CONCISE REPORT

Antibodies against cyclic citrullinated peptide (CCP) in psoriatic patients with or without joint inflammation

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Objective: To compare the prevalence of anti-CCP antibodies in psoriatic patients with and without joint inflammation, patients with early RA, and controls.

Methods: Anti-CCP antibodies (cut off level 5 U/ml) were measured in 160 patients with psoriatic arthritis (PsA), 146 patients with psoriasis but no arthritic disease, 101 patients with early RA, and 102 healthy controls by ELISA.

Results: 11 (7%) patients with PsA, 75 (74%) patients with early RA, 2 (2%) healthy controls (2%), and 1 (0.7%) patient with psoriasis without arthritis had anti-CCP antibodies above the cut off level. The presence of anti-CCP antibodies was not related to radiological changes and/or deformity and functional impairment in PsA. 8/11 patients with PsA and anti-CCP antibodies had a polyarthritic disease, and all fulfilled the ACR criteria for RA at 4 year follow up. Five of these 8 patients also had manifestations such as dactylitis, DIP involvement, radiological changes associated with PsA, and/or enthesitis. In multiple logistic regression analysis with polyarthritis as the dependent variable, anti-CCP antibodies and rheumatoid factor significantly distinguished RA from PsA.

Conclusions: Anti-CCP antibodies were more prevalent in patients with PsA than in patients with psoriasis without arthritis, but less prevalent than in patients with early RA. Patients with PsA positive for anti-CCP antibodies more often had polyarthritic disease, but the presence of anti-CCP antibodies did not relate to radiological changes and/or deformity and functional impairment.

Psoriatic arthritis (PsA) is a heterogeneous disease with disease patterns that vary between patients, as well as within an individual patient over time. The patients may have symptoms and signs, such as mild mono-oligoarthritis or very severe, erosive and destructive polyarthritis, which are possibly indistinguishable from those seen in patients with rheumatoid arthritis (RA).[1] Other common manifestations are spondyloarthropathy with axial involvement,[1] dactylitis and/or enthesitis.[2] Rheumatoid factor (RF) is usually absent, although there are reports of a slightly increased prevalence of RF in patients with psoriasis and inflammatory joint manifestations.[3] In the Moll and Wright criteria for PsA,[1] RF should be negative for diagnosis of PsA, but in clinical practice there are patients diagnosed as having PsA if the disease pattern is more consistent with PsA (for example, dactylitis, enthesitis, distal interphalangeal (DIP) joint involvement) rather than RA even when the RF result is positive. Laboratory assessment of inflammatory activity, such as increased erythrocyte sedimentation rate, is often sparse, and to date a laboratory test with specificity for PsA is unavailable.

During the past decade new, aggressive treatments against arthritic diseases such as RA have become available and the possibility of treating the disease efficiently has changed the outcome for many patients.

A positive RF test is included in the diagnostic criteria for RA, even though RF is also detected in other rheumatic diseases.[4] The development of tests for antibodies against cyclic citrullinated peptide (anti-CCP) has increased the possibility of distinguishing between RA and other rheumatic diseases.[5–7] The specificity for RA has been shown to increase by combining the presence of anti-CCP antibody with that of RF.[5 8] Furthermore, the presence of anti-CCP antibodies and of RFs of all isotypes predate the onset of RA by several years.[8] Anti-CCP antibodies have the highest predictive values for the development of RA; however, the predictive value is increased by the concurrent presence of anti-CCP antibodies and IgA RF.[8] It is also evident that anti-CCP antibody positive patients with RA have a more erosive disease than patients with RA negative for anti-CCP.[5]

The specificity of anti-CCP antibodies for other arthritic diseases is low compared with RA.[4–7] A recent report has shown that anti-CCP antibodies occurred in 7.8% of patients with PsA.[9] In that report some of the patients had a disease pattern typical of PsA while others were psoriatic patients with concurrent RA.

The present study aimed at examining the presence of anti-CCP antibodies in psoriatic patients with and without manifestation of joint inflammation in comparison with patients with early RA and healthy controls.

MATERIAL AND METHODS

A total of 306 consecutively examined patients with psoriasis, of whom 160 (76 women, 84 men) were diagnosed as having joint inflammation, and 146 (81 women, 65 men) of the patients had psoriasis of the skin with no arthritic disease, were recruited into this cross sectional study. Additionally, 101 patients (74 women, 27 men) attending the early RA clinic were consecutively included, together with 102 randomly selected self stated healthy controls from the same geographical area, and with the same ethnic background. Anti-CCP antibodies were measured in plasma from patients and controls using the Diastat kit from Axis-Shield Diagnostics Limited (Technology Park, Dundee DD2 1XA, Scotland, UK). The cut off level for a positive test for anti-CCP antibodies was 5 U/ml.

The mean age of all subject groups was between 50 and 53 years, and the mean disease duration for the patients with PsA was 16 years and for patients with early RA <1 year. For the patient groups, erythrocyte sedimentation

Abbreviations: ACR, American College of Rheumatology; CCP, cyclic citrullinated peptide; DIP, distal interphalangeal; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor

Table 1 Details of the 11 patients positive for anti-CCP diagnosed as PsA at inclusion in the study, and disease manifestations at the 4 year follow up examination

At inclusion in the study				At 4 year follow up examination	
Age/sex	Disease pattern	RF	Anti-CCP antibody (titre)	⩾4 of the ACR criteria for RA	Disease manifestations and actual treatment
68/M	Axial disease	0	60.0	0	No disease activity
48/F	Mono-oligoarthritis	0	80.4	0	Medium disease activity. Methotrexate+sulfasalazine
30/M	Oligoarthritis	320	67.3	0	No disease activity, no radiological changes in the joints of the feet
67/F	Polyarthritis + axial disease	80	35.6	1	Low disease activity. Sulfasalazine
63/M	Polyarthritis + axial disease	80	19.6	1	Low-medium disease activity, enthesitis, DIP and MTP joints, knees, back involvement. Sulfasalazine
65/M	Polyarthritis	160	113.2	1	High disease activity, back involvement, enthesitis, no swollen joints, DIP joint involvement
50/F	Polyarthritis	80	13.1	1	Medium-high disease activity, radiological destruction hands, feet, destruction MCP II sin, joint/tuft osteolysis MTP I (pencil in cup). Remicade
33/F	Polyarthritis	160	5.4	1	Medium disease activity, clinically active PsA, joint function impairment, radiological destruction MCP I sin. Methotrexate + gold injections
61/M	Polyarthritis	320	122.5	1	Low disease activity. Prednisolone
56/F	Polyarthritis	320	123.3	1	Disease activity
75/M	Polyarthritis	320	256.3	1	Low disease activity. Auranofin

rate and RF were also determined; the number of tender and swollen joints was counted according to the American College of Rheumatology (ACR) 68 joint count for tender and 66 joint count for swollen joints,[10] excluding the DIP joints of the fingers and interphalangeal, proximal interphalangeal, and DIP joints of the toes, which are rarely affected in RA.

Statistics

Differences between continuous data were tested using the Mann-Whitney test and between categorical data using the χ^2 test. Spearman rank order correlation was used to test for correlations between variables in small samples. Multiple logistic regression analysis was used to test the predictive value of variables that were unevenly distributed between the groups.

The study was approved by the regional research ethics committee.

RESULTS

Eleven (7%) patients with PsA (median anti-CCP antibody titre 67.3 U/ml, IQR = 19.6–122.5), 75 (74%) patients with early RA (median titre 85.2 U/ml, IQR = 50.2–118.2), two (2%) healthy controls, and one (0.7%) patient with psoriasis without arthritis had titres of anti-CCP antibodies above the cut off level. The difference between patients with PsA and psoriatic patients without arthritis was significant ($p = 0.006$), as was that between patients with PsA and patients with early RA ($p<0.001$), whereas the difference between patients with PsA and controls was not significant ($p = 0.086$). Eighteen (11%) patients with PsA and 84 (83%) patients with early RA were positive for RF ($p<0.001$); furthermore, nine (6%) patients with PsA and 70 (69%) patients with early RA were positive for both anti-CCP and RF. The number of tender joints and the number of swollen joints were higher in patients with early RA than in patients with PsA (median 10.0 *v* 3.0, $p<0.001$ and 11.5 *v* 5.0, $p<0.001$, respectively). There were no correlations between the titres of anti-CCP antibodies and the number of swollen or tender joints, either in the patients with PsA or with early RA. Nor was the presence of anti-CCP antibodies related to aggressive manifestations such as radiological changes and/or deformity and functional impairment in PsA.

At a 4 year follow up examination, 8/11 patients with PsA positive for anti-CCP had a polyarthritic disease and all fulfilled ⩾4 of the ACR criteria for RA.[11] Five of these eight patients also had manifestations such as dactylitis, DIP involvement, radiological changes associated with PsA, and/or enthesitis (table 1). In multiple logistic regression analysis with polyarthritis (based on ACR joint count) as a dependent variable, anti-CCP antibodies ($p<0.001$, odds ratio (OR) = 6.53, 95% confidence interval (CI) 2.32 to 18.37) and RF ($p<0.001$, OR = 11.10, 95% CI 4.09 to 30.16) significantly distinguished between RA and PsA (data not shown).

DISCUSSION

In this study the prevalence of anti-CCP antibodies was increased in patients with psoriasis with arthritis compared with patients with psoriasis without arthritis; however, the prevalence was significantly lower than in patients with early RA. Only 11 patients with PsA were positive for anti-CCP antibodies, most of whom fulfilled the ACR criteria for RA at 4 year follow up. Most frequently they fulfilled the criteria of positive RF, polyarthritis, arthritis in the hands, and morning stiffness. However, some of the patients fulfilling the criteria for RA had clinical signs associated with PsA, demonstrating the complexity and difficulty in diagnosing the two diseases. The number of patients with PsA positive for anti-CCP antibodies was not sufficient to stratify for subgroup analysis. Although the presence of anti-CCP antibodies did not correlate with the number of swollen or tender joints, it seemed, when each positive patient was evaluated separately, that anti-CCP antibodies in patients with PsA were related to polyarthritis and the presence of RF rather than to RA as defined by the ACR criteria. On the other hand, there is a possibility that the patients have both PsA and RA because both diseases are quite common in the population. This explanation would further strengthen the association between anti-CCP antibodies and RA. However, in multiple logistic regression anti-CCP antibodies, and more strongly, RF distinguished between RA and PsA.

Recent studies report an association between radiological progression and the presence of anti-CPP antibodies in patients with RA.[4] In the present study the patients with RA had short disease duration (<1 year) and, consequently, radiological progression was not evaluated. In the patients with PsA there was no association between radiological changes and/or deformity/functional impairment with anti-CCP antibodies.

CONCLUSIONS

Anti-CCP antibodies were more common in patients with PsA than in patients with psoriasis without arthritis, but less common than in patients with early RA, which confirms findings of a recent report.[9] Patients with PsA and positive for anti-CCP antibodies more often had polyarthritic disease, but the presence of anti-CCP antibodies was not associated with radiological changes and/or deformity and functional impairment. Anti-CCP antibodies and RF predicted RA in patients with polyarthritic disease.

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