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ANTINEUTROPHIL CYTOPLASMIC AUTOANTIBODIES IN RHEUMATOID ARTHRITIS

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ABSTRACT

Antineutrophil cytoplasmic autoantibodies (ANCA) were detected in patients with autoimmune and vascular diseases such as Wegener's granulomatosis, polyarteritis nodosa and systemic lupus erythematosus. Indirect immunofluorescence (IIF) technique was employed to detect these autoantibodies. By this method, two general patterns of ANCA were seen: a cytoplasmic (c-ANCA) and a perinuclear form (p-ANCA). These antibodies were also observed in rheumatoid arthritis (RA) but their prevalence and clinical significance have not been determined. In this study the presence of ANCA in 52 RA patients (10 males and 42 females) and its relationship with disease activity was evaluated. 26.9% of patients were ANCA-positive, 36% of whom had c-ANCA and 64% a p-ANCA pattern. The results also showed that there is no significant correlation between ANCA titer and disease activity ($p<0.05$).

Thus according to the results obtained, the detection of these autoantibodies are not useful for the diagnosis or prognosis of these disorders.

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INTRODUCTION

Anti-neutrophil cytoplasmic antibodies (ANCA) are autoantibodies directed against endosomal enzymes of human neutrophils and monocytes. These autoantibodies have been detected in various forms of vasculitis, including segmental necrotizing glomerulonephritis, Wegener's granulomatosis (WG), and microscopic polyarteritis.[1,2] Two major staining patterns can be distinguished (on indirect immunofluorescence, IIF), a cytoplasmic pattern (c-ANCA), and a perinuclear one (p-ANCA).[3] The c-ANCA staining pattern is considered sensitive for Wegener's disease. This type of ANCA can even be used for monitoring disease activity in Wegener's granulomatosis.[4,5] The perinuclear staining pattern has been detected in patients with necrotizing and crescentic glomerulonephritis, microscopic polyangiitis, and Churge-Strauss syndrome.[6] The main target antigen associated with c-ANCA is proteinase-3 and for p-ANCA is myeloperoxidase.[7,8] ANCA has been found in sera from some patients with autoimmune rheumatic diseases such as systemic lupus erythematosus[9,10] and rheumatoid arthritis.[11] In patients with RA, the reported prevalence and subtype of ANCA is variable.[12,13] Some investigators have studied the association between ANCA and disease activity.[14] According to their findings the presence of ANCA tended to increase among patients with long-lasting or severe forms of disease.[13] This study was undertaken to evaluate the prevalence and subtype of ANCA in 52 RA patients and its association with disease activity.

MATERIALS AND METHODS

52 RA patients (42 females and 10 males between 19 to 77 years old) from different provinces referring to the Rheumatology Research Center of Shariati Hospital (RRCS), Tehran were selected and classified as active or inactive forms according to the presence of more than two of six symptoms of RA. Disease activity or inactivity was confirmed

by the RRCS. 54 healthy adult volunteers (20 females and 34 males between 17 to 60 years old) were selected as the control group. The subjects' sera were screened for antineutrophil cytoplasmic antibody (ANCA) and antinuclear antibody (ANA) by indirect immunofluorescence technique (IIF). The presence of ANCA in undiluted serum and detection of ANA in dilutions of more than 1:40 of sera were considered positive. p-ANCA positive subjects that were also ANA positive were excluded and considered as ANCA negative.

RESULTS

ANCA was detected by IIF on ethanol fixed granulocytes in 14 RA sera specimens (26.9%), but was not detected in any of the control group.

The presence of ANCA—even in undiluted serum—was evaluated as positive. ANA was also screened by IIF on frozen sections of guinea pig kidney tissue. Only 4 patients (with p-ANCA) were ANA positive, while all normal subjects were negative. Statistical analysis (chi-square test) showed that there was no correlation between ANCA level and disease activity. The majority of ANCA positive RA patients (9 cases) had a p-ANCA pattern. McNemar test revealed that there was no significant difference between ANCA and ANA tests in the diagnosis of RA. T-test showed that there was a significant difference between p-ANCA and c-ANCA prevalence in RA ($p<0.05$).

DISCUSSION

Like other researchers[10,15] we have already found ANCA in SLE patients.[9] In RA, the reported prevalence of ANCA is variable and its clinical relevance is not defined. In this study we attempted to clarify the presence and prevalence of ANCA and its subtypes in RA patients and evaluate the clinical importance of these autoantibodies. Our results, like those of other researchers showed that the prevalence of ANCA in RA patients was 26.9% and mostly of the p-ANCA type. Similar to some other studies[14] we found no association between disease activity and presence of ANCA. The results showed no correlation between the occurrence of ANCA and that of ANA, which means that the immune response against neutrophil cytoplasmic antigens is independent of the response against nuclear antigens. Antineutrophil cytoplasmic autoantibodies are important markers for certain forms of systemic vasculitis and pauci-immune glomerulonephritis. The detection of ANCA by indirect immunofluorescence is highly specific for primary vasculitides such as Wegener's granulomatosis and microscopic polyangiitis.[4-6] It seems that in these diseases ANCA-mediated adherance of polymorphonuclear cells to the endothelium and the release of toxic compounds from the granules could finally lead to endothelial damage. Vasculitis is an uncommon but important manifestation of autoimmune rheumatic diseases, such as systemic lupus erythematosus (SLE), Sjögren's syndrome, scleroderma and rheumatoid arthritis. Recently some investigators[16] have studied the association of ANCA and disease severity rather than disease activity. Disease severity in RA patients is characterized with features such as higher RF titers, elevated ESR, kidney and pulmonary involvement and rheumatoid vasculitis. Mustila and colleagues (1997) reported a strong association between p-ANCA and RA-associated nephropathy in 149 RA patients with histologically proven or clinically suspected nephropathy. Therefore, although we found p-ANCA in only 26.9% of RA patients and didn't notice any association between the presence of ANCA and disease activity, the presence of ANCA in RA and other connective tissue diseases may be associated with severe forms of disease, i.e. vasculature involvement and nephropathy, that remains to be elucidated in future studies.

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