

MARKOWIAK, Szymon, WARDEŚZKIEWICZ, Marta, JABŁOŃSKA, Wiktoria, KASPRZAK, Amelia, ŚWIERCZ, Maciej, TRUCHTA, Monika, MAŃKOWSKA, Aleksandra, KOLANO, Agata and PEJAS, Anna. Ankylosing Spondylitis: Review of Clinical Features, Diagnosis, and Treatment. *Journal of Education, Health and Sport*. 2024;51:76-91. eISSN 2391-8306.
<https://dx.doi.org/10.12775/JEHS.2024.51.006>
<https://apcz.umk.pl/JEHS/article/view/47730>
<https://zenodo.org/records/10464453>

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences). Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
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The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 27.12.2023. Revised: 31.12.2023. Accepted: 06.01.2024. Published: 06.01.2024.

Ankylosing Spondylitis: Review of Clinical Features, Diagnosis, and Treatment

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ABSTRACT

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disorder affecting the spine and joints, leading to significant physical impairment. With a prevalence of 0.1-1.4%, AS holds

significance in healthcare and socioeconomic contexts, therefore a thorough understanding is crucial for diagnosis and effective management. This article provides a current state of knowledge of the subject for clinicians and patients.

Review methods

English-language scientific literature found in PubMed, Web of Science, Google Scholar and Wiley databases (2015-2023) was used for the review. Articles were searched based on keywords. Each article was analysed for knowledge currency and relevance for use in the review.

Description of the State of Knowledge

After searching the articles, 20 articles were selected for final analysis. The data collected provides the latest information on ankylosing spondylitis.

The etiology of AS has a strong association with the HLA-B27 antigen and research is being conducted on the association with HLA-15, IL-1, IL-23R, ERAP-1 and ERAP-2. Clinical manifestations include a broad spectrum of symptoms involving the musculoskeletal, ocular, respiratory, cardiovascular, gastrointestinal and psychiatric systems. Specific diagnostic guidelines have been published by ASAS and EULAR. Treatment includes NSAID, GCS and biologic drug therapy.

Summary

AS, with its complex etiology and diverse clinical manifestations, presents a diagnostic challenge to clinicians. The variable prognosis and complex treatment in AS requires physicians to continually update their knowledge.

Early diagnosis and treatment initiation can improve the patient's prognosis.

Keywords: Ankylosing Spondylitis, Bechterew Disease, Rheumatoid Spondylitis, bamboo spine

INTRODUCTION AND OBJECTIVE

Ankylosing spondylitis (AS) is a form of axial spondyloarthropathy, which involves a chronic and often progressive inflammatory process affecting the sacroiliac and spinal joints, as well as the fibrous rings and ligaments of the spine. This process gradually leads to stiffening of these tissues.

AS usually presents in early adulthood and can significantly impair physical function and quality of life. This article presents a comprehensive review of ankylosing spondylitis, covering its etiology, clinical manifestations, diagnostic criteria, treatments, monitoring and prognosis.

AS affects roughly 0.1-1.4% of the population. The average prevalence of AS in the European population is 23.8 cases per 10,000 individuals. Males are impacted more frequently than females, with a ratio of approximately 3:1. The illness usually starts during adolescence or early adulthood and hardly ever appears in individuals above 40 years of age. Consequently, AS holds great significance for healthcare and socioeconomic matters. [1, 2]

The purpose of this review is to provide an up-to-date overview of the current knowledge on the subject, with the aim of increasing doctors' awareness of AS. Furthermore, patients will gain a better understanding of their condition and the planned treatment after reading the article.

MATERIALS AND METHODS

For this review, we conducted a manual search of the PubMed, Web of Science, Google Scholar, and Wiley databases for English articles on ankylosing spondylitis. We used the keywords 'Ankylosing Spondylitis', 'Bechterew Disease', 'Rheumatoid Spondylitis', and 'bamboo spine'. Our search was limited to English articles published between 2015 and 2023, along with their references. The evaluation was based on titles, abstracts, and full texts. Only those that properly matched and described the topic were included. The articles included prospective and retrospective studies, as well as reviews.

REVIEW

Etiology

The precise etiology of Ankylosing Spondylitis is complex and comprises of both genetic and environmental factors. AS is a disease strongly linked to genetic inheritance, with 113 genetic associations identified so far.

The HLA-B27 gene is the strongest genetic association, found in 80-98% of Caucasian patients. The role of HLA-B27 would be to present endogenous peptides to T lymphocytes activated by external factors such as bacteria.

Currently, the association of AS with HLA-15 gene, genes for IL-1, IL-23R and endoplasmic reticulum aminopeptidases 1 and 2 (ERAP-1, ERAP-2) is under investigation.

After biopsy examination of the inflamed tissues, it can be concluded that CD4 +, CD8 + T lymphocytes and macrophages play an important role in the pathogenic process.

Some studies have shown that an association exists between AS and intestinal dysbiosis, which is characterized by an increased number of intestinal bacteria displaying pro-inflammatory properties. This condition leads to enhanced permeability of the intestinal walls, which allows immunologically competent cells to migrate, thus resulting in inflammation of other tissues. The inflammatory process is triggered by the pro-inflammatory cytokines IL-23, IL-17, and IL-6.

Furthermore, tumour necrosis factor α (TNF- α), whose mRNA is present around lymphocyte-macrophage infiltrates, also plays an important role in AS pathogenesis.

There is an increased activity of syndesmophytes at inflamed sites in the spine, which leads to the formation of new bone tissue. Furthermore, dominant mRNA for transforming growth factor β (TGF- β) can be found in these areas. [1, 3, 4, 5, 6]

Symptoms

Clinical features of ankylosing spondylitis can vary as the disease affects various systems on different stages. Symptoms typically accumulate over time, making it challenging to identify the onset of the disease.

Initial symptoms are most commonly chronic dull pain in the lower back or gluteal region combined with stiffness of the lower back. Patients tend to experience a limitation of range of motion in lumbar area accompanied by severe pain even at rest. It progressively intensifies towards the upper regions of the spine (inflammation of the cartilages of the sternum, sternocostal joints, sternoclavicular joints), which can result in discomfort within the thoracic area, especially while breathing. The aggravation of pain typically occurs at night and in the morning alongside stiffness in the spine. Physical therapy can provide relief from those symptoms to some extent.

Moreover, joint inflammation may occur within the hip, knee, ankle, shoulder, plantar tendon, and Achilles tendon attachments. Inflammation of the temporomandibular joints is less common.

Inflammatory changes can lead to systemic features such as hypotension, weight loss and fatigue.

The disease affects the eyes as well in a form of anterior uveitis. Symptoms typically resolve within one to two months, but may recur if left untreated. This could lead to severe irreversible consequences such as glaucoma or even complete loss of vision.

The impact on respiratory system proves to be of great significance. A decrease in chest mobility results in an abdominal breathing pattern with ventilation being mainly diaphragm-driven. Fibrosis in the upper lobes of the lungs typically leads to changes in the pulmonary parenchyma, raising the risk of infection. Furthermore, bronchial dilatation and pleural thickening may occur.

Patients with AS often experience circulatory diseases such as aortic regurgitation and cardiac conduction abnormalities.

In some cases, patients may develop proteinuria due to amyloid deposition, IgA nephropathy, or kidney impairment caused by NSAID usage, which can also result in gastric and duodenal ulcers.

Continuous chronic pain and decreased functionality have the potential to result in mental health disorders such as depression. Moreover, there is a link between AS and an increased prevalence of schizophrenia and anorexia.

AS exhibits periods of exacerbation and remission. The condition typically follows a chronic and progressive course. Changes in the spine result in changes to posture and the development of limb contracture. [7, 8]

Diagnosis

We start the diagnosis by identify axial spondyloarthropathy. For this we use the classification criteria according to ASAS (2010).

Criteria for axial spondyloarthropathy (only need one of two):

- 1) Inflammatory changes in the sacroiliac joints documented by X-ray or MR imaging and a minimum of 1 other characteristic axial spondyloarthritis features (Table 1.).
- 2) Presence of HLA-B27 antigen and a minimum of 2 other characteristic axial spondyloarthritis features (Table 1).

Table 1. Based on ASAS (2010).

Characteristic features of axial spondyloarthritis
Inflammatory sacral pain (minimum of 4 criteria: age of onset below 40 years old, insidious onset, improvement with exercise, no improvement with rest, and pain at night (with improvement upon getting up));
Past history of inflammation in the joints, heels, or tendon-bone attachments
Inflammatory bowel disease (Crohn’s disease or ulcerative colitis)
Family history for axial spondyloarthritis
Psoriasis
Uveitis
Dactylitis
Positive for the HLA-B27
Good response to treatment with NSAIDs
Elevated CRP or ESR

Imaging tests

According to the EULAR recommendations (2014), classic X-ray of the sacroiliac joints is the first-choice method for detecting the axial form of the disease. An alternative and more sensitive method is to perform MR imaging of these joints.

On the X-ray we look for erosions and sclerosis in sacroiliac joints, syndesmophytes, calcified ligaments, tendons, entheses and „bamboo spine appearance”, while an MRI can reveal inflammatory changes of the corners of the vertebral bodies and fatty infiltration. [9, 10, 11]

Treatment

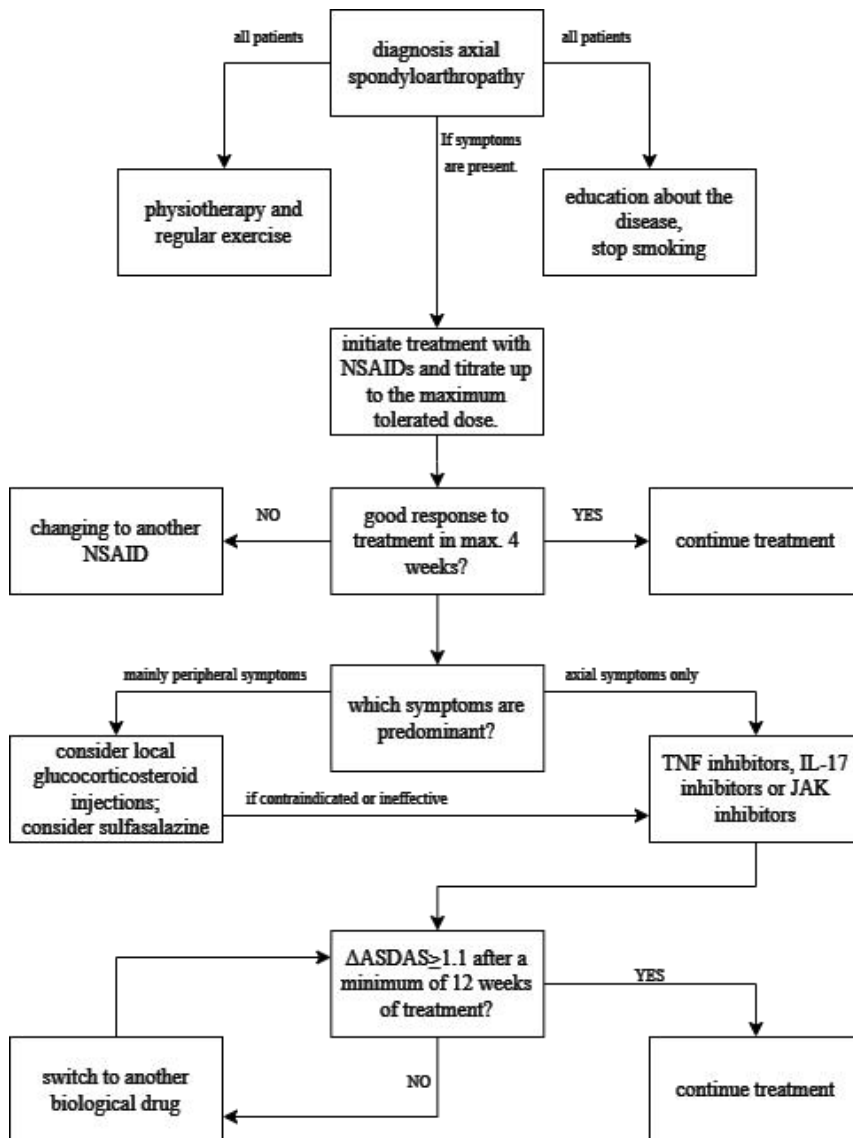


Figure 1. Treatment algorithm for AS. Based on [18].

The patient should be educated as soon as possible about how to function with the disease.

Adequate physiotherapy forms the basis of treatment, therefore all patients should learn suitable exercises with the guidance of a physiotherapist and practice them at home on a daily basis.

Patients should sleep on a firm mattress with a small pillow under the head.

Patients are advised to quit smoking.

The goal of treatment is to relieve pain and stiffness, so the initial mainstay of therapy are anti-inflammatory drugs such as NSAIDs administered on an ad hoc basis.

In cases where peripheral symptoms are the primary concern, topical glucocorticosteroids (GCS) injections may be considered (If two or fewer peripheral joints, sacroiliac joints or tendon attachments are involved.). It is recommended to avoid administering injections around the Achilles tendon, quadriceps tendon, and patella ligament.

In addition, only in cases of peripheral joint involvement can sulfasalazine be taken in a dosage of 3g per day for a period of 3 months. If the treatment is ineffective, switch to axial treatment.

To treat axial symptoms we use: TNF inhibitors, IL-17 inhibitors or JAK inhibitors. In order to receive the above-mentioned treatments, the patient must meet three criteria:

- 1) Increased CRP and/or sacroiliitis on imaging studies.
- 2) Failure of previous treatments.
- 3) Patients with high disease activity (ASDAS \geq 2.1 or BASDAI \geq 4).

Most commonly, a TNF inhibitor or IL-17 inhibitor is used.

A TNF inhibitor is recommended for patients with uveitis or inflammatory bowel disease, and an IL-17 inhibitor for patients with psoriasis.

JAK inhibitors should be considered only as a secondary option due to limited data on their use.

In the event of remission lasting more than six months, the dosage of TNF or IL-17 inhibitors may be reduced.

Operative intervention in the form of a hip endoprosthesis should be considered for patients experiencing severe pain, disability, and joint destruction. [1, 12, 13, 14, 15, 16, 17, 18, 19, 20]

Monitoring

Disease monitoring involves evaluating disease activity, function, and structural changes.

Magnetic resonance imaging (MRI) is used to assess disease activity, while X-rays (RTGs) help evaluate the progression of structural damage to the spine.

The frequency of laboratory tests and imaging should be based on individual patient needs.

The use of ASDAS or BASDAI scales is advisable.

ASDAS (Ankylosing Spondylitis Disease Activity Score)

<https://www.asas-group.org/instruments/asdas-calculator/>

ASDAS evaluates the activity and treatment response in patients suffering from AS.

BASDAI (Bath Ankylosing Spondylitis Disease Activity Index)

<https://www.evidencio.com/models/show/1503>

BASDAI determines effectiveness of current drug therapy, or the need to institute a new drug therapy. [8, 10, 11]

Prognosis

The prognosis for AS is highly variable. Progressive stiffness and fusion of spinal vertebrae can lead to reduced mobility and a lower quality of life.

Patients with AS have a shorter lifespan than the general population, and the risk of death increases with age.

Patients have an elevated risk of spinal fractures and cardiovascular diseases, particularly during the first decade of the condition when mobility impairment frequently progresses.

Maintaining an active and productive life is only possible with prompt diagnosis and suitable treatment. [8, 17]

CONCLUSION

- Ankylosing spondylitis (AS) emerges as a complex and impactful condition affecting sacroiliac and spinal joints, leading to chronic inflammation and tissue stiffening.
- With a prevalence of 0.1-1.4% in the population, AS holds significant healthcare and socioeconomic importance, predominantly affecting males in early adulthood.
- The etiology of AS is multifaceted, involving genetic associations, particularly with the HLA-B27 gene, and environmental factors. Inflammatory processes, influenced by cytokines like IL-23, IL-17, and IL-6, contribute to the pathogenesis.
- AS manifests in a variety of symptoms impacting musculoskeletal, ocular, respiratory, cardiovascular, gastrointestinal, and psychiatric systems. Periods of exacerbation and remission mark the chronic and progressive nature of the disease.
- Diagnosis follows specific patterns outlined by ASAS and EULAR, involving inflammatory changes in sacroiliac joints and characteristic features. Imaging, primarily X-rays and MRIs, aids in the identification of structural damage and inflammatory changes.
- Treatment strategies encompass education, physiotherapy, pharmacological interventions (NSAIDs, glucocorticosteroids), and advanced biologic drugs (TNF inhibitors, IL-17 inhibitors, JAK inhibitors). Surgical intervention, such as hip endoprosthesis, may be considered in severe cases.
- Disease monitoring involves assessing activity, function, and structural changes using tools like ASDAS and BASDAI scales. The prognosis varies, emphasizing the importance of early intervention for a more favorable outcome.

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All authors have read and agreed with the published version of the manuscript.

Funding Statement

The study did not receive special funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Conflict of Interest Statement

No conflict of interest.

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