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Brief Overview About Axial Spondyloarthropathy

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Abstract:Background: Axial Spondyloarthropathy (AxSpA) is a chronic inflammatory disease that affects axial skeleton (spine and sacroiliac joint) mainly causing severe pain and disability. It also affects peripheral joints and enthesis and can be assosciated with extra-articular manifestations as uveitis, psoriasis, and inflammatory bowel. Chronic back pain is the main clinical symptom of AxSpA and is usually the early clinical symptom. Back pain in AxSpA is usually of inflammatory character (Insidious onset, morning stiffness more than 30 minutes, improvement of back pain with movement and increase with rest, pain at night causing patient to awake during sleep, and alternating buttock pain. As an inflammatory autoimmune disease, AxSpA causes complications in many organ systems and tissues throughout the body including aortic regurgitation, pulmonary fibrosis, cauda Equina syndrome, mood disorders, chronic pain, aortic affection, osteoporosis, and Disability. Physiotherapy is an essential part of the treatment of AxSpA. It aims to alleviate pain, increase spinal mobility and functional capacity, reduce morning stiffness, correct postural deformities, increase mobility and improve the psychosocial status of the patients. Physical therapy components, like stretching exercises, posture education, range of motion exercises, strengthening exercises, Aerobic exercise, developing a plan for activity, movement, and posture that will preserve mobility and even strategies such as selecting the right mattress and workplace chair help to improve quality of life. AxSpA is a chronic condition for which there is currently no cure. The aim of treatment is essentially symptomatic with good control of symptoms, maintenance of function (facilitated by early diagnosis) and management of complications. Refer all new or suspected cases of AxSpA to a rheumatologist. This is for confirmation of the diagnosis, review of current treatment, access to specialist physiotherapy and occupational therapy and the arrangement of follow-up (often as part of a shared care arrangement with primary care). Treatment of extra-articular manifestations may require the involvement of other specialist teams. In this review we tried to givae a brief account about AxSpA diagnosis, and management.

Keywords: Axial Spondyloarthropathy

Introduction

Severe pain and impairment are the main symptoms of axial skeletal arthritis (AxSpA), a chronic inflammatory illness that mostly affects the spine and sacroiliac joint. Additional extra-articular symptoms

such as uveitis, psoriasis, and inflammatory bowel disease can accompany it, and it also impacts the enthesis and peripheral joints. ***(1).***

Radiographic AxSpA, also known as AS, is characterized by structural abnormalities in the sacroiliac joints or spine that are visible on radiographs. Non-radiographic AxSpA, on the other hand, does not involve any x-ray structural abnormalities. Half of the individuals with AxSpA will also experience peripheral arthritis, dactylitis, or enthesitis, even though the axial skeleton is the most prevalent place to be afflicted. The overall disease activity can be impacted by these peripheral symptoms. ***(2).***

Prevalence

The rheumatic disease AxSpA is not uncommon. The incidence rate can be as high as 1% in certain regions, while it varies greatly across nations. One possible explanation for the observed variance in AxSpA incidence between populations is the fact that the prevalence of the HLA-B27 antigen varies across ethnic groups. Males have a two- to thrice higher prevalence of AS compared to females. The prevalence of AxSpA is equal in boys and girls, or even higher in females, when a more inclusive definition of the disease is used, which encompasses the early phases before radiographic abnormalities. ***(3).***

Diagnosis

Articular manifestation

1) Back pain and stiffness

One of the first signs of AxSpA is chronic back pain, which is also the most common clinical symptom. Typical symptoms of inflammatory back pain in AxSpA include a gradual onset, persistent morning stiffness lasting more than 30 minutes, back pain that improves with exercise but worsens with rest, nighttime discomfort that keeps the patient awake, and intermittent buttock pain. When these symptoms manifest in a patient younger than 40 years old, it raises serious suspicions of AxSpA. ***(4).***

2) Peripheral arthritis

Approximately 36% of people with AxSpA will also experience peripheral arthritis, even though discomfort of the axial bone is the primary clinical symptom. It strikes the lower extremities most often and can happen at any point in the disease's progression, even before the axial symptoms manifest. ***(5).***

3) **Enthesitis**

It is a common symptom in AxSpA patients, usually assosciated with worse disease activity and quality of life. Enthesitis occurs in about 25.4% of patients with AxSpA,with more prevelance in females and those with non-radiographic AxSpA. It can occur at site of attachment of achillis tendon, planter fascia, insertions of the flexor and extensor tendons at the phalanges, muscular attachment into greater and lesser trochanters, and quadriceps tendon at the upper patellar pole ***(6).***

4) Fatigue

Along with pain and stiffness, fatigue is one of the most commonly reported symptoms of AxSpA. Fatigue is a subjective feeling of exhaustion. Although the exact cause of weariness in AxSpA is unknown, it is commonly linked to a high level of disease activity. A patient's sense of health, quality of life, socioeconomic position, and physical function all have a role on their level of fatigue. ***(7).***

5) Dactylitis

As a result of arthritis or tenosynovitis, a finger or toe might swell all over, giving it a sausage-like look; this condition is known as dactylitis. It is a sort of AxSpA that shows up in the joints on the periphery. ***(8*)**.

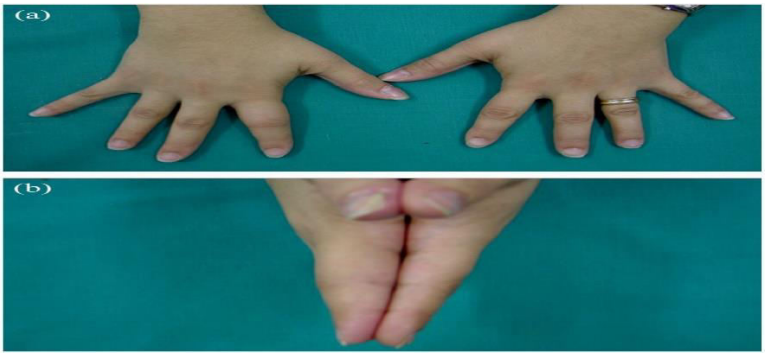

Figure (1): Dactylitis: (a) Dactylitis of the second digit of the right hand (frontal view). (b) Dactylitis of the second digit of the right hand compared to the contralateral (lateral view) ***(9).***

Extra-articular manifestation

1) Uveitis

All three of these structures can become inflamed in uveitis. Panuveitis is one kind of this condition, whereas intermediate and posterior forms are also possible. Around one-third of AxSpA patients will experience uveitis, making it the most prevalent extra-articular symptom of the disease. Photosensitivity, discomfort, lacrimation, redness of the eye, and impaired vision are symptoms of acute anterior unilateral uveitis, the most common form of uveitis in AxSpA patients. ***(10)*****.**

2) **Psoriasis**

An immune-mediated skin condition, psoriasis is defined by an overabundance of scales. Psoriasis is an extra-articular symptom of AxSpA, although the hereditary susceptibility to the disease is different from that of AxSpA. The onset and progression of psoriasis can happen at any point in time, and the disease's prevalence tends to rise as it progresses. Psoriasis patients with AxSpA are more prone to develop synovitis, but they do not have worse results relating to activity or severity. ***(11).***

3) Inflammatory bowel disease

Inflammatory bowel disease is one of the extraarticular manifestations of AxSpA. This may be presented as Crohn's disease, ulcerative colitis, or subclinical gut inflammation. AxSpA patients with inflammatory bowel disease have higher levels of disease activity, as assessed by ESR and CRP, but there is no increase in activity as assessed by BASDAI, and ASDAS-ESR scores ***(12).***

Signs:

1) provocation tests of sacroiliac joint

Many tests can be used to provoke an injury, such as the FABER (flexion, abduction, and external rotation), distraction, thigh thrust, and compression tests, as well as Gaenslen's test. If sacroiliac joint dysfunction is suspected, these tests might be useful in making a diagnosis. The results are deemed positive if the patient's symptoms are either intensified or replicated during the maneuver. Unfortunately, sacroiliac joint dysfunction cannot be reliably diagnosed by a single provocation test. On the other hand, when three provocation tests are used, the diagnostic validity improves; for example, Broadhurst and Bond found that sacroiliac joint discomfort may be identified with a sensitivity of 77-87% when three provocative maneuvers are performed on the joint. ***(13).***

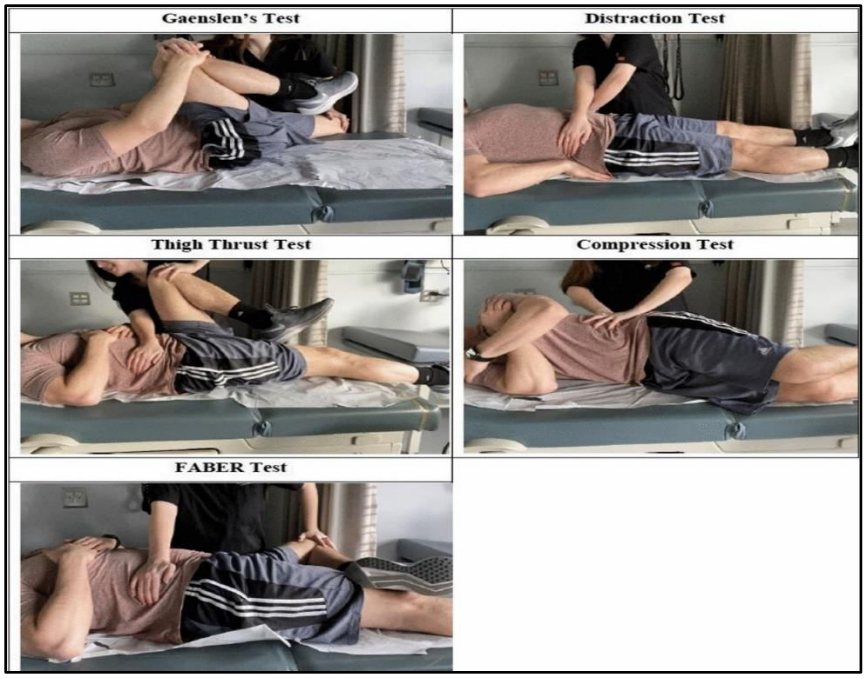

Figure (2): provocation tests of sacroiliac joint *(14).*

Although that, there are some limitation of provocation tests this is due to structure of sacroiliac joint itself that leaded to lack of motion in sacroiliac joint and low palpation ability of the examiner. In addition to that, compression may cause an irritation of a ligament, which in some cases may mimic the sacroiliac joint pain ***(15).***

2) Spinal Mobility, chest expansion, and posture

Loss of the typical lumbar lordosis at an early stage is frequently the initial symptom. Limitations in range of motion may be experienced when the lumbar spine is hyperextended, flexed laterally, or bent forward. To identify any restriction of lumbar forward flexion, the Schober test or a modified version of it is helpful. Pain and restricted neck mobility are symptoms of cervical spine involvement. The early stages of AS are characterized by a mild to moderate loss of chest expansion. As the condition progresses, the patient may experience a gradual loss of lumbar lordosis and the development of thoracic kyphosis, as well as a stiffening of the entire spine. Typically, these abnormalities manifest after a decade or more of illness. Clinical examination of spinal mobility includes cervical, thoracic, and lumbar mobility **(16*).***

Measure	Description
Cervical mobility	
Occiput-to-wall distance*	Horizontal distance between occiput and wall, patient standing with heels and buttocks against the wall.
Tragus-to-wall distance	Horizontal distance between right tragus and wall, patient standing with heels and buttocks against the wall without rotation.
Cervical rotation	Distance between tip of nose and acromioclavicular joint in neutral less the same distance in maximal ipsilateral rotation.
Thoracic mobility	
Chest expansion*	The difference in centimetres to the nearest 0.1 cm between full expiration and full inspiration, measured at the nipples.
Lumbar mobility	
Modified Schober index*	Distance between the midpoint of the posterior superior iliac spines and a point 10cm vertically above when standing erect, following maximal forward flexion of the spine (normal > 15cm)
Finger-to-floor distance	Distance between tip of middle finger and the floor following maximal lumbar forward flexion with knees extended
Lumbar lateral flexion	Distance between tip of ipsilateral middle finger and the floor following maximal lumbar lateral flexion, with both feet on the floor, knees extended and without rotation
*Recommended in the ASAS Core Sets.	

Figure (3) Clinical examination of spinal mobility (16*).*

Complication of AxSPA

As an inflammatory autoimmune disease, AxSpA causes complications in many organ systems and tissues throughout the body including aortic regurgitation, pulmonary fibrosis, cauda Equina syndrome, mood disorders, chronic pain, aortic affection, osteoporosis, and Disability ***(17).***

Investigations

1-Acute phase reactants

ESR and CRP are used as an indicator of disease activity in AxSpA. Elevated CRP levels and high ESR are associated with high risk of radiographic progression in the sacroiliac joints and spine. Although that these laboratory tests aren't diagnostic for AxSpA, about half of patients with AxSpA are found to have high ESR and elevated CRP levels***(18).***

2- HLA-B 27

HLA-B27 has Moderate-to-high sensitivity but it has low specificity in diagnosis of AxSpA. This means that not everyone with the gene will develop the disease, but people with the HLA-B27 gene are more susceptible to developing AxSpA. Despite the fact that 90–95% of patients with AxSpA are positive for HLA-B27, it accounts for less than one third of the genetic risk for AxSpA. While the risk of developing this disease is only about 5% in HLA-B27+ve individuals without seropositive relatives, this risk is increased 5 to 16 folds if there is a first degree relative with AxSpA. HLA-B27 is a polymorphic form of HLA-B molecule that is found in up to 95% patients of European ancestry with AS, as well as 70% with reactive arthritis, 60% with psoriatic spondylitis, 25% with peripheral psoriatic arthritis (although no association with psoriasis itself), 70% with spondylitis associated with inflammatory bowel disease (but no association with inflammatory bowel disease itself) and 50% with acute anterior uveitis occurring without other stigmata of spondyloarthritis.But the strength of the association of AxSpA with the HLA- B27 antigen is lower in most of the Arab countries (25–75 %) than in Western European populations (>90 %) ***(19).***

3-Imaging techniques

There are different imaging techniques for diagnosis of AxSpA, each of them has different role ***(20).***

Techniques		Inflammatory/ acute changes	Structural/ chronic changes
Conventional radiography		–	+
Computed tomography		–	++
Spectral CT		+	+
Ultrasound		+	(+)
Scintigraphy		+	–
MRI	T1w	(+)	+
	STIR/T2FS/T1Gd	++	+
SPECT-CT		+	+
PET–CT, PET–MRI		+	+

–, no diagnostic value; +, with diagnostic value; (+), limited diagnostic value; ++, with diagnostic value, gold standard. CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; SPECT, single-photon emission computed tomography; STIR, short tau inversion recovery sequence; T1Gd, gadolinium-enhanced T1-weighted sequence; T1w, T1-weighted sequence; T2FS, fat-saturated T2-weighted sequence.

Figure (4): Different imaging techniques for diagnosis of AxSpA*(20).).*

a-Plain X-Ray

The first radiographic changes observed in AxSpA are found in the Sacroiliac joints. AxSpA cause ossification of the ligaments that join the sacrum to the ilium. Some changes can be detected in X-ray of sacroiliac joints and help in diagnosis of AxSpA as narrowing or pseudo-widening of the joint space , presence of erosions, and presence of sclerosis**.** The erosions first appear on the iliac side, then on the sacral side. As erosions progress, the joint space appears wider. Then small amounts of bone repair can be seen around the erosions. As the process progresses, the space of the sacroiliac joints gets smaller, more bone repair and sclerosis occur. Eventually, the sacroiliac joints are totally fused and ankylosed **.** The New York grading system for sacroiliac joint status is as follows: grade I = suspicious, Grade II = evidence of erosion and sclerosis, Grade III = erosions, sclerosis, and early ankylosis, and Grade IV = total ankylosis ***(21).***

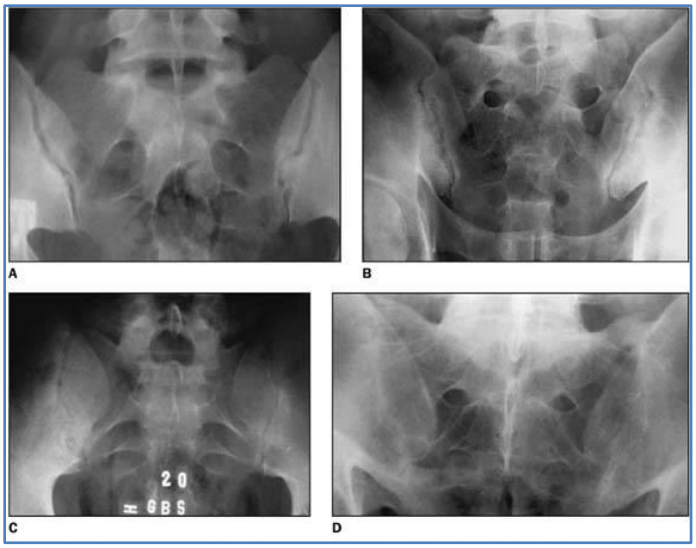

Figure (5): Radiographic changes in sacroiliac joint in AxSpA. A: Grade I = suspicious, B: Grade II = evidence of erosion and sclerosis, C: Grade III = erosions, sclerosis, and early ankylosis; and D: Grade IV = total ankylosis***(21).***

b-CT

CT is more sensitive than plain x-ray for detecting bony changes secondary to sacroiliitis, and the cross-sectional images allow a more complete image of the anatomy of the sacroiliac joints. In addition to showing erosion and sclerosis in bones, Spectral CT can also show and measure bone marrow edema in the sacroiliac joints ***(22).***

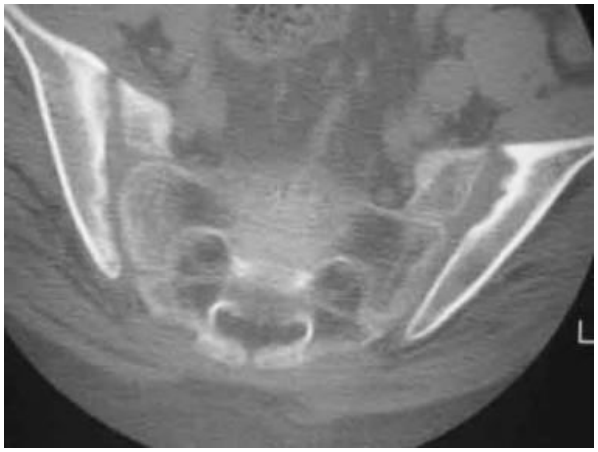

Figure (6): Axial CT scan in AS patient shows erosions and iliac side subchondral sclerosis of both sacroiliac joints. Bilateral sacroiliitis. ***(22).***

MRI

MRI of sacroiliac joints has an essential role in early diagnosis of AxSpA, and detection of active inflammation in sacroiliac joints. Presence of bone marrow edema or osteitis on T2-weighted fat-suppressed sequences of the MRI is mandatory for diagnosis of active sacroilitis, while presence of synovitis, enthesitis and capsulitis without bone marrow edema or osteitis is suggestive but not sufficient for diagnosis. Bone marrow edema or osteitis on T2-weighted fat-suppressed sequences of the MRI is usually detected on at least two consecutive slices in MRI scan of AxSpA. Bone marrow edema lesions are typically located periarticularly. Detection of inflammation on one slide is highly suggestive of AxSpAespecilly if multipul inflammatory lesions present. Structural lesions as sclerosis and erosion can be also detected in MRI (**23).**

- ASAS definition of active sacroiliitis is as follows:

Active inflammatory lesions of SI joints: Appear as “osteitis” or bone marrow edema (BME) on STIR or on T2-weighted images in subchondral regions or periarticular bone marrow.

Positive MRI: At least two BME lesions on the same slice or one lesion in the same quadrant on at least two consecutive slices.

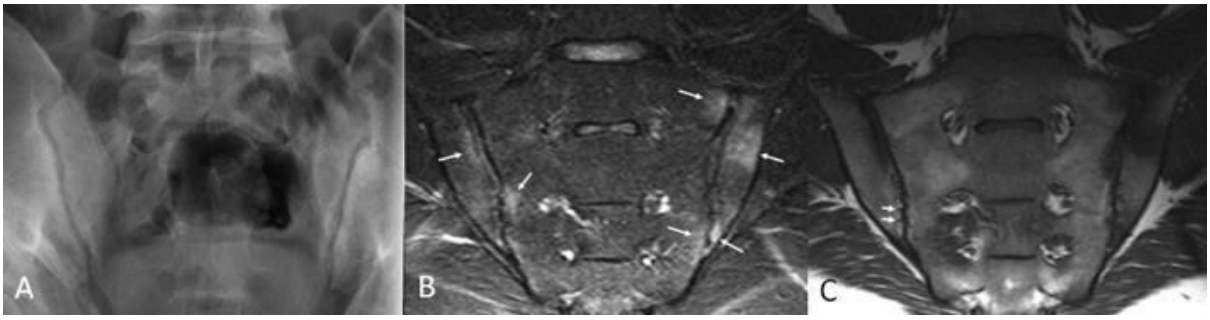

Figure (7): Early sacroiliitis on conventional radiography and MRI. Radiograph (A) of the sacroiliac joints reveals only subtle findings of possible erosion and minimal sclerosis. Short tau inversion recovery (STIR) MRI image (B) performed at the same time shows multiple bone marrow lesions, which appear as oedema (bright; arrows) involving the sacrum and ilium bilaterally, i.e. definite sacroiliitis was documented by MRI.

The corresponding T1-weighted MRI image (C) shows some areas of diminished marrow fat signal corresponding to the intense oedema in the left upper quadrant. Some very subtle defects in the subchondral marrow in the lower quadrants, which likely represent tiny erosions (arrows), are also seen. **(24).**

d-Ultrasonography (US)

US showed good sensitivity and specificity for identification of sacroiliitis. However, there are some considerations, as that there is no clear definition of sacroiliitis by US, some authors consider it as morphological changes that present only in grayscale, whereas others consider the presence of Doppler is mandatory. Also, US has some limitations as it can visualize only the upper third of sacroiliac joint, but it can't assess the lower third where inflammation occurs early **(24).**

US has its own unique advantage in the diagnosis of enthesitis in AxSpA, US is superior to clinical examination in the detection of peripheral enthesitis. Manifestations of tendon enthesitis in AxSpA on US include a thickened tendon, hypoechoicity, local calcification and bony erosion. Abnormal blood flow in tendon entheseal sites can be detected by power Doppler ultrasound ***(22).***

Treatment of AxSpA

1) Role of Physiotherapy in AxSpA

Physiotherapy is an essential part of the treatment of AxSpA. It aims to alleviate pain, increase spinal mobility and functional capacity, reduce morning stiffness, correct postural deformities, increase mobility and improve the psychosocial status of the patients. Physical therapy components, like stretching exercises, posture education, range of motion exercises, strengthening exercises, Aerobic exercise, developing a plan for activity, movement, and posture that will preserve mobility and even strategies such as selecting the right mattress and workplace chair help to improve quality of life ***(25)***.

2) Medical treatment of AxSpA

AxSpA is a chronic condition for which there is currently no cure. The aim of treatment is essentially symptomatic with good control of symptoms, maintenance of function (facilitated by early diagnosis) and management of complications. Refer all new or suspected cases of AxSpA to a rheumatologist. This is for confirmation of the diagnosis, review of current treatment, access to specialist physiotherapy and occupational therapy and the arrangement of follow-up (often as part of a shared care arrangement with primary care). Treatment of extra-articular manifestations may require the involvement of other specialist teams ***(26).***

NSAIDs are considered the first-line treatment for patients with active, predominantly axial manifestations of AxSpA. the use of NSAIDs provides rapid relief of inflammatory back pain and stiffness and may lead to a potential reduction of the radiographic progression in the spine of patients with AxSpA. Moreover, continuous use of NSAIDs may lead to gastrointestinal, cardiovascular, and renal complications ***(26).***

Local injections of glucocorticoids seem to be an option for treating enthesopathy and arthritis. Glucocorticoid injections into involved peripheral joints, sacroiliac joints, or entheses could provide immediate symptom relief. ***(26).***

Trials of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate and sulfasalazine in AxSpA have shown disappointing results regarding axial symptoms, especially spinal pain. But they can improve signs and symptoms of peripheral arthritis, thus csDMARDs can have a role in controlling peripheral inflammatory arthritis. Evidence favours using sulfasalazine for the treatment of peripheral arthritis in AxSpA compared with methotrexate. Tumor necrosis factor inhibitors (TNFi) are effective for treatment of not only advanced ankylosing spondylitis, but also its early stage, so early use of TNFi in AxSpA has been recommended. All TNF inhibitors have been shown to improve spinal and peripheral musculoskeletal manifestations, such as enthesitis and dactylitis, as well as CRP levels and MRI-detectable inflammation in the sacroiliac joints and spine. All TNF inhibitor monoclonal antibodies, but not the TNF soluble receptor (etanercept), are effective for uveitis and inflammatory bowel disease ***(27)***.

Other biologics as secukinumab (a monoclonal antibody against IL-17), and ustekinumab (a monoclonal antibody against IL-12/23) can be used If TNFi fails to treat AxSpA. However, the efficacy of ustekinumab in the treatment of AxSpA hasn't been established ***(27)***.

Brodalumab is an anti-IL-17 receptor A (IL-17RA) monoclonal antibody. It inhibits several cytokines of the IL-17 family, including IL-17A–IL17F heterodimer, IL-17C and IL-17E ***(27)***.

Clinical trials of janus kinase inhibitors (JAKi) in axSpA have yielded favorable results in key clinical domains of the disease, with an acceptable safety profile. Thus, JAKi could be considered in the therapeutic management of AxSpA. Upadacitinib is currently licensed for the treatment of radiographic AxSpA, while European Medicines Agency (EMA) has recently approved tofacitinib for AxSpA in certain countries. Their place (first, second, or further line of treatment) in the treatment strategy of AxSpA remains to be clarified ***(26).***

3) Surgical treatments

Untreated AS can cause spinal deformity, with more than 30% of AS patients suffering from thoracolumbar kyphosis. Corrective osteotomy and stabilization are very common in surgical procedures and are recommended under certain conditions, such as adult patients suffering severe kyphosis. Also, patients with advanced hip arthritis may need arthroplasty. Summary of 20*22* Updates of the ASAS-EULAR recommendations for the management of axial spondyloarthritis***(28).***

Table (1): Summary of 20*22* Updates of the ASAS-EULAR recommendations for the management of axial spondyloarthritis ***(28).***

2022 Update of the American College of Rheumatology/ Spondylitis Association of America/Spondyloarthritis.	
1	The treatment of patients with axSpA should be individualised according to the current signs and symptoms of the disease (axial, peripheral, extramusculoskeletal manifestations) and the patient characteristics including comorbidities and psychosocial factors.
2	Disease monitoring of patients with axSpA should include patient-reportedoutcomes, clinical findings, laboratory tests and imaging, all with the appropriate instruments and relevant to the clinical presentation. The frequency of monitoring should be decided on an individual basis depending on symptoms, severity and treatment.
3	Treatment should be guided according to a predefined treatment target.
4	Patients should be educated about axSpA and encouraged to exercise on a regular basis and stop smoking; physiotherapy should be considered.
5	Patients suffering from pain and stiffness should use an NSAID as first-line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs, continuous use is preferred if needed to control symptoms
6	Analgesics, such as paracetamol and opioid-(like) drugs, might be considered for residual pain after previously recommended treatments have failed, are contraindicated, and/or poorly tolerated.
7	Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Patients with axial disease should not receive long-term treatment with systemic glucocorticoids.

8	Patients with purely axial disease should normally not be treated with csDMARDs; sulfasalazine may be considered in patients with peripheral arthritis.
9	TNFi, IL-17i or JAKi should be considered in patients with persistently high disease activity despite conventional treatments ; current practice is to start a TNFi or IL-17i.
10	If there is a history of recurrent uveitis or active IBD, preference should be given to a monoclonal antibody against TNFiIn patients with significant psoriasis, an IL-17i may be preferred.
11	Absence of response to treatment should prompt re-evaluation of the diagnosis and consideration of the presence of comorbidities.
12	Following a first b/tsDMARD failure, switching to another bDMARD (TNFi or IL-17i) or a JAKi should be considered.
13	If a patient is in sustained remission, tapering of a bDMARD can be considered.
14	Total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage, independent of age; spinal corrective osteotomy in specialised centres may be considered in patients with severe disabling deformity.
15	If a significant change in the course of the disease occurs, causes other than inflammation, such as a spinal fracture, should be considered and appropriate evaluation, including imaging, should be performed.

ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; b/tsDMARDs, biological/targeted synthetic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; GCs, glucocorticoids; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitors; JAKi, Janus kinase inhibitors; LoA, level of agreement; NSAIDs, non-steroidal anti-inflammatory drugs; RCTs, randomised controlled trials; TNFi, tumour necrosis factor inhibitors.

Evaluation of severity of AxSpA

1) Radiographic scores

the Bath Ankylosing Spondylitis Radiology Index (BASRI), the Stoke Ankylosing Spondylitis Spine Score (SASSS), and a modification of SASSS (mSASSS) are scoring method for quantifying chronic structural changes on conventional radiographs. SASSS assesses the lumbar spine region, mSASSS assesses the cervical and lumbar spine, and BASRI-spine assesses the lumbar, cervical spine, and the sacroiliac joints ***(29)***.

2) Bath Ankylosing Spondylitis Metrology Index (BASMI)

BASMI a validated index consisting of five clinical measurements including cervical rotation, tragus-to-wall distance, lateral spine flexion, lumbar flexion and intermalleolar distance, which reflects axial segmental involvement**.** Each one of these measurements is classified in three levels of severity (0 = Mild, 1 = Moderate, 2 = Severe) according to values defined for each interval. Summing up the results obtained for the five measurements, an index between zero and ten is obtained ***(30).***

3) **BASFAI**

It consists of 10 questions about certain daily activities. Each item has a score from 0 to 10, 0 means easy and 10 means impossible, and average of all items is calculated. High BASFI score is considered as an important predictor of work disability, and a high BASFI score at baseline can predict a poor response to treatment***(31).***

Evaluation of disease activity

1-Acute phase reactant

The CRP level in AxSpA patients is a key indicator of inflammation and is also considered to be a predictor of clinical response to TNFi treatment. In a number of studies, patients with elevated CRP at baseline have demonstrated significantly greater responses to TNFi compared with patients with low CRP levels as well as those receiving placebo treatment ***(18).***

Although, Acute phase reactant as ESR and CRP can be used as a predictor of disease activity, ESR and CRP are elevated only in half of patients with AxSpA***(18).***

2-MRI

MRI of the sacroiliac joints has become the imaging investigation of choice for patients with suspected AxSpA who do not have X-ray evidence of sacroiliitis. MRI can detect active inflammatory lesions of osteitis as bone marrow edema on T2-weighted fat-suppressed sequences of the MRI. MRI can also detect other lesions, such as synovitis, enthesitis and capsulitis, associated with AxSpA***(20).***

MRI is particularly useful for the early diagnosis of AxSpA, it is capable of detecting both bone marrow edema or osteitis and erosions before other imaging techniques. Also, inflammation of the sacroiliac joints as detected by MRI correlates with histological and clinical finding in AxSpA. So, MRI is the only imaging technique that is able to detect both active inflammation and structural lesions in AxSpA patients, but it is an expensive technique that can't be repeated regularly due to cost ***(20).***

3-BASDAI

The BASDAI score consists of six questions that reflects the five major skeletal symptoms of AxSpA, fatigue, spinal pain, peripheral joint pain or swelling, enthesitis, duration and severity of morning stiffness. Each question has a score from 0 to10 (0 being no problem and 10 being the worst problem), the average of the two scores related to morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final 0 – 10 BASDAI score. Scores of 4 or greater suggest suboptimal control of disease **(32*).***

4-ASDAS

ASAS developed a new disease activity score (ASDAS) that combines four questions about patient's self-assessments with acute phase reactants (CRP or ESR) ***(33).***

ASDAS_CRP: 0.121 × total back pain + 0.110 × patient global + 0.073 × peripheral pain / swelling + 0.058 × duration of morning stiffness + 0.579 × Ln (CRP+1).

ASDAS-ESR: 0.079 × spinal pain + 0.069 × stiffness duration + 0.113 × PGA + 0.086 × peripheral arthritis + 0.293 × √(ESR)

Table (2) ASDAS score *(33).*

ASDAS score 0 being no problem and 10 being the worst problem	**Score**
1) How would you describe the overall level of AS neck, back or hip pain you have had? (Spinal pain)	(0-10)
2) How would you describe the overall level of pain/swelling in joints other than neck, back or hips you have had? (Joint pain or swelling)	(0-10)
3) How long does your morning stiffness last from time you wake up? (Morning stiffness duration)	(0-more than 2 hours)
4) How active was your disease on average during the last week (PGA)?	(0-10)
ESR or CRP	

The 3 cut-offs selected to assess activity: <1.3 means "inactive disease, <2.1 means low disease activity, ≤ 3.5 means high disease activity, and >3.5 means very high disease activity ***(30).***

Figure (8): ASDAS disease activity state *(30).*

Unfortunately, the evaluation of disease activity in AxSpA is complex and multifactorial, both BASDAI, and ASDAS are based largely on subjective measures, and lacks objective biomarker of disease activity, patients and physicians have different perspectives of the disease activity, and none of the current single-item or combined indexes adequately unifies both perspectives ***(34).***

Conclusion

Axial spondyloarthritis (axSpA) is a chronic, rheumatic disease characterized by inflammation of the sacroiliac joint, spine, and entheses. Axial spondyloarthritis affects up to 1.4% of adults in the United States and is associated with decreased quality of life, increased mortality, and substantial health care–related costs, imposing a high burden on patients, their caregivers, and society. Over the past decade, the concept of axSpA has broadened to include AS and previously unrecognized axSpA without sacroiliitis on radiographs. This conceptual evolution has spurred research on the early detection and diagnosis of axSpA, revealing differences in disease presentation and severity between men and women, barriers to early diagnosis, and other axSpA-like conditions that may confound diagnosis. The early detection and diagnosis of axSpA, along with breakthroughs in available therapeutic options, have led to improvements in patient care and disease management, but delays in diagnosis and treatment remain common. Additional research and education are critical for recognizing diverse axSpA presentations and optimizing management early in the course of disease.

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