IS PERIODONTAL DISEASE A RISK FACTOR FOR RHEUMATOID ARTHRITIS? THE ANTICITRULLINATED ANTIBODY REPertoire IN PERIODONTAL DISEASE

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Background Anticitrullinated peptide antibodies (ACPA) epitope spreading has been shown to occur several years prior to RA clinical onset. Recent studies suggest an association between rheumatoid arthritis (RA) and periodontal disease (PD). Since P gingivalis is a common periodontal pathogen with a peptidylarginine deiminase that citrullinates proteins, the authors hypothesised that PD may have a causal role in the aetiology of RA. The purpose was to determine the immune reactivities to citrullinated antigens in subjects with and without PD.

Methods Participants were recruited from the Birmingham Dental Hospital, Birmingham, UK. The presence of PD was based on a periodontal examination and/or radiographs. ACPA presence was determined on serum samples. In addition to anti-CCP2 and anti-MCV, the authors tested for antibodies with specificity for different citrullinated peptides, including α-enolase peptide 1 (CEP-1), fibrinogen (cit-fib) and vimentin (cit-vim). Antibodies against the uncitrullinated form of the same peptides were determined as negative controls. Comparisons between groups were done using χ² or Mann–Whitney as appropriate. Non-normally distributed variables were log transformed for analyses using linear regression models.

Results The total sample included 194 subjects of whom 81 had PD and 113 did not (non-PD). None of the participants had RA at the time of the study. As expected, there was a low frequency of ACPA, including anti-CCP2, anti-MCV, anti-CEP-1, anti-cit-vim and anti-cit-fib. Anti-CCP2 antibodies were present in 1.3% of the PD group and none of the controls. Anti-MCV was present in one subject in each of the groups. Anti-CEP-1 antibodies and anti-REP1 (arginine control peptide for CEP-1) were present in 8.6% and 1.8% (p=0.02) and 38.3% and 14.2% (p<0.001) of the cases and controls, respectively. Among those with PD, those who were anti-CEP-1 positive were non-smokers and among those who were anti-REP-1 positive only 13% were smokers. Anti-fib antibodies (arginine control peptide for cit-fib) were also more common among those with PD compared with non-PD (45.7% vs 13.3%, p<0.001). There was no statistical difference between groups for anti-cit-fib, anti-cit-vim or anti-vim positivity. Compared with non-PD, presence of PD was associated with both the citrullinated peptides (anti-CEP-1 (p<0.001), anti-cit-vim
and anti-cit-fib \( p=0.004 \)) and their uncitrullinated controls (anti-vim \( p<0.001 \), anti-REP-1 \( p<0.001 \) and anti-fib \( p<0.001 \)) in linear regression models. These differences were independent of smoking.

**Conclusions** Distinct ACPA reactivity was observed between individuals with and without PD. Antibodies against CEP-1 and cit-fib and their uncitrullinated forms (REP-1 and fib, respectively) were more common in PD, and higher levels of antibodies were observed among those with PD compared with non-PD, independent of smoking, suggesting that the uncitrullinated peptide may break tolerance in PD, with epitope spreading to citrullinated epitopes in the small proportion of patients which may evolve into RA.

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