



Surgical Management of Spondyloarthropathies in the Age of Disease Altering Drugs

ABSTRACT

Inflammatory spondyloarthropathies produce synovitis of the spinal joints in rheumatoid arthritis (RA), or enthesitis in ankylosing spondylitis (AS). In RA, progressive disease leads to synovial destruction, ligamentous laxity, pannus formation and deformity. In AS progressive enthesitis results in ascending ossification, kyphotic deformity and rigidity which increase the risk of fracture. Although pain is the common presentation, spinal cord compression can produce neurological deficits. Although the need for surgery has decreased with the advent of new disease altering drugs, there remains a number of indications when surgical consultation remains important.

KEYWORDS: Spondyloarthropathy and spondyloarthritis, Synovium and synovitis, Enthesis and enthesitis, Pannus



Pre-test Quiz ?

Introduction

In a general sense, the term spondyloarthropathy refers to any disease involving the joints of the spine. However, it is more commonly used in the context of certain inflammatory rheumatological disorders and, in the presence of active inflammation, is referred to as spondyloarthritis. Examples of conditions that may involve the axial skeleton, whether as a primary presentation or in association with more systemic synovial inflammation, are listed in Table 1. This article highlights the two most common and significant pathologies, rheumatoid arthritis (RA) and ankylosing spondylitis (AS). These distinct disease entities commonly present with pain and without treatment can ultimately lead to instability. This reflects progressive cartilaginous destruction and ligamentous laxity in RA, or rigidity and loss of normal



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supporting structures in AS. In either instance, the pathology alters the dynamic stressors and biomechanical properties of the spine potentially leading to pain, rigidity, deformity, and neurological compromise.

An overview of the ligamentous and bony anatomy of the spine helps conceptualize the dynamic pathology that ensues with progressive inflammation (Figure 1). The craniovertebral junction comprises the base of the occiput, the atlas (C1), and the axis (C2). The atlas articulates with the occiput across the two horizontal condyles. The axis and atlas articulate laterally via two synovial joints. Anteriorly, the odontoid, a rostral extension of the body of C2, articulates with the anterior arch of the atlas through an intervening synovial lining. This

joint is stabilized by the cruciate ligament, which limits posterior displacement of the odontoid.¹ The subaxial spine can be segmented into two columns of support. Anterior to the spinal canal, the vertebral bodies are separated by the intervertebral disc and ‘braced’ by the anterior longitudinal ligament (ALL) and posterior longitudinal ligament (PLL). Posterior to the spinal canal, the paired, synovial-lined facet joints interlock at each spinal level.

Inflammation typically attacks the spine either within the synovial joints (synovitis), or at the interosseous tendinous attachments (enthesitis). Either pathology can result in bone erosion, laxity of tendons, abnormal segmental fusion, rigidity and a loss of normal spine biomechanics, resulting in instability and/

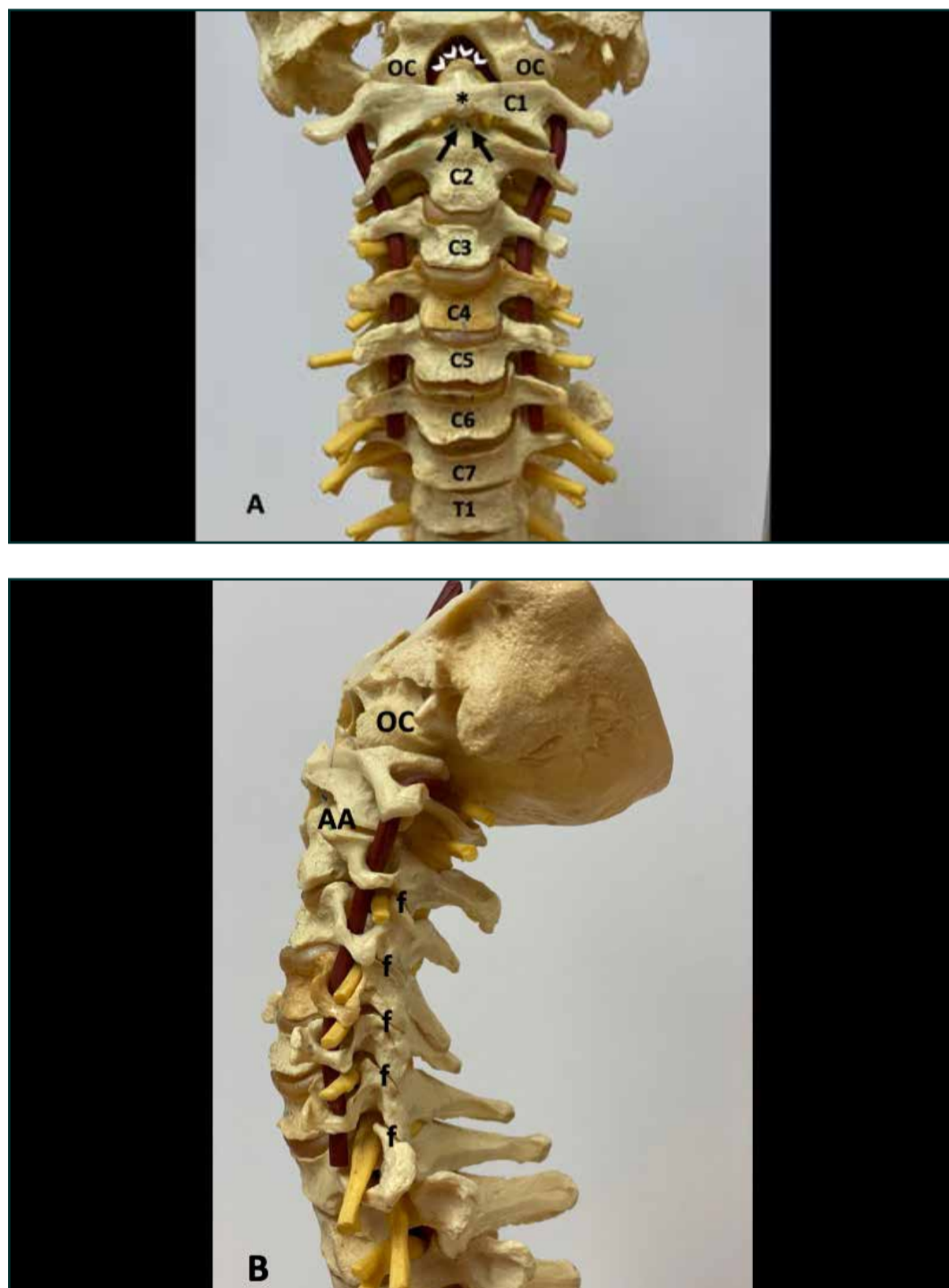
Table 1: Common spondylopathies and the incidence of spinal involvement

	Genetic link	Overall prevalence	% spine involvement	Pathology
Rheumatoid arthritis	HLA-DRB ⁽⁶⁾	0.5-1% ⁽⁷⁾	70-80% ⁽⁸⁾	Autoimmune synovial inflammation
Ankylosing spondylitis	HLA-B27 ⁽⁵⁾	0.5% ⁽³⁾	100% ⁽¹⁾	Primarily axial enthesitis, symmetric
Gout	Not described	4% ⁽⁹⁾	rare	Urate crystal deposition and synovitis
Pseudogout	Not described	0.5% ⁽¹⁰⁾	rare	Synovial calcium pyrophosphate deposition
Psoriasis and Psoriatic arthritis	HLA-B27 ⁽⁵⁾	3% ⁽¹¹⁾	25-30% ⁽¹²⁾	Primarily peripheral enthesitis, asymmetric



or fracture. Although axial back pain in the normal spine is usually benign, the presence of an inflammatory disorder increases the risk of significant pathology. Disease control, as well as monitoring and treatment of associated systemic complications

Figure 1: Anatomical demonstration of the cervical spine.



(A) Anterior view. Cervical vertebrae are numbered. OC denotes the Occipital Condyle. The * is on the anterior arch of C1 with the base of the odontoid marked with the black arrows and the tip of the odontoid marked with the white arrow heads. (B) Lateral view. The lateral atlantoaxial articulation (AA) and the posterior facet joints (f) are evident.

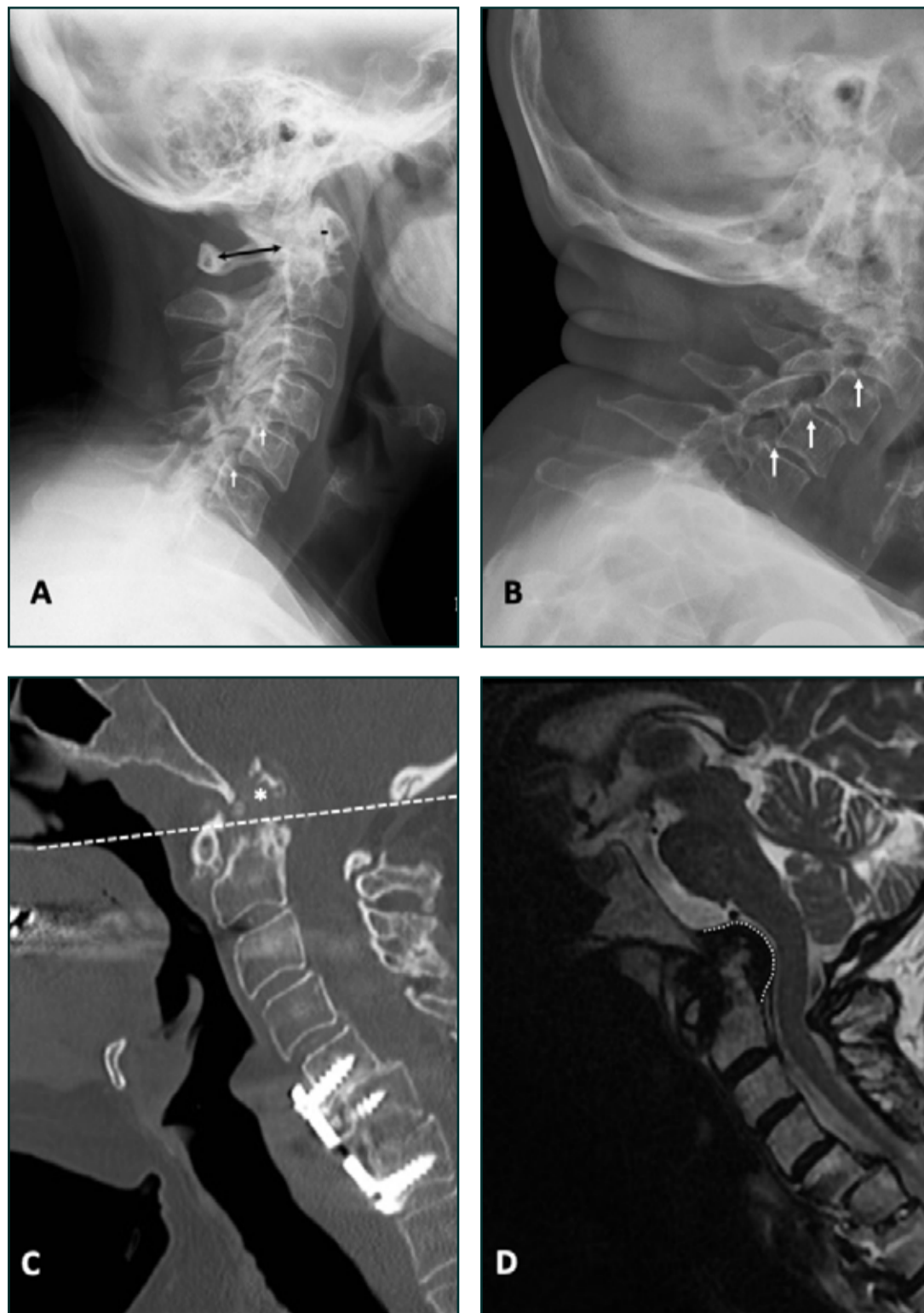
is vital. Rheumatoid arthritis and ankylosing spondylitis, both inflammatory arthropathies, are frequently associated with osteoporosis.² Respiratory disease is also common in these patients; in RA due to fibrosis from disease progression or in relation to treatment, in AS, as restriction of respiratory movement associated with reduced chest expansion.³ Although the systemic effects of these disorders are beyond the scope of this article, it is important to note that, although it can be seen in early disease, axial spine involvement typically correlates with overall disease severity and is proportional to inflammatory markers.⁴

Rheumatoid Arthritis

Rheumatoid Arthritis is typically a symmetrical inflammatory polyarticular arthritis, afflicting the peripheral joints of the hands and presenting after the fourth decade of life. Mainly a disease of synovial tissue, progressive inflammation causes destruction of the cartilage, erosion of adjacent bone, and ligamentous laxity. Within the cervical spine this leads to instability and migration of osseous structures. The articulation between the odontoid and the anterior arch of the atlas involves a complex synovial joint and is the most common site affected within the spine. The subaxial cervical spine is the



Figure 2: Serial images of a patient with RA demonstrating the progression of disease and need for routine imaging.



(A) Lateral radiograph demonstrating a normal ADI (short dash) and PADI (double arrowhead line) but early subaxial staircase deformity (white arrows). (B) lateral radiograph 3 years later with progression of staircase deformity and osteoporosis. (C) Sagittal CT reconstruction 2 years after anterior fixation of subaxial deformity. Erosion of the odontoid (*) and basilar invagination with the odontoid above McGregor's line (white dash) are evident. (D) T2-weighted sagittal MRI scan illustrating hypointense pannus (outlined by white dots) compressing the cervico-medullary junction. (RA – rheumatoid arthritis; ADI – atlanto-dental interval; PADI – posterior atlanto-dental interval)

second most commonly affected spinal location.¹³

Natural history and Pathophysiology

The degree of spine involvement in RA typically correlates with disease severity and level of therapeutic control. The presence of bone erosion in the peripheral joints increases the likelihood of spine involvement.⁸ Disease onset at a younger age, longstanding disease and higher inflammatory markers have been correlated with higher rates of spinal involvement. Most studies correlate the degree of spine involvement in longstanding disease (>10 years), however some studies have shown radiographic evidence of cervical spine involvement within the first years of diagnosis.⁸

The natural progression of the disease causes laxity in the atlantoaxial ligaments, leading to progressive loss of the normal articulation and the correct relationship of the craniovertebral junction. An increase in the atlanto-dental interval and settling of the dens within the foramen magnum can be observed. Progressive synovial inflammation within the atlanto-dental joint leads to “pannus” formation, inflammatory granulation tissue, which develops from the synovial lining of the odontoid process (Figure 2D). Inflammation and destruction of the cruciform ligamentous complex



from proteolytic enzymes, leads to laxity and C1-2 hypermobility. This pannus may cause a mass effect on the cervico-medullary junction of the spinal cord. Synovial inflammation may involve the joint between the lateral mass of the atlas and axis. Bony destruction of both the lateral mass and cruciate ligament leads to vertical and anterior subluxation.¹⁴ Advanced subluxation results in cranial settling with protrusion of the odontoid within the foramen magnum. Direct pannus compression or deformity and loss of normal cervical alignment can produce progressive neurological deficits. The subaxial cervical spine is the second most commonly affected axial site in RA. Progressive involvement of the facet joints and the associated ligamentous laxity leads to multilevel subluxation with a staircase deformity (Figure 2A,B).^{8,15}

Clinical presentation

Patients with RA and spinal involvement may be asymptomatic

with only radiographic findings or present with neck or occipital pain, stiffness, numbness or parasthesias in the upper extremities.¹⁶ Severe disease may lead to deformity, myelopathy and lower cranial nerve dysfunction. Ranawat et al. described a simple classification for clinical myelopathy for RA of the cervical spine.¹⁷ The four classes of successively more severe neurological compromise are shown in Table 2. A comprehensive neurological exam, assessing for objective signs of myelopathy, is important. Although, historically, RA specific clinical tests, such as the Sharp-Purser test (semi-flexion of the neck followed with passive extension produced by pushing on the patient's forehead while applying counter pressure to the C2 spinous process—a positive test produces myelopathic symptoms with flexion that resolve with passive extension) were used to assess atlantoaxial instability, the reliability, as well as the potential for harm, have been questioned and radiographic assessment is superior.^{18,19} Disease

Table 2: Ranawat Classification¹⁷ of neurological impairment in patients with spinal cord compression secondary to Rheumatoid Arthritis.

Ranawat Classification	Class 1	Class 2	Class 3a	Class 3b
	Neurologically intact	subjective weakness and dysesthesia	objective weakness ambulatory	objective weakness non-ambulatory



activity is also determined through calculating systemic joint burden as well as biochemical markers of inflammation such as ESR and CRP.

Radiology

Involvement of the cervical spine in RA is common but with adequate treatment and in the absence of advanced disease, it is usually mild with only radiographic findings. However, progression of the disease may lead to significant neurological morbidity so annual radiological screening is good routine practice (Figure 2). In the absence of clinical findings of cord compression or deformity, conventional x-ray radiography, including flexion

and extension views, is sufficient to highlight pertinent aspects of RA involvement.²⁰ Imaging of the cranio-cervical junction includes assessment of any abnormal translation of the bony structures, related to the degree of cartilaginous and ligamentous involvement. The cruciate ligament is assessed using the atlanto-dental interval (ADI). This is a horizontal measurement of the space between the posterior border of the anterior arch of C1 and the anterior border of the odontoid. A distance of greater than 3mm is indicative of cruciate ligament insufficiency and subluxation. A measurement of the canal diameter or posterior atlanto-dental interval (PADI), between the posterior border of the

Table 3: Common indication for surgical consultation

	Radiological evidence of	Clinical evidence of
Rheumatoid Arthritis	Vertical subluxation (basilar invagination/cranial settling) Atlantoaxial subluxation – ADI > 5mm – PADI < 14mm Spinal cord compression – Pannus formation – Canal stenosis	Myelopathy on clinical examination Pain refractory to conservative measures with evidence of spinal disease
Ankylosing Spondylitis	Acute fracture Chronic instability – Anderson lesion – Pseudarthrosis from old fracture	Neurological deficit in the setting of trauma Kyphotic deformity affecting quality of life (chin on chest deformity)

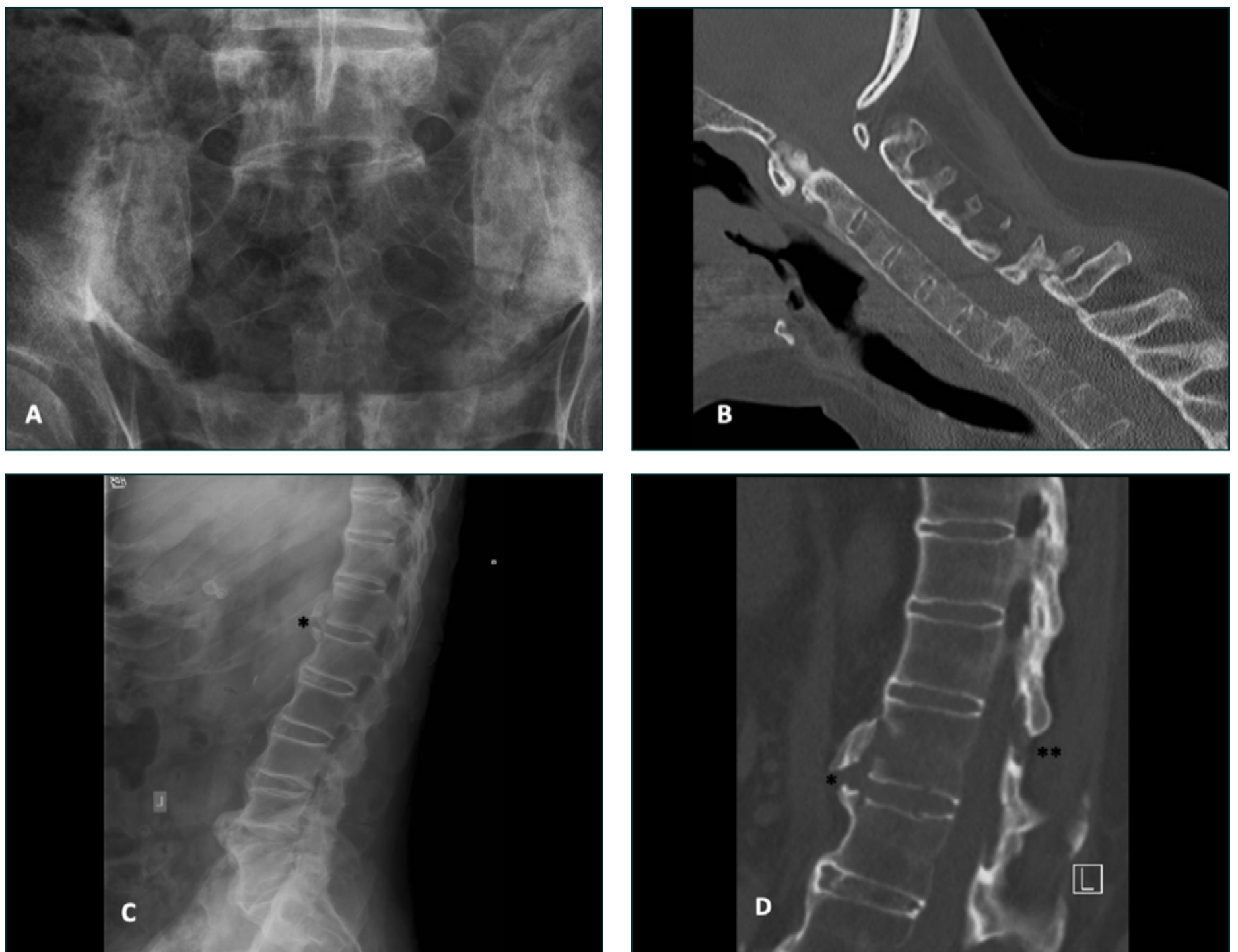


odontoid and the anterior border of the posterior arch of C1, of less than 14mm can be associated with spinal cord compression.

Destruction of the lateral mass, cranial settling and basilar invagination can be measured using different horizontal lines across the cranial base. McRae's line is drawn between

the anterior and posterior edge of the foramen magnum, the basion and opisthion respectively. Chamberlain's line is drawn between the posterior tip of the hard palate and the opisthion. McGregor's line is a modification that connects the hard palate and the inferior most aspect of the occipital bone (Figure 3C).

Figure 3: Imaging from patients with AS.



(A) Anteroposterior view of the pelvis demonstrating fusion of the sacroiliac joints. (B) Sagittal CT scan illustrating the typical 'bamboo spine' and a fracture at C7. (C) Lateral radiograph with an apparent anterior avulsion fracture (*), which upon CT imaging (D) clearly involves the posterior column (**) making this a highly unstable injury. (AS – ankylosing spondylitis)



When an abnormality is identified, further imaging (CT/MRI) and a referral to a spine surgeon are indicated. It's important to note that conventional x-ray will not show synovial disease or pannus formation while the CT may show bone erosion and joint destruction but may not show the soft tissue pannus causing compression. When cord compression is suspected, an MR is vital (Figure 2C,D).^{8,20,21}

Surgery in the context of RA and the Impact of Therapeutics

The incidence of surgical indications (Table 3) for RA has been decreasing. In a recent meta-analysis, Zhang et al. reported that due to advances in RA therapeutics and treatment regimens the prevalence of atlantoaxial instability has decreased from 36% in the 1970's to 24% in the 2000's.²¹ Longitudinal studies comparing novel treatments, such as biologic agents, have demonstrated a clear reduction in the incidence of cervical spine pathology, particularly atlantoaxial subluxation.^{22,23}

The most widely used Disease Modifying Anti-Rheumatic Drug (DMARD) is methotrexate. Other agents include leflunomide, sulfasalazine and hydroxychloroquine. Combinations of these medications provide the mainstays of treatment, immunomodulation and reduction

of inflammation. Novel treatment includes biologic agents, the most common is anti-TNF alpha, which target specific immune pathways. These biologics are typically used alone and require close monitoring of both the disease and the drug effect.²⁴ Their use is usually restricted to patients where DMARDs produce an inadequate response.

A common perioperative dilemma is: how to manage the immunomodulatory therapy? The increased risk of infection and/or poor healing that follow early reinstatement of immunosuppression must be balanced against the possibility of a disease flare-up. In the case of methotrexate, the majority of evidence demonstrates no difference in the rate of postoperative complications between those patients where it was withheld perioperatively or continued throughout, strengthening support for the latter approach.²⁵ For other DMARDs, such as leflunomide and hydroxychloroquine, the evidence is conflicting, and the decisions are best left to the surgical team and the treating rheumatologist.²⁵ For TNF alpha inhibitors, the evidence suggests no significant difference in complication rate if the drug is continued or withheld. However, the American College of Rheumatology Guidelines recommend discontinuing



biologic therapy at least one week perioperatively. In all cases, there are unique considerations so the risks and benefits need to be individualized.²⁴ Although therapeutic management has reduced the rate of significant cervical spine deformity, surgery still has a role with significant deformity and/or myelopathy in preventing morbidity and mortality.²⁶ Timely recognition and referral is prudent.

The goals of surgery, pain relief, decompression the spinal cord, and halting progression of deformity are achieved through arthrodesis (fusion) of the diseased joint and regression of odontoid pannus is typically observed after atlantoaxial fixation.^{27,28} Because of this, many authors advocate for early surgery, when disease progression is first seen. This must be balanced with the morbidity associated with loss of motion, specifically rotation, that results from C1-2 fusion. Delaying surgery until disease progression itself limits motion or until neurologic deterioration is imminent, however, may result in more postoperative complications related to advanced systemic disease.

Peri-operative management and rehabilitation are of the utmost importance and may be complicated by the presence of peripheral arthritis, muscle wasting, organ and systemic disease or treatment side effects and complications.²⁵ There is a

higher risk of infection in patients with RA, specific to the pathology as well as to immunomodulatory therapy. Many patients on long-term steroid therapy may require stress dosing. A comprehensive preoperative anesthesia assessment, to identify and mitigate surgical risks, is certainly warranted.

Seronegative Spondyloarthropathies

The seronegative spondyloarthropathies are a group of rheumatologic disorders that share clinical characteristics, including inflammatory sacroiliitis and enthesitis. This cluster of disorders includes ankylosing spondylitis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, and reactive arthritis. The term ‘seronegative’ reflects an absent rheumatoid factor on serologic testing. The HLA-B27 gene is found in about 90% of patients afflicted by ankylosing spondylitis.²⁹ We focus on AS, the most common of these entities to affect the spine.

Ankylosing Spondylitis

AS is a progressive ascending axial arthropathy, affecting entheses—the sites where tendons or ligaments insert into the bone—and leading to progressive ossification. Classically, it begins at the sacroiliac joints leading to obliteration of the joint (Figure 3A), before progressing up the spine.





CME

Post-test Quiz

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Clinical presentation

The usual presentation is the insidious onset of long lasting back pain sometime in the third and fourth decades of life. It is described as morning stiffness for more than half an hour, improving with movement but not with rest. Contrary to long-held teachings, the sexes are equally effected. There may be pelvic, typically alternating buttock, pain. NSAIDs produce a good response.^{3,30} The clinical assessment of a patient with AS includes measuring the degree of spinal stiffness as well as the amount of kyphosis. The Schober test measures the degree of flexion in the lumbar spine while measuring the occiput to wall distance assesses the degree of kyphosis and the loss of extension in the cervicothoracic spine. With severe kyphosis patients may be unable to achieve level gaze. With further progressive rigidity and kyphosis a restrictive lung disease pattern can develop, reflecting the need to assess the degree of chest expansion and auscultate for aortic valve insufficiency.³ Although serological markers such as rheumatoid factor are negative, inflammatory markers, such as CRP may be high.³¹

The mainstay of treatment is physiotherapy for activity modification and exercise to minimize deformity and NSAIDs to provide symptomatic relief.³² The use of targeted biologic agents, including against tumor necrosis

factor (TNF), IL-17 and IL-23, have been shown to inhibit disease progression, both clinically and radiographically.³³

Radiology

Radiographically, the progressive inflammation and ossification of entheses in AS is seen as bridging bone between spinal segments. Early radiographic findings include obliteration of the sacroiliac joints (Figure 3A). As the disease progresses up the spine, the bridging ossification across the vertebral endplates produces the appearance of a 'bamboo spine' (Figure 3B). As a consequence of successive segmental fusion and rigidity, a progressive kyphosis develops. Occasionally a delay in the ankylosis of an adjacent segment, or a stress fracture with delayed healing, may result in a pseudarthrosis, termed an Andersson lesion, traversing a vertebral body or across an intervertebral disc space. The pseudarthrosis allows movement within rigid segments and may become a point of translation and significant instability.³⁴ In AS the risk of vertebral fractures is significantly greater than the risk of fracture in a peripheral long bone.³⁵ Owing to unrecognized three column involvement within the ossified spine, seemingly benign fractures can be very unstable (Figure 3C,D). Radiographic analysis of all patients with ankylosing spondylitis after





SUMMARY OF KEY POINTS

1. Inflammatory arthritis from multiple etiologies may affect the spine with different patterns and pathophysiology.
2. Rheumatoid arthritis is a disease of synovial inflammation and in advanced disease leads to synovitis within the atlanto-dental articulation and the facet joints of the spine.
3. If left untreated atlantoaxial subluxation, cranial settling and pannus formation may lead to spinal cord and lower medullary compression.
4. Seronegative arthropathies leads to an enthesitis of the spine, usually starting in the sacroiliac spine and ascending with progressive ossification.
5. As a consequence of pathological alteration of the spine biomechanics, trauma in the setting of ankylosing spondylitis leads to different fracture patterns with a high chance of instability even after minimal trauma.

trauma is recommended. Since these fractures commonly involve an ossified disc space, plain radiographs may not reveal the extent of the injury and CT imaging, especially in the thoracic spine where interpretation can be challenging, is warranted in the majority of cases.³⁶

AS and trauma

As a consequence of the altered biomechanics, traumatic spinal

injury in AS has different fracture patterns and implications for stability when compared to a fracture in the normal spine. Fractures often occur following minimal trauma and the majority follow a horizontal, trans-vertebral or trans-discal pattern. The risk and degree of osteoporosis is significantly increased, a fact that must be considered in any surgical management. The ankylosed spine is prone to fracture and the



CLINICAL PEARLS

1. Early and adequate treatment of rheumatoid arthritis can prevent advanced atlanto-axial disease, deformity and neurological injury.
2. Even minimal trauma to the spine in a patient with ankylosing spondylitis has a high risk of instability and neurological injury; detailed imaging is always warranted.
3. With the advent of modern disease modifying agents for the treatment of spondyloarthropathies, the requisite for surgery has decreased but there remain important indications.



lengthy rigid sections on either side of the break greatly increase the instability.³⁷ Fractures in the AS spine are also more often associated with an epidural hematoma, which can cause delayed neurological deterioration. Frequent repeated neurological examination are necessary.

Surgical Considerations

Given the high risk of instability, any spinal fracture in AS, even with a trivial radiographic appearance, should be referred to a spine surgeon for assessment (Table 3). Surgery, if required, is intended to prevent significant translation across the fracture, avoid neurological compromise and prevent a pseudarthrosis. This usually requires an instrumented arthrodesis spanning multiple levels on both sides of the fracture. Identifying an Andersson lesion is reason for a surgical consult although there is no consensus regarding the treatment and the approach is on a case-by-case basis. Lastly, deformity correction via osteotomies and fixation, in either the lumbar or lower cervical spine, can play a significant role in improving quality of life of AS patients with severe kyphosis.

Conclusion

Inflammatory arthropathies commonly affect the spine via synovitis or enthesitis. Clinical presentation is most commonly

axial pain at the site of the inflammation. Disease progression can lead to worsening pain, neurological compromise, focal instability or severe, progressive, disabling kyphotic deformity. DMARDs and biological agents have significantly improved disease control and, as a result, reduced the incidence of severe, advanced disease in both rheumatoid arthritis and ankylosing spondylitis. Although required less commonly, surgery remains an important consideration in cases of trauma, myelopathy or disabling deformity.

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