Ankylosing Spondylitis: A Dual Perspective of Current Issues and Challenges

MUHAMMAD ASIM KHAN

ABSTRACT. This series of articles on ankylosing spondylitis (AS) provides insight into the burden of disease and focuses on early diagnosis and effective management. AS leads to progressive functional impairment over time and has tremendous impact on society at large in terms of economic costs and indirect costs associated with physical impairment and loss of employment. Early diagnosis is crucial now that we have more effective therapy with tumor necrosis factor (TNF) antagonists, which suppress disease activity and improve the functional ability of patients whose disease is refractory to conventional drug therapy. Early identification of variables that help predict severe disease with bad functional prognosis is needed. If biological therapy with TNF inhibitors is proven to retard disease progression and prevent or delay functional limitations, insight into such prognosticators will help us offer the correct treatment to the correct patient at the correct time. There is also a need to demonstrate longterm benefits of such a therapy as well as a favorable cost/benefit ratio to help convince healthcare authorities, insurance companies, and others of the utility of these drugs for treating patients with AS refractory to conventional drug therapy. (J Rheumatol 2006;33 Suppl 78:1-3)

> Key Indexing Terms: ANKYLOSING SPONDYLITIS

DIAGNOSIS

TREATMENT

This series of articles on ankylosing spondylitis (AS) provides insight into the burden of disease and focuses on early diagnosis and effective management. AS is a chronic systemic inflammatory rheumatic disorder of uncertain etiology with a predilection for the axial skeleton^{1,2}, which can lead to progressive bony fusion of the vertebral column; some patients may also show involvement of the hip and/or shoulder, and less often, peripheral joints. Extraarticular structures may also be affected such as the eyes, heart, and lungs¹⁻⁵.

This article has been written from a dual perspective: I have been a patient with AS for the last 50 years; and AS has been the main focus of my academic pursuit as a rheumatologist^{1-3,6-19}. I do not mind sharing with the readers some of the many hurdles I have faced as a patient, in order to bring awareness to the medical community at large about some of the many challenges faced by patients with AS.

My disease was not diagnosed for 6 years, and I received many inappropriate treatments during that time,

From Division of Rheumatology, Case Western Reserve University, MetroHealth Medical Center, Cleveland, Ohio, USA.

Support for this supplement was provided by Amgen Inc. and Wyeth Research.

M.A. Khan, MD, MACP, FRCP.

Address reprint requests to Dr. M.A. Khan, Division of Rheumatology, Case Western Reserve University, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, OH 44109-1998. E-mail: mkhan@metrohealth.org

including prolonged bed rest and a year of antituberculosis therapy. I was even given a short course of honey by intravenous infusions that did not affect my disease, but I am sure it has left me ever so sweet.

Sadly, the delay in diagnosis I experienced is not atypical, and the situation has not much improved over the years¹⁷. Early diagnosis is very crucial now that we have much more effective therapy. Elsewhere in this series, my colleague Dr. Elyan and I discuss how one can diagnose AS early²⁰ and with reasonable confidence, even before radiographs confirm the presence of definite sacroiliitis^{13,16,18,19}.

Patients with AS experience progressive functional impairment over time, and many of them are unable to maintain the level of employment that they had prior to the onset of disease, as discussed in the article by Drs. Boonen and van der Linden²¹ also in this series. Patients with AS have lower vitality and quality of life as compared with the general population, and the illness has tremendous effect on society at large in terms of economic costs and the indirect costs associated with physical impairment and loss of employment²²⁻²⁵.

As a result of my disease, I have had bilateral total hip arthroplasties with a subsequent revision arthroplasty, recurrent episodes of acute anterior uveitis, and progressive limitation of spinal mobility and chest expansion. At one time, I fractured my cervical spine, and the fracture did not heal despite many months of neck immobilization by a halo with vest. This ultimately needed a surgical fusion and another 3 months of neck immobilization.

Khan: AS: Issues and challenges

My illness has resulted in a complete fusion of my whole spine, including the neck. I cannot even nod my head, and have to bend at my hip joints to give an impression of a nod. I have virtually no chest expansion. One can imagine what might happen to me if I were to fall or faint. In particular, if I were to have the misfortune of needing a cardiac resuscitation; the probability would be high that, inadvertently, my death would be hastened because of a possible neck fracture during intubation, or broken ribs during cardiac massage.

I have managed to continue to take care of my patients and also to follow my academic pursuits, although at times it has been an uphill task. But I can say that I have enjoyed every bit of my life, with all its hardships, hurdles, and dramatics. I am very grateful to modern medicine for keeping me going, and in some ways I should consider myself to be a "bionic man."

Exercise and nonsteroidal antiinflammatory drugs (NSAID) have been the mainstay of treatment of AS for more than 5 decades, but they are often ineffective and offer little hope in arresting the disease process or delaying the progression of the disease²⁶. As reviewed by Dr. Daniel Clegg in this series²⁷, the advent of biological therapy with tumor necrosis factor (TNF) antagonists etanercept and infliximab is currently revolutionizing management of this disease. These drugs have shown marked efficacy in suppressing disease activity and improving the functional ability of patients with disease refractory to conventional drug therapy with NSAID, although as yet, too little is known about their longterm effects.

A high percentage of patients with AS may qualify for treatment with TNF antagonists²⁸. Those with shorter disease duration treated with a biologic agent have a greater likelihood of achieving a significantly better clinical response to TNF antagonists than the ones with longer disease duration. This again emphasizes the need for early diagnosis²⁹. Input from patients and their selfhelp organizations^{30,31} should be sought in order to learn from the patients' perspectives: their definition of severe disease and their attitudes towards the different treatment options. Many patients with AS have left the medical system and rely on over-the-counter medication and nonpharmacologic interventions to alleviate their symptoms. Better education of healthcare providers and patients alike will help improve the early diagnosis and increase awareness of the new and much more effective therapeutic options.

Early identification is also needed of variables (prognosticators) that predict severe disease and a bad functional prognosis. If biological therapy with TNF inhibitors is proven to retard disease progression and prevent or delay functional limitations, insight into such prognosticators will help us offer the correct treatment to

the correct patient at the correct time. Moreover, longterm benefits of such a therapy need to be demonstrated, as well as a favorable cost/benefit ratio (A. Boonen, personal communication). Such evidence will help convince healthcare authorities, insurance companies, and others of the utility of these drugs for treating patients with AS refractory to conventional drug therapy.

REFERENCES

- Khan MA. Update on spondyloarthropathies. Ann Intern Med 2002;136:896-907.
- Khan MA. Ankylosing spondylitis: clinical features. In: Hochberg M, Silman A, Smolen J, Weinblatt M, Weinblatt M, editors. Rheumatology. London: Mosby; 2003:1161-81.
- Khan MA. Spondyloarthropathies. In: Hunder GG, editor. Atlas of rheumatology. Philadelphia: Current Medicine; 2005:151-80.
- Weisman MH, Reveille JD, van der Heijde D, editors. Ankylosing spondylitis and the spondyloarthropathies: a comparison to rheumatology. London: Mosby-Elsevier; 2006.
- Van Royen BJ, Dijkmans B, editors. Ankylosing spondylitis diagnosis and management. New York: Taylor and Francis; 2006.
- Khan MA. Ankylosing spondylitis and related spondyloarthropathies. In: Arnold DM, Lonstein JE, editors. Spine: state of the art reviews. Philadelphia: Hanley and Belfus, Inc.; 1990.
- Khan MA, editor. Spondyloarthropathies. Philadelphia: WB Saunders; 1992.
- Khan MA, Braun WE, Kushner I, Grecek DE, Muir WA, Steinberg AG. HLA B27 in ankylosing spondylitis: differences in frequency and relative risk in American Blacks and Caucasians. J Rheumatol 1977;4 Suppl 3:39-43.
- Khan MA, Khan MK. Diagnostic value of HLA-B27 testing and ankylosing spondylitis and Reiter's syndrome. Ann Intern Med 1982;96:70-6.
- Khan MA, Khan MK, Kushner I. Survival among patients with ankylosing spondylitis: a life-table analysis. J Rheumatol 1981;8:86-90.
- Khan MA, Kushner I, Braun WE. Comparison of clinical features in HLA-B27 positive and negative patients with ankylosing spondylitis. Arthritis Rheum 1977;20:909-12.
- 12. Khan MA, van der Linden SM. A wider spectrum of spondyloarthropathies. Semin Arthritis Rheum 1990;20:107-13.
- Khan MA, van der Linden SM, Kushner I, Valkenburg HA, Cats A. Spondylitic disease without radiologic evidence of sacroiliitis in relatives of HLA-B27 positive ankylosing spondylitis patients. Arthritis Rheum 1985;28:40-3.
- Khan MA. HLA-B27 and its subtypes in world populations. Curr Opin Rheumatol 1995;7:263-9.
- 15. Feltkamp TE, Khan MA, Lopez de Castro JA. The pathogenetic role of HLA-B27. Immunol Today 1996;17:5-7.
- Khan MA. Thoughts concerning the early diagnosis of ankylosing spondylitis and related diseases. Clin Exp Rheumatol 2002;20 Suppl 28:S6-10.
- Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatol Int 2003;23:61-6.
- Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria? Arthritis Rheum 2005;52:1000-8.
- Rudwaleit M, van der Heijde D, Khan MA, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004;63:535-43.

- Elyan M, Khan MA. Diagnosing ankylosing spondylitis. J Rheumatol 2006;33 Suppl 78:12-23.
- 21. Boonen A, van der Linden SM. The burden of ankylosing spondylitis. J Rheumatol 2006;33 Suppl 78:4-11.
- Davis JC, van der Heijde D, Dougados M, Woolley JM.
 Reductions in health-related quality of life in patients with
 ankylosing spondylitis and improvements with etanercept therapy.
 Arthritis Rheum 2005;53:494-501.
- Boonen A, van der Heijde D. Review of the costs of illness of ankylosing spondylitis and methodologic notes. Expert Rev Pharmacoeconomics Outcomes Res 2005;5:163-81.
- Boonen A, Chorus A, Miedema H, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. Ann Rheum Dis 2001;60:1033-9.
- 25. Boonen A, Chorus A, Miedema H, van der Heijde D, van der Tempel H, van der Linden S. Employment, work disability, and work days lost in patients with ankylosing spondylitis: a cross sectional study of Dutch patients. Ann Rheum Dis 2001;60:353-8.

- Dougados M, Dijkmans B, Khan M, Maksymowych W, van der Linden S, Brandt J. Conventional treatments for ankylosing spondylitis. Ann Rheum Dis 2002;61 Suppl 3:iii40-50.
- 27. Clegg DO. Treatment of ankylosing spondylitis. J Rheumatol 2006;33 Suppl 78:24-31.
- 28. Barkham N, Kong KO, Tennant A, et al. The unmet need for anti-tumour necrosis factor (anti-TNF) therapy in ankylosing spondylitis. Rheumatology Oxford 2005;44:1277-81.
- Rudwaleit M, Listing J, Brandt J, Braun J, Sieper J. Prediction of a major clinical response (BASDAI 50) to tumour necrosis factor alpha blockers in ankylosing spondylitis. Ann Rheum Dis 2004;63:665-70.
- Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups. Curr Opin Rheumatol 2000;12:239-47.
- Newman PA, Bruckel JC. Spondylitis Association of America: the member-directed, nonprofit health organization addressing the needs of ankylosing spondylitis patients. Rheum Dis Clin North Am 2003:29:561-74.

Khan: AS: Issues and Challenges