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.


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 erythematosus9,10 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 anti­
neutrophil cytoplasmic antibody (ANCA) and
antineuclear 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 we have already found ANCA
in SLE patients. 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 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. It seems that in these diseases
ANCA-mediated adherence of polymorphonuclear cells to
the endothelium and the release of toxic compounds from

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