

Research Article**MRI Patterns of Bone Marrow Edema and Neuroinflammatory Associations in Seronegative Spondyloarthropathies****Sohail Ahmad¹, Shahzad Saeed², Zahid Nazir³, Faraz Ahmed⁴, Masood Uz Zaman Babar⁵, Shazia Aman⁶****Affiliations:**¹ Assistant Professor, Department of Neurosurgery, Wah Medical College.² Associate Professor, Department of Radiology, Punjab Institute of Neurosciences, Lahore.³ Senior Consultant Radiologist, Government Kot Khawaja Saeed Teaching Hospital, King Edward Medical University, Lahore.⁴ Assistant Professor, Department of Neurology, Isra University Hospital, Hyderabad.⁵ Assistant Professor, Department of Neurology, Isra University, Hyderabad.⁶ Senior Registrar, Department of Radiology, Sheikh Zayed Hospital, Lahore.**Corresponding author: Sohail Ahmad¹**

Abstract: Seronegative spondyloarthropathies (SpA) are chronic inflammatory disorders characterized by axial and peripheral joint inflammation, with bone marrow edema (BME) on MRI as an early imaging hallmark. This prospective study evaluated MRI patterns of BME and explored their association with systemic and neuroinflammatory biomarkers in patients with SpA. One hundred and ten participants (80 SpA and 30 controls) underwent high-resolution 3T MRI of the sacroiliac joints, spine, and selected entheses. Serum levels of IL-17, TNF- α , and neurofilament light chain (NfL) were quantified using ELISA assays. BME was detected in 85% of SpA patients, predominantly at subchondral sacroiliac regions (78%), vertebral corners (65%), and enthesal insertions (54%). Distinct MRI distribution patterns were observed: diffuse subchondral BME in ankylosing spondylitis, patchy enthesal BME in psoriatic arthritis, and focal reactive lesions in undifferentiated SpA. Mean IL-17 and TNF- α levels were significantly elevated in all patient groups compared to controls ($p < 0.001$), with strong correlations between BME volume and cytokine concentrations ($r = 0.78$ for IL-17; $r = 0.71$ for TNF- α). Neurofilament light chain levels were elevated in 42% of patients and correlated with total BME score ($r = 0.69$, $p < 0.001$), suggesting subclinical neuroinflammatory activity. These findings reveal distinct MRI phenotypes of BME across SpA subtypes and highlight neuroinflammatory markers as potential indicators.

Keywords: bone marrow edema, seronegative spondyloarthropathy, MRI, neuroinflammation

Introduction

Seronegative spondyloarthropathies (SpA) comprise a heterogeneous group of chronic inflammatory rheumatic disorders that primarily affect the axial skeleton, sacroiliac joints, and entheses. The spectrum includes ankylosing spondylitis, psoriatic arthritis, reactive arthritis, inflammatory bowel disease-associated arthritis, and undifferentiated SpA. Although they share common clinical, genetic, and immunopathological features, their radiological manifestations differ in distribution, extent, and chronicity. Magnetic resonance imaging (MRI) has emerged as the most sensitive modality for detecting early inflammatory changes, particularly bone marrow edema (BME), long before structural lesions such as sclerosis or ankylosis appear.¹⁻⁵

Bone marrow edema represents a histopathological correlate of inflammatory cell infiltration, vascular congestion, and osteitis within subchondral bone. MRI can visualize BME as hyperintense signals on short tau inversion recovery (STIR) or fat-suppressed T2-weighted images and as hypointense regions on T1-weighted sequences. The recognition of characteristic BME patterns in sacroiliac joints and spine allows for early diagnosis of axial SpA, which is crucial to prevent irreversible structural damage. However, the morphology and topography of BME lesions vary across SpA subtypes, and their correlation with systemic inflammatory and neuroinflammatory processes remains insufficiently characterized.⁶⁻⁸

Recent insights into SpA pathogenesis have highlighted the pivotal role of the IL-23/IL-17 axis and TNF- α -mediated inflammation in both peripheral and central compartments. In addition to synovial and enthesal inflammation, accumulating evidence suggests the involvement of neuroinflammatory pathways contributing to pain amplification and disease chronicity. Circulating neurofilament light chain (NfL), a marker of axonal injury, has been proposed as a sensitive indicator of neural involvement secondary to systemic inflammation. Integration of MRI findings with neuroinflammatory biomarkers may therefore refine disease characterization and identify subsets of patients with heightened neuroimmune activation.⁹⁻¹²

The neuroinflammatory dimension of SpA pathophysiology, although not yet fully delineated, is increasingly recognized as a contributor to pain persistence independent of structural lesions. Cytokines such as IL-17 and TNF- α have been implicated in modulating central pain sensitization,

blood–brain barrier permeability, and microglial activation. MRI studies have shown that marrow edema severity correlates not only with local inflammation but also with systemic inflammatory load, reflecting a bidirectional immune–neural axis. However, the association between quantitative MRI BME indices and neuroinflammatory biomarkers has not been comprehensively explored in seronegative spondyloarthropathies.

This study was designed to characterize MRI patterns of bone marrow edema in different SpA subtypes and to assess their correlation with systemic inflammatory cytokines and neurofilament light chain levels. The research aimed to delineate imaging biomarkers that reflect underlying neuroinflammatory activity and to provide insight into disease mechanisms bridging peripheral inflammation and central sensitization.

Methodology

This prospective observational study at Wah Medical College included 110 subjects recruited from the rheumatology and radiology departments of a tertiary care center over 18 months. Eighty patients fulfilled the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for seronegative spondyloarthropathies and were stratified as ankylosing spondylitis (n = 30), psoriatic arthritis (n = 20), reactive arthritis (n = 15), and undifferentiated SpA (n = 15). Thirty age- and sex-matched healthy volunteers without musculoskeletal or neurological disease served as controls. Exclusion criteria included rheumatoid arthritis, infection, malignancy, and prior biologic therapy within three months.

MRI scans were obtained using a 3.0 Tesla system with dedicated spine and pelvic coils. Sequences included T1-weighted, T2-weighted fat-saturated, and STIR imaging in axial and coronal planes. Imaging coverage extended from the sacroiliac joints to the thoracolumbar spine and major enthesal sites. Bone marrow edema was defined as hyperintensity on STIR with corresponding T1 hypointensity. BME lesions were graded semi-quantitatively (0–3 scale) for intensity and extent, and summed to generate a total BME score (maximum 36).

Blood samples were collected after MRI acquisition. Serum IL-17A, TNF- α , and neurofilament light chain (NfL) concentrations were measured using high-sensitivity ELISA kits. All samples

were analyzed in duplicate, and intra-assay variation was <6%. Neurological screening excluded overt neuropathic conditions.

Sample size was estimated using Epi Info 7 software, assuming an expected correlation coefficient of 0.5 between BME score and cytokine levels, with 90% power and 5% α error, yielding a required sample of 70 patients, increased to 80 to account for attrition.

Statistical analysis was performed using SPSS version 27.0. Continuous variables were expressed as mean $\pm$ SD. Intergroup comparisons used ANOVA with Bonferroni correction. Correlations were tested using Pearson's coefficient. ROC curve analysis determined biomarker thresholds predicting high BME burden. Statistical significance was defined as $p < 0.05$.

Results

Table 1. Demographic and clinical characteristics

Parameter	Controls (n = 30)	AS (n = 30)	PsA (n = 20)	ReA (n = 15)	Undiff SpA (n = 15)	p-value
Age (years)	39.6 $\pm$ 8.4	41.3 $\pm$ 9.1	42.1 $\pm$ 7.8	40.5 $\pm$ 6.9	38.9 $\pm$ 8.2	0.77
Males (%)	57	70	60	67	60	0.63
Disease duration (years)	—	6.8 $\pm$ 3.4	5.1 $\pm$ 2.7	3.9 $\pm$ 2.1	4.2 $\pm$ 2.5	0.04
BASDAI score	—	5.8 $\pm$ 1.2	5.1 $\pm$ 1.0	4.6 $\pm$ 0.9	4.8 $\pm$ 0.8	0.03

Patients were comparable in demographic distribution; disease activity indices differed modestly between subtypes.

Table 2. MRI bone marrow edema distribution and grading

Site	AS (%)	PsA (%)	ReA (%)	Undiff SpA (%)	p-value
Sacroiliac subchondral	78	62	48	55	0.02
Vertebral corners	65	48	33	40	0.03

Site	AS (%)	PsA (%)	ReA (%)	Undiff SpA (%)	p-value
Entheseal insertions	42	54	51	47	0.21
Mean BME score	18.6 ± 5.3	14.2 ± 4.7	10.9 ± 3.8	11.3 ± 4.1	< 0.001

BME was most prevalent and extensive in ankylosing spondylitis, followed by psoriatic arthritis.

Table 3. Correlation of BME score with inflammatory and neuroinflammatory biomarkers

Biomarker	Mean ± SD (SpA)	Controls	r (BME vs marker)	p-value
IL-17 (pg/mL)	44.7 ± 10.2	15.8 ± 4.9	0.78	< 0.001
TNF- α (pg/mL)	61.2 ± 13.5	21.3 ± 6.2	0.71	< 0.001
NfL (pg/mL)	32.8 ± 8.7	12.4 ± 3.2	0.69	< 0.001

Strong positive correlations were noted between BME severity and systemic as well as neuroinflammatory markers.

Discussion

This study identifies distinct MRI patterns of bone marrow edema across seronegative spondyloarthropathy subtypes and establishes strong correlations between imaging inflammation and neuroinflammatory biomarkers. The findings reinforce MRI's value as a sensitive biomarker of disease activity while highlighting the neuroimmune axis as a critical determinant of chronicity.¹³⁻¹⁴

The predominance of subchondral sacroiliac BME in ankylosing spondylitis reflects the early enthesitic and osteitic processes at the axial skeleton. In contrast, psoriatic arthritis demonstrated more peripheral and patchy BME distribution consistent with multifocal enthesal inflammation. Reactive arthritis and undifferentiated SpA exhibited intermediate patterns with focal reactive lesions and lower global BME scores, indicating transient inflammatory episodes.

Serum IL-17 and TNF- α levels showed robust association with BME burden, confirming their central role in driving osteitis and synovio-enthesal inflammation. The parallel elevation of neurofilament light chain levels and their correlation with MRI BME scores suggest subclinical

neuronal involvement mediated by systemic cytokine activity and central sensitization. Elevated NfL implies axonal stress possibly due to inflammatory cytokine-mediated neurotoxicity or blood–brain barrier dysfunction, supporting the emerging concept of neuroinflammatory contributions to pain persistence in SpA.¹⁵⁻¹⁸

Integration of MRI and biomarker analysis offers a multidimensional assessment of inflammatory activity, potentially improving disease monitoring and therapeutic stratification. The findings provide a rationale for targeting both peripheral and central inflammatory cascades to achieve sustained disease control.¹⁹⁻²⁰

Limitations include modest sample size and cross-sectional design, which preclude causality assessment. Longitudinal evaluation could elucidate whether changes in neuroinflammatory markers parallel MRI resolution following biologic therapy. Quantitative MRI techniques such as diffusion-weighted imaging and dynamic contrast enhancement may further refine assessment of marrow perfusion and cellular infiltration.

Overall, the combined use of MRI and neuroinflammatory biomarkers enables a more comprehensive understanding of disease biology, highlighting that seronegative spondyloarthropathies encompass systemic immune and neural inflammation beyond the joints.

Conclusion

Distinct MRI patterns of bone marrow edema characterize different seronegative spondyloarthropathy subtypes. The significant correlation of BME severity with IL-17, TNF- α , and neurofilament light chain levels underscores the role of neuroinflammatory mechanisms in disease pathogenesis. Integrating imaging and biomarker analysis can enhance diagnostic precision and guide targeted anti-inflammatory and neuroprotective therapies.

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