Ankylosing spondylitis

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Abstract
Ankylosing spondylitis (AS) is one of the diseases covered by the more general term "spondylarthropathy" which includes: reactive arthritis, psoriatic arthritis, inflammatory bowel disease (IBD) related arthritis, and some subtypes of juvenile chronic arthritis. In continental Europe, prevalence ranges from 0.2 to 1% of the whole population suggesting that this disease is far from being rare. However, it remains undiagnosed. The main symptoms are inflammatory spinal pain with subsequent limitation of spine mobility and chest expansion. Diagnosis is based both on the clinical signs, radiological signs (sacroiliitis) and presence of HLA-B27 antigen (genetic predisposition). Non steroidal anti-inflammatory drugs and physiotherapy represent the cornerstones of therapy. In case of refractory severe disease, anti-TNF (tumor necrosis factor) agents are very promising.

Keywords
Ankylosing spondylitis - spondylarthropathies - seronegative arthritis -B27 antigen

Disease name and synonyms

- Ankylosing spondylitis (AS)
- Axial involvement of spondylarthropathy
- Seronegative arthritis

Excluded diseases

This text focuses on the axial involvement in spondylarthropathy. However, it should be kept in mind that all the sub-groups related to spondylarthropathy (*i.e.* reactive arthritis, psoriatic arthritis, inflammatory bowel disease (IBD) related arthritis,etc.) are interrelated disorders. Therefore, it can be argued that the most appropriate way to describe a patient is not to refer to the subgroup (*e.g.* ankylosing spondylitis), but to the clinical presentation (*e.g.* axial involvement of spondylarthropathy). Apart from axial involvement, there may be other clinical signs: peripheral articular involvement, enthesiopathy, extra-articular features such as acute anterior uveitis.

Diagnostic criteria/definition
Most of the studies that focus on the axial involvement of spondylarthropathy refer to the modified New York criteria (1). Most of the studies taking the whole spectrum of spondylarthropathy into account refer to the European spondylarthropathy study group criteria (ESSG) (2).

ESSG (European Spondylarthropaty Study Group)
Diagnositic Criteria for Spondylarthropathy (Arthritis Rheum 1991:34:1218-1227)

Inflammatory spinal pain
OR
Synovitis (asymmetrical or predominantly in the lower limbs)
AND
one or more of the following:
- Positive family history
- Psoriasis
- Inflammatory bowel disease
- Alternate buttock pain
- Enthesopathy
- Sacroiliitis

Current researchers are now focused on the elaboration of diagnostic criteria allowing the recognition of the disease at an early stage (3).

Differential diagnosis
When sacroiliitis is not observed by X-rays, the main difficulty consists in excluding the diagnosis of fibromyalgia (4).

Prevalence
While AS is considered as a rare disease in North America, prevalence in Germany is thought to be close to 1% (5). Prevalence of spondylarthropathy in Brittany (France) is 0.49%; that is, very close to the one of rheumatoid arthritis, 0.64% (6).

Clinical description
The main symptoms reflecting the axial involvement include alternate buttock pain, inflammatory spinal pain and anterior chest wall pain. At an advanced stage of the disease, decreased spinal mobility can be found together with loss of physiological lumbar lordosis, dorsal kyphosis, reduced chest expansion.
The other symptoms frequently observed are:
Enthesopathy such as heel pain (40%),
Peripheral articular arthritis (20%),
Acute anterior uveitis (20-50%),
Endocarditis (less than 0.5%).
From a radiological point of view, apart from sacroiliitis which is very helpful for diagnosis at an advanced stage, ossification of the vertebral ligaments can be observed (syndesmophytes, squaring with then a spine with bamboo aspect). X-rays are usually normal at an early stage, in this case, MRI might be of interest. As far as peripheral articular involvement is concerned, persistent inflammation can result in chondrolysis and sub-chondral bone erosions.

Management and treatment
Management includes the following:
- information and education of the patient;
- physiotherapy including home exercises, group therapy, spa;
- symptomatic treatment: ankylosing spondylitis represents the "gold standard" indication for non-steroidal anti-inflammatory drugs (NSAID). Such treatment can control the disease in 60-80%, the disease can be controlled in 80% of the patients. In case of persistent active disease despite NSAID therapy, disease-modifying anti-rheumatic drugs (DMARD) have to be considered. The drugs proposed in rheumatoid arthritis (sulfasalazine, gold, methotrexate) are usually useful in case of peripheral articular involvement but hardly effective in case of axial involvement (6). Anti-tumor necrosis factor agents seem to be effective whatever the clinical presentation of the disease. ASAS (Assessment in Ankylosing Spondylitis) has proposed recommendations for the management of the patients in daily practice and clinical research (8), but also for conducting clinical trials in ankylosing Spondylitis (9) and for the initiation, and monitoring of anti-TNF (10).

Etiology
Etiology has not been well established yet. Research is carried out in two fields:
- genetics, with the role of B27 (the B27 transgenic rat model is therefore very useful in order to better understand the physiopathology of the disease);
- infections, with the potential role of the *Klebsiella* and *Shigella*.

Diagnostic methods
Diagnosis is based on a composite index including clinical symptoms, radiological signs and genetic background (1, 2, 3).

Genetic counseling
No particular prevention is required despite the relation between B27 antigen and spondylarthropathies. Besides probability of occurrence is very low in patients' children.

Antenatal diagnosis
It is not appropriate to perform any antenatal search for the presence of HLA B27 antigen.

Unresolved questions
- Etiology
- How to select the patients in whom disease might progress and, who are therefore, candidates for "aggressive" therapy.

References
1. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27: 361-368.
2. Dougados M, van der Linden S, Juhlin R, *et al.* The European Spondylarthropathy Study Group. Criteria for the classification of spondylarthropathy. Arthritis Rheum 1991;34: 1218-1227.
3. Rudwaleit M, van der Heijde D, Khan MA, *et al.* How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004;63:535-43.
4. Amor B, Dougados M, Listrat V, *et al.* Are classification criteria for spondylarthropathy international working group/Spondylitis association of America recommendations conducting clinical trials in ankylosing Spondylitis. Arthritis Rheum 2005;52:386-94
10. Braun J, Pham T, Sieper J, *et al.* International ASAS consensus statement for the use of anti-tumour necrosis factor agents in patients with ankylosingspondylitis. Ann Rheum Dis 2003;62:793-4.
useful as diagnostic criteria? Rev Rhum Engl Ed 1995;62:10-15.
5. Braun J, Bollow M, Remlinger G *et al.* Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. Arthritis Rheum 1998;41:58-67.
6. Saraux A, Guedes C, Allain J, *et al.* Prevalence of rheumatoid arthritis and spondylarthropathy in Brittany, France. Société de Rhumatologie de l'Ouest. J Rheumatol 1999;26:2622-2627.
7. Dougados M, Revel M, Khan MA. Spondylarthropathy treatment: progress in medical treatment, physical therapy and rehabilitation. Baillieres Clin Rheum 1998;12:717-736.
8. van der Heijde D, Bellamy D, Calin A *et* al. Preliminary core sets for endpoints in ankylosing spondylitis. Assessments in Ankylosing Spondylitis Working Group. J Rheumatol 1997; 24:2225-6.
9. van der Heijde D, Dougados M, Davis J, *et al.* Assessment in ankylosing Spondylitis