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Prevalence of anticardiolipin antibodies in the elderly British population

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Summary: In a cross-sectional study of 100 healthy elderly individuals, anticardiolipin antibodies (aCL) were measured using an ELISA technique. aCL were not detected in the majority of subjects (63%), and in the remaining 37% titres were within the laboratory reference range (mean + 5 standard deviations) previously determined for adults of all ages. In contrast, significant titres of IgM rheumatoid factor were found in 10%, antimitochondrial antibody in 13%, antinuclear factor in 5%, anti-smooth muscle antibody in 18%, antiparietal cell antibody in 10%, and antireticulin antibody in 1%. Antibodies to single or double-stranded DNA were not detected in any subject.

We conclude that, although other auto-antibodies may be present in the healthy aging population in Britain, abnormally elevated levels of aCL antibody do not occur, and when present may be an indicator of autoimmune-mediated pathology.

Introduction

Anticardiolipin antibodies (aCL) belong to a group of cross-reacting antibodies that may be responsible for false-positive results in tests for syphilis and lupus anticoagulant. Their clinical significance is unclear. In systemic lupus erythematosus elevated aCL has been associated with vascular occlusion, especially in the central nervous system,[1-9] and recently a specific syndrome consisting of recurrent thrombosis, abortion, thrombocytopenia and neurological disease has been described.[10] In our own studies elevated titres of aCL were found in 19% of elderly patients suffering stroke, and were associated with an unfavourable outcome.[11] However, it has been suggested that during the aging process in humans a number of immunological aberrations occur that may result in the production of various auto-antibodies, including rheumatoid factor (RF) and antinuclear factor (ANF).[12] The presence of aCL in the elderly might therefore be an epiphenomenon of no pathological significance. The prevalence of aCL in a healthy Greek elderly population living in nursing homes has been reported to be 51.6%,[13] but no data is available on the prevalence of aCL in the elderly in the British Isles.

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For these reasons, we have determined aCL and other auto-antibodies in a randomly selected sample of the elderly English population.

Materials and methods

One hundred healthy British elderly individuals, living independently in their own homes, were selected at random from the age and sex registers of 8 group general practices in the Aylesbury Health District, Buckinghamshire, UK. All subjects were interviewed by the same investigator (KKC) and a detailed history of previous illnesses was recorded. In particular, history of deep vein thrombosis, spontaneous abortions and miscarriages, hypertension and diabetes was specifically sought.

Subjects known to have any connective tissue disease, active or recent infection, myocardial infarction within the previous 6 months, previous stroke or transient ischaemic attack at any time, symptoms or definite diagnosis of bleeding diathesis, or who were currently receiving any anticoagulant medication, were excluded. All subjects gave written informed consent to the study, which had the prior approval of the local research ethics committee.

A single blood sample was taken from each subject at the time of interview. In this sample RF was determined qualitatively by latex fixation test and quantitatively by the sheep cell agglutination test. A titre of 1/32 or greater was taken as significantly positive. ANF was determined by *in*

situ immunofluorescence using composite tissue blocks of rat liver, stomach and kidney as substrate. A titre of 1/80 or greater was taken as significantly positive. Antibodies to double-stranded DNA were assayed in any sample with ANF titre 1/80 or greater by modified Farr assay. C-reactive protein (CRP) concentrations were determined by single radial immunodiffusion. Both IgG and IgM aCL were measured by enzyme-linked immunosorbent assay. The reference range for normal individuals for this method was established from data obtained for blood donors aged between 18 and 70 years.[14] aCL values were considered to be abnormally raised if greater than the mean + 5 standard deviations for this control group. This established a reference range of 0–9 units/ml for IgG aCL and 0–8 units/ml for IgM aCL.

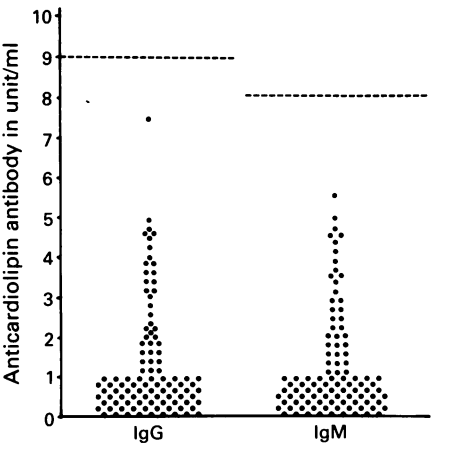

Figure 1 Distribution of IgG and IgM isotypes of anticardiolipin antibody in 100 healthy elderly subjects. The broken lines indicate the upper limit of the laboratory reference range.

Results

Thirty-eight female and 62 male subjects were studied, mean age 75 years (range 60–93 years). Seventeen subjects were hypertensive, 19 were non-insulin-dependent diabetics, 17 subjects gave a history of ischaemic heart disease, and 8 subjects (2 male, 6 female) gave a history of deep vein thrombosis. Twenty-one subjects had suffered a miscarriage or spontaneous abortion; in 13 on more than one occasion. There was a family history of stroke in parents or grandparents in 12 subjects, and of myocardial infarction or heart failure in 28 subjects. There was a family history of dementia in 8 subjects.

IgG aCL were not detected in 63 subjects and IgM aCL were not detected in 64 subjects. In the remaining cases values for both IgG aCL and IgM were within the reference range (Figure 1). In contrast, RF (SCAT) was abnormally elevated in 10 subjects and ANF in 5 subjects (Figure 2). CRP concentration was elevated (greater than 5 mg/l) in 6 subjects. Significant titres of antimitochondrial antibodies were found in 13 subjects, antiparietal cell antibodies in 10, anti-smooth muscle antibodies in 18, and antireticulin antibodies in 1 subject. Antibodies to single- and double-stranded DNA were absent in all subjects.

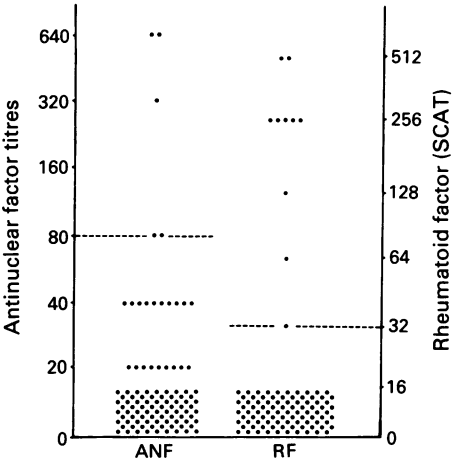

Figure 2 Distribution of antinuclear factor (ANF) and rheumatoid factor (RF) in the study population. The broken lines indicate the upper limit of the laboratory reference range.

Discussion

The reasons for the observed increased incidence of several auto-antibodies in the elderly, including RF, ANF and DNA antibodies, are not well understood. It has been suggested that there is an age-related decline in both function and control of the immune system, and that some of the features of senescence may even be the result of these processes.[12] Our results are in agreement with previous studies in that several auto-antibodies were detected in the absence of any signs of clinical disease. None of our subjects, however, had abnormally raised aCL antibodies in their serum, and in 63% these antibodies were completely undetectable by the methods used.

aCL has been incriminated in various vascular and neurological conditions in patients with SLE and other autoimmune diseases. It has also been described in patients with chorea, epilepsy, optic neuritis, Guillain–Barré syndrome, myasthenia gravis, and various other rare neurological

disorders such as Jamaican myelopathy.[15,16] However, the most consistent clinical association has been with venous or arterial thrombosis. aCL has been reported in cases of venous thrombosis in the deep veins of the legs, retinal veins, superior and inferior vena cava, and hepatic veins,[2,3,17,18] and in cases of arterial thrombosis involving both large and small vessels, including the aorta, bronchial, retinal, common femoral and various visceral arteries.[1,2,19,20] Recently a new syndrome, termed primary antiphospholipid syndrome, has been recognized, predominantly in the younger age group, consisting of recurrent thrombosis, recurrent abortion and thrombocytopenia, in association with aCL.[2,4,5,21-27]

Since vascular thrombotic events contribute significantly to both morbidity and mortality rates in the elderly, it is interesting to speculate whether aCL might be a predisposing factor for events such as stroke, transient ischaemic attack or myocardial infarction in this age group. We have previously reported elevated titres of aCL in a significant minority of elderly patients suffering stroke, and the presence of aCL was associated with an unfavourable outcome.[11] We were unable to determine, however, whether aCL might be causally related to stroke or might have appeared as a consequence. In contrast, in the present study we have found no evidence of a higher prevalence of this antibody in the healthy elderly population. Moreover, in this sample a history of deep vein thrombosis was obtained in 2 male subjects and 6 female subjects, 3 of whom had been taking oral contraceptive medication at the time of occurrence of their thrombosis, and 21 of our female subjects had suffered one or more miscarriage or spontaneous abortion at some time, including 3 patients who had suffered both deep venous thrombosis and miscarriage in early adult life. These data thus give no support to the hypothesis that aCL is causally related to vascular events in the elderly.

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