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NEÜ YAYINEVİ

Clinical and Demographic Features of Twenty-Nine Patients with Psoriatic Arthritis "Sine Psoriasis"

Cilt Bulgusu Olmayan 29 Psöriyatik Artrit Hastasının Klinik ve Demografik Özellikleri

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Öz

Amaç: Psoriatik Artrit (PsA), sedef hastalığı (PsO) olan hastaların %10-30'unu etkileyen kronik ilerleyici inflamatuar bir hastalıktır. "PsA Sine sedef hastalığı" terimi, "cilt belirtileri olmadan PsA teşhisi konan hastaları" tanımlamak için kullanılır. Bu çalışmada "PsA" "sine psoriasis"in demografik ve klinik özelliklerinin CASPAR kriterlerine göre tanımlanması amaçlandı.
Hastalar ve Yöntem: 2016-2022 yılları arasında CASPAR kriterlerine göre PsA sine psoriasis tanısı alan 29 hasta çalışmaya dahil edildi. Romatizmal hastalığı ve herhangi bir cilt tutulumu olan hastalar çalışma dışı bırakıldı.
Bulgular: Çalışmaya dahil edilen 29 hastanın tamamına CASPAR kriterlerine göre PsA tanısı konuldu. Hastaların 16'sı kadındı. Hastaların ortalama (±SS) yaşı 45±11 idi. Hastaların ortalama (±SD) PsA süresi 6,2±3,0 yıldı. PsA'lı hastaların birinci derece akrabalarında psoriazis öyküsü %54,1; ikinci derece akrabalarında psöriazis öyküsü ise %45,9 olarak saptandı. Hastaların %39,4'ünde poliartiküler, %35,7'sinde oligoartiküler, %24,9'unda aksiyal tutulum vardı. Tüm hastaların 19'unda (%65,5) DİP tutulumu mevcuttu. Hastaların %88.9'unda tırnak bulguları mevcuttu. Ayrıca hastaların 17'sinde (%58,6) entezit, 18'inde (%62) daktilit saptandı.
Sonuç: PsA'yı düşündüren klinik semptom ve bulguları olan ve ailede psöriazis öyküsü olan hastalar, PsA sine psoriasisi olarak sınıflandırılabilir. Daktilit ve DIP artritli hastalar, ailesel sedef hastalığı PsA'nın bir alt grubunu temsil edebilir.

Anahtar Kelimeler: Sedef hastalığı, psoriatik artrit, distal interfalangeal eklem

Abstract

Aim: Psoriatic Arthritis (PsA) is a chronic progressive inflammatory disease that affects 10-30% of patients with psoriasis (PsO). The term "PsA sine psoriasis" is used to describe "patients diagnosed with PsA without skin manifestations". In this study, it was aimed to define the demographic and clinical features of "PsA" "sine psoriasis" according to CASPAR criteria.
Patients and Methods: Twenty-nine patients diagnosed with PsA sine psoriasis according to CASPAR criteria between 2016-2022 were included in the study. Patients with rheumatic diseases and any skin involvement were excluded from the study.
Results: All twenty-nine patients included in the study were diagnosed with PsA according to the CASPAR criteria. 16 of the patients were female. The mean (±SD) age of the patients was 45±11 years. The mean (±SD) PsA duration of the patients was 6.2±3.0 years. A history of psoriasis in the first-degree relatives of patients with PsA was 54.1%; A history of psoriasis in second-degree relatives was found in 45.9%. 39.4% patients had polyarticular, 35.7% had oligoarticular, 24.9% had axial involvement. DIP involvement was present in 19 (65.5%) of all patients. Nail findings were present in 88.9% of the patients. Besides, enthesitis was detected in 17 (58.6%) and dactylitis was in 18 (62%) of patients.
Conclusion: Patients with clinical symptoms and findings suggestive of PsA and a family history of psoriasis can be classified as PsA sine psoriasis. Patients with dactylitis and DIP arthritis, familial psoriasis may represent a subgroup of PsA.

Key words: Sine psoriasis, psoriatic arthritis, psoriasis, distal interphalangeal joint

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INTRODUCTION

Psoriatic Arthritis (PsA) is a chronic progressive inflammatory disease that affects 10-30% of patients with psoriasis (PsO) (1). Since joint damage occurs in more than half of untreated cases, the importance of diagnosing and treating the disease is increasing (1). In 60-70% of psoriatic arthritis (PsA) cases, psoriasis precedes arthritis. Since there is no specific test for the diagnosis of the disease, the presence of skin lesions is of great importance in the diagnosis (1,2). In approximately 20% of PsA patients, joint involvement may precede skin involvement. There may be delays and difficulties in the diagnosing PsA when there is no psoriatic skin lesions and the patient is not aware of skin lesion history. The term "PsA sine psoriasis" is used to describe "patients diagnosed with PsA without skin manifestations" (3). Does the definition of “PsA sine psoriasis” refer to a patient with typical PsA who has not yet developed skin psoriasis but will eventually develop if followed long enough or a patient who may have latent psoriasis that cannot be detected during clinical evaluation or only a patient with psoriasis in his family? These questions remain unanswered. A positive family history of psoriasis may be a helpful clue when diagnosing ‘’PsA sine psoriasis". It is important to identify patients who could benefit from approved but expensive new treatments for PsA. In particular, the questions remain unanswered whether the two SpA subtypes, namely peripheral SpA and PsA sine psoriasis, should be grouped together and ultimately treated in the same way or considered as two separate diseases. On the other hand, without psoriatic skin lesions, PsA can be diagnosed according to Classification Criteria For Psoriatic Arthritis (CASPAR) criteria (4). The diagnosis of PsA can be made using imaging methods, familial history of psoriasis, joint involvement features, enthesitis, dactylitis, and nail findings, and laboratory tests performed to exclude similar diseases (4).

This study aimed to retrospectively define the demographic and clinical features of “PsA sine psoriasis” patients diagnosed with PsA according to CASPAR criteria.

PATIENTS AND METHODS

Twenty-nine patients diagnosed with PsA sine psoriasis according to CASPAR criteria between 2016-2022 were included in the study. Patients older than 18 years of age, no signs of psoriatic skin disease, diagnosed as PsA according to CASPAR criteria, had a history of psoriasis in a first or second-degree relative, and without other rheumatic diseases were included in the analysis.

Sociodemographic characteristics, PsA duration, PsA domain findings, family history of rheumatic disease or PsO, radiological and laboratory findings, treatment history and comorbidities were recorded retrospectively. CASPAR criteria were used to for diagnosing PsA. Ethics committee approval was obtained from Ankara Medical Park Hospital Ethics Committee (dated: 07.12.2022, decision number: E2-22-2987).

Statistical Analysis

Statistical analysis was performed using SPSS Statistics for Windows, Version 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). The conformity of numerical variables for normal distribution was examined by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Descriptive statistics were expressed by mean ±standard deviation or median and interquartile range (IQR) according to distribution of the numeric variables and percentage [n(%)] for categorical variables. As the type of this study was a descriptive study, we did not make any statistical inference.

RESULTS

All twenty-nine patients included in the study were diagnosed with PsA according to the CASPAR criteria. 16 (55.2%) of the patients were female. The mean age was 45±11 years. The mean PsA duration was 6.2±3.0 years. All patients had either first or second-degree family history of psoriasis. 8 (27.6%) of the patients were consulted to the rheumatology clinic from other clinics (orthopedics, physiotherapy, internal medicine, etc.). The percentage of patients who applied directly to the rheumatology outpatient clinic was 21 (72.4%). None of the patients had any signs of psoriasis. No patients had a personal history of psoriasis. (Table 1)

Considering the articular involvement distribution: 11(39.4%) polyarticular, 10 (35.7%) oligoarticular, 7 (24.9%) axial involvement patterns and 19 (65.5%) DIP involvement. Human leukocyte antigen (HLA-B27) was studied in 14 of 29 patients and was positive in only three patients. Erythrocyte Sedimentation Rate (ESR, mm/h) and C-reactive protein (CRP, mg/dl) were high in all patients. Nails were affected in 24/27 (88.9%) of the patients (64% toe nails, 36% fingernails). The most common nail sign was pitting. The association of DIP-nail involvement was remarkable, nail involvement

Table 1. Demographic and Clinical Features Patients with Psoriatic Arthritis “Sine Psoriasis” (n= 29)

Age (mean±SD) (years)		45±11
Female, n(%)		16 (55.2)
Family History of psoriasis (%)		100
PsA duration (mean±SD) (years)		6.2±3.0
Articular Involvement Joint Pattern n(%)		(n=28)
	Polyarticular	11 (39.4)
	Oligoarticular	10 (35.7)
Axial		7 (24.9)
Distal Interphalangeal Involvement n(%)		19 (65.5)
Dactylitis n(%)		18 (62)
Enthesitis n(%)		17 (58.6)
Uveitis n(%)		1 (3.4)
Nail Involvement n(%)		24/27 (88.9)
Inflammatory Bowel Disease n(%)		-
Comorbidity number >2 n(%)		14 (48.3)
Erythrocyte Sedimentation Rate (ESR) (mean±SD) mm/h		47±11
C-reactive protein (CRP) (mean±SD) mg/dl		12±3
HLA B27a n(%) (+)		3/14 (21)
RFb n(%) (+)		-
Anti-CCPc n(%) (+)		-
ANAd n(%) (+)		-

a Human leukocyte antigen (HLA) B27
b Rheumatoid factor
c Anti-Cyclic Citrullinated Peptide Antibody
d Antinuclear Antibodies

was observed in all cases with DIP involvement.

Enthesitis was detected in 17/29 (58.6%) cases. Achilles the plantar region was the most commonly affected enthesis regions. Enthesitis was diagnosed with physical examination in 13 of 17 patients, 3 with USG and 1 with MRI. 12 of 17 patients had enthesitis in multiple regions (such as patellar ligament and iliac crest). Dactylitis was detected in 18 (62%) of patients' history and current examination findings. Nail findings were observed in 16 (88.8%) of patients with dactylitis. In addition, these patients have DIP joint involvement. Obesity, hyperlipidemia, hypertension, and diabetes mellitus were the most common comorbidities when considering the frequency of co-morbidities in the patients. 14/29 (48.3%) of the patients had two or more comorbidities. Antinuclear Antibodies (ANA), Anti-Cyclic Citrullinated Peptide Antibody (Anti-CCP), Rheumatoid factor (RF), were all negative in all patients.

Table 2. Drug Use in Patients with Psoriatic Arthritis “Sine Psoriasis” (n= 29)

NSAID1 n(%) (%)	29 (100)
PRD2 n(%) (%)	16 (55.1)
csDMARD3 n(%) (%)	15 (51.7)
Anti-TNFs 4 n(%) (%)	14 (48.3)
Non-TNF Biologics n(%) (%)	5 (17.2)

1 Non-Steroidal Anti-Inflammatory Drugs
2 Prednisolone below 7.5 mg/day
3 Conventional synthetic disease modifying antirheumatic drugs
4 Tumor Necrosis Factor (TNF) Inhibitors

Intra-articular steroid injection, and systemic steroids below 7.5 mg/day were used in appropriate cases. Conventional DMARDs in 15 (51.7)%, tumor necrosis factor (TNF) inhibitors (anti-TNFs) in 14 (48.3%), and non-TNF biologics in 5 (17.2%) of patients were used in the management of PsA.

DISCUSSION

The relationship between the onset of skin and joint complaints in patients with psoriatic arthritis (PsA) has always been a matter of interest (5). Considering that joint involvement may precede the onset of rash in 10-20% of cases, ‘’PsA sine psoriasis” should not be a rare diagnosis. Using data from the COMOSPA and PerSpA studies, the prevalence of PsA sine psoriasis was calculated to range from 3.1% to 5.5% of all SpA (3). From the perspective of rheumatologists, some findings suggest psoriatic arthritis (PsA) even if the patient does not have psoriasis. According to the CASPAR criteria, the presence of psoriasis is not mandatory for the diagnosis of PsA (3,4).

Few studies have evaluated the demographic characteristics of patients with PsA sine psoriasis. In a study comparing peripheral SpA (pSpA) and PsA sine psoriasis, the mean age of patients with pSpA was 32.8 - 42.2 (6). In studies of PsA sine psoriasis involving 20, 57, and 100 patients, respectively, the

age of onset was similar (7). In our study, the patients' mean age was also similar to the studies mentioned. Looking at the distribution of males and females using the same studies, the prevalence of male sex in PsA sine psoriasis varied between 20-55% (7). In our study, the female-male ratio was also similar.

HLA-B27 is the shared genetic factor for SpA subtypes. The prevalence of HLA-B27 in pSpA ranges from 27 to 62.3% (6). In PsA, data from the PerSpA study confirmed the lower prevalence of HLA-B27 at 18.2%, similar to our study. In other studies, conducted in patients with psoriasis, HLA-B27 was associated with early psoriasis and PsA onset; HLA-Cw6 was found to be associated with delayed onset of PsA (8). In addition, HLA-B27 was associated with axial involvement and symmetrical sacroiliitis in PsA, while it was negatively associated with a family history of psoriasis (9). Scarpa et al. studied 57 patients (31 female, 26 male) with undifferentiated spondyloarthritis in their study on the clinical and genetic aspects of PsA sine psoriasis (10). The outcome of the study was that the subset of PsA sine psoriasis was defined by dactylitis and/or DIP arthritis, HLA Cw6, and a family history of psoriasis (10). Although the HLA Cw6 antigen could not be examined in our study, family history of DIP arthritis, lower extremity dactylitis, and PsA sine psoriasis was observed as a clinical pattern frequently found in cases (11). In addition, HLA-B27 was studied in 14 of 29 patients in the study group, and it was found to be positive in only 3 of them, and 3 of the cases were cases with axial involvement. In the literature, while HLA-B27 in patients with peripheral involvement did not show a significant increase, HLA-B27 positivity was detected in 45% of patients with axial involvement (3).

In current literature on PsA sine psoriasis, 85.7% of the cases have arthritis, 62-75% dactylitis, and 35-55% enthesitis (12). In PsA sine psoriasis, the small joints of the hands and feet are dominantly affected which is different from pSpA which mainly involves the large joints of the lower extremities. In our study, 35.7% patients had oligoarticular involvement and 39.4% had polyarthritis; small joints were affected more than large joints. The association of asymmetric oligoarticular involvement and dactylitis was also remarkable in our patients.

24.9% of our patients had axial involvement. Although it may be difficult to distinguish patients with PsA axial involvement from ankylosing spondylitis, the presence of cervical involvement without lumbar involvement, the presence of asymmetric sacroiliitis and the presence of non-marginal coarse syndesmophytes in the vertebrae may help in the differentiation (3). Peripheral involvement may or may not be present in PsA with axial involvement. Three of the patients in our study group had axial and peripheral involvement together with entheseal involvement.

In the literature, DIP arthritis predominates in approximately 15% of all PsA cases (12). Although it is stated that DIP involvement is common in PsA sine psoriasis cases, the rate is not stated (13). In our study, about 65.5% of patients had DIP involvement accompanying the oligoarticular and polyarticular joint involvement. Besides, nail involvement is very common and predictive of PsA (6,14,15). In the literature, nail changes were observed in 88% of PsA sine psoriasis, similar to our study (16,17). Unlike skin lesions, there is a close relationship between nail changes and DIP joint involvement (6,12,16). Nail finding was one of the important findings that contributed to the diagnosis since there were no skin findings in our PsA sine psoriasis patients. The association of DIP-nail involvement was remarkable in our group, and nail involvement was observed in all cases with DIP involvement in our series. According to current classification criteria, patients with PsA “sine psoriasis” are included in the broad spectrum of the undifferentiated SpA or peripheral SpA subset (3,6,18). It can be thought that the diagnosis of PsA "sine psoriasis" may be easier if dactylitis and DIP involvement, which are two features of classical PsA, are found in patients with a first and/or second-degree family history in the patient group diagnosed with undifferentiated Spa or pSpA (3,12). In their study, Oliveri et al. (7) reported that fifteen patients with PsA sine psoriasis met the Amor criteria for spondyloarthritis and the European Spondyloarthropathy Study Group (ESSG) criteria (11). Patients with peripheral musculoskeletal disease (arthritis or enthesitis, or dactylitis) with and without skin psoriasis may meet both the CASPAR and ASAS pSpA classification criteria. The family history of psoriasis should be absolutely questioned in patients diagnosed with pSpA or undifferentiated SpA according to AMOR and European Spondylarthropathy Study Group (ESSG). When CASPAR criteria are applied to cases with a family history of psoriasis, some patients may be diagnosed with SpA sine psoriasis. Study results of Oliveri et al. suggested that the clinical spectrum of PsA sine psoriasis is as broad as that of PsA.

Enthesitis has a key pathogenic role in PsA (3,19-

21). In the literature, the percentage of enthesitis in PsA sine psoriasis has been reported as 35-55% (3,20-21). Enthesitis was detected in 58.6% of patients in this study most commonly in lower extremities. The rate of enthesitis reported in PsA sine psoriasis cases may be higher than in the literature with the use of MRI, USG and if the enthesitis examination is performed regularly and carefully.

Dactylitis is seen in about 30% of PsA cases. (22-24). Generally, the involvement of the toes is more than the hand (25). The relationship between dactylitis and involvement of DIP joints in PsA patients is remarkable (3,23). In the literature, dactylitis has been reported in 62-75% of PsA sine psoriasis cases. Dactylitis was seen at a rate of 18/29 in the patients included in our study. It can be considered as one of the strong clues leading to the diagnosis of PsA in cases with PsA sine psoriasis, especially in patients with a family history of psoriasis. In our study, it was more common in the lower extremities. Nail findings were observed in 16/18 of the patients with dactylitis. In addition, almost all these patients have DIP joint involvement.

Ocular involvement is seen in 7-33% of PsA patients (3,23). In contrast to AS and enteropathic arthritis; bilateral, posterior, insidious, and chronic uveitis can be seen in psoriatic arthritis. The percentage of uveitis in PsA sine psoriasis has been reported to be 2-25% (3,25). Chronic anterior uveitis was observed in 1 of 29 patients in our study group. The patient also had psoriasis in his first-degree relatives, and DIP involvement, HLA-B27 negative, and nail findings were remarkable. Inflammatory Bowel Disease (IBD), which is well known to be associated with SpA, was not detected in our series. There is no IBD rate reported in the literature in patients with PsA sine psoriasis.

It has been reported that comorbidities such as hypertension, diabetes mellitus, cardiovascular disease, metabolic syndrome, and obesity were all frequent in patients with psoriasis and psoriatic arthritis (3,25-27). In 48.3% of the patients included in our study, two or more comorbidities accompanied the diagnosis of PsA. The most common comorbidities were hypertension, diabetes mellitus, obesity, and cardiovascular disease.

There are no diagnostic laboratory tests for PsA. Although RF and anti-CCP negativity seem to be distinctive laboratory features, low titer RF positivity was found in 5-16% of patients in recent studies (3,28). In all patients in our study, ANA, anti-CCP, RF were negative.

The aim of treatment in patients with PsA is to improve the quality of life, provide symptom control, prevent structural damage, and minimal disease activity or remission (28). Biologic drugs can be considered in case of unresponsiveness to conventional DMARD treatment during PsA treatment (29-31). In our study treatment choices were parallel to current guidelines.

The limited number of patients and the short follow-up period can be said to be the main limitations of our study. We think that studies with longer follow-up period examining the characteristics of PsA sine psoriasis patients in different ethnic and geographical regions are needed.

CONCLUSION

This study provides one of the largest Sine Psoriasis patients data with recent classification criteria. Findings of present study proves the importance of anamnesis. The set of PsA classification criteria proposed in 2006, with better specificity and sensitivity than those previously published, allows the classification of the disease in the absence of psoriasis if typical PsA findings are present. A first- or second-degree relative of psoriasis patients without skin lesions will help the diagnosis. Patients with clinical symptoms and findings suggestive of PsA and a family history of psoriasis can be classified as PsA sine psoriasis. In this spectrum, patients with dactylitis and DIP arthritis, familial psoriasis may represent a subgroup of the disease.

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