ANTI NEUTROPHIL CYTOPLASMIC AUTOANTIBODIES IN UVEITIS

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ABSTRACT

Anti-neutrophil cytoplasmic autoantibodies have been detected in patients with some autoimmune and vascular diseases such as Wegner's granulomatosis, polyarthritis nodosa and systemic lupus erythematosus. Indirect immunofluorescence technique has been employed to detect these autoantibodies. By this method, two general patterns of antineutrophil cytoplasmic antibodies were seen: a cytoplasmic (C-ANCA) and a perinuclear form (P-ANCA). These antibodies have also been observed in uveitis. In this study, the presence of antineutrophil cytoplasmic antibodies in 25 patients with uveitis and its relationship with anatomical location of the autoimmune reaction was evaluated. According to the results, antineutrophil cytoplasmic antibodies were detected in 16% (4 out of 25) of the patients, all of which were C-ANCA type. The results also showed that there was no significant correlation between the presence of antineutrophil cytoplasmic antibodies and anatomical location of the disease (p=0.65).

Keywords: Uveitis; Anti-Neutrophil Cytoplasmic Antibody

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, Wegner'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 as sensitive for Wegner's disease. This type of ANCA can even be used for monitoring disease activity in Wegner'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 also been found in the sera of
some patients with autoimmune diseases such as systemic lupus erythematosus (9,10), rheumatoid arthritis, ulcerative colitis and uveitis (11,12,13). Uveitis is a clinically heterogeneous group of diseases characterized by intraocular inflammation that may lead to severe immune-mediated ocular damage (12). Most studies showed that the majority of uveitis patients (over 75%) were ANCA negative and the remaining (<25%) had ANCA, most of which were C-ANCA type (13,14,15). In this study, the prevalence and the types of ANCA in 25 uveitis patients were evaluated.

MATERIALS AND METHODS

25 uveitis patients (14 females and 11 males) between 14-64 years of age from different provinces having referred to Labbafinejad Educational Hospital-Tehran, IRAN, were selected. The patients had uveitis caused by Behcet syndrome (N=7), uveitis due to toxoplasmosis (N=2), rheumatoid arthritis (N=1), sarcoidosis (N=1), pars planitis (N=1) and etiological unknown uveitis (N=13). Anatomical locations of uveitis were as follows: 36% Pan-uveitis, 60% anterior and 4% posterior chamber. 30 adult volunteers (8 females and 22 males) between 20-30 years old were selected as the control group. The subject’s 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 the detection of ANA in dilution greater than 1:40 of serum were considered as positive. P-ANCA positive subjects which were ANA positive, were also considered as ANCA negative.

Statistical Fisher test was used to evaluate the correlation between ANCA and anatomical location of the lesion (P=0.65).

RESULTS

ANCA was detected by IIF on ethanol fixed granulocytes in 4 uveitis sera (16%), but was not detected in the control group (Figure 1). 3 out of 4 ANCA positive subjects had anterior uveitis and one had posterior uveitis due to toxoplasmosis. In the present study, the presence of ANCA even in undiluted serum was considered as positive. ANA was also screened by IIF on frozen section of guinea pig kidney tissue and only 4 patients (ANCA negative) were ANA positive; however, all normal subjects were negative. All of the ANCA positive patients had C-ANCA pattern. Statistical analysis (Fisher test) indicated that there was no correlation between the presence of ANCA and the anatomical location of the disease (P=0.65).

DISCUSSION

In this study, 4 out of 25 subjects (16%) were ANCA positive. The frequency of ANCA in this study is similar to the results of other investigations (13,14,15). 3 ANCA positive cases had anterior uveitis and the remaining had toxoplasomal posterior uveitis. Uveitis is a clinically heterogeneous group of diseases characterized by intraocular inflammation that may lead to severe immune-mediated ocular damage. Study on ANCA in uveitis has been started since early 1980.

In a study performed in the Netherlands on 485 patients including 260 females (8-87 years old) and 225 males (3-87 years old), 19 cases (4%) were ANCA positive by IIF technique. In this group, 17 cases (90%) had C-ANCA and the remaining (10%) had P-ANCA (15). Yang in a study showed that 14 of 63 uveitis cases were ANCA positive and all of them were in the acute phase of the disease (13). Acute uveitis is a non-pyogenic inflammation which is characterized by edema, vascular dilatation and pyogenic exudate (PMN) (12). The presence of neutrophils in these inflammatory sites and their activation by unknown factors may be due to proteinase production and vascular injury which cause the disease resulting in ANCA positivity.

Some studies indicated that ANCA are more frequent in anterior uveitis (16). Our results showed that 3 out of 4 ANCA positive cases had anterior uveitis, too. This study revealed that there was no correlation between ANCA and anatomic location of uveitis (P=0.65). All ANCA positive cases in our study were C-ANCA type. None of C-ANCA positive samples was ANA positive, while 4 cases of ANCA negative patients were ANA positive. This showed that ANCA and ANA do not have any diagnostic values in uveitis and none of them has any advantage to the others. The next objective of
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described in this study has been the definition of ANCA target antigen. Although protease-3 was defined as a major target antigen in C-ANCA, some studies showed that none of uveitis ANCA serum reacted with protease-3. It is assumed that future studies must be focused on defining another target antigen in uveitis (16). One of the 25 subjects with posterior uveitis was also ANCA positive. Future studies should be focused on revealing the prevalence of ANCA in this group of diseases.

REFERENCES