Characteristics of post-traumatic-spondyloarthritis: a cross-sectional study from a single tertiary hospital

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Research article

Keywords: spondyloarthritis, post-traumatic, peripheral spondyloarthritis, triggering factor

Posted Date: July 3rd, 2019

DOI: <https://doi.org/10.21203/rs.2.11019/v1>

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Version of Record: A version of this preprint was published at Journal of Rheumatic Diseases on January 1st, 2021. See the published version at <https://doi.org/10.4078/jrd.2021.28.1.25>.

Abstract

Background Trauma has been proposed as a triggering factor of psoriatic arthritis (PsA), and the deep Koebner phenomenon was the suggested underlying mechanism. The relationship between spondyloarthritis (SpA) and trauma was only observed in PsA. This study investigated cases of SpA other than PsA that occurred after physical trauma and analyzed their clinical, laboratory, and radiologic features. Methods We retrospectively reviewed the medical records of 214 patients who visited our hospital due to a suspicion of SpA and grouped them into post-traumatic-SpA (PT-SpA) and non-post-traumatic-SpA (non-PT-SpA). Baseline characteristics were compared between the two groups. Results Peripheral SpA was more common in PT-SpA than in non-PT-SpA. Active inflammation on sacroiliac joint (SIJ) magnetic resonance imaging (MRI) was more common in non-PT-SpA (83.5% vs 54.5%, $P = 0.046$). The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) was significantly higher in the non-PT-SpA group (2.0 vs 0.0, $P = 0.007$). Symptom duration from the first SpA symptom to diagnosis tends to be longer in the non-PT-SpA group (2.0 vs 0.5 years, $P = 0.079$). Conclusion PT-SpA patients more frequently showed peripheral SpA, a less active inflammatory lesion on SIJ MRI, and a lower mSASSS score. Further studies are needed to clarify whether physical trauma has a direct/indirect role in the pathogenesis of SpA or merely confers an opportunity to recognize SpA symptoms.

Background

Spondyloarthritis (SpA) is characterized by a young-age onset, inflammatory back pain, and an association with human leukocyte antigen (HLA)-B27. SpA can be divided into two forms: axial and peripheral SpA according to the dominant symptom, axial joint arthritis or peripheral arthritis/dactylitis/enthesitis [1]. SpA can also subclassified to ankylosing spondylitis (AS), psoriatic arthritis (PsA), inflammatory bowel disease associated SpA, reactive arthritis, and undifferentiated SpA [1]. The pathogenesis of SpA is not fully evaluated yet, but several factors are suggested as the underlying pathologic mechanisms. A genetic background such as HLA-B27 showed an obvious relationship with SpA pathogenesis, and recently dysbiosis, disruption of normal flora, emerged as a novel environmental triggering factor of SpA [2]. Another environmental factor, biomechanical stress, has been suggested as one of the triggering factors of SpA; most of the evidence was based on clinical data of PsA and the mice model of SpA [3-5].

Environmental factors related to the pathogenesis of SpA are not well known. Smoking is a known aggravating factor, but the role of smoking on the onset of SpA is not clear [6]. Dysbiosis has been suggested as another environmental pathologic factor. Several studies showed altered microbiota in SpA by comparing fecal microbiota with healthy controls [7, 8]. Physical trauma, including lifting heavy loads, fracture, and contusion, has shown several consistent results on the occurrence of PsA [5, 9, 10]. Furthermore, mice models of SpA displayed physical loading aggravated enthesitis; and abnormal new bone formation was promoted in entheses when biomechanical stress was applied [4]. The underlying mechanism relating trauma and PsA was hypothesized as the 'deep Koebner' response [11]. However, clinical data concerning SpA occurring after physical trauma, other than PsA, has not been published. Finally, previous studies only included PsA patients from Western countries.

To establish the characteristics of post-traumatic-SpA (PT-SpA) other than PsA, in an Asian population, we investigated the clinical, laboratory, and radiologic findings of PT-SpA in Korea. We also compared the clinical, laboratory, and radiologic findings in PT-SpA and non-PT-SpA.

Methods

Patients

We retrospectively reviewed the medical records of patients who visited a tertiary hospital, Armed Forces Capital Hospital, for suspicion of SpA between January 2016 and April 2017. The inclusion criteria were as follows: (1) fulfilment of the Assessment of SpondyloArthritis (ASAS) classification criteria for axial or peripheral SpA [1, 12], (2) age 18 to 40 years, (3) initial diagnosis in our hospital, and (4) presence of initial radiologic findings and laboratory data. Peripheral SpA was diagnosed if the dominant symptoms were peripheral, such as peripheral arthritis, enthesitis, or dactylitis [12]. PT-SpA was defined when SpA

symptoms first occurred after definite physical trauma such as fracture, contusion, or excessive weight bearing exercise which required medical consultation [5, 9]. The exclusion criteria of the PT-SpA group were as follows: (1) having a prior history of inflammatory arthritis, (2) a history of arthralgia or back pain before the event. Furthermore, to distinguish SpA symptom from trauma related symptoms, we only included PT-SpA patients when the arthralgia lasted at least 3 months after the initial trauma related symptoms were relieved. A total of 214 patients were diagnosed with axial or peripheral SpA based on the ASAS classification criteria [1, 12]. Acquisition of informed consent was omitted because this study was based on retrospective chart review. All experiments were conducted in accordance with the Declaration of Helsinki (revised version of 2013). This study was approved by the Institutional Review Board of Armed Forces Medical Command (AFMC-17093-IRB-17-089).

Radiologic findings

Initial radiologic data included magnetic resonance imaging (MRI) of the sacroiliac joint (SIJ) and plain radiography of the SIJ, cervical spine, and lumbar spine. Active sacroiliitis (bone marrow edema in SIJ) was defined as high signal intensity on T2-weighted sequences sensitive to water [13]. The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) was measured using cervical and lumbar spine radiography and the existence of syndesmophytes was clarified [14]. The grade of sacroiliitis was scored according to the modified New York criteria [15].

Demographic, clinical, and laboratory profiles

Patients' clinical data and laboratory findings, including HLA-B27, were collected at the time of the first visit to our hospital. Elevation of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were defined as over 0.3mg/dL and 20 mm/hr, respectively. Items constituting ASAS classification criteria for axial or peripheral SpA were recorded. Groups were divided based on the presence or absence of a definite physical trauma before onset of SpA symptoms.

Statistical analysis

The Mann-Whitney test was used to compare continuous values between groups. Continuous variables were presented as median and interquartile range. Categorical variables, such as proportions, were compared between groups using the chi-squared test or Fisher's exact test. Values of $P < 0.05$ were considered statistically significant. All tests were performed with the software R (R for Windows 3.3.2; The R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline clinical characteristics, laboratory profiles, and clinical features of patients with PT-SpA

We found 12 patients with PT-SpA among 214 SpA patients. All PT-SpA patients were male. The clinical characteristics and items constituting the ASAS classification criteria for SpA of the 12 PT-SpA patients are presented in Table 1. The laboratory and radiologic findings from the 12 PT-SpA patients are summarized in Table 2. Eleven patients (91.7%) were positive for HLA-B27, and the CRP level was elevated in seven patients (63.6%).

Comparison between patients with PT-SpA and non-PT-SpA

Table 3 shows the comparison of clinical parameters and items constituting the ASAS classification criteria for SpA between PT-SpA and non-PT-SpA groups. Peripheral SpA was significantly higher in the PT-SpA than in the non-PT-SpA (25.0% vs 1.5%,

$P < 0.001$). Symptom duration from the first SpA symptom to diagnosis tends to be shorter in PT-SpA. No significant difference regarding the items of ASAS classification criteria was noted between the two groups.

Laboratory and radiologic findings were compared and summarized in Table 4. An active inflammatory lesion (bone marrow edema) on SIJ MRI was less frequent in the PT-SpA, and the mSASSS score was also lower in the PT-SpA than in the non-PT-SpA (54.5% vs 83.5%, $P = 0.046$, 0 vs 2.0, $P = 0.007$, respectively).

Discussion

The present study aimed to clarify the features of PT-SpA patients other than PsA and to compare the characteristics of patients with PT-SpA and non-PT-SpA. PT-SpA showed a higher prevalence of peripheral SpA than non-PT-SpA. Other SpA characteristics were similar between the two groups. An active inflammatory lesion (bone marrow edema) of SIJ was more frequent and spinal structural damage (mSASSS) was more severe in the non-PT-SpA group. Only one patient (Patient No.2 of PT-SpA) complained of the site where he was injured as the site of the first SpA symptom whereas others complained of the first arthralgia in a distant joint. This supports the hypothesis that preceding physical trauma could provoke the symptoms of SpA not only by direct biomechanical stress but also a systemic immune response such as 'deep Koebner' response [11].

Previous studies revealed an increased risk of PsA occurrence in patients with psoriasis (PsO) who experienced physical trauma [5, 10]. Another study showed lifting heavy loads had increased odds of PsA among PsO patients [9]. Recently, Tinazzi, I. et al. showed increased A1 pulley thickness in PsA patients compared with RA, PsO, and healthy controls [16]. The "Deep Koebner" phenomenon was suggested as an underlying mechanism that could explain how physical stress or trauma contributes to the occurrence of PsA in patients with underlying PsO [11, 16]. Although the precise mechanism of the 'deep Koebner' response is not elucidated, it might also explain the role of biomechanical stress on the pathogenesis of SpA other than PsA. Previous studies seeking a relationship between physical trauma and the occurrence of PsA were conducted in Europe and North America. Racial differences exist between Caucasians and Asians patients with SpA in that Caucasians with SpA have a higher prevalence of psoriasis than Asians [17-20]. Also, previous studies that revealed an association between physical trauma and SpA were limited by their inclusion of only PsA in the analysis [5, 9, 10, 16]. This study was the first performed in Asia and the first to include SpA other than PsA.

Entheses are the known target of musculoskeletal inflammation in the pathogenesis of SpA including PsA. In SpA patients, low-level mechanical stress on entheses might induce enthesitis. Activation of localized $\gamma\delta$ T cells and type 3 innate lymphoid cells of entheses may induce an immune response [21]. Mice models of SpA showed unloading of the hind limb attenuated enthesitis, peripheral arthritis, and abnormal new bone formation compared with weight bearing controls [4]. In this study, PT-SpA patients showed peripheral SpA and enthesitis more frequently than non-PT-SpA. This is consistent with the previous knowledge that physical stress/trauma might contribute to aggravation of peripheral arthritis and enthesitis in SpA. Although the underlying mechanisms of physical trauma in SpA occurrence have not been fully elucidated, based on this research, future studies might reveal the role of physical trauma in SpA pathogenesis, especially enthesitis and peripheral arthritis.

The present study has several limitations. First, the sample size of enrolled PT-SpA patients was small. However, this was the first study to enroll PT-SpA other than PsA, and in an Asian population. Second, all the PT-SpA patients included in the present study were male and young because the Korean army requires all male citizens to join. Therefore, our results may not apply to PT-SpA in female and elderly patients. Third, this study was cross-sectional and included only baseline data; thus, follow-up data were unavailable. The clinical course of PT-SpA was not demonstrated. Fourth, trauma was checked according to interview and electric medical record, the intensity of trauma was not measured. Finally, experiments to discover the mechanism whereby physical trauma effects SpA pathogenesis are not included. Therefore, whether physical trauma is a triggering factor in SpA pathogenesis or solely an opportunity to recognize SpA symptoms is unclear.

Conclusions

Physical trauma might play a direct role in the pathogenesis of SpA or might present an opportunity to recognize SpA symptoms in previously undiagnosed SpA patients. We evaluated characteristics of 12 cases of PT-SpA in SpA patients other than PsA in Korea for the first time. These PT-SpA patients had a higher prevalence of peripheral SpA, and active inflammation on MRI was less common than in patients with non-PT-SpA. The mSASSS score was lower in patients with PT-SpA. Further studies are required to clarify whether physical trauma has a direct pathologic role on SpA occurrence.

List Of Abbreviations

AS : ankylosing spondylitis

ASAS : Assessment of SpondyloArthritis International Society

CRP : C-reactive protein

ESR : erythrocyte sedimentation rate

HLA : human leukocyte antigen

MRI : magnetic resonance imaging

mSASSS : modified Stoke Ankylosing Spondylitis Spine Score

PsA : psoriatic arthritis

PsO : psoriasis

PT-SpA : post-traumatic-spondyloarthritis

SIJ : sacroiliac joint

SpA : spondyloarthritis

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Armed Forces Medical Command (AFMC-17093-IRB-17-089). Acquisition of informed consent was omitted because this study was based on retrospective chart review.

Consent for publication

Not applicable

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing of interests

The authors declare that they have no competing interest related to this manuscript.

Funding

None

Author's contributions

HKM designed the study, analyzed and interpreted the patient data, and wrote the manuscript. HC collected the patient data and analyzed the data. SHP designed the study, reviewed and commented for the manuscript. All authors read and approved the final manuscript.

Acknowledgments

None

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Tables

Table 1. Clinical and spondyloarthritis(SpA) features of PT-SpA patients

Patient	Trauma	First Symptom	Peripheral SpA	Peripheral arthritis	Dactylitis	Enthesitis (heel)	Uveitis	Psoriasis	Inflammatory Bowel disease	NSAID response	FHx. Of SpA
1	Weight bearing exercise	Back pain	-	+	-	-	-	-	-	-	-
2	Fall down	Buttock pain	-	-	-	+	-	-	-	+	-
3	Traffic accident	Buttock pain	-	-	-	-	+	-	-	+	-
4	Weight bearing exercise	Left inguinal pain	-	-	-	-	-	-	-	+	-
5	Weight bearing exercise	Back pain	-	-	-	-	+	-	-	-	+
6	Weight bearing exercise	Right ankle pain	+	+	-	+	-	-	-	+	-
7	Weight bearing exercise	Right buttock pain	-	-	-	-	-	-	-	+	-
8	Weight bearing exercise	Both knee, ankle pain	+	+	-	+	-	-	-	-	-
9	Sternum fracture	Right knee/ankle/foot, Left toe pain	+	+	-	+	-	-	-	+	-
10	Weight bearing exercise	Left buttock pain	-	-	-	-	-	-	-	-	-
11	Traffic accident	Back pain	-	-	-	-	-	-	-	+	-
12	Traffic accident	Back pain, Both knee pain, Left 3 rd -5 th finger pain	-	+	-	+	-	-	-	-	-

FHx: family history, NSAID: nonsteroidal anti-inflammatory drug, SpA: spondyloarthritis

Table 2. Laboratory data of PT-SpA patients

Patient	HLA-B27	ESR (mm/hr)	CRP (mg/L)
1	+	8	7.4
2	+	15	10.2
3	+	17	39.2
4	+	7	5.5
5	+	2	0.9
6	+	2	0.6
7	+	7	2.6
8	+		
9	+	55	20.1
10	+	2	8.2
11	+	30	36.0
12	-	2	0.8

CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, HLA: human leukocyte antigen

Table 3. Comparison of clinical and SpA features between PT-SpA and non-PT-SpA

	Physical trauma-related SpA (N=12)	Non related SpA (N=202)	<i>P</i>
Age	21.0 (20.0-25.0)	21.0(20.0-23.0)	0.789
Sex (Male, %)	12 (100.0%)	201 (99.5%)	1.000
Symptom duration (first SpA symptom to diagnosis, year)	0.5 (0.25-3.0)	2.0 (0.5-4.0)	0.079
Peripheral SpA	3 (25.0%)	3 (1.5%)	<0.001
Enthesitis (heel)	5 (41.7%)	50 (24.8%)	0.336
Uveitis	2 (16.7%)	38 (18.8%)	1.000
Psoriasis	0 (0.0%)	4 (2.0%)	1.000
Inflammatory bowel disease	0	0	1.000
CRP elevation	7 (63.6%)	112 (56.0%)	0.853
Alternating buttock pain	7 (58.3%)	110 (54.5%)	1.000
Good response to NSAID	7 (58.3%)	132 (65.3%)	0.855
Family history of SpA	1 (8.3%)	26 (12.9%)	0.990
Peripheral arthritis	5 (41.7%)	86 (42.6%)	1.000
Dactylitis	0 (0.0%)	3 (1.5%)	1.000

Table 4. Comparison of laboratory and radiologic findings between PT-SpA and non-PT-SpA

	Physical trauma-related SpA (N=12)	Non related SpA (N=202)	<i>P</i>
HLA-B27	11 (91.7%)	175 (87.5%)	1.000
ESR (mm/hr)	7.0 (2.0-16.0)	7.0 (2.0-18.0)	0.874
CRP (mg/L)	0.7 (0.2-1.5)	0.3 (0.1-1.5)	0.541
Sacroiliitis grade of right SIJ	2.0 (1.0-3.0)	3.0 (1.0-3.0)	0.315
Sacroiliitis grade of left SIJ	2.0 (1.0-3.0)	2.0 (1.0-3.0)	0.567
Active inflammation on SIJ MRI	6 (54.5%)	132 (83.5%)	0.046
mSASSS score	0.0	2.0 (1.0-16.0)	0.007
Syndesmophyte	0 (0.0%)	17 (12.5%)	0.886

MRI: magnetic resonance imaging, mSASSS: modified Stoke Ankylosing Spondylitis Spine Score, SIJ: sacroiliac joint