Increased level of autoantibodies targeting mutated citrullinated vimentin in patients with psoriatic arthritis compared to psoriasis vulgaris

Szandra Dalmády[1], Mária Kiss[1], László Kovács[2], Gábor Sonkodi[3], Lajos Kemény[1, 4], Rolland Gyulai[1]

[1]*Department of Dermatology and Allergology, University of Szeged, 6 Korányi Fasor, Szeged, 6720, Hungary*

[2]*Department of Rheumatology, University of Szeged, 57 Kálvária Sugárút, Szeged, 6725, Hungary*

[3]*Erzsébet Hospital, Hódmezővásárhely, Rheumatology and Rehabilitation Center of Kakasszék, 143 IV. kerület, Székkutas,6821, Hungary*

[4]*Dermatological Research Group of the Hungarian Academy of Sciences, University of Szeged, 6 Korányi Fasor, Szeged, 6720, Hungary*

Szandra Dalmády: e-mail: dalmady.szandra@med.u-szeged.hu

Abstract

Antibodies against citrullinated proteins/peptides (ACPA), especially antibodies targeting mutated citrullinated vimentin (anti-MCV), are novel biomarkers of rheumatoid arthritis (RA). While ACPAs are specific and sensitive markers for RA, there have been hardly any reports regarding ACPAs in psoriatic arthritis (PsA) and psoriasis without joint symptoms (PSO). The aim of the present study was to investigate the prevalence of anti-MCV antibodies in PsA and PSO. Serum anti-MCV titres were measured in 46 PsA and 42 PSO patients, and in 40 healthy controls. Anti-MCV levels were assayed using a commercial enzyme-linked immunosorbent assay (ELISA). Serum autoantibody levels were correlated with several clinical and laboratory parameters. Anti-MCV antibody levels in PsA patients were significantly higher than titres in the PSO group. Among the clinical variables, the presence of tender knee joints and nail psoriasis was significantly associated with anti-MCV positivity in PsA patients. Higher anti-MCV titers in PSO patients were associated with more severe disease course, and with early onset of psoriatic skin symptoms. Our results suggest that anti-MCV antibodies can be used as novel markers in the diagnosis of psoriatic arthritis, and in a subset of psoriasis patients.

1. Introduction

Antibodies targeting mutated citrullinated vimentin (MCV) belong to the group of anti-citrullinated protein/peptide antibodies (ACPAs). Detection of ACPA titres is a novel specific and sensitive marker for diagnosing rheumatoid arthritis (RA) [1-5]. Furthermore, ACPAs have important prognostic relevance as well: higher ACPA levels are associated with faster progression and poorer outcome in RA [6-9]. Novel members of the ACPA group are the antibodies against citrullinated cyclic peptides (anti-CCP). The anti-CCP antibodies seemed to fulfil the requirements of an ideal marker in the diagnosis of early RA. Recently, antibodies targeting mutated citrullinated vimentin (anti-MCV) were found to have even higher diagnostic sensitivity than anti-CCP and rheuma factor tests in RA [10-12]. Anti-MCV antibodies are detectable in early RA patients, even before symptoms are manifest, thus, they are supposed to have important prognostic value. Several recent studies suggest that the production of these autoantibodies is associated with faster disease progression, and seems to be a useful predictive marker of severe joint damage [6, 13]. Anti-MCV antibodies target the citrullinated vimentin. Vimentin is the main cytoskeletal component of the mesenchymal cells [14, 15]. It is not coded by DNA, it can only be expressed by post-translational modification. The post-translational modification is the enzymatic citrullination of the amino acid arginine. Vimentin contains 43 arginine residues, and the citrullination is catalyzed by the enzyme peptidylarginine deiminase (PAD or PADI). PAD enzymes can be found in monocytes and macrophages. Tissue inflammation and cell apoptosis changes the structure of the protein by enzymatic citrullination, and activate the immune system by the increased production of autoantibodies [16]. Recent studies suggest that the enzymatic citrullination and the production of ACPAs also can be associated with other inflammative arthritis associated autoimmune diseases [17-19].

Psoriatic arthritis (PsA) is a seronegative spondyloarthropathy developing in up to 30 percent of patients with psoriasis (National Psoriasis Foundation, www.psoriasis.org). PsA occurs more frequently in patients with HLA-B27 haplotype [20-22]. PsA has several different clinical phenotypes: oligoarticular, polyarticular, symmetrical and asymmetrical peripheral joint inflammation or axial involvement [23, 24]. Several different system and criteria exist to aid the diagnosis and classification of PsA [21, 25-29]. Although none of them are unequivocally accepted, the Moll and Wright [29] described classification criteria and more recently the classification criteria for psoriatic arthritis (CASPAR) have been used most frequently [28]. The wide spectrum of disease expression makes it often difficult to distinguish PsA from rheumatoid arthritis (RA) or other spondylarthropathies. Currently, there is no specific test that could be used in the diagnosis of PsA. Moreover, a biomarker (or biomarkers) that could distinguish between different clinical phenotypes

of PsA or PsA and psoriasis vulgaris, or could be used as a predictive marker for future PsA development in psoriasis patients, is still lacking.

Because of the several clinical similarities between PsA and RA, and because of the fact that the anti-MCV antibodies are highly sensitive markers in RA, we aimed to investigate the prevalence of anti-MCV antibodies in PsA and PsO patients. Furthermore, associations between the anti-MCV antibody titres and the clinical and laboratory variables of PsA and PsO patients were also studied.

2. Materials and Methods

2.1. Study population.

This clinical study was approved by the Regional and Institutional Human Medical Biological Research Ethics Committee of the Albert Szent-Györgyi Clinical Center, University Of Szeged. Informed consent was obtained from all participants in the study.

In the psoriatic arthritis (PsA) group we studied 46 patients, 24 women and 22 men, seen at the Department of Rheumatology and at the Department of Dermatology and Allergology of the University of Szeged (Szeged, Hungary), for psoriatic arthritis. Basic demographic and clinical characteristics of PsA group are summarized in Table 1. The mean (± standard deviation; SD) age of patients was 54.3 ± 11.9 years (range: 28-77 years). At the time of sampling collection the mean DAS28 score was 4.51 ± 1 (range: 2.08-6.81); 33 (72%) patients' scores were lower or equal to 5.1 (low PsA activity), whereas 13 (28%) had DAS28 scores higher than 5.10 (high PsA activity). All patients were previously or currently treated with at least one type of disease-modifying antirheumatic drug (DMARD). The group was heterogeneous regarding arthritis phenotypes. We used the Moll and Wright criteria [29] to classify PsA patients into five subgroups. Twenty five patients (54%) had asymmetrical oligoarthritis, 20 patients (43%) had symmetrical polyarthritis, 8 patients (17%) had axial type of arthritis, and 2 patients (4%) had distal arthritis. There was only 1 patient having arthritis mutilans (2%). Fifteen PsA patients (33%) had distal interphallangeal (DIP) joint inflammation. All patients had psoriatic skin lesion as well. Detailed clinical and laboratory characteristics of patients in the PsA group are shown in Table 2.

Forty two patients with psoriasis vulgaris (PsO), treated at the Department of Dermatology and Allergology, University of Szeged, were enrolled in the study. Basic demographic and clinical characteristics of psoriasis group without arthritis are shown in Table 1. The mean age was 45.60 ± 15.72 years (range: 18-78 years), and the female:male ratio was 11:31 (26% vs. 74%). The group consisted of 6 patients with mild and 36 patients with severe disease course. Assessment of disease course severity was based on previous and concomitant antipsoriatic therapies: patients previously or currently treated with systemic (including biological) therapy or full body phototherapy were considered severe psoriasis patients, whereas others were considered as having a mild disease

course. At the time of serum sample collection the mean Psoriasis Area and Severity Index (PASI) score was 5.84 ± 6.75 (range: 0.00-34.20), however, most patients were on concurrent systemic, biological or phototherapy. None of the patients had psoriatic joint involvement, as assessed by a trained rheumatologist. Clinical and laboratory characteristics of PsO patients are summarized in Table 2.

A randomly selected, self-stated healthy group of volunteers (N=40) served as control (none of them had ever psoriatic skin or joint symptoms). The mean age was 45.05 ± 19.56 years (range: 16-82 years) and the female:male ratio was equal (20 vs. 20).

2.2. Detection of anti-MCV IgG by ELISA. The anti-MCV IgG antibodies were analysed by ELISA (ORG 548 anti-MCV; Orgentec Diagnostika GmbH, Mainz, Germany), which contains recombinant MCV as antigen. The analysis was conducted according to the manufacturer's instructions for use. Patients with anti-MCV titers higher than the 20 U/ml cut-off value, as recommended by the manufacturer, were considered being positive.

2.3. Statistical analysis. The associations between the antibody levels and different clinical parameters were analysed by non-parametric (Mann-Whitney u test) and correlation (Spearman's rho) tests. The associations between the anti-MCV positivity and the clinical features were compared by Fischer exact test and correlations (Spearman's rho). P values <0.05 were considered significant. All statistical analyses were performed using the statistical program SPSS Windows (v15.0).

3. Results

3.1. Anti-MCV titers are significantly higher in PsA than in PsO patients and non-psoriatic individuals. As anti-MCV positivity is a characteristic hallmark of rheumatoid arthritis, first we analysed whether anti-MCV antibodies are also associated with a different type of inflammatory joint disease, psoriatic arthritis. PsA patients had significantly higher mean serum anti-MCV levels than patients with only skin manifestations of psoriasis (Figure 1). The mean autoantibody level of the PsA group was 30.32 ± 82.14 U/ml compared to 8.71 ± 7.41 U/ml in the PSO group. Statistically significant difference was not detected between the mean antibody levels in the control (9.50 ± 4.23 U/ml) and the PSO group.

When patients were subdivided into anti-MCV positive and anti-MCV negative populations, based on the recommended cut-off value (> 20 U/ml), 11 PsA patients (24%) and 3 PsO patients (8%) were found to be positive for anti-MCV, whereas all of the controls were anti-MCV negative. The differences between the PsA and PsO groups, as well as the PsA and control groups were found

statistically significant (P = 0.032 and P = 0.0009, respectively). Statistically significant difference was not detected between the PsO and the control groups (P = 0.0848).

3.2. Higher anti-MCV titer in PsO patients is associated with more severe disease course. When psoriasis patients were subdivided into severe (previously or currently treated with systemic or phototherapy) and mild (never received systemic or phototherapy) groups, higher anti-MCV antibody titers were significantly associated with more severe disease course (9.73 ± 7.54 U/ml vs. 2.73 ± 2.37 U/ml, P = 0.033) (Figure 2). Furthermore, we found that severe PsO patients treated with biological therapy (Figure 3) had significantly higher anti-MCV levels than severe psoriasis patients not requiring biological therapy (14.01 ± 6.22 U/ml vs. 3.01 ± 3.34 U/ml, P < 0.01). It seems, therefore, that present psoriasis activity is not a critical determinant of anti-MCV level. Rather, patients with the most severe disease course - and thus requiring biological therapy - have the highest anti-MCV levels among PsO patients. A similar analysis in the PsA group was not feasible, as the group almost entirely consisted of severe psoriatic arthritis patients receiving systemic DMARD or biological therapy. Similarly to the PsO group, current disease activity, as demonstrated by the DAS28 level, was not associated with higher anti-MCV levels in the PsA group either (P = 0.843, data not shown).

3.3. High anti-MCV titers in psoriasis are associated with early onset of disease. Psoriasis patients can be subdivided into two distinct groups based on the first onset of skin symptoms. Patients with early onset (below 30 years of age) psoriasis usually have stronger genetic background (HLA-cw6), and among others, more frequently develop psoriatic arthritis [30, 31]. Therefore, next we analysed, whether an association between the age at onset of psoriasis and the level of anti-MCV antibody titers exist. As demonstrated in Figure 4, anti-MCV levels are in significant inverse correlation with the age at the onset of psoriasis (P = 0.019), namely, patients with early appearance of psoriatic skin symptoms usually present with higher anti-MCV levels than patients with late disease onset. When the same analysis was carried out in the PsA group, no correlation was found between the age of arthritis onset and the level of anti-MCV serum level (P = 0.096, data not shown).

3.4. The presence of tender knee joints and nail psoriasis is associated with anti-MCV positivity in PsA patients. In order to find clinical or laboratory features associated with high anti-MCV levels, we next correlated a detailed set of parameters with anti-MCV positivity in psoriatic arthritis patients. PsA patients were subdivided into anti-MCV positive and negative groups, using the recommended cut-off value (>20 U/ml). The list of studied parameters is shown in Table 3. A similar experiment, although seemingly reasonable, was not feasible in the PsO group, as the low number of anti-MCV positives (N = 3) did not allow fair statistical analysis in this group.

Among all parameters analysed in the PsA group, only two proved to be correlated with high anti-MCV titers. The presence of painful knee joints was significantly more frequent in anti-MCV positive patients (63.64% vs. 25.71%, P = 0.032). When anti-MCV titers in PsA patients with or without the presence of painful knees were compared, significantly higher mean antibody titer was detected in the group with painful knees (61.18 ± 133.76 U/ml vs. 13.87 ± 20.22 U/ml, P = 0.013) (Figure 5). There was no correlation, however, between presence of painful knees and either the patient's age or the patient's body weight (data not shown).

The second clinical feature significantly more frequently appearing in the anti-MCV positive PsA group was the presence of nail psoriasis (63.64% and 17.14% in patients with and without psoriatic nail symptoms, respectively, P = 0.006). However, when PsA and PsO patients were subdivided based on the presence of nail symptoms, although a clear trend was observed towards an increased anti-MCV level in PsA patients with nail symptoms, the difference was not statistically significant (Figure 6).

4. Discussion

In this study, we have demonstrated that anti-MCV titers are significantly higher in psoriasis patients with arthritis than in psoriasis patients without arthritis or in healthy controls. The mean autoantibody level in the PsA group was 30.3 U/ml compared to 8.7 U/ml in the PSO, and 9.5 U/ml in the control group. Serum anti-MCV concentrations, although clearly elevated in a subset of PsA patients, were markedly lower than the several hundred-to-thousand U/ml values reported previously in RA patients [32]. Similar to our observations, modestly elevated anti-MCV titers were reported previously in a subpopulation of PsA [12, 33], as well as, more recently, in ankylosing spondylitis (AS) patients [34]. In our study cohort, 24% (11 out of 46) of PsA patients were found to be anti-MCV positive. To our knowledge, anti-MCV levels in PsA have been reported only 2 times previously, and the results are not in full concordance. In these reports the prevalence of anti-MCV antibodies in PsA ranges from 3.6% [33] to 15.2% [12]. The cause of the even higher percentage of anti-MCV positivity in our study population cannot be fully explained. Anti-MCV antibody titers were previously reported to significantly correlate with disease activity in rheumatoid arthritis [11, 13]. In our anti-MCV positive patients, however, the average number of swollen joints was not very high (3.45 ± 2.94), disease activity according to DAS28 score was moderate (4.49 ± 0.98). Thus, in our study population, anti-MCV reactivity was not associated with high disease activity; however, our patients were all actively treated with DMARDs or biologicals at the time of sample collection.

When clinical and laboratory features were correlated with anti-MCV levels, nail psoriasis and tender knee joints were observed significantly more frequently in anti-MCV positive PsA patients than in anti-MCV seronegatives (64% vs. 17%). It has recently been recognized that distal

interphalangeal (DIP) joint disease in PsA is associated with diffuse inflammation that envelops the nail root and adjacent bone [35]. Thus, nail matrix inflammation, and, therefore, psoriatic nail changes are resulting from PsA enthesitis, and consequently, nail psoriasis reflects DIP joint enthesitis. More recently, it has been shown that nail involvement in psoriasis is directly correlated with systemic enthesitis, as enthesopathy scores are significantly higher in PsA patients with nail disease than in patients without nail disease [36]. Taken together, the association of anti-MCV positivity with psoriatic nail symptoms in our study population may indicate that high anti-MCV level is a marker of systemic enthesitis in PsA. However, we could not confirm this hypothesis by directly correlating enthesopathy scores with anti-MCV titers, as the presence of subclinical enthesitis was not recorded at the time of sample collection in this study. Whether the increased number of PsA patients with tender knee joints within the group of anti-MCV seropositives is an epiphenomenon, or represents a clear pathogenetic association, requires further investigations.

Although the mean anti-MCV titers of psoriasis patients without arthritis did not differ from that detected in healthy controls, when psoriasis patients without arthritis were divided into severe and mild groups, higher anti-MCV antibody titers were significantly associated with more severe disease course (Figure 2). Furthermore, patients treated with biological therapy had significantly higher anti-MCV levels than severe psoriasis patients not requiring biological therapy (Figure 3). These findings imply that within the group of non-arthritic psoriasis patients, higher anti-MCV levels may distinguish patients with more severe disease course. Whether these patients have significant subclinical joint involvement, potentially detectable with highly sensitive imaging methods, is unclear. Furthermore, we cannot exclude the possibility that these patients would, in the future, develop clinically evident psoriatic arthritis. Concerning the role of (biological) therapy in ACPA levels, some studies have reported significantly decreased RF and anti-CCP serum levels in RA patients, as an effect of 6-12 months of TNF inhibitor therapy [37-39]. Roland et al. found significantly decreased anti-MCV antibody levels after 18-24 months of anti-TNF treatment in RA [40]. Several other studies, however, did not report marked changes in the anti-CCP levels after 22, 30 and 54 weeks of infliximab treatment in rheumatoid arthritis [41-43]. These studies indicate that anti-CCP antibodies are not influenced by anti-TNF-α therapy, and are qualitatively stable hallmark of RA. Even though a definite conclusion cannot be drawn from these findings, considering the relatively low overall anti-MCV titers in the PsO population, in seems unlikely that biological treatment would significantly modify (or even increase) the anti-MCV antibody levels. Therefore, the increased antibody titers in the group of psoriasis patients treated with biological therapy are, in our opinion, not directly related to the treatment, but to the underlying severe disease course leading to the use of biologicals. The idea that more severe disease course in psoriasis is associated with higher anti-MCV levels, was further supported by the finding that anti-MCV levels are in significant inverse correlation with the age at the onset of psoriatic skin symptoms (Figure 4). It is well known

that patients with early onset psoriasis usually have stronger genetic background (HLA-cw6), and among others, more frequently develop psoriatic arthritis [30, 31]. Also, early onset psoriasis is frequently associated with more severe disease course, thus patients with early onset psoriasis are potentially more likely to suffer from psoriatic arthritis and from more severe skin symptoms.

In conclusion, our study suggests that anti-MCV antibodies, apart from being biomarkers of early RA, can also be used to differentiate a subset of PsA patients from psoriasis patients without arthritis. As differentiating in early and mild forms of PsA can present significant challenge in some cases, detection of anti-MCV positivity can aid the diagnosis of PsA, especially in patients with psoriatic nail symptoms and tender knee joints. Furthermore, high levels of anti-MCV in psoriasis patients without clinically manifest arthritis may also distinguish patients who are more likely to run a severe disease course, and potentially require biological therapy. However, this study needs to be expanded on a large group of PsA and psoriasis patients to confirm these associations.

TABLE 1**:** Basic demographic and clinical characteristics of Psoriatic Arthritis (PsA) and Psoriasis (PsO) groups.

Variable	Psoriatic Arthritis (*N = 46*)	Psoriasis (*N = 42*)
Male : female ratio	24 : 22	31 : 11
Age (mean ± SD; years)	54.35 ± 11.87	45.60 ± 15.72
BMI (mean ± SD; kg/m^2)	29.38 ± 6.41	28.86 ± 9.80
Current smokers (%)	20%	12%
Age at diagnosis of PsO (mean ± SD; years)	38.91 ± 14.47	28.84 ± 15.82
Age at diagnosis of PsA (mean ± SD; years)	45.26 ± 13.80	–
Disease scored severity (mild : severe)	0 : 46	6 : 36
Psoriasis guttata (%)	4%	20%
Arthritis mutilans (%)	2%	–
Axial type of arthritis (%)	17%	–
Distal type of arthritis (%)	4%	–
Asymmetrical oligoarthritis (%)	54%	–
Symmetrical polyarthritis (%)	43%	–
Therapy		
Received MTX therapy (%)	85%	57%
Received systemic steroid treatments (%)	13%	2%
Received 311nm NB- UVB therapy (%)	7%	38%
Received PUVA therapy (%)	2%	31%
Received biological therapy (%)	13%	52%

PsO: psoriasis vulgaris, PsA: psoriatic arthritis, BMI: body mass index, MTX: methotrexate, PUVA: psoralen + ultraviolet A, 311nm NB-UVB: 311nanometer narrow-band ultraviolet B. Symmetrical arthritis: two side arthritis in frequency more than 50%.

TABLE 2**:** Clinical and laboratory characteristics of patients in the Psoriatic Arthritis (PsA) and Psoriasis Vulgaris (PsO) groups

Variable	Psoriatic Arthritis (*N = 46*)	Psoriasis (*N = 42*)
ANTI-MCV positivity (%)	24%	8%
Level of ANTI-MCV (mean ± SD; U/ml)	30.32 ± 82.14	8.71 ± 7.41
ANA positivity (%)✦	38%	not measured
RF positivity (>9 U/ml; %)✦	11%	not measured
Active psoriatic lesions in the skin	100%	95%
PASI score (mean ± SD)	–	5,84 ± 6,75
Nail psoriasis (%)	28%	43%
Scalp psoriasis (%)	72%	57%
Plaques on the face (%)	11%	14%
Plaques on the upper limbs (%)	61%	71%
Plaques on the trunk (%)	30%	48%
Plaques on the perineum (%)	15%	7%
Plaques on the lower limbs (%)	59%	88%
Arthritic features		
DAS28 score (mean ± SD)	4.51 ± 1.00	–
DIP involvement (%)	33%	–
Erosion (%)	24%	–
Tender joint count (mean ± SD)	9.78 ± 5.90	–
Back (%)	48%	–
Shoulders (%)	37%	–
Elbows (%)	15%	–
Wrists (%)	46%	–
Hands (%)	67%	–
Hip (%)	17%	–
Knees (%)	35%	–
Foot (%)	61%	–
Swollen joint count (mean ± SD)	2.67 ± 3.19	–
Swollen shoulder (%)	0%	–
Swollen elbow (%)	2%	–
Swollen wrist (%)	9%	–
Swollen hand (%)	43%	–
Swollen hip (%)	0%	–
Swollen knee (%)	11%	–
Swollen feet (%)	26%	–

Anti- MCV: antibodies against mutated citrullinated vimentin, ANA: anti-nuclear antibody, RF: rheuma factor, DIP: distal interphallangeal, PASI: psoriasis area and severity index, DAS28: disease activity score.

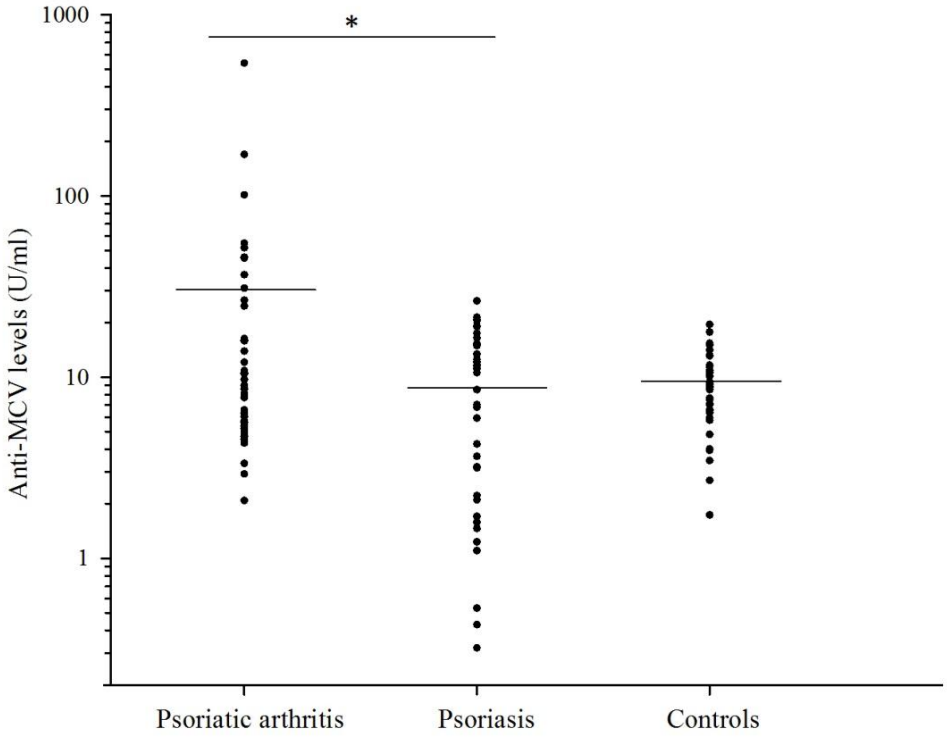

FIGURE 1: Anti-MCV titers are higher in PsA patients than in patients with psoriasis without arthritis and in healthy volunteers. The plots show the antibody levels of the investigated patients. The horizontal lines represent the mean levels of anti-MCV antibodies. The mean autoantibody level of the PsA group was 30.32 ± 82.14 U/ml compared to 8.71 ± 7.41 U/ml in the psoriasis and 9.50 ± 4.23 U/ml in the control group. *There was statistically significant difference between the PsA and the psoriasis groups ($P < 0.05$).

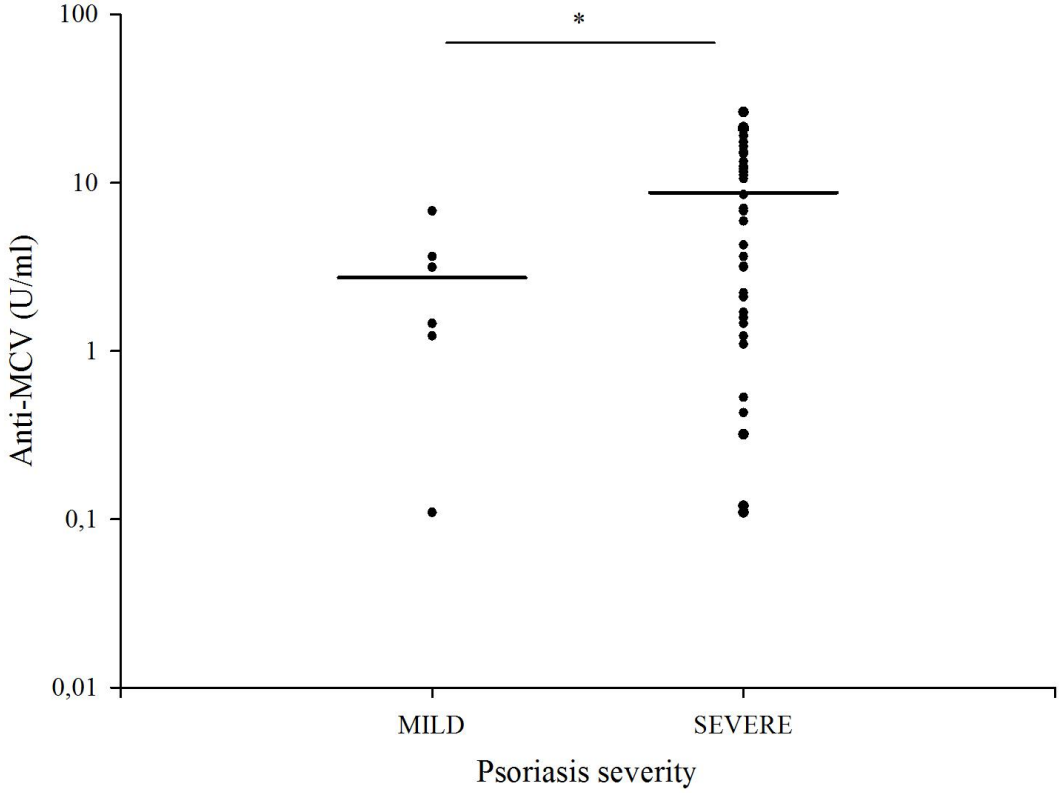

FIGURE 2**:** Anti-MCV titers are higher in patients with severe psoriasis than in mild psoriasis. The plots show the anti-MCV levels in severe (previously or currently treated with systemic or phototherapy) and mild (never received systemic or phototherapy) PsO patients. The horizontal lines represent the mean levels of anti-MCV antibodies. *Significant difference was detected between the mild and the severe psoriasis patients' groups (2.73 ± 2.37 U/ml vs. 9.73 ± 7.54 U/ml, $P < 0.05$).

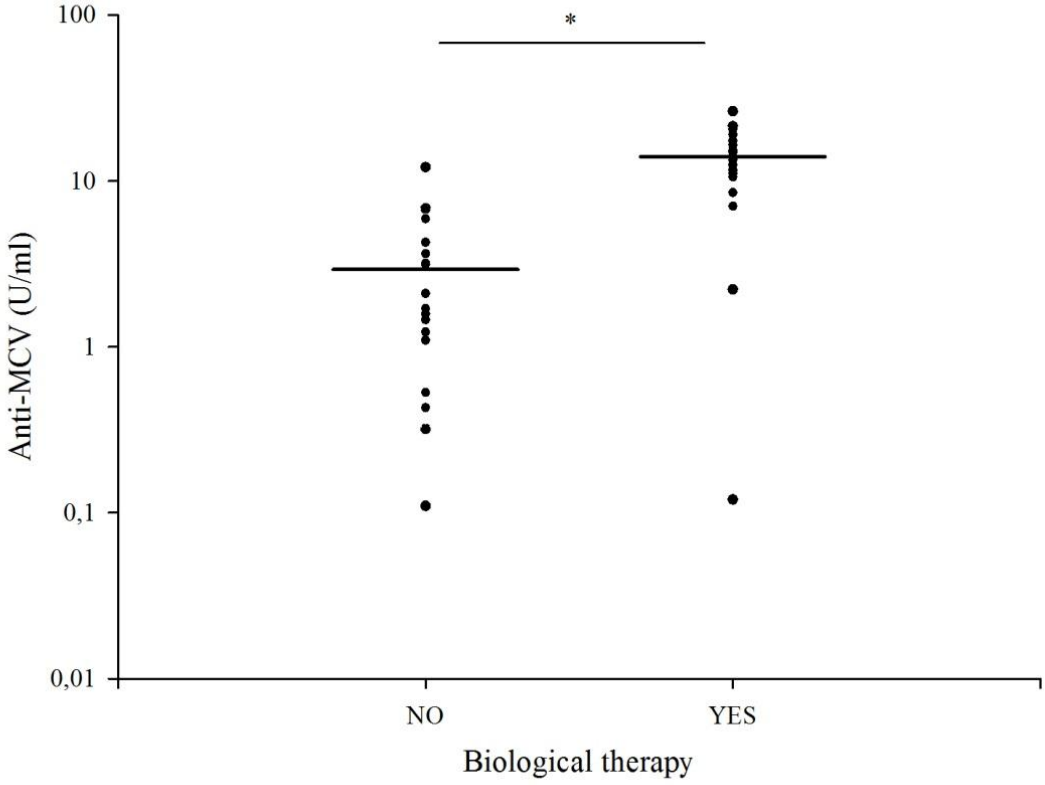

FIGURE 3**:** Anti-MCV titers are higher in severe PsO patients treated with biological therapy than in severe psoriasis patients not requiring biological therapy. The plots show the antibody levels of investigated patients. The horizontal lines represent the mean levels of anti-MCV antibodies. *PsO patients not requiring biological therapy had significantly lower anti-MCV levels than severe psoriasis patients treated with biological therapy (3.01 ± 3.34 U/ml vs. 14.01 ± 6.22 U/ml, $P < 0.01$).

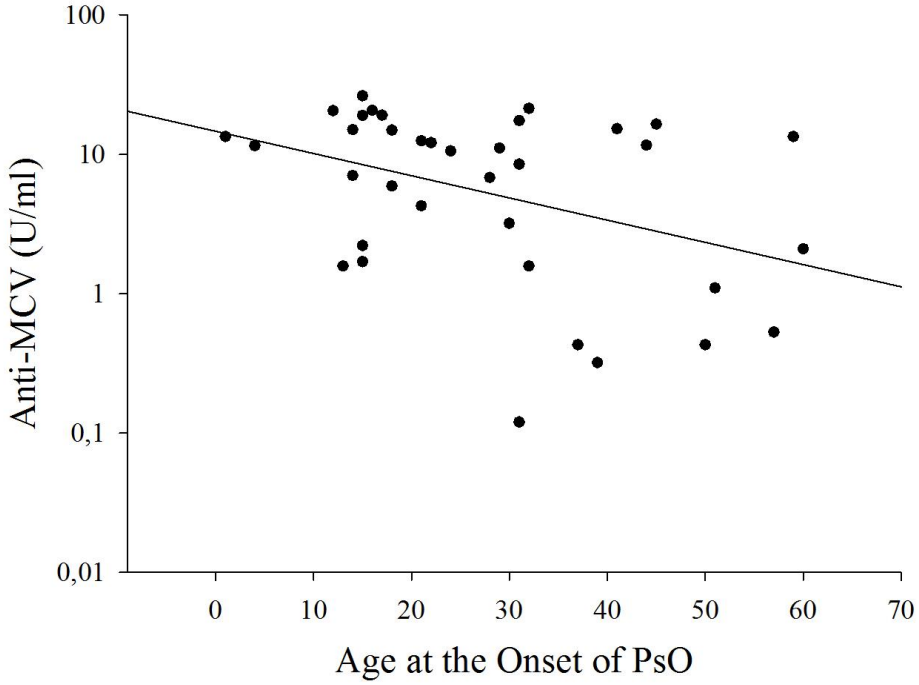

FIGURE 4**:** Anti-MCV levels are in significant inverse correlation with the age at the onset of psoriasis in psoriasis patients. The plots represent the anti-MCV levels of the psoriasis patients and the age at the onset of psoriasis. (P = 0.019)

TABLE 3: Comparisons of clinical findings between anti-MCV positive versus anti-MCV negative PsA patients.

Variable	Anti-MCV positive PsA patients (*N = 11*)	Anti-MCV negative PsA patients (*N = 35*)	
Sex ratio (male : female)	3 : 8	21 : 14	
Age (mean ± SD; years)	57.91 ± 9.26	53.23 ± 12.48	
Current smoker (%)	9%	23%	
Age at diagnosis of PsO (mean ± SD; years)	44.27 ± 13.73	37.23 ± 14.48	
Age at diagnosis of PsA (mean ± SD; years)	46.55 ± 15.78	44.86 ± 13.34	
PsA scored severity (mild : severe)	0 : 11	0 : 35	
Psoriasis guttata (%)	9%	3%	
Arthritis mutilans	9%	0%	
Axial type (%)	27%	14%	
Distal type (%)	9%	3%	
Asymmetrical oligoarthritis (%)	64%	51%	
Symmetrical polyarthritis (%)	36%	46%	
Therapy			
Received local steroid treatments (%)	73%	83%	
Received sulfasalazine (%)	27%	20%	
Received systemic steroid treatments (%)	27%	9%	
Received 311nm NB-UVB therapy (%)	18%	3%	
Received PUVA therapy (%)	0%	3%	
Received MTX therapy (%)	73%	89%	
Received biological therapy (%)	18%	11%	
DIP involvement (%)	18%	37%	
Erosion (%)	18%	26%	
Level of ANTI-MCV (mean ± SD; U/ml)	**102.41 ± 150.99**	**7.67 ± 3.77**	*
ANA positivity (%)✦	50%	33%	
RF positivity (%)✦	0%	14%	
DAS28 score (mean ± SD)	4.49 ± 0.98	4.52 ± 1.02	
Psoriatic skin lesions			
Nail psoriasis (%)	**64%**	**17%**	*
Scalp psoriasis (%)	64%	74%	
Plaques on the face (%)	9%	11%	
Plaques on the upper limbs (%)	55%	63%	
Plaques on the trunk (%)	36%	29%	
Plaques on the perineum (%)	9%	17%	
Plaques on the lower limbs (%)	55%	60%	
Arthritic features			
Tender joint count (mean ± SD)	7.27 ± 3.58	10.57 ± 6.29	
Back (%)	36%	51%	
Shoulders (%)	36%	37%	
Elbows (%)	18%	14%	
Wrists (%)	45%	46%	
Hands (%)	45%	74%	
Hip (%)	0%	23%	
Knees (%)	**64%**	**26%**	*
Foot (%)	73%	57%	
Swollen joint count (mean ± SD)	3.45 ± 2.94	2.43 ± 3.27	
Swollen shoulder (%)	0%	0%	
Swollen elbow (%)	9%	0%	
Swollen wrist (%)	18%	6%	
Swollen hand (%)	45%	40%	
Swollen hip (%)	0%	0%	
Swollen knee (%)	27%	6%	
Swollen feet (%)	18%	29%	

PsO: psoriasis vulgaris, PsA: psoriatic arthritis, Anti- MCV: antibodies against mutated citrullinated vimentin, BMI: body mass index, PASI: psoriasis area and severity index, DAS28: disease activity score, DIP: distal interphallangeal, HLA B27: human leukocyte antigen B27, ANA: anti-nuclear antibodies, RF: rheuma factor, ESR: erythrocyte sedimentation rate, CRP: C- reactive protein, MTX: methotrexate, PUVA: psoralen + ultraviolet A, nm: nanometer. Symmetrical arthritis: two side arthritis in frequency more than 50%.✦ The current values in these cases at least in 60% were completed. In case of other values, the datas were complete, 100%. * There were significant differences between the anti-MCV positive and negative groups ($P < 0.05$).

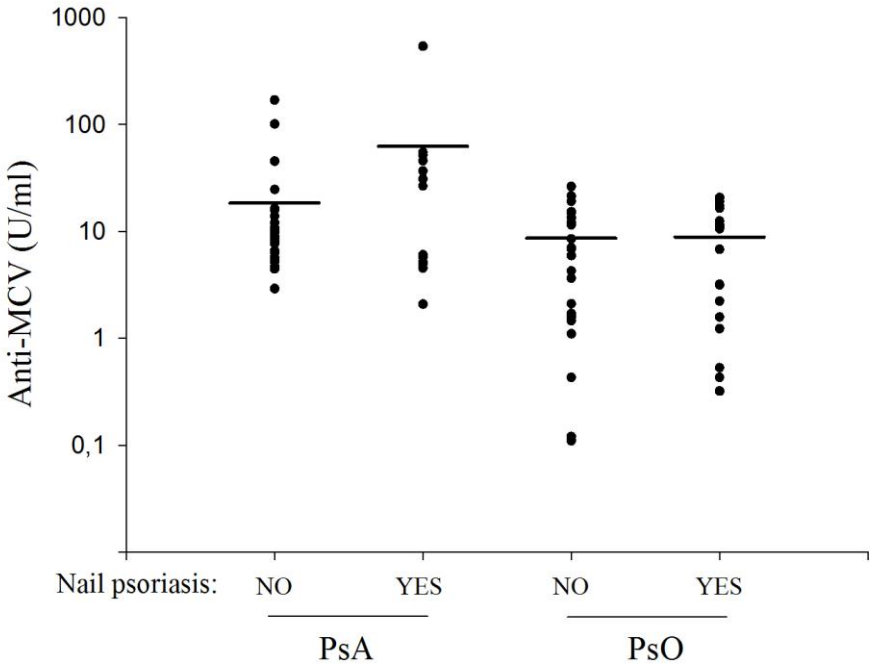

FIGURE 5**:** The anti-MCV levels of PsA and PsO patients with and without nail psoriasis. The plots show the antibody levels of PsA and PsO patients with and without nail psoriasis. The horizontal lines represent the mean levels of anti-MCV antibodies. Significant correlations were not found between the groups.

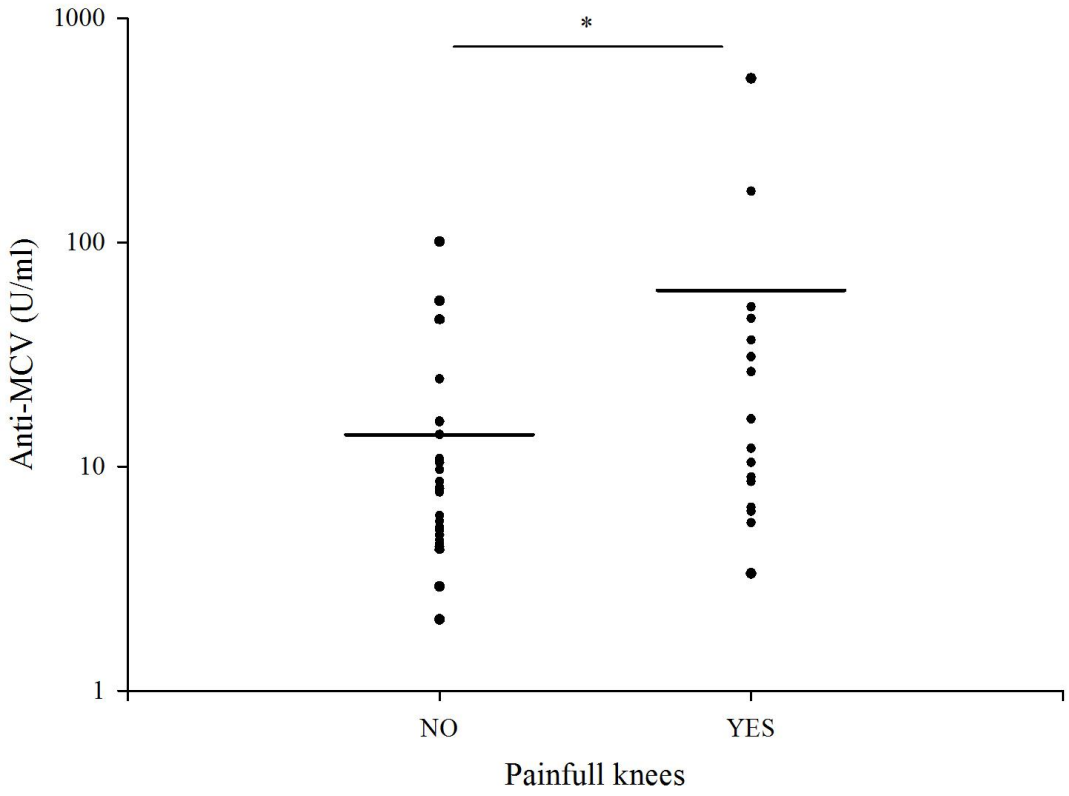

FIGURE 6**:** The anti-MCV levels in PsA patients with painful knees are significantly higher than in patients without painful knee. The plots show the antibody in PsA patients without pain of knees (labelled as "NO") and with pain of knees (labelled as "YES"). The horizontal lines represent the mean levels of anti-MCV antibodies. * There was significant difference of anti-MCV levels between the two groups (13.87 ± 20.22 U/ml vs. 61.18 ± 133.76 U/ml, $P < 0.05$).

References

[1] L. Klareskog, M. Widhe, M. Hermansson, and J. Ronnelid, "Antibodies to citrullinated proteins in arthritis: pathology and promise," *Current Opinion in Rheumatology,* vol. 20, no. 3, pp. 300-305, 2008.

[2] T. Skogh, "Does a positive anti-CCP test identify a distinct arthritis entity?" *Arthritis Research & Therapy,* vol. 7, no. 6, pp. 230-232, 2005.

[3] A.H. van der Helm-van Mil, and T.W. Huizinga, "Advances in the genetics of rheumatoid arthritis point to subclassification into distinct disease subsets," *Arthritis Research & Therapy,* vol. 10, no. 2, pp. 205, 2008.

[4] M.A. van Boekel, E.R. Vossenaar, F.H. van den Hoogen, and W.J. van Venrooij, "Autoantibody systems in rheumatoid arthritis: specificity, sensitivity and diagnostic value," *Arthritis Research,* vol. 4, no. 2, pp. 87-93, 2002.

[5] N. Bizzaro, G. Mazzanti, E. Tonutti et al., "Diagnostic accuracy of the anti-citrulline antibody assay for rheumatoid arthritis," *Clinical Chemistry,* vol. 47, no. 6, pp. 1089-1093, 2001.

[6] B. Vander Cruyssen, I. Peene, T. Cantaert et al., "Anti-citrullinated protein/peptide antibodies (ACPA) in rheumatoid arthritis: specificity and relation with rheumatoid factor," *Autoimmunity Reviews,* vol. 4, no. 7, pp. 468-474, 2005.

[7] H. Visser, S. le Cessie, K. Vos et al., "How to diagnose rheumatoid arthritis early: a prediction model for persistent (erosive) arthritis," *Arthritis and Rheumatism,* vol. 46, no. 2, pp. 357-365, 2002.

[8] E.J. Kroot, B.A. de Jong, M.A. van Leeuwen et al., "The prognostic value of anti-cyclic citrullinated peptide antibody in patients with recent-onset rheumatoid arthritis," *Arthritis and Rheumatism,* vol. 43, no. 8, pp. 1831-1835, 2000.

[9] C.H. van Jaarsveld, E.J. ter Borg, J.W. Jacobs et al., "The prognostic value of the antiperinuclear factor, anti-citrullinated peptide antibodies and rheumatoid factor in early rheumatoid arthritis," *Clinical and Experimental Rheumatology,* vol. 17, no. 6, pp. 689-697, 1999.

[10] H. Bang, K. Egerer, A. Gauliard et al., "Mutation and citrullination modifies vimentin to a novel autoantigen for rheumatoid arthritis," *Arthritis and Rheumatism,* vol. 56, no. 8, pp. 2503-2511, 2007.

[11] L. Mathsson, M. Mullazehi, M.C. Wick et al., "Antibodies against citrullinated vimentin in rheumatoid arthritis: higher sensitivity and extended prognostic value concerning future radiographic progression as compared with antibodies against cyclic citrullinated peptides," *Arthritis and Rheumatism,* vol. 58, no. 1, pp. 36-45, 2008.

[12] L. Damjanovska, M.M. Thabet, E.W. Levarth et al., "Diagnostic value of anti-MCV antibodies in differentiating early inflammatory arthritis," *Annals of the Rheumatic Diseases,* vol. 69, no. 4, pp. 730-732, 2010.

[13] L. Soos, Z. Szekanecz, Z. Szabo et al., "Clinical evaluation of anti-mutated citrullinated vimentin by ELISA in rheumatoid arthritis," *The Journal of Rheumatology,* vol. 34, no. 8, pp. 1658-1663, 2007.

[14] E.R. Vossenaar, N. Despres, E. Lapointe et al., "Rheumatoid arthritis specific anti-Sa antibodies target citrullinated vimentin," *Arthritis Research & Therapy,* vol. 6, no. 2, pp. R142-50, 2004.

[15] H.A. Menard, E. Lapointe, M.D. Rochdi, and Z.J. Zhou, "Insights into rheumatoid arthritis derived from the Sa immune system," *Arthritis Research,* vol. 2, no. 6, pp. 429-432, 2000.

[16] E. Wagner, M. Skoumal, P.M. Bayer, and K. Klaushofer, "Antibody against mutated citrullinated vimentin: a new sensitive marker in the diagnosis of rheumatoid arthritis," *Rheumatology International,* vol. 29, no. 11, pp. 1315-1321, 2009.

[17] J.E. Gottenberg, S. Mignot, P. Nicaise-Rolland et al., "Prevalence of anti-cyclic citrullinated peptide and anti-keratin antibodies in patients with primary Sjogren's syndrome," *Annals of the Rheumatic Diseases,* vol. 64, no. 1, pp. 114-117, 2005.

[18] T. Avcin, R. Cimaz, F. Falcini et al., "Prevalence and clinical significance of anti-cyclic citrullinated peptide antibodies in juvenile idiopathic arthritis," *Annals of the Rheumatic Diseases,* vol. 61, no. 7, pp. 608-611, 2002.

[19] R. Mediwake, D.A. Isenberg, G.A. Schellekens, and W.J. van Venrooij, "Use of anti-citrullinated peptide and anti-RA33 antibodies in distinguishing erosive arthritis in patients with systemic lupus erythematosus and rheumatoid arthritis," *Annals of the Rheumatic Diseases,* vol. 60, no. 1, pp. 67-68, 2001.

[20] P. Rahman, and J.T. Elder, "Genetic epidemiology of psoriasis and psoriatic arthritis," *Annals of the Rheumatic Diseases,* vol. 64 Suppl 2, pp. ii37-9; discussion ii40-1, 2005.

[21] S. Marsal, L. Armadans-Gil, M. Martinez et al., "Clinical, radiographic and HLA associations as markers for different patterns of psoriatic arthritis," *Rheumatology (Oxford, England),* vol. 38, no. 4, pp. 332-337, 1999.

[22] Y. Liu, C. Helms, W. Liao et al., "A genome-wide association study of psoriasis and psoriatic arthritis identifies new disease loci," *PLoS Genetics,* vol. 4, no. 3, pp. e1000041, 2008.

[23] D.D. Gladman, R. Shuckett, M.L. Russell et al., "Psoriatic arthritis (PSA)--an analysis of 220 patients," *The Quarterly Journal of Medicine,* vol. 62, no. 238, pp. 127-141, 1987.

[24] J.C. Torre Alonso, A. Rodriguez Perez, J.M. Arribas Castrillo et al., "Psoriatic arthritis (PA): a clinical, immunological and radiological study of 180 patients," *British Journal of Rheumatology*, vol. 30, no. 4, pp. 245-250, 1991.

[25] D.D. Gladman, P. Helliwell, P.J. Mease et al., "Assessment of patients with psoriatic arthritis: a review of currently available measures," *Arthritis and Rheumatism*, vol. 50, no. 1, pp. 24-35, 2004.

[26] D. McGonagle, P.G. Conaghan, and P. Emery, "Psoriatic arthritis: a unified concept twenty years on," *Arthritis and Rheumatism*, vol. 42, no. 6, pp. 1080-1086, 1999.

[27] D. Veale, S. Rogers, and O. Fitzgerald, "Classification of clinical subsets in psoriatic arthritis," *British Journal of Rheumatology*, vol. 33, no. 2, pp. 133-138, 1994.

[28] W. Taylor, D. Gladman, P. Helliwell et al., "Classification criteria for psoriatic arthritis: development of new criteria from a large international study," *Arthritis and Rheumatism*, vol. 54, no. 8, pp. 2665-2673, 2006.

[29] J.M. Moll, and V. Wright, "Psoriatic arthritis," *Seminars in Arthritis and Rheumatism*, vol. 3, no. 1, pp. 55-78, 1973.

[30] J.T. Elder, "Genome-wide association scan yields new insights into the immunopathogenesis of psoriasis," *Genes and Immunity*, vol. 10, no. 3, pp. 201-209, 2009.

[31] R. Queiro, S. Alonso, M. Alperi et al., "Stratification by age of onset with 30 years as age limit is an effective means of identifying PSORS1-associated psoriasis in patients with psoriatic arthritis," *Joint, Bone, Spine : Revue Du Rhumatisme*, vol. 78, no. 6, pp. 581-583, 2011.

[32] L. Mathsson, M. Mullazehi, M.C. Wick et al., "Antibodies against citrullinated vimentin in rheumatoid arthritis: higher sensitivity and extended prognostic value concerning future radiographic progression as compared with antibodies against cyclic citrullinated peptides," *Arthritis and Rheumatism*, vol. 58, no. 1, pp. 36-45, 2008.

[33] A. Tesija-Kuna, S. Grazio, M. Miler et al., "Antibodies targeting mutated citrullinated vimentin in patients with psoriatic arthritis," *Clinical Rheumatology*, vol. 29, no. 5, pp. 487-493, 2010.

[34] N. Bodnar, Z. Szekanecz, Z. Prohaszka et al., "Anti-mutated citrullinated vimentin (anti-MCV) and anti-65 kDa heat shock protein (anti-hsp65): new biomarkers in ankylosing spondylitis," *Joint, Bone, Spine : Revue Du Rhumatisme*, vol. 79, no. 1, pp. 63-66, 2012.

[35] D. McGonagle, "Enthesitis: an autoinflammatory lesion linking nail and joint involvement in psoriatic disease," *Journal of the European Academy of Dermatology and Venereology : JEADV*, vol. 23 Suppl 1, pp. 9-13, 2009.

[36] Z.R. Ash, I. Tinazzi, C.C. Gallego et al., "Psoriasis patients with nail disease have a greater magnitude of underlying systemic subclinical enthesopathy than those with normal nails," *Annals of the Rheumatic Diseases*, vol. 71, no. 4, pp. 553-556, 2012.

[37] H.A. Chen, K.C. Lin, C.H. Chen et al., "The effect of etanercept on anti-cyclic citrullinated peptide antibodies and rheumatoid factor in patients with rheumatoid arthritis," *Annals of the Rheumatic Diseases*, vol. 65, no. 1, pp. 35-39, 2006.

[38] C. Alessandri, M. Bombardieri, N. Papa et al., "Decrease of anti-cyclic citrullinated peptide antibodies and rheumatoid factor following anti-TNFalpha therapy (infliximab) in rheumatoid arthritis is associated with clinical improvement," *Annals of the Rheumatic Diseases*, vol. 63, no. 10, pp. 1218-1221, 2004.

[39] Y. Braun-Moscovici, D. Markovits, O. Zinder et al., "Anti-cyclic citrullinated protein antibodies as a predictor of response to anti-tumor necrosis factor-alpha therapy in patients with rheumatoid arthritis," *The Journal of Rheumatology*, vol. 33, no. 3, pp. 497-500, 2006.

[40] P. Nicaise Roland, S. Grootenboer Mignot, A. Bruns et al., "Antibodies to mutated citrullinated vimentin for diagnosing rheumatoid arthritis in anti-CCP-negative patients and for monitoring infliximab therapy," *Arthritis Research & Therapy*, vol. 10, no. 6, pp. R142, 2008.

[41] P. Caramaschi, D. Biasi, E. Tonolli et al., "Antibodies against cyclic citrullinated peptides in patients affected by rheumatoid arthritis before and after infliximab treatment," *Rheumatology International*, vol. 26, no. 1, pp. 58-62, 2005.

[42] L. De Rycke, X. Verhelst, E. Kruithof et al., "Rheumatoid factor, but not anti-cyclic citrullinated peptide antibodies, is modulated by infliximab treatment in rheumatoid arthritis," *Annals of the Rheumatic Diseases*, vol. 64, no. 2, pp. 299-302, 2005.

[43] F. Bobbio-Pallavicini, R. Caporali, C. Alpini et al., "High IgA rheumatoid factor levels are associated with poor clinical response to tumour necrosis factor alpha inhibitors in rheumatoid arthritis," *Annals of the Rheumatic Diseases*, vol. 66, no. 3, pp. 302-307, 2007.