylitis

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Ankylosing spondylitis is the most frequent subtype of spondyloarthropathy, a disease characterised by axial inflammation, asymmetrical peripheral synovitis and enthesitis and genetic linkage with human leukocyte antigen B27. Bacterial triggering and gut inflammation are pathophysiologically important, as illustrated by reactive arthritis and the overlap with inflammatory bowel disease. Accordingly, the first observations with infliximab in spondyloarthropathy were done in four patients with Crohn's disease-associated spondyloarthropathy who experienced a major improvement of gut as well as peripheral joint and axial symptoms.

Whereas several placebo-controlled trials have demonstrated the efficacy of infliximab treatment for ankylosing spondylitis, focusing essentially on axial disease, similar efficacy has been demonstrated for other spondyloarthropathy subtypes. As for ankylosing spondylitis, there was a rapid and major improvement of global disease activity and inflammatory parameters compared to placebo. Response to treatment was similar in the different subgroups and was maintained for up to 5 years. The effect on signs and symptoms was not restricted to the axial disease, but extended to peripheral joint disease, enthesitis and uveitis. For peripheral joint disease, the clinical efficacy was confirmed at the histopathological level and was associated with structural remodelling.

Although tumour necrosis factor (TNF)-α blockade is a major breakthrough in the treatment of severe ankylosing spondylitis and spondyloarthropathy, caution remains warranted with regard to potential side effects. Severe infectious episodes, including disseminated tuberculosis, have been reported and may be related to the downregulation of the Toll-like receptors by infliximab treatment. This may be even be more relevant in daily practice than in study populations. As in rheumatoid arthritis, infliximab treatment also leads to a major induction of anti-nuclear antibodies and double-stranded DNA (dsDNA) autoantibodies in spondyloarthropathy. However, the dsDNA antibodies were almost exclusively of the non-pathogenic IgM subtype, were not associated with other lupus-related autoantibodies, disappeared upon interruption of therapy, and did not lead to lupus-like syndromes over a period of 2 years.

Further insights into the mechanisms of TNFα blockade will help us to fully appreciate the clinical short- and long-term effects and the optimal benefit : risk ratio for infliximab treatment in ankylosing spondylitis and spondyloarthropathy. ▲