Five Cases of Non-radiographic Spondyloarthritis (nr-SpA) of Patients from a Tertiary Care Center in the Philippines: A Case Series

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ABSTRACT

Axial Spondyloarthritis (SpA) is a chronic inflammatory disease of the spine associated with the gene HLA-B27. Non-radiographic spondyloarthritis (nr-SpA), an early stage of axial SpA often goes unrecognized in many settings including the Philippines. We describe five Filipinos from a tertiary health care facility who fulfill the Assessment of SpondyloArthritis International Society (ASAS) 2009 criteria for non-radiographic SpA with the aim of increasing awareness of this disease in the Philippines. All five patients presented with chronic low back pain. There were two women and three men in this series. All had varying degrees of inflammatory back pain. Uveitis was diagnosed in four. HLA-B27 was positive in four patients. MRI findings confirmed sacroiliitis where plain radiographs of the sacroiliac joints were interpreted as normal. Treatment included non-steroidal anti-inflammatory drugs (NSAIDs), biologic disease-modifying anti-rheumatic drugs (DMARDs), anti-tumor necrosis factor (TNF), and anti-interleukin-17 (IL-17) antibodies. Among Filipinos, we recommend that in both male and female patients with symptoms of inflammatory low back pain and uveitis, evaluation for Spondyloarthritis particularly non-radiographic SpA should be undertaken. Early diagnosis and treatment will potentially prevent long-term irreversible joint and bone damage and disability of the spine and improve quality of life.

Keywords: Spondyloarthritis, spondylitis, ankylosing, sacroiliitis, case series

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INTRODUCTION

Axial Spondyloarthritis (SpA) is a chronic inflammatory genetic disease of the spine which may develop in individuals who carry the HLA-B27 gene. Non-radiographic spondyloarthritis (nr-SpA) is recognized as an early stage of axial SpA. It usually presents as chronic inflammatory back pain in the absence of radiographic changes but with magnetic resonance imaging (MRI) findings of bone edema, erosions, and fat metaplasia. Progression to radiographic Spondyloarthritis (r-SpA) is referred to as Ankylosing Spondylitis (AS). Nr-SpA has a prevalence of 0.5% in the general population.[1] Depending on the geographic region, the prevalence of nr-SpA in persons with chronic inflammatory low back pain ranged from 16.02% in Africa to 36.46% in Asia.[2] AS has a prevalence of 0.2-0.4% in China.[3] Early treatment during the non-radiographic stage has many advantages including less bone and joint damage, less musculoskeletal disability, better response to treatment, and longer drug-free remissions.[1,2]

The 1984 New York criteria for the diagnosis of SpA only included radiographic findings of sacroiliitis which identifies changes in the spine reflecting chronic, progressive, and

irreversible spine disease.[4] MRI provides better visualization of changes in the spine and the sacroiliac joint before the onset of radiographic changes. Hence, in 2009, the Assessment of SpondyloArthritis International Society (ASAS) added MRI in its criteria for axial spondyloarthritis.[5]

Axial SpA has been classified and staged by the ASAS into non-radiographic and radiographic SpA. MRI findings of inflammatory activity in the sacroiliac joints, together with clinical examination and C-reactive protein (CRP) levels are used to determine treatment and monitoring of disease activity. The pharmacologic modalities for axial SpA include NSAIDs, intralesional corticosteroids, and biologic DMARDs.

The disease has been extensively described in international literature but there is a dearth of data in the Philippines including its prevalence in the country.

We describe the demographics, clinical characteristics, and treatment modalities of five Filipinos collected from medical record reviews from January 2022 to March 2023 from a tertiary health care facility in the Philippines who fulfill the ASAS 2009 criteria for non-radiographic SpA with the aim of increasing awareness of this disease in our setting from 2022-2023 (Table 1). When contact information was available, verbal informed consent guided by the informed consent form was obtained by their primary rheumatologists as the study subjects were not available at the time of the medical records review.

CASE 1

A 54-year-old Filipino female while treated with topical corticosteroids for recurrent anterior uveitis affecting both eyes complained of chronic low back pain to her ophthalmologist since she was 38 years old. She had normal range of motion of her spine. No tenderness in the sacro-iliac joints and the occiput to wall distance was normal. Visual Analog Scale (VAS) for pain was 3/10, 10 being the most severe pain. She had a positive HLA-B27 gene test. Plain radiographs of the sacroiliac (SI) joint and pelvis were normal (Figure 1). Plain radiograph of the lumbosacral spine showed mild disc disease L5-S1. MRI of the sacroiliac joints confirmed mild bilateral sacroiliitis described as minimal osseous edema in both sacral and iliac bones along the sacroiliac joints (Figure 2). Bony erosions and osteophytes along with joint space narrowing were also noted along both SI joints and there was no abnormal fluid collection. MRI of the lumbosacral spine revealed abnormal signals at the corners of T11, L1, L3 and L4 vertebral bones which may be seen in Ankylosing Spondylitis. The chest radiograph showed scoliosis of the thoracic spine. 2D-echo was normal; C-reactive protein and ESR were normal. Interferon-gamma release assay (IGRA) and viral hepatitis panel were negative. She was treated with methotrexate for recurrent uveitis and TNF-inhibitor adalimumab for nr-SpA. The patient had resolution of her uveitis and low back pain with treatment.

CASE 2

A 31-year-old Filipino male complained of on-and-off low-back pain, cervical spine pain, and ankle pain, which were accompanied by easy fatigability. He denied any history of uveitis. He had normal lumbar spine flexion. He was worked up for spondyloarthropathy. He had a positive HLA-B27 test, normal inflammatory markers, and a normal radiograph of the lumbosacral spine and sacroiliac joints. The MRI scans illustrated mild sacroiliitis on the right, and focal marrow edema in the inferior left iliac bone. He was treated with NSAIDs and advised treatment with biologic DMARDs. His low back pain improved. A pain visual analogue scale (VAS) improved from 8/10 to 3-4/10.

CASE 3

A 46-year-old, Filipino female, presented with recurrent uveitis and recent onset low back pain and peripheral arthritis. No family history of ankylosing spondylitis. Her VAS for pain was 4/10, she had some right hip joint pain when the range of motion maneuvers were done. The rest of her musculoskeletal examination was normal. The Schober test, which measures a decrease in lumbar range in forward

Table 1. Summary of Characteristics of the Five Patients with Non-radiographic Spondyloarthritis

Patient	Gender	Age at disease onset, in years	Low back pain symptom duration in years	Peripheral Arthritis	Uveitis	Elevated ESR	Elevated CRP	Treatment	HLA-B27	Sacroiliac MRI Findings
1	Female	38	16	–	+	–	–	MTX, TNF	+	Bilateral sacroiliitis and osseous edema
2	Male	31	<1	+	–	–	–	NSAID	+	Sacroiliitis on right, marrow edema on left
3	Female	45	2	–	+	+	–	NSAID, TNF	–	Active sacroiliitis
4	Male	21	19	–	+	+	+	NSAID, IL17-A	+	MRI not done
5	Male	29	5	+	+	+	+	NSAID, TNF, IL17-A	+	MRI not done

flexion, was normal. A radiograph showed normal SI joints. MRI of SI joints revealed active sacroiliitis. Her HLA-B27 was negative. Inflammatory marker slightly elevated with ESR at 30 mm/hr. She fulfilled the ASAS 2009 criteria for non-radiograph SpA based on an MRI sacroiliitis, back pain of more than three months, age at onset less than 45 years old, uveitis, and a good response to NSAIDs. She was given NSAIDS and biologic treatment with IL-17A inhibitor or anti-TNF was offered. Her lower back pain resolved with NSAIDs and function was improved.

CASE 4

A 40-year-old, Filipino male complained of back pain since 2004, however consulted in 2022. He had a history of uveitis. He denied any family history of ankylosing spondylitis. His VAS pain scale for back pain was 5/10. Musculoskeletal examination revealed a positive Schober test, and pain on hip joint movement during flexion, abduction, and external rotation (FABER test). Plain radiograph revealed normal SI joints. There was no MRI of SI joints. The test for HLA-B27 was positive, ESR was elevated, and CRP was high at 32 mg/L. He fulfilled the ASAS 2009 criteria for non-radiographic SpA- HLA-B27 positive, back pain > 3 months, age at onset <45, uveitis, elevated CRP, and good response to NSAIDs. His current treatment is with an IL-17A inhibitor and an NSAID Etoricoxib. His disease activity using the BASDAI (Bath Ankylosing Spondylitis Disease Activity) score improved from 4.8 to 1.76.

CASE 5

A 34-year-old, Filipino male complained of back pain and ankle swelling in 2018. He had no family history of ankylosing spondylitis. Musculoskeletal examination revealed a swollen right Achilles tendon, a decrease in lumbar spine range of motion through a positive Schober's test, and limited range of motion of both hips. His VAS for back pain was 3/10. A plain radiograph showed normal SI joints. MRI of SI joints was requested but not done. The HLA-B27 was positive, elevated ESR, and CRP was high at 24 mg/L. He fulfilled the ASAS 2009 criteria for nr-SpA based on HLA-B27 positive, back pain > 3 months, age at onset <45, uveitis, good response to NSAIDs, and elevated CRP. He was treated with IL-17A inhibitor, Anti-TNF, and NSAIDs at different times of his disease course. His disease activity when given IL-17A inhibitor using the BASDAI score improved from 5 to 2.45. Treatment with anti-TNF likewise showed an improved BASDAI score from 5 to 3.05.

DISCUSSION

Nr-SpA is a subset of axial SpA in which the clinical manifestations and treatment are the same or similar to radiographic-SpA (R-SpA) or AS. In a narrative review of nr-SpA, certain differences are noted between Nr-Spa and R-SpA/AS. These include a reversal of male-to-female ratios wherein females have been shown to have the same prevalence, lower inflammatory markers, and less structural

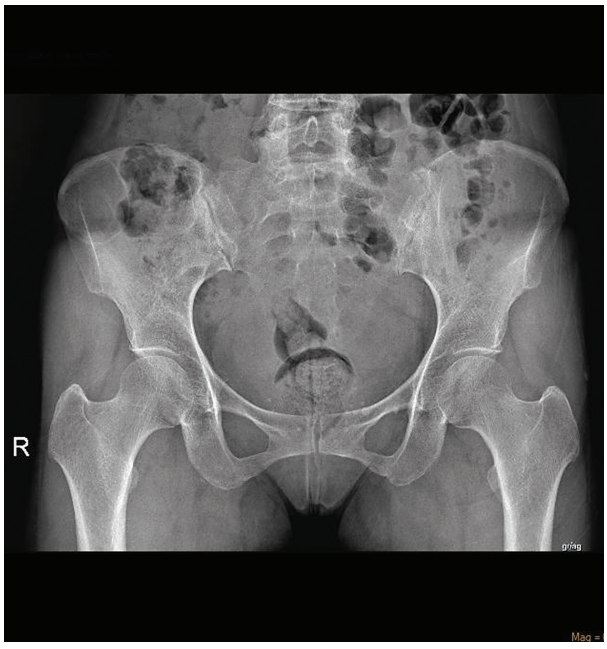

Figure 1. Plain radiograph of Case 1 showing normal sacroiliac joints.

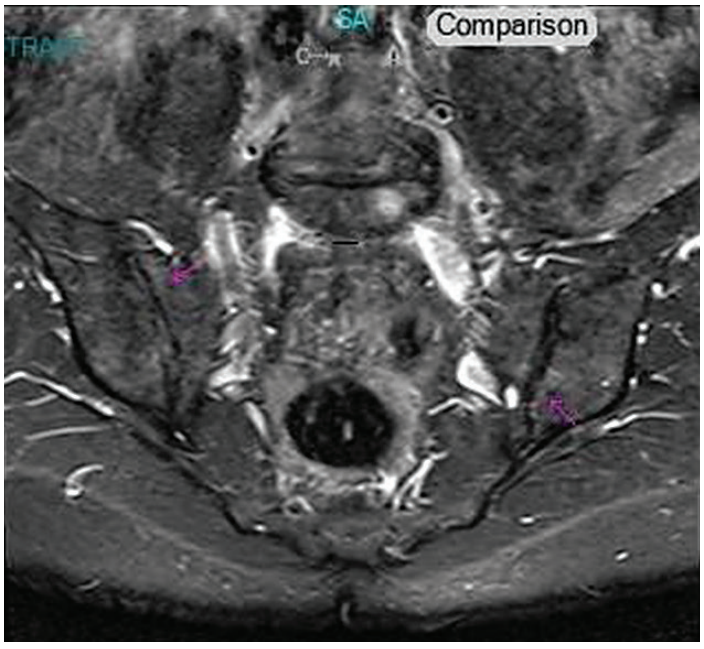

Figure 2. MRI of Case 1 showing bilateral sacroiliitis and minimal osseous edema.

damage resulting in better or less limitation of mobility and function.[6] Uveitis may be an early manifestation of this condition.

We described five Filipino patients with nr-SpA based on the 2009 ASAS criteria. The cases had similar presentations as those described in the literature.[6] The age of onset in this series of symptoms of inflammatory back pain (IBP) is in persons less than 45 years old. In this series, the onset of IBP ranges from 21-45 years old. In the report of Burgos-Varga,[2] among 266 individuals with nr-Spa, the age of onset was 34.75 ± 10.03 years.[2] This is comparable with the patients described.

The hallmark of AS and nr-SpA is inflammatory back pain. There are several differential diagnoses for chronic IBP which include malignant processes, infections, and gynecologic and intra-abdominal pathologies that need to be considered. For this series, all cases fulfilled the 2009 ASAS criteria for nr-SpA based on medical record review. All cases in this series presented with varying degrees of chronic inflammatory low back pain which prompted their physicians to have them evaluated for spondyloarthritis. Most (4/5) were positive for the gene marker HLA-B27. The study of Burgos-Varga[2] has shown that the HLA-B27 gene was positive in 71.43 % of their cohort of 266 patients with nr-SpA which was comparable to this case series wherein the majority were positive. Four of the five patients presented with uveitis and were first seen by ophthalmologists who referred them to a rheumatologist for further evaluation of chronic or intermittent back pain. Uveitis is an extra-articular manifestation of nr-SpA. From a meta-analysis by De Winter et al.,[7] the pooled prevalence of uveitis for nr-axSpA was 15.9%. This case series highlights its value as a presenting symptom that needs to be further evaluated.

In the patients where MRI was not done, diagnosis of nr-SpA was based on HLA-B27 positive tests. Although the MRI and/or HLA-B27 positive tests are included in the ASAS 2009 criteria for the diagnosis of nr-SpA, in locations where MRI scan or HLA-B27 are not available, plain radiographs of the sacroiliac joints showing normal findings in persons with symptoms of chronic inflammatory back pain will make this diagnosis a likelihood.

AS is primarily a disease in men but nr-SpA has similar prevalence in men and women. This case series reports three men and two women with nr-SpA. Although this is a small series, the male: female ratio is comparable to available literature. In the cohort of Tournadre et al.,[8] recent-onset SpA comparing men and women, their study population of 475 included 239 men and 236 women approaching an almost equal distribution. It reported 45.1% of men and 32.9 % of women having radiographic sacroiliitis. The majority of these patients therefore had non-radiographic sacroiliitis – men 54.9%, women 67.1%. In the study of Burgos-Varga,[2] among the Asian sub-group of 140 individuals with nr-SpA, the male-to-female ratio was 64.29% to 35.71%. Nr-SpA should therefore be considered in women who present with chronic low back pain as shown in the two women who presented with uveitis and chronic back pain.

ASAS/EULAR guidelines for the management of AS recommend the use of NSAIDs and Coxibs for symptomatic treatment and glucocorticoid injections to the local site of musculoskeletal inflammation may be considered.[9] It also recommends TNF-inhibitors and IL-17a blockade which has good evidence supporting large treatment effects for spinal pain and function especially in those with high disease activity. The recommended treatment for non-radiographic SpA is the same as radiographic SpA. For pharmacological treatment, most patients (4/5) were given NSAIDs and three received biological treatment with TNF blockade or IL-17a blockade. One patient had a combination of methotrexate with anti-TNF therapy. Methotrexate, a conventional DMARD, was given for uveitis. The favorable outcomes particularly with back pain for all the patients when given pharmacological intervention have shown the need for early intervention and potentially improving their quality of life and preventing disease progression and worsening. Non-pharmacological treatments are supported by evidence for maintaining function. These treatments were not mentioned in chart review and therefore this is one of the gaps in management of this patient population.

CONCLUSION

This case series describes nrSpA in five Filipinos from a tertiary health care facility and emphasizes certain points. Among these, uveitis is a common presenting manifestation. We recommend that all patients, both men and women, with low back pain, uveitis or a combination of these be screened for nr-SpA. This requires an increased awareness of this disease across various specializations, its similar prevalence in women compared with men as observed in this series, and the need for further imaging with MRI. To ensure early diagnosis and better treatment outcomes, there must be a multi-disciplinary collaboration between specialties including ophthalmologists, rheumatologists, spine specialists, and allied medical professionals.

FUTURE PLANS

To further describe this disease in the country and increase research efforts, we will recommend the creation of a registry that can be a multi-disciplinary database. This will standardize data collection for much-needed information about the gaps in the diagnosis and management of this disease.

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