Chapter

The Clinical Characteristics and Treatment Status of Psoriatic Arthritis

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Abstract

Psoriatic arthritis (PsA) is a complex musculoskeletal disorder. Its clinical features include psoriasis, peripheral arthritis, spinal involvement, enthesitis, and dactylitis. Typically, skin lesions precede osteoarticular lesions, although osteoarticular lesions can precede skin lesions in some cases. This study aimed to investigate the onset pattern of PsA, the time interval between the occurrence of skin and osteoarticular lesions, and the treatment status of PsA. A total of 64 patients with PsA who had been assessed according to the CASPAR criteria were enrolled. Of those, 75% had a typical lesion onset pattern where skin lesions preceded osteoarticular lesions (skin leading) and 16% had an osteoarticular leading lesion pattern. The mean time interval between the onset of lesions in patients with the skin leading pattern was 14.2 years and that in patients with the osteoarticular leading pattern was 4.5 years. Non-steroidal anti-inflammatory drugs were prescribed to 39% of patients, conventional synthetic disease modifying antirheumatic drugs (DMARDs) to 64%, and biologic DMARDs to 51.5%. In conclusion, there were several cases where osteoarticular lesions preceded skin lesions in PsA; therefore, care should be taken with regard to oligo- or poly-arthritis patients with a negative rheumatoid factor without the presence of skin lesions.

Keywords: bDMARDs, CASPAR criteria, csDMARDs, obesity, psoriatic arthritis

1. Introduction

Psoriatic arthritis (PsA) is a complex musculoskeletal disorder that has the clinical features of psoriasis, peripheral arthritis, spinal involvement, enthesitis, and dactylitis [1, 2]. Typically, skin lesions precede osteoarticular lesions [1–6], although osteoarticular lesions precede skin lesions in some cases. In these cases, the diagnosis is difficult and often results in a delay in treatment. Regardless, the appropriate management of PsA requires early diagnosis. Classification criteria of PsA (CASPAR criteria) consist of established inflammatory articular diseases with at least 3 points from the following features: current psoriasis (assigned a score of 2), a history of psoriasis (a score of 1), a family history of psoriasis (a score of 1), dactylitis (a score of 1), juxtaarticular new

bone formation (a score of 1), rheumatoid factor negativity (a score of 1), and nail dystrophy (a score of 1). The CASPAR criteria have been reported to be useful in assisting clinicians in the diagnosis of PsA because of high sensitivity and specificity than any other criteria [7].

PsA in many patients is associated with obesity, diabetes, hypertension, metabolic syndrome, fatty liver, and an increased risk of cardiovascular events compared to that of the general population [8]. In a realistic orthopedic outpatient clinical setting, little is unknown about the clinical features and the treatment status in patients with PsA. Whether PsA is associated with obesity or lifestyle-related diseases remains unknown.

We investigated the clinical characteristics of PsA, such as the onset pattern of PsA, the interval between the occurrence of skin lesions and osteoarticular lesions, and the distribution of arthritis such as peripheral and axial lesions and enthesitis. In addition, we examined whether obesity, hypertension, or diabetes mellitus was significantly increased in patients with PsA. We also examined the treatment status for PsA.

2. Methods

This was a single-center non-interventional retrospective study that examined patients with PsA who were diagnosed by rheumatologists and dermatologists at our hospital between January 2010 and December 2018. All patients in this study satisfied the CASPAR criteria with a score of more than 3 points. A total of 64 consecutive cases were enrolled, and informed consent was obtained from each patient. This study was approved by Niigata University Medical and Dental Hospital Institutional Review Board (#2018–0418).

The patients were categorized and investigated according to the following PsA onset patterns: a skin rash that preceded the manifestations of arthritis (skin leading type), the osteoarticular lesion that preceded the manifestation of a skin rash (osteoarticular leading type), and the simultaneous onset of skin and osteoarticular symptoms (simultaneous type). For both the skin and osteoarticular leading types of PsA, we recorded the time between the presentation of the first and second symptoms. We also investigated the disease prevalence according to the lesion site, namely peripheral lesions (e.g., fingers, wrists, elbows, shoulders, toes, ankles, knees, and hips), axial lesions (e.g., cervical, thoracic, lumbar spines, and sacroiliac joint), and enthesitis (e.g., Achilles' tendon, plantar aponeurosis, quadriceps tendon, and patellar tendon).

When arthritis symptoms were present, painful areas were evaluated by radiography, which allowed us to confirm the presence of imaging findings typical of PsA (typical peripheral joint new bone formation, sacroiliac joint bone erosions, and syndesmophytes on the sacroiliac joint or spine).

Obesity was defined as a body mass index (BMI) ≥ 25, and the prevalence of comorbidities was assessed relative to that of the general population as reported in a survey conducted by the Ministry of Health, Labor, and Welfare of Japan [9]. The incidences of obesity and hypertension, diabetes mellitus, and other diseases such as dyslipidemia and chronic kidney disease were examined.

Furthermore, we classified the patients according to the treatments they had received, such as nonsteroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biological DMARDs (bDMARDs), prednisolone, and others.

2.1 Statistical analysis

The statistical analyses were performed using SPSS (Version 21, Tokyo, Japan). The Student t-test was performed for continuous variables, and Fisher's exact probability test was performed for categorical variables. A p-value <0.05 was considered to be statistically significant.

3. Results

Of the 64 patients with PsA who were enrolled, 49 were male and 15 were female patients. The patient characteristics are shown in **Table 1**. The mean age ± SD of the patients was 55.5 ± 12.9 years (range, 27–80 years), and the mean age at the onset of first symptoms was 36.2 ± 15.7 years (range, 3–70 years). The mean age of the onset of psoriasis (skin lesion) and the osteoarticular lesion was 36.2 years and 47.0 years, respectively. The mean time interval between the onset of skin and osteoarticular lesions was 11.3 years (range, 0–39 years). Regarding the CASPAR criteria, the percentage of confirmed items was 100% for current psoriasis, followed by rheumatoid factor negativity (92.4%), nail lesions (34.8%), juxta-articular new bone formation (25.8%), and dactylitis (16.7%); the mean CASPAR score was 3.75 points (range, 3–6 points).

Regarding the onset patterns of PsA, the skin leading type was dominant in 48 cases (75%), with 10 cases of the osteoarticular leading type (15.6%), followed by 6 cases of the simultaneous type (9.4%). The mean time interval between the presentation of the two different lesion types was 14.2 ± 10.2 years (range, 0.3–39.4 years) in the skin leading type and 4.5 ± 3.3 (range, 0.1–15.1 years) in the osteoarticular leading type. A statistically significant difference ($p < 0.001$) was observed between the

Demographic and clinical characteristics (n = 64)	**Value (range, %)**
Demographic characteristics	
Sex, male/female	49/15
Age	55.5 ± 12.9 years (27–80)
Age at onset of symptoms	36.2 ± 15.7 years (3–70)
Age at psoriasis onset	36.8 years (3–70)
Age at arthritis onset	47.0 years (17–75)
The mean interval between the occurrence of skin lesion and arthritis	11.3 years (0–39)
CASPAR criteria	
Current psoriasis	64 (100)
Dactylitis	11 (16.7)
Juxta-articular new bone formation	17 (25.8)
Rheumatoid factor negativity	61 (92.4)
Typical psoriatic nail lesions	23 (34.8)
Average score	3.75 (3–6)

Table 1.
Characteristics of patients with psoriatic arthritis.

two types (**Table 2**). In addition, no statistically significant difference was observed between the patient's sex and age.

Axial joints were affected in 29% of those in the skin leading group and 60% of the patients in the osteoarticular leading group, although there was no statistically significant difference in the distribution patterns of the affected axial joints ($p = 0.16$). Axial lesions were observed in a total of 21 cases (53%), with the sacroiliac joints the most affected joints in 14 cases (22%), followed by the thoracic spine in 10 cases (16%), lumbar spine in 9 cases (14%), and cervical spine in 7 cases (11%) (**Table 3**).

Peripheral joints were affected in 92% of the patients in the skin leading type and 100% of the patients in the osteoarticular leading type, without a statistically significant difference ($p = 0.99$). Regarding the peripheral joint lesions, 53 cases (83%) were observed in the upper extremity and 30 cases (47%) in the lower extremity. In the upper extremity, the joints that were first affected joint were the finger joints in 39 cases (61%), followed by shoulder joints in 22 cases (34%), wrist joints in 12 cases (19%), and elbow joints in 7 cases (11%). In the lower extremity, the joints that were first affected were the toe joints in 12 cases (19%), followed by knee joints in 11 cases (17%), hip joints in 7 cases (11%), and ankle joints in 4 cases (6.3%) (**Table 4**).

Enthesitis was observed in 15 of the total cases (23%). The most affected tendons were the Achilles' and plantar tendons, both with 8 cases (13%), followed by the quadriceps tendon in 6 cases (9.4%) and patellar tendon in 2 cases (3.1%) (**Table 5**).

In our study, the prevalence of obesity was determined to be 55%. Regarding other comorbid lifestyle-related diseases, hypertension was observed in 27 cases (42%), diabetes mellitus in 12 cases (19%), dyslipidemia in 11 cases (17%), and chronic

Timing of onset	**n or years (range, %)**
Skin leading type	48 (75)
Time interval between the occurrence of skin and osteoarticular lesions	14.2 ± 10.2 years (0.3–39.4)
Simultaneous type	6 (9.4)
Osteoarticular leading type	10 (15.6)
Time interval between the occurrence of osteoarticular and skin lesions	4.5 ± 3.3 (0.1–15.1)*

**shows statistically significant difference ($p < 0.0001$) compared to that of the time interval between the occurrence of skin and osteoarticular lesions.*

Table 2.
The onset patterns of psoriatic arthritis.

The site of axial lesions	**Cases**	**%**
Cervical spine	7	11
Thoracic spine	10	16
Lumbar spine	9	14
Sacroiliac joints	14	22
Total	21	33

Table 3.
The distribution pattern of axial lesions.

Site of peripheral lesions	Cases	%
Upper extremity	53	83
Finger	39	61
Wrist	12	19
Elbow	7	11
Shoulder	22	34
Lower extremity	30	47
Toe	12	19
Ankle	4	6.3
Knee	11	17
Hip	7	11

Table 4.
The distribution pattern of the peripheral lesions.

Site of enthesitis	Cases	%
Achilles' tendon	8	13
Plantar tendon	8	13
Quadriceps tendon	6	9.4
Patellar tendon	2	3.1
Total	15	23

Table 5.
The distribution pattern of enthesitis.

	Present study (%)	Japanese cohort in 2016 (%)	p-value
Obesity (BMI ≥ 25)	55	26	< 0.001
Hypertension	42	36	0.43
Diabetes mellitus	19	15	0.57

Fisher's direct exact test was performed for each patient for obesity and concomitant diseases.
BMI, body mass index.

Table 6.
The incidence of obesity, hypertension, and diabetes mellitus in patients with psoriatic arthritis and comparison with a Japanese cohort.

kidney disease (CKD) in 3 cases (4.7%). Diabetes mellitus was type 2 in all 12 cases. A statistically significant correlation was found between PsA and obesity ($p < 0.0001$). No statistically significant correlations were observed between PsA and hypertension ($p = 0.43$) or diabetes mellitus ($p = 0.57$) (**Table 6**).

Table 7 shows the treatments the patients with PsA received. NSAIDs were prescribed in 25 cases (39%). Several csDMARDs were prescribed in 41 cases (64%), where 21 cases (32.8%) received methotrexate, 9 cases (14%) received salazosulfapyridine, and 3 cases (4.7%) received cyclosporine. Several bDMARDs were prescribed in 33 cases (51.5%), with the most prescribed bDMARDs being

Drug	Cases	%
NSAIDs	**25**	**39.0**
csDMARDs	**41**	**64.0**
Methotrexate	21	32.8
Salazosulfapyridine	9	14.0
Cyclosporine	3	4.7
Others	6	9.4
bDMARDs	**33**	**51.5**
Adalimumab	10	15.6
Infliximab	10	15.6
Etanercept	3	4.7
Certolizumab pegol	1	1.6
Tocilizumab	1	1.6
Ixekizumab	4	6.3
Secukinumab	3	4.7
Guselkumab	1	1.6
Steroids	1	1.6
Apremilast	2	3.1
Ascorbic acid, calcium Pantothenate	2	3.1
Biotin	2	3.1

bDMARDs, biologic disease modifying antirheumatic drugs; csDMARDs, conventional synthetic disease modifying antirheumatic drugs; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 7.
The treatment status for psoriatic arthritis.

adalimumab and infliximab, which were both prescribed in 10 cases (15.6%), followed by ixekizumab in 4 cases (6.3%), etanercept and sekukinumab both in 3 cases (4.7%), and certolizumab pegol, tocilizumab, and guselkumab each prescribed in 1 case (1.6%). Other treatments included prednisolone in a single case (1.6%) and apremilast, ascorbic acid, calcium pantothenate, and biotin, each prescribed in two cases (3.1%) (**Table 7**).

4. Discussion

We identified several clinical features of PsA based on the results of this study. First, PsA dominantly afflicted male patients (77%), with the mean age of onset for cutaneous psoriasis at 36.8 years, while that of osteoarticular lesions at 47.0 years. Second, the skin leading type was observed more than the osteoarticular leading type, with the interval between the onset of both symptoms significantly shorter in the osteoarticular leading type than in the skin leading type. Third, upper extremity lesions were more dominant (53 cases; 83%) than lower extremity lesions (30 cases; 47%). Fourth, axial lesions were observed in 33% and enthesitis in 23% of the sample. Fifth,

obesity was strongly associated with PsA. Finally, csDMARDs were the most prescribed drugs in patients with PsA, followed by bDMARDs and NSAIDs.

Regarding the onset pattern of PsA in a Japanese multicenter study, Ohara reported arthritis preceded psoriasis in 11% of patients [1]. In previous reports concerning PsA [3–6], the incidences of "joint before skin" cases were between 15% and 30% of the sample. In our study, arthritis preceded skin lesions in 17%, which was in near agreement with the results of previous reports. In these cases, the lack of skin lesions makes diagnosis difficult.

Regarding the distribution of arthritis, Ritchlin reported that axial joints are affected in 50% of PsA patients [2]. In the Japanese multicenter study, back pain such as lumbago and neck pain was observed in 34.3% of patients and enthesitis in 28.3% [10, 11]. Similarly, our study showed that axial lesions were present in 33% and enthesitis in 23%.

Moreover, we checked the distribution of arthritis by the onset patterns in this study. However, there was no statistically significant difference in both peripheral and axial lesions, and it was therefore concluded that the distribution pattern was not useful for detecting PsA in the osteoarticular leading type.

The risk factors for the development of psoriasis are obesity and lifestyle-related diseases such as hypertension, diabetes mellitus, hyperlipidemia [12], with obesity-related to the severity of psoriasis [13]. A large cohort study also demonstrated that BMI was associated with psoriasis [14]. In another study, PsA showed a significant association with obesity, type 2 diabetes, hypertension, metabolic syndrome, fatty liver, and an increased risk of cardiovascular events [15].

Similarly, in our study, obesity was significantly associated with PsA; however, the other factors were not statistically significantly associated with PsA.

Regarding the treatment status, NSAIDs were effective for joint symptoms but ineffective for skin lesions. The csDMARDs were effective for arthritis and skin involvement, whereas the bDMARDs were used for patients with an inadequate response to the csDMARDs as it can suppress skin and joint inflammation and delay radiographic progression.

Despite the use of traditional disease-modifying medications in more than 50% of patients with PsA, bone erosions were still observed in 47% of patients within the first 2 years [16]. Therefore, the appropriate diagnosis of PsA and tight control are required for better clinical outcomes of PsA. According to the American College of Rheumatology recommendation for PsA in a 2019 update, non-steroidal anti-inflammatory drugs and local glucocorticoid injections are proposed as initial therapy. Further, for patients with arthritis and poor prognostic factors such as polyarthritis or monoarthritis/oligoarthritis accompanied by factors such as dactylitis or joint damage, rapid initiation of csDMARDs are recommended. If the treatment target is not achieved with this strategy, bDMARDs targeting tumor necrosis factor (TNF), interleukin (IL)-17A, or IL-12/23 should be initiated [17].

In our study, NSAIDs were used in 39% of patients, csDMARDS in 64%, and bDMARDs in 51.5%. These data suggest that skin or arthritic symptoms were moderate to high in our cases. Yamamoto et al. Demonstrated that bDMARDs were used in more than 50% of all patients registered with PsA, which is in agreement with our results [10, 11].

Our study had several limitations. First, the small sample size was a result of this study taking place at a single center. Second, the type of skin and severity of psoriasis with a Psoriasis Area and Severity Index score was not evaluated. Third, the effect of the prescribed drugs was not examined.

5. Conclusions

we clarified the clinical features of PsA in a clinical orthopedic outpatient clinic setting. PsA was more dominant in male patients, with the osteoarticular leading type pattern of PsA observed in 17% of patients, as opposed to 75% in the skin leading type pattern. The interval between the onset of osteoarticular symptoms and the appearance of skin lesions was 4.5 years on average in the osteoarticular leading type, which was significantly shorter than that in the skin leading type. It was concluded that for patients with RF negative polyarthritis, it is important to be aware that psoriasis may develop approximately 4 years on average. Increased use of csDMARDs and bDMARDs was observed compared to that of NSAIDs.

Acknowledgements

The authors acknowledge English language editing and proofreading for Editage.

Conflicts of interest

None.

Ethical statement

This study was performed with the approval of the institutional review board of our hospital.

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