RESEARCH PAPER

Axial Spondyloarthritis and Metabolic Disease: A Clinical Interplay of Systemic Inflammation and Cardio-Metabolic Risk

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ABSTRACT
Non-radiographic axial spondyloarthritis (nr-axSpA) represents an early subset of axial spondyloarthritis characterized by absence of sacroiliac joint changes on radiographs but detectable inflammation on MRI. Increasing evidence links nr-axSpA to systemic metabolic disturbances driven by chronic inflammation, reduced physical activity, and adipose dysfunction. This case underscores the systemic and metabolic implications of nr-axSpA. We report a 38-year-old male with chronic inflammatory back pain, progressive restriction of spinal mobility, obesity, and newly developed hypertension. Despite prior suboptimal management with NSAIDs, further evaluation revealed HLA-B27 positivity, with MRI-confirmed sacroiliitis consistent with nr-axSpA. The patient was also known diabetic and had Class II obesity (BMI 35.9 kg/m²). Following initiation of adalimumab (40 mg s/c every 2 weeks) alongside antihypertensive and antidiabetic therapy, the patient demonstrated significant symptomatic and functional improvement over follow-up. Non-radiographic axial spondyloarthritis is a systemic inflammatory condition often intertwined with obesity, hypertension, and diabetes. Chronic inflammation mediated by TNF-? and IL-17 promotes insulin resistance, endothelial dysfunction, and hypertension, while pain-induced inactivity and obesity aggravate disease activity and cardiovascular risk. Early recognition, metabolic risk assessment, and multidisciplinary management are essential to improve long-term outcomes and reduce cardiovascular morbidity in these patients. Biological therapy at the outset may offer dual benefits: disease control and mitigation of cardiometabolic sequelae.

Keywords: *Non-radiographic axial spondyloarthritis, Ankylosing Spondylitis, HLA-B27, Hypertension, Obesity, Diabetes mellitus, TNF-α, Adalimumab, Liraglutide, Cardiometabolic risk*
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INTRODUCTION

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Axial spondyloarthritis (axSpA) is a chronic immune-mediated inflammatory disorder of the axial skeleton, marked by inflammatory back pain and progressive spinal stiffness. It includes two entities: radiographic axSpA (ankylosing spondylitis) and non-radiographic axSpA (nr-axSpA), distinguished by the presence or absence of radiographic sacroiliitis. As per the Assessment of SpondyloArthritis International Society (ASAS) criteria, nr-axSpA is characterized by clinical and imaging evidence of inflammation without structural damage on X-rays.

The pathophysiology of axSpA is multifactorial, involving HLA-B27–mediated immune dysregulation, TNF-α and IL-17A pathway activation, and mechanical stress at entheses, leading to both local and systemic inflammation. Recent studies report higher rates of metabolic syndrome, insulin resistance, hypertension, and obesity among patients with axSpA, linking chronic inflammation with cardiometabolic dysfunction. Cytokines and adipokines (e.g., TNF-α, IL-6, leptin) promote endothelial dysfunction and altered glucose metabolism, while restricted mobility further worsens obesity and cardiovascular risk.

We present a case of nr-axSpA in a middle-aged male with chronic inflammatory back pain and subsequent obesity, hypertension, and diabetes mellitus. This case underscores the underrecognized association between inflammatory spondyloarthritis and metabolic comorbidities, highlighting the need for early biologic therapy and comprehensive metabolic screening.

CASE REPORT

A 38-year-old society manager, resident of Pune, presented to OPD with complaints of;

- Chronic lower back pain, since past 36 months

- Restriction in mobility, since past 28 months

- Weight gain, since past 24 months

The lower back pain, was dull aching in nature, worsening upon rest, and improving on activity. There was no associated paresthesia, motor/sensory loss or bowel/bladder involvement.

8 months later, patient developed painful restriction in his range of motion, forcing him to transition his from truck driving to a desk-job.

4 months following this, patient started noticing incremental weight gain, worsening because of physical inactivity, owing to increased back ache and reduced mobility.

6 months later, upon hospital visit, patient was found to have a blood pressure of 180/100mmHg, following which he was started on antihypertensives.

There was no history of fever, joint pain, incoordination or involuntary movements.

The patient is a known diabetic since last 2 years, on OHAs, with good glycemic control. There is no other significant past medical, surgical or any drug allergy history obtained.

General physical examination findings were unremarkable, save for BMI of 35.98 kg/m2 and blood pressure of 170/110mmHg.

Upon neurological examination; there were no abnormalities noted in higher mental functions, motor or sensory system, cerebellar function, or cranial nerve examination. However, there was spinal tenderness present over L2 to L5 vertebrae. The Schober's test could not be performed by the patient, due to painful restriction of forward bending motion. [Figure 1]

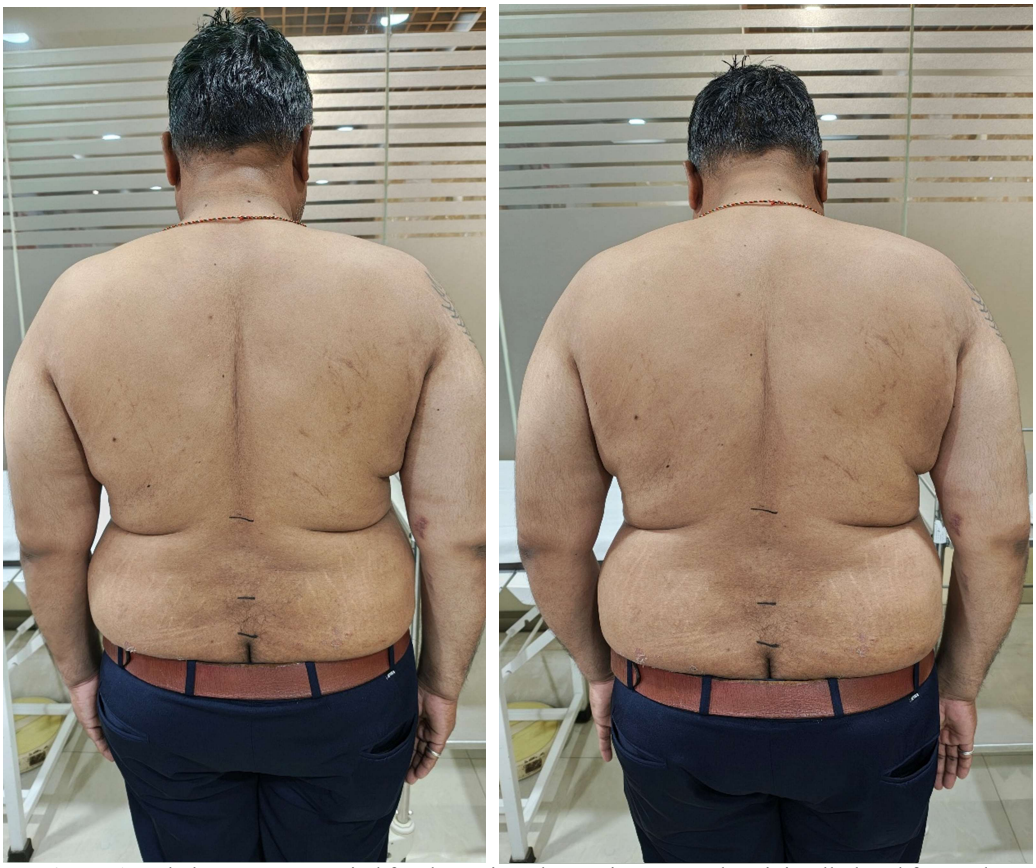

Figure 1: Schober's test was tried for the patient, but patient can only minimally bend forwards

Rest of systemic examination was unremarkable.

The laboratory and radiological investigations are summarized in tables 1 and 2. Written informed consent was obtained for anonymized patient information to be published in this article.

Lab Investigations [Table 1]

Lab Investigation	Value	Lab Reference Value
Haemoglobin	12.2 g/dL	13.2 – 16.6 g/dL
Total Leucocyte Count	8,200 cells/µL	4000 – 10,000 cells/µL
Platelet Count	199,000 cells/µL	150,000 – 410,000 / µL
Liver and Renal Function Tests, S. Electrolytes, Urine Routine	Normal	
HBsAg, Anti HCV, HIV	Negative	
HLA B 27	Positive	
ESR CRP	30 mm/hr 141.79 mg/L	<15 mm/hr <5 mg/L
S. Calcium S.Magnesium S. Phosphorus	8.2 mg/dL 1.93 mg / dL 3.3 mg/dL	8.6 – 10.2 mg/dL 1.6 – 2.6 mg/dL 2.4 – 5.1 mg/dL
S. Cortisol (8am) S. Cortisol (4pm)	16.7 7.9	3.7 to 19.4 microg/dL 3.7 to 19.4
HbA1c	6.4 %	4 – 5.6 %
BSL Fasting	106 mg/dL	
BSL – Post Prandial	146 mg/dL	
NT Pro BNP	140.3 pg/mL	<125 pg/mL
ANA Blot ANA IF	Ku positive Antibody against cell nuclei – Weak positive, Nuceloplasm speckled	
Thyroid Function Test	Normal	

S. Homocysteine	14.81 µmol/L	5.08 – 15.39 µmol/L
S. Total Cholesterol	186 mg/dL	< 200 mg/dL
HDL Cholesterol	36 mg/dL	> 50mg/dL
S. Triglycerides	116 mg/dL	< 150mg/dL
VLDL Cholesterol	23 mg/dL	< 30mg/dL
LDL Cholesterol	136 mg/dL	< 100mg/dL
Fundus Examination	No evidence of retinopathy / any ischemic changes	

Radiological Investigations [Table 2]

USG (A+P) (8/10/2025)	• Borderline hepatomegaly with Grade I fatty liver Excessive bowel gases present
MRI WSS with Dedicated LS Spine (10/10/2025)	• Mild straightening of lumbar spine - likely due to paraspinal muscle spasm. Mild scoliosis of lumbar spine with convexity to left • Mild central wedging involving superior end plates of L3, L4 and L5 vertebral bodies. • Small marginal osteophytes at multiple lumbar vertebral levels • Focal small triangular T1/ T2 hyperintense signal involving anterosuperior corners of L1, L2, L5 and S1 vertebral bodies and anteroinferior corner of L5 vertebral body - likely represent Romanus lesions. • Abnormal subchondral marrow edema involving right L2/L3, L3/L4, L4/L5 & L5/S1 facetal joints and left L4/L5 & L5/S1 facetal joints Mild adjacent soft tissue edema - Features likely represent facet joint arthropathy (inflammatory pathology). • Clumping of cauda equina nerve roots at L2, L3, L4 and L5 vertebral levels - likely represent: ? arachnoiditis (Figure 2) • L4-L5 intervertebral disc shows mild posterior disc bulge indenting ventral thecal sac however with no obvious nerve root compression. • Visualized portions of bilateral sacroiliac joints reveal right sided acute sacroiliitis involving posterosuperior aspect of right sacroiliac joint with mild adjacent soft tissue edema. Fatty metaplasia involving sacral and iliac articular surfaces of left sacroiliac joint and rest of right sacroiliac joint. CT correlation reveals areas of ankylosis involving bilateral sacroiliac joints. • Whole spine screening reveals: Mild straightening of cervical spine - likely due to paraspinal muscle spasm. Small marginal osteophytes at multiple cervical and thoracic vertebral levels. Disc desiccation at multiple cervical intervertebral disc levels. • Focal small triangular T1/ T2 hyperintense signal involving multiple cervical and thoracic vertebral body corners - likely represent Romanus lesions. • Syndesmophytes at D4/D5 and D8/D9 levels

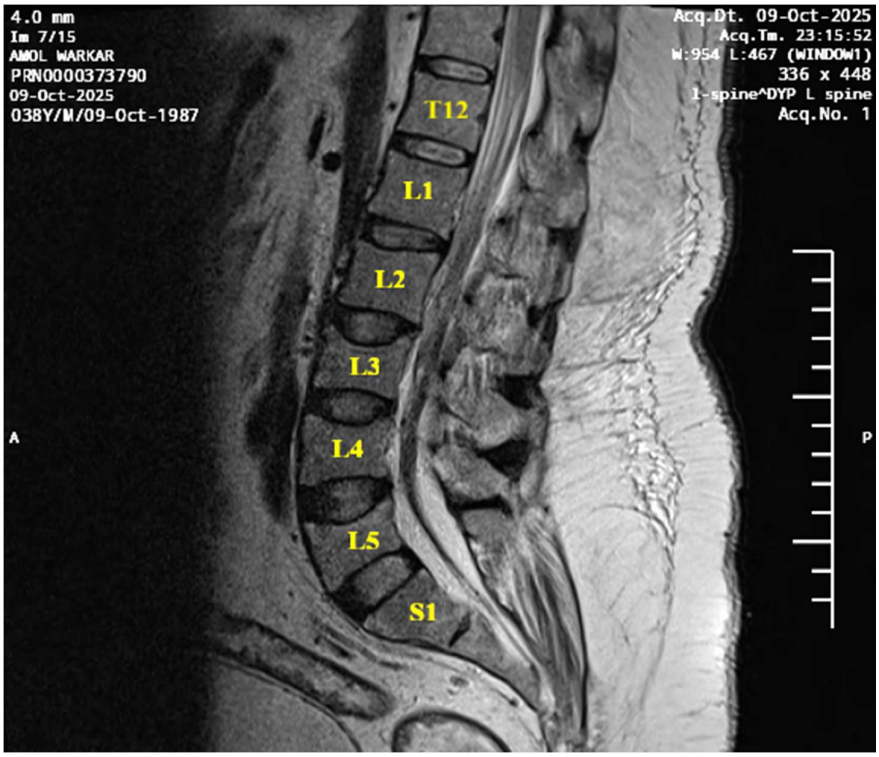

Figure 2 - Clumping of cauda equina nerve roots at L2, L3, L4 and L5 vertebral levels – likely- ?Arachnoiditis

In preliminary blood investigations, we detected HLA B27 positivity. This along with radiological findings on MRI of spine, confirmed our clinical suspicion of Axial Spondyloarthritis. In keeping with absence of sacroilitis on radiograph and its evidence on MRI, we confirmed our diagnosis of

- Non-Radiographic Axial Spondyloarthritis (Nr-AxSpa).
- Obesity with Diabetes Mellitus and Hypertension

Treatment given in Hospital [Table 3]

NSAIDs	Cap. INDOMETHACIN Sustained Release – 75mg – p/o – 0-0-1 x 2 weeks
Supportive Measures	Physiotherapy was initiated for the patient
Obesity Management (as per Endocrinology Advice)	Inj LIRAGLUTIDE – 0.3mg – s/c – 1-0-0 x 5 days - 0.6mg – s/c – 1-0-0 x 15 days - 1.2mg – s/c – 1-0-0 x 15 days Dose adjustment upon follow up
OHAs	Tab. DAPAGLIFLOZIN – 10mg – p/o – 1-0-0 Tab. METFORMIN – 500mg – p/o – 0-0-1
Anti-Hypertensive	Tab. AMLODIPINE – 5mg – p/o – 1-0-0 Tab. BISOPROLOL – 1.25mg – p/o – 0-0-1
Statin	Tab. ATORVASTATIN - 10mg – p/o – 0-0-1
Supportive Measure	Cap. UPRISE D3 – 60K IU – once a week x 8 weeks
TNF Inhibitor	Inj ADALIMUMAB – 40mg s/c – once in 2 weeks

Following clinical improvement, patient was discharged on Adalimumab in addition to the ongoing.

During follow up visits, there was noted a significant improvement in his symptoms and overall condition, along with improved spinal mobility and flexion. He is currently continued on Adalimumab (40 mg s/c once/2 weeks) and is on regular follow up. In last two months, patient has reported a weight loss of 9 kg, following the initiation of Liraglutide.

DISCUSSION

Spondyloarthritis (SpA) is broadly classified as axial or peripheral, depending on the predominant site of involvement. Axial Spondyloarthritis (AxSpA) is a chronic inflammatory disorder characterized by inflammatory back pain and includes two entities: Radiographic Axial Spondyloarthritis (Ankylosing Spondylitis, AS) and Non-Radiographic Axial Spondyloarthropathy (nr-axSpA).

According to the Assessment of Spondylo-Arthritis International Society (ASAS) criteria, inflammatory back pain is defined by ≥4 of the following [(1)]:

- age of onset <40 years
- insidious onset
- improvement with exercise
- no improvement with rest
- night pain improving upon arising.

Axial SpA includes: AS and nr-axSpA, distinguished by the presence or absence of sacroiliac changes on radiography, respectively. [2] About 10–40% of nr-axSpA cases progress to radiographic sacroiliitis within 2–10 years, with risk factors including male sex, HLA-B27 positivity, elevated CRP, MRI evidence of sacroiliitis, and smoking. [3]

The pathogenesis involves genetic predisposition (notably HLA-B27), immune dysregulation, gut microbiome alterations, and mechanical stress at entheses. Longitudinal imaging shows fat metaplasia at prior inflammation sites preceding ossification.

Imaging hallmark features include sacroiliac joint changes. Radiography detects structural abnormalities (narrowing, sclerosis, erosions, ankylosis), while MRI identifies early inflammation and fat deposition, making it essential for nr-axSpA diagnosis.

Bilgen, I. et al in Diagnostic Radiology [4] reported a case with long-standing ankylosing spondylitis (AS) showing radiological features linking arachnoiditis to cauda equina syndrome (CES), and concluded chronic adhesive arachnoiditis may contribute to CES in AS. Our patient had MRI features suggestive of both arachnoiditis and CES. (Figure 2 above)

Nayak et al. [5] reported a global MetS prevalence of 15.5% in AS. Similarly, Liu et al. found BMI as an independent MetS risk factor, with higher blood pressure, glucose, and triglycerides versus controls. [6]

In nr-axSpA, IL-17/TNF-α activation and HLA-B27–driven immune mechanisms promote insulin resistance, dyslipidemia and endothelial dysfunction. Elevated BMI correlates with greater disease activity, poorer biologic response, and higher rates of hypertension and insulin resistance — establishing a vicious cycle of inflammation → pain → inactivity → metabolic worsening.

Hypertension has been found as the most common comorbidity in AxSpA. Elevated CRP correlated with systolic pressure, while reduced spinal mobility reflected high inflammatory burden. Obesity further increased risks of hypertension, diabetes, and hypercholesterolemia via accelerated atherosclerosis. [7] Our patient, a known diabetic, developed hypertension during disease progression, consistent with this pattern.

Cardiovascular (CV) morbidity and mortality in AxSpA arise from chronic inflammation as well as traditional risk factors. While NSAIDs may raise CV risk, TNF-α inhibitors could be protective. [8] Hence, upon rheumatology advice, we started adalimumab for our patient.

Longitudinal studies confirm that obesity directly worsens disease activity via cytokine production and mechanical stress, beyond reduced exercise capacity. [9] Targeting obesity can therefore improve both disease outcomes and cardiovascular health. [10] Following the recommendation of the Endocrinology team, we initiated liraglutide therapy for our patient.

SUMMARY

- This case illustrates the coexistence of cardiometabolic comorbidities including obesity, diabetes, and hypertension in axial spondyloarthropathies, reflecting an expanded disease burden beyond the musculoskeletal system.
- Cytokine-driven inflammation, adipose-related metabolic derangements, compounded by inactivity and chronic medication exposure collectively heighten cardiometabolic risk.
- Timely initiation of biologic therapy can relieve inflammation, improve mobility, and mitigate metabolic and cardiovascular complications, particularly in nr-axSpA, where systemic inflammation may precede structural damage.

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TABLES and FIGURES

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