ORIGINAL PAPER

Psoriasis and family history of psoriasis may not affect disease severity of rheumatoid arthritis

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SUMMARY

The incidence of psoriasis in patients with rheumatoid arthritis (RA) is higher than in the general population. In addition, psoriasis may negatively affect the severity of rheumatological diseases in patients with autoinflammatory or autoimmune diseases. In this study, we evaluated the effect of psoriasis or a family history of psoriasis on the characteristics of RA.

This is a cross-sectional study. We included 737 RA patients who met the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) RA Classification Criteria, but did not meet the CASPAR psoriatic arthritis criteria. Subsequently, we compared disease activity, the need for biologic therapy, the number of conventional synthetic disease-modifying anti-rheumatic drugs taken, the frequency of erosive disease and extra-articular involvement, glucocorticoid doses and the Stanford Health Assessment Questionnaire scores between patients with and without a history of psoriasis, and patients with and without a family history of psoriasis.

Thirteen (1.8%) patients had psoriasis, while 58 (7.9%) had a family history of psoriasis in first- or second-degree relatives. All outcome parameters were found to be similar between the groups.

We show that concomitant psoriasis has no effect on the evaluated disease characteristics of RA.

Key words: *Psoriasis, rheumatoid arthritis, disease activity.*

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic, autoimmune and chronic inflammatory disease characterized mainly by joint involvement (1). Some factors may affect the severity and the progression of the disease, the frequency of extra-articular involvement, and the response to treatment, such as seropositivity, smoking, high acute phase reactants and several genetic polymorphisms (2-4). In addition, comorbidities associated with RA such as obesity, depression, hypertension, hypothyroidism, hyperthyroidism, cardiovascular diseases, coronary artery diseases, cerebrovascular diseases, chronic renal disease, chronic obstructive pulmonary disease, and diabetes mellitus may be associated with a more severe disease (5-7).

Psoriasis is a chronic skin disease characterized by several multisystem inflammatory components (8). When psoriasis occurs in patient with rheumatologic diseases, it may have negative effects on the course of the latter. For example, the frequency of abdominal pain and fever is higher in pediatric familial Mediterranean fever patients with psoriasis (9). In addition, psoriasis was found to have a role in poor response to treatment in systemic lupus erythematosus patients (10). Furthermore, psoriatic arthritis patients with a family history of psoriasis have an increased risk of joint deformity (11).

Recently, psoriasis has been shown to be more frequent in RA patients compared to the general population (12). However, the effect of psoriasis or a family history of psoriasis on the disease characteristics of RA was not evaluated in this study.

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New data showing an increased frequency of psoriasis in RA and the negative effects of psoriasis on some rheumatic diseases have increased our awareness of the relationship between RA and psoriasis. In this study, we aim to evaluate if psoriasis or a family history of psoriasis have a negative effect on the evolution of RA.

MATERIALS AND METHODS

We enrolled 737 RA patients who fulfilled the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) RA Classification Criteria (13). All the patients were literate and none of them had any neurological pathology and hearing disorders in the examinations that may influence their response to the questionnaire. The patients with inflammatory arthritis who met both the 2010 ACR/EULAR RA Classification Criteria and CASPAR psoriatic arthritis (PsA) criteria (14) were excluded from the study. In addition, pregnancy, breastfeeding, and other concomitant inflammatory or auto-immune rheumatologic conditions were also exclusion criteria. The diagnosis of psoriasis in RA patients was made by evaluating their medical history or by physical examination, evaluating psoriatic skin and scalp disease. In addition, the history of psoriasis and the type of psoriatic disease in the family members of the patient were determined by interviewing the patients.

Demographic features, smoking habits, disease duration, co-morbid illnesses, C-reactive protein and erythrocyte sedimentation rate during study enrolment period, extra-articular involvement, rheumatoid factor and anti-citrullinated protein antibodies (ACPA), current and previous RA treatment were obtained from the medical database of the hospital. Additionally, tender and swollen joints counts of the patients with RA were obtained by physical examination by the same rheumatologist (NS). The activity of RA was evaluated with the Disease Activity Score-28 with CRP (DAS28-CRP) (15). Patients were classified as having an erosive form of disease, if they fulfilled the EULAR definition: '*When an erosion (defined as a cortical break) is seen in at least three separate joints at any of the following sites: the proximal interphalangeal, the metacarpophalangeal, the wrist (counted as one joint) and the metatarsophalangeal joints on radiographs of both hands and feet'* (16). Hand and feet X-rays were evaluated by the same rheumatologist (NS). Lastly, the patient's quality of life was evaluated by the validated Turkish version of the Stanford Health Assessment Questionnaire disability index (HAQ-DI) (17). NS evaluated both radiographs and clinical examination at different times, and was blinded to clinical data when performing radiographic scoring.

In this study, we compared several variables between RA patients with and without psoriasis and RA patients with and without a family history of psoriasis. Our main outcome parameters were HAQ-DI, joint deformity, frequency of patients receiving steroid doses greater than 7.5 mg/day, number of conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) received by the patient, and frequency of patients using biological or targeted synthetic DMARDs.

This study was approved by the Local Research Ethics Committee and carried out in compliance with the Helsinki Declaration. All the patients gave their written informed consent.

Statistical analyses

Statistical analyses were carried out using SPSS Version 17.0 (SPSS Inc., Chicago, IL, USA). In order to determine whether the data were normally distributed, the Kolmogorov-Smirnov test was performed. All continuous variables were distributed non-normally. The comparisons of the continuous variables between patients were performed by Mann-Whitney U test. Moreover, the comparisons of the categorical variables were performed by using the Chi-square test. The results are given as median (interquartile range) and a p value lower than 0.05 was considered as statistically significant.

RESULTS

The median age of the 737 study participants was 53 years (range 43-62 years). 595 (80.7%) of them were women. Median disease duration was 72 months (24-144 months). Thirteen (1.8%) out of 737 RA patients also had psoriasis. Additionally, 58 (7.9%) of the patients had a family history of psoriasis in first- or second-degree relatives. More than two-thirds of the patients had RF and more than half had ACPA positivity. Extra-articular involvement was observed in 62 (8.5%) out of 737 patients and 40/62 (64.5%) patients had lung involvement. A diagnosis of erosive disease was made in 130 (17.6 %) patients. 142 (19.3%) patients received bDMARDs or tsDMARDs at any time after diagnosis. Additionally, 110 (14.9%) patients were currently receiving bDMARDs or tsDMARDs. Only 43 (5.9%) patients were taking steroid doses above 7.5 mg/day (Table I).

We compared demographic and disease-related parameters in patients with and without a history of psoriasis. The only difference between the groups was a family history of psoriasis. More patients in the psoriasis group had a family history of psoriasis (p=0.01). The frequency of all other outcome parameters was similar between patients with and without psoriasis (Table II).

We also compared demographic and disease-related parameters in patients with and without a family history of psoriasis. More patients without a family history of psoriasis had psoriasis (p=0.01). In addition, the frequency of male patients was found to be higher among those with a family history of psoriasis (p=0.01). All other demographic and disease-related items were similar in the groups (Table III).

DISCUSSION AND CONCLUSIONS

In our study, in which we evaluated the influence of psoriasis on RA disease-related features, both a history of psoriasis and a family history of psoriasis did not correlate with disease activity, need for biologic therapy, number of csDMARDs taken, steroid doses, frequency of erosive disease, extra-articular joint involvement, and HAQ scores of RA patients.

As far as we know, at the moment there is no study published in the literature evaluating the clinical effect of psoriasis on RA patients. Previous studies have shown that

Table I - Demographic and disease related features of the patients (n=737).

Age (years)	53.0 (43.0-62.0)
Gender (M/F)	142/595
Smoking (%)	128 (17.4)
Co-morbidity (%)	360 (48.8)
Disease duration (month)	72.0 (24.0-144.0)
Family history of psoriasis (%)	58 (7.9)
Psoriatic arthritis	1 (1.8)
Psoriasis	52 (89.6)
Psoriatic arthritis and Psoriasis	5 (8.6)
Patient psoriasis (%)	13 (1.8)
RF positivity (%)	488 (66.2)
ACPA positivity (%)	409 (55.5)
Extra-articular involvement (%)	62 (8.5)
Joint deformity (%)	130 (17.6)
Swollen joints (n)	0 (0-2.0)
Tender joints (n)	1.0 (0-4.0)
DAS 28-CRP score	2.8 (2.0-3.7)
Sedimentation rate (mm/h)	24.0 (12.0-39.0)
CRP (mg/dL)	3.7 (1.7-9.0)
HAQ score	0.15 (0-0.5)
Treatment	
bDMARD or tsDMARD (at any time)*	142 (19.3)
Steroid dose (mg/dL)	5.0 (5.0-5.0)
Steroid dose >7.5 mg/day (n)	43 (5.9)
Methotrexate (%)	352 (47.8)
Leflunamide (%)	259 (35.1)
Hydroxychloroquine (%)	362 (49.1)
Sulfasalazine (%)	81 (11.0)
Number of csDMARD	1.0 (1.0-2.0)
bDMARD or tsDMARD	110 (14.9)

M, male; F, female; RF, rheumatoid factor; ACPA, anti-citrullinated protein antibody; DAS 28, Disease activity score 28; CRP, C-reactive protein; HAQ, Health Assessment Questionnaire; bDMARD, biologic disease modifying drugs; tsDMARD, targeted synthetic disease modifying drugs; csDMARD, conventional synthetic disease modifying drugs. *Adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, tofasitinib, baricitinib.

Table II - Demographic and disease-related features of the rheumatoid arthritis patients with or without psoriasis (n=737).

	Psoriasis history n=13	Without psoriasis history n=724	p
Age (years)	52.0 (38.0-62.5)	53.0 (43.0-62.0)	0.93
Gender (M/F)	3/10	139/585	0.72
Smoking (%)	4 (30.8)	123 (17.0)	0.25
Co-morbidity (%)	6 (46.2)	353 (49.0)	0.83
Disease duration (month)	96.0 (30.0-137.5)	72.0 (24.0-144.0)	0.73
Family history of psoriasis (%)	4 (30.8)	54 (7.4)	0.01°
RF positivity (%)	9 (75.0)	478 (68.7)	0.76
ACPA positivity (%)	8 (72.7)	400 (60.2)	0.54
Extra-articular involvement (%)	1 (7.7)	61 (8.5)	NS
Joint deformity (%)	1(7.7)	129 (17.8)	0.48
Swollen joints (n)	1.0 (0-2.5)	0 (0-1.0)	0.15
Tender joints (n)	2.0 (0-3.5)	0 (0-4.0)	0.87
DAS 28-CRP score	3.2 (1.7-4.2)	2.8 (2.0-3.7)	0.89
Sedimentation rate (mm/h)	24.0 (8.0-44.0)	24.0 (12.0-39.0)	0.99
CRP (mg/dL)	4.0 (1.3-10.0)	3.7 (1.6-9.0)	0.88
HAQ score	0.2 (0.1-0.7)	0.1 (0-0.5)	0.13
Treatment			
bDMARD or tsDMARD (at any time)*	1 (7.7)	141 (19.5)	0.48
Steroid dose (mg/dL)	5.0 (4.3-5.0)	5.0 (5.0-5.0)	0.60
Steroid dose >7.5 mg/day (n)	0(0)	43 (5.9)	NS
Number of csDMARD	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.85
bDMARD or tsDMARD (%)	1 (7.7)	108 (14.9)	0.75

M, male; F, female; RF, rheumatoid factor; ACPA, anti-citrullinated protein antibody; DAS 28, Disease activity score 28; CRP, c-reactive protein; HAQ, Health Assessment Questionnaire; bDMARD, biologic disease modifying drugs; tsDMARD, targeted synthetic disease modifying drugs; csDMARD, conventional synthetic disease modifying drugs. *Adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, tofasitinib, baricitinib. °p<0.05.

Table III - Demographic and disease-related features of the rheumatoid arthritis patients with or without family history of psoriasis.

	Without family history of psoriasis n=679	Family history of psoriasis n=58	p
Age (years)	53 (43.0-62.5)	50 (42.0-58.2)	0.25
Gender (M/F)	138/541	4/54	0.01°
Smoking (%)	119 (17.5)	9 (15.5)	0.69
Co-morbidity (%)	330 (48.6)	30 (51.7)	0.67
Disease duration (month)	72.0 (24.0-144.0)	66.0 (24.0-142.7)	0.56
Patient psoriasis (%)	9 (1.3)	4 (6.9)	0.01°
RF positivity (%)	449 (68.8)	39 (69.6)	0.89
ACPA positivity (%)	379 (60.8)	30 (56.6)	0.54
Extra-articular involvement (%)	61 (9.0)	1 (1.8)	0.06
Joint deformity (%)	123 (18.1)	7 (12.1)	0.24

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	Without family history of psoriasis n=679	Family history of psoriasis n=58	p
Swollen joints (n)	0 (0-1.0)	0 (0-2.0)	0.76
Tender joints (n)	1.0 (1.0-4.0)	1.0 (1.0-3.0)	0.51
DAS 28-CRP score	2.8 (2.0-3.8)	2.8 (1.9-3.5)	0.38
Sedimentation rate (mm/h)	24.0 (12.0-40.0)	24.0 (14.2-30.0)	0.81
CRP (mg/dL)	3.7 (1.6-9.2)	3.6 (1.7-8.0)	0.73
HAQ score	0.1 (0-0.5)	0.2 (0-0.5)	0.62
Treatment			
bDMARD or tsDMARD (at any time)*	132 (19.5)	10 (17.2)	0.68
Steroid dose (mg/dL)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	0.17
Steroid dose >7.5 mg/day (n)	39 (5.8)	4 (7.0)	0.56
Number of csDMARD	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.94
bDMARD or tsDMARD (%)	104 (15.3)	6 (10.3)	0.56

M, male; F, female; RF, rheumatoid factor; ACPA, anti-citrullinated protein antibody; DAS 28, Disease activity score 28; CRP, c-reactive protein; HAQ, Health Assessment Questionnaire; bDMARD, biologic disease modifying drugs; tsDMARD, targeted synthetic disease modifying drugs; csDMARD, conventional synthetic disease modifying drugs. *Adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, tofasitinib, baricitinib. °p<0.05.

the presence of psoriasis, or a family history of psoriasis may be associated with increased disease severity of other autoimmune diseases.

Numerous genetic loci have been identified in psoriasis and psoriatic arthritis (18, 19). These genetic traits may have an impact on concomitant autoimmune or autoinflammatory diseases (9, 10). HLA-C is the strongest HLA-related genetic locus in psoriasis (20). HLA-C was associated with ACPA-positive RA (21). However, in other studies, HLA-C was found to be protective from the development of RA (22) and rheumatoid vasculitis (23). Additionally, HLA-C was not found to be associated with methotrexate resistance in a group of RA patients (24). Alterations in protein-tyrosine phosphatase, non-receptor type 22 (PTPN22) were identified as a genetic variation in PsA (20). Although PTPN22 was shown to be associated with the development of RA, it has not been associated with a severe disease (25, 26). Other frequent genetic alterations identified in psoriasis such as gene of caspase recruitment domain-containing protein 14, psoriasis susceptibility regions and adaptor-related protein complex 1 σ3 subunit were not found to be associated in RA development and RA severity. Therefore, it can be speculated that the genetic background of psoriasis or PsA is not associated with disease severity in RA.

We found a lower incidence of psoriasis in our RA cohort as compared to the data shown in a recently published article (12). We thought that our strict inclusion criteria, which excluded patients who met both CASPAR and RA classification criteria, in the absence of adjudication to either diseases based on clinician's opinion, might underestimate the frequency of psoriasis in our RA cohort.

Our study has some limitations: information about the family history of psoriasis was obtained from the patient. However, all similar studies used the same validated approach (27). As noted above, the incidence of psoriasis was lower in our RA cohort. This may weaken the power of the study. Additionally, this may be the reason for the absence of differences between the groups. Finally, we determined the relationship only cross-sectionally, without having a follow-up period.

In conclusion, we showed that RA patients with or without psoriasis or a family history of psoriasis may have similar disease characteristics.

Conflict of interest
None

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None

Author's contribution
NS, important contributions to conceptual and planning stages of the study and collection/processing, analysis and interpretation of the data; RM, responsible for patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments; GG, responsible for logical interpretation of the results and drawing conclusions from them; BE, methodology planning to reach the conclusions; OV, reviewing article before submission from the scientific point of view and also checking spelling and grammar; SYO, responsible for patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments; MET, main writer, planning methodology to reach the conclusions and reviewing article before submission from the scientific point of view and also checking spelling and grammar.

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