PREFACE

New treatment strategies in ankylosing spondylitis: Proceedings of the Ankylosing Spondylitis Workshop, Berlin, Germany, 18–19 January 2002

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This *Annals of the Rheumatic Diseases* supplement is the official Proceedings of the Ankylosing Spondylitis Workshop held in Berlin, Germany earlier this year. The workshop was a remarkable assembly of international experts on ankylosing spondylitis (AS) and the other spondyloarthropathies, organised to discuss numerous aspects of diagnosis, clinical management, and treatment of the disease. The supplement consolidates information from 26 formal presentations given by the workshop participants.

AS is a complex disease in which several years typically elapse before radiological signs permit a definite diagnosis. Thus, diagnosis is often made only after significant structural damage has occurred. Patients with severe AS can face a lifetime of pain, disability, spinal deformity, reduced functioning, and subsequently, lower quality of life. At present, treatment is aimed at relieving symptoms and improving function, but no currently approved treatment alters the natural course of the disease.

Although AS is the prototypical spondyloarthropathy (SpA), the latter term also refers to reactive arthritis, arthritis/spondylitis in inflammatory bowel disease, psoriatic arthritis/spondylitis, and undifferentiated SpA (uSpA). These diseases share the same pattern of peripheral and axial joint involvement, certain extra-articular manifestations such as anterior uveitis, association with human leucocyte antigen (HLA)-B27, and an overlapping aetiology and symptomatology. The search for an effective treatment for the SpAs has been neglected until recently. Presently, there are no disease modifying treatments available, similar to the situation that existed with rheumatoid arthritis two generations ago. Current opinion holds that only non-steroidal anti-inflammatory drugs (NSAIDs) are effective as chronic SpA treatment, but NSAIDs have symptomatic rather than disease modifying effects. One of the objectives of the AS workshop, as well as this supplement, was and is to create a foundation of understanding so that the current limited treatment options might be expanded. Indeed, there are compelling reasons for finding a true disease modifying SpA treatment.

FREQUENT DISEASE INCIDENCE

Epidemiological data indicate that the SpAs occur at least as frequently as rheumatoid arthritis. Depending on the HLA-B27 prevalence in a selected population, studies indicate the SpA incidence to be between 0.5% and 1.9%. Defined as a subgroup, uSpA has been and can be regarded in many cases as an early form of AS. AS and uSpA appear to be the most commonly diagnosed SpAs, with an incidence of about 1%. In demographic terms, for example, approximately 800 000 people in Germany, 3 million in the European Community, and 2.4 million in the United States would be affected with the two most relevant SpA subgroups.

EARLIER DIAGNOSIS

Refinement of SpA classification criteria to include uSpA, and the emergence of new imaging techniques such as magnetic resonance imaging (MRI), allow earlier and more accurate diagnosis. Pre-emptive disease modifying treatment in early stage SpA may preclude development of advanced disease and functional impairment.

DISEASE OCCURRENCE EARLY IN LIFE

Initial SpA symptoms typically occur between 20 and 30 years of age. Although incidence favours men by a factor of two to three, both sexes are affected. Juvenile onset (that is, at 16 years of age or younger) is also known to occur, particularly if environmental triggers are present. Thus, patients are potentially affected throughout the most productive periods of life.

POTENTIAL FOR SEVERE DISABILITY

The SpAs are sometimes considered to be benign diseases with a high probability for a favourable outcome. However, recent studies indicate that patients with severe AS are at least as disabled as age matched patients with RA. Early treatment that prevents disability can greatly reduce the disease associated costs and adverse effects on quality of life.

LIMITATIONS OF CONVENTIONAL NSAIDs, POTENTIAL FOR COX-2 SELECTIVE NSAIDs

NSAIDs are the only universally accepted SpA treatment, but their gastrototoxic and other side effects, as well as their therapeutic limitations, are well known. NSAIDs that are cyclooxygenase-2 (COX-2) selective have potentially fewer gastrointestinal side effects. The recently approved COX-2 selective NSAIDs need to be assessed to determine their value in the treatment of SpA.

POTENTIAL OF IMMUNOSUPPRESSIVE AND IMMUNOMODULATING THERAPIES

Although AS and the other SpAs are immune mediated diseases, disease modifying antirheumatic drugs (DMARDs) with immunosuppressive or immunomodulating effect have yet to be proved effective for treatment of SpA. DMARDs such as methotrexate, parenteral gold, azathioprine, and cyclosporin A have proved effective in treating RA but need to be evaluated using appropriate assessment methods in placebo controlled trials involving patients with SpA. However, clinical

Abbreviations: AS, ankylosing spondylitis; COX, cyclo-oxygenase; DMARDs, disease modifying antirheumatic drugs; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; SpA, spondyloarthropathy; TNF α , tumour necrosis factor α ; uSpA, undifferentiated spondyloarthropathy

experience suggests that these drugs are of limited efficacy. The strong association of SpAs with HLA-B27, a principal function of which is T cell activation, and the presence of activated T cells in biopsy specimens from SpA affected tissues, suggest that immunocompetent cells are an appropriate therapeutic target. Favourable response to experimental anti-tumour necrosis factor α (TNF α) therapy supports this treatment approach.

POTENTIAL OF ANTI-TNF α THERAPY

Recent but limited investigational use of the anti-TNF α agents infliximab and etanercept in patients with AS, uSpA, and psoriatic arthritis has produced encouraging and, in some cases dramatic, responses. Results of anti-TNF α therapy appear to be at least equivalent to the results seen when used in treating RA, suggesting that disease modification in cases of SpA is possible.

IMPROVED METHODS OF ASSESSING TREATMENT OUTCOME

Outcome criteria, such as those developed by the Assessment in Ankylosing Spondylitis (ASAS) Working Group, have been successfully applied in evaluating response to AS treatment. MRI has proved to be a highly sensitive method for detecting gradations of sacroiliac and spinal inflammation. These advances provide the assessment tools needed for the conduct of meaningful clinical trials.

The factors mentioned above have created a new urgency for information exchange and for continued investigation of those treatments that have proved effective in treating RA or other chronic immune mediated diseases and can now be evaluated for the treatment of SpAs. Perhaps most significantly, biological agents that target key features of the inflammatory pathway should be evaluated as SpA treatments.

Infliximab, a monoclonal anti-TNF α antibody, and etanercept, a soluble TNF α receptor fusion protein, are currently available for the treatment of RA. Infliximab is also available for the treatment of Crohn's disease, and etanercept for psoriatic arthritis, conditions frequently associated with AS. TNF α also appears to have a central role in the pathogenesis of AS, suggesting a role for anti-TNF α therapy in treating this disease. Thus, based on their mechanism of action, anti-TNF α therapies have the potential to deliver a twofold clinical benefit: symptom control and prevention of disease progression.

The articles in this supplement summarise the presentations given at the Ankylosing Spondylitis Workshop and provide insights into the principal aspects of diagnosing, managing, and treating AS. Some topics that were discussed only briefly at the workshop, such as treatment of juvenile spondyloarthropathies, are presented here in more detail. Thus, the supplement is a comprehensive document intended to provide a better and more complete understanding of the current situation in AS, including the limited treatment options of the past and the beginning of an exciting era of new treatments. We hope that the workshop and this supplement will contribute to a more rapid and dramatic change in our ability to modify or even arrest the normally progressive course of this important chronic rheumatic disease.

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