

A Review Article on Ankylosing Spondylitis

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Abstract: *Ankylosing spondylitis is a major form of arthritis that causes severe pain and inflammation of the spine. If not treated in earlier stages it can lead to the formation of Bamboo spine condition that includes complete fusion of the bones and accelerates the stiffness of the joints. The major contributors of the immune system that lead to ankylosing spondylitis includes cytokines and chemokines like TNF - alpha and interleukins along with human leukocyte antigen HLA - B27. This study gives an overall overview of ankylosing spondylitis as a chronic inflammatory disorder.*

Keywords: Ankylosing spondylitis, spine, arthritis, immune system, inflammation.

1. Introduction

Ankylosing Spondylitis is a type of arthritis where in the axile spine suffers through inflammation causing sever back pain. It belongs to the spondyloarthropathy category of rheumatic diseases.1Humanity has been plagued with ankylosing spondylitis (AS) since ancient Egypt. The traditional description of AS was created in the 1800s.2The illness is acknowledged as belonging to the class of rheumatic disorders known as spondyloarthropathy. Psoriatic arthritis, reactive arthritis, and arthritis linked to inflammatory bowel illness are a few of them. Joints that may be affected by ankylosing spondylitis include the shoulders, hips, and, less frequently, the knees. The sacroiliac joints are the main locations of inflammation in AS. Males seem to be more frequently impacted than females. Young adults are its main target demographic, and patients under 45 have a greater incidence of it. As the condition worsens, it may lead to complete fusion of the axial skeleton, which would impair spinal movement and bodily function. Patients who have not received proper treatment or who have not been recognized with the condition may acquire the distinctive "bamboo spine, " which is characterized by complete spinal fusion. That can cause postural defects in the individual.

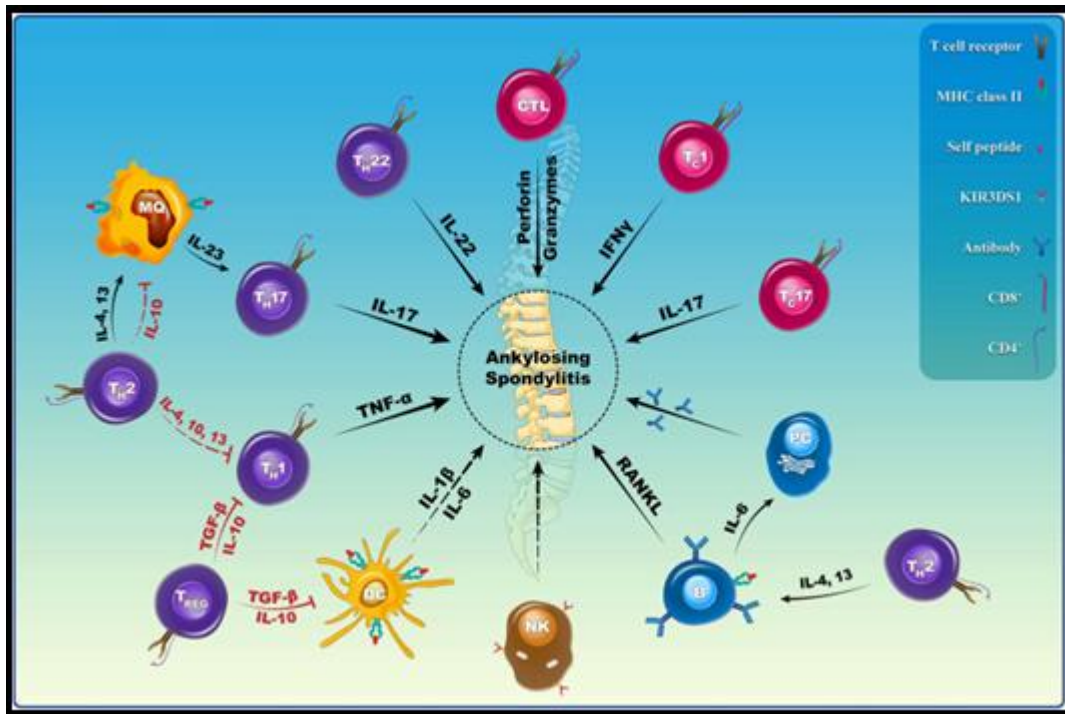
Pathophysiology

The main players of the immune system in Ankylosing Spondylitis (AS) are the HLA - B27human leukocyte

antigen.4Two subtypes HLA - B2706 and HLA - B2709, have been associated with AS.5Research on β 2 microglobulin (β 2m), a noncovalent component of the MHC - I complex, by using HLA - B27 - transgenic rats has demonstrated that increased β 2m decreases HLA - B27 misfolding and thus increases spondylitis and arthritis, indicating that B27 misfolding is linked to intestine inflammation. According to this finding, aberrant β 2m may work in tandem with HLA - B27 to promote AS development.

Immune cells involved

³Enthesitis is the main cause of spondyloarthropathies, such as AS. Immune cells including macrophages and CD4 and CD8 T lymphocytes are a part of this tenacious inflammation. The inflammatory process also involves cytokines, including transforming growth factor - β (TGF - β) and tumor necrosis factor - α (TNF - α).6Regulatory T cells (T - regs) are a subset of T cells that have a suppressive role. T - regs play an important housekeeping role in preserving the equilibrium and homeostasis between pro - and anti - inflammatory responses. Target effector T cells (T - effs) are suppressed by inhibiting IL - 2 expression, which is essential for T - reg cell proliferation thus, killing T - effs directly through apoptosis, or reducing T - eff activity by changing IL - 10 and growth factor (TGF) - β .



³Figure 1: Immune cells are involved in the initiation, evolution, and regulation of AS.

TNF signalling pathway in AS

⁸Three phases can be distinguished in the pathological processes that can result in the structural joint abnormalities associated with AS which are inflammation, bone erosion,

and new bone formation. TNF is a pro - inflammatory cytokine that may be connected to effect or pathways in each of the three phases, as shown in Fig 2.

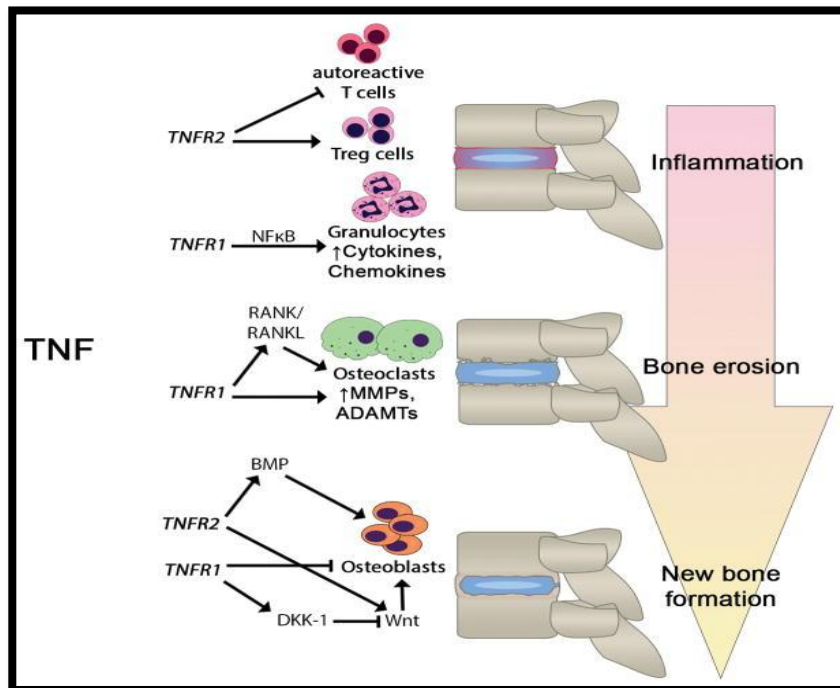


Figure 2: Role of TNF in Ankylosing spondylitis development

2. Diagnosis

Imaging

⁷The disease's major hallmark is sacroiliitis as seen in Fig 4. Traditionally, the lower third of the sacroiliac joints experience changes. The joint may appear blurry and indistinct at first, then develop sclerosis, bony erosions, and

an apparent widening of the joint. Long - term disease untreated may result in complete fusion of the bones. Changes in spinal radiography include squaring of the vertebral bodies, marginal erosions of the vertebral bodies, and the development of bony bridges, or syndesmophytes, between neighbouring vertebrae. Nearly total fusion of the vertebral column may happen in cases of severe, protracted disease, known as a Bamboo Spine as seen in Fig 3.

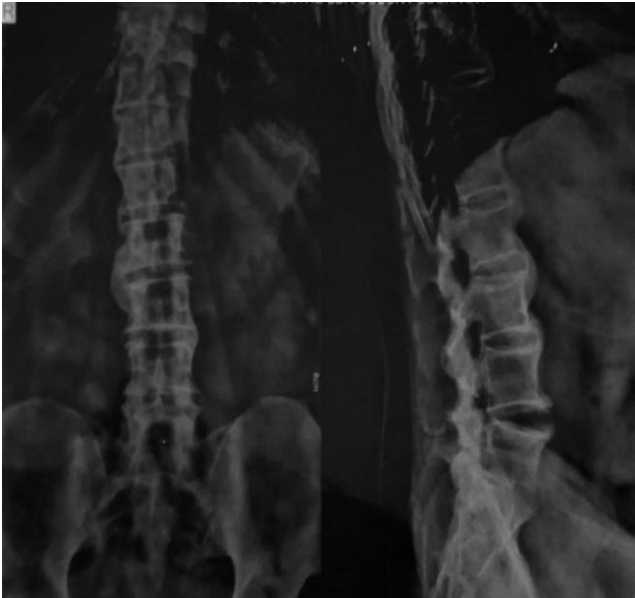


Figure 3: Bamboo spine detected in a male patient, 53 years of age suffering from Ankylosing Spondylitis with a 25 years of history of back pain and spine stiffness.



Figure 4: Sacroiliitis detected in a male patient, 53 years of age suffering from Ankylosing Spondylitis with a 25 years of history of lower back pain and spine stiffness.

Lab Assessments

⁷Major biomarkers for AS are Erythrocyte sedimentation rate and C reactive protein that will be elevated in most of the ankylosing spondylitis patients. In comparison to other inflammatory conditions like rheumatoid arthritis, levels of inflammatory markers are less helpful in tracking disease activity in ankylosing spondylitis.

DEPARTMENT OF HAEMATOLOGY				
Test Name	Result	Unit	Bio. Ref. Interval	Method
CRP (C Reactive Protein) Latex * Sample: Serum	NEGATIVE	mg/L	< 6.0 Negative > 6.0 Positive	SLIDE AGGLUTINATION

DEPARTMENT OF HAEMATOLOGY				
Test Name	Result	Unit	Bio. Ref. Interval	Method
ESR **, Blood				
Observed	16.00	Mm for 1st hr.		
Corrected	10.00	Mm for 1st hr.	<9	
PCV (HCT)	38.00	%	40-54	

Figure 5: Test results of CRP and ESR obtained from a male patient, 53 years of age suffering from Ankylosing Spondylitis with a 25 years of history of lower back pain and spine stiffness.

3. Treatment

TNF targeted

Anti - TNF injections are administered intravenously and functions by prohibiting TNF's effects as well as the inflammation caused in ankylosing spondylitis. Currently, adalimumab, etanercept, golimumab, and infliximab are mostly used TNF - α inhibitors. Despite clinical trials evaluating the effectiveness and safety of each TNF - α inhibitor, there seemed to be a significant disparity in the literature regarding the indicators of efficacy and safety.

¹¹Enbrel, or etanercept blocks TNF - alpha. TNF - α is bound by this fusion protein, which prevents TNF - α from interacting with the TNF - α receptor found on other cells.

Usually, a subcutaneous injection of 25 mg of etanercept is given twice a week.

¹¹Humira, or adalimumab Adalimumab is a monoclonal antibody against TNF - α , Adalimumab is injected subcutaneously once every two weeks at a dose of 40 mg.¹²In a 5 - year follow - up study, reported a drug survival rate of 65%, partial remission in 51% of patients based on the Ankylosing Spondylitis Disease Activity Score (ASDAS), and ASDAS inactive disease in 61% of patients.

Interleukin - 17A targeted

Secukinumab is a first - in - class fully human monoclonal antibody against interleukin - 17A used to treat AS.¹⁰Its mechanism of action includes Fully human monoclonal antibody of IgG1/ κ isotype that binds selectively to IL - 17A

and inhibits its interaction with the IL - 17 receptor thus inhibiting the release of proinflammatory cytokines and chemokines.

4. Conclusion

Even though there aren't many options for the diagnosis and treatment of ankylosing spondylitis, yet significant advancements in biological agents and diagnostic technologies have made it possible to detect and treat the disease. The majority of patients with ankylosing spondylitis are treated with medication in non - orthopaedic departments, though surgery is occasionally used. Overall, through proactive diagnosis and treatment, orthopaedic surgeons should work harder to lessen the financial burden of ankylosing spondylitis and relieve patients' pain and deformities related to the spine and musculoskeletal system.

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