Prevalence of anticardiolipin antibodies in juvenile chronic arthritis

R Caporali, A Ravelli, F De Gennaro, G Neirotti, C Montecucco, A Martini

Abstract
The prevalence of anticardiolipin antibodies was evaluated in 70 children with juvenile chronic arthritis (JCA), in 25 adult patients with rheumatoid arthritis, in 42 healthy children and in 40 adult controls. Thirty seven (53%) patients with JCA were positive for IgG or IgM anticardiolipin antibodies, or both, and 30 (43%) for IgG anticardiolipin antibodies. In contrast, only seven (28%) adult patients with rheumatoid arthritis presented anticardiolipin antibodies, which were of IgG class in four (16%) cases. IgG anticardiolipin antibodies were negative in all control subjects while IgM anticardiolipin antibodies were detected in two (5%) children and in four (10%) adult controls. No correlations were found in patients with JCA between the presence or titres of anticardiolipin antibodies and various clinical or laboratory variables. No patient with anticardiolipin antibodies showed any feature of the anticardiolipin syndrome.

Juvenile chronic arthritis (JCA) is a heterogeneous condition, which is currently divided into different subtypes according to symptoms at onset. Among numerous immunological abnormalities seen in JCA only antinuclear antibodies and IgM rheumatoid factor are currently thought to be useful in patient classification and management. Some autoantibodies with defined specificity, such as antihistone and anticollagen antibodies, have also been detected in patients with JCA, but their significance is still poorly understood.

Anticardiolipin antibodies are antiphospholipid antibodies, which can be found in patients with systemic lupus erythematosus and other autoimmune syndromes. Their presence has been correlated with various clinical manifestations, including thromboembolic phenomena, autoimmune cytopenia, and neurological disease. In this study we tested 70 patients with JCA for the presence of anticardiolipin antibodies.

Patients and methods
PATIENTS
Seventy children (26 boys, 44 girls), ranging in age from 1 year and 5 months to 17 years and 11 months (mean age 8.3 years), whose parents gave permission for drawing extra blood at the time of routine venepuncture, were studied. All fulfilled the criteria for diagnosis of JCA and had been categorised by onset type according to

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IgG and IgM antibody titre was expressed as arbitrary units using reference standard serum samples: serum samples with IgG values ranging from 8 to 15 arb units or IgM from 5 to 15 arb units were defined as low positive, while values above 15 arb units were considered as high positive. No standard reference serum samples were available for titration of IgA anticardiolipin antibodies.

Statistical analysis was by Wilcoxon’s test for comparison of differences between means and by linear regression analysis for calculation of correlation coefficients.

Results

The table and figure show the results of IgG and IgM anticardiolipin antibody determinations in patients with JCA, in adults with rheumatoid arthritis, and in healthy controls.

Of the 70 patients with JCA tested, 37 (53%) were positive for IgG or IgM anticardiolipin antibodies, or both, and 30 (43%) for IgG anticardiolipin antibodies. In contrast, only seven out of 25 (28%) adult patients with rheumatoid arthritis presented anticardiolipin antibodies, which were of IgG class in four cases (16%). IgG anticardiolipin antibodies were negative in all control subjects while IgM anticardiolipin antibodies were present in two children (5%) and in four adult controls (10%).

Of the 30 patients with JCA positive for IgG anticardiolipin antibodies, eight (27%) were in the high positive group and 22 (73%) in the low positive group. All adult patients with rheumatoid arthritis were in the low positive group.

No significant correlations were found in patients with JCA between anticardiolipin antibody titres and clinical subtypes, disease activity defined on clinical grounds, onset age, disease duration, presence of iridocyclitis or other extra-articular manifestations, erythrocyte sedimentation rate, antinuclear antibody positivity, partial thromboplastin time, outcome, and treatment. All patients with a high titre of IgG anticardiolipin antibodies had a raised erythrocyte sedimentation rate. No patient presented with acute occlusive vascular episodes or cytopenia.

Discussion

Our results show a high prevalence (53%) of anticardiolipin antibodies in patients with JCA. IgG anticardiolipin antibodies were present in 43% of patients with JCA and a quarter of these positive cases presented high antibody titres. The prevalence and the titre of IgG anticardiolipin antibodies in patients with JCA were also markedly higher than those found in a group of adult patients with rheumatoid arthritis. This finding may be regarded as a further distinctive feature between JCA and adult onset rheumatoid arthritis.

Previous studies on anticardiolipin antibodies in childhood have focused primarily on systemic lupus erythematosus and related autoimmune conditions. In a study of patients with JCA Leak found a low titre of anticardiolipin antibodies in 29% of patients with antinuclear antibodies in association with active arthritis and a poor outcome. Moreover, recently, Shergy et al reported IgG anticardiolipin antibodies in five of 12 patients with JCA; four of these patients had also a positive antinuclear antibody test.

Our study was carried out on a larger series of patients with JCA and did not show any association between anticardiolipin antibodies and antinuclear antibodies or between anticardiolipin antibodies and any other clinical or laboratory feature. Indeed, the prevalence of anticardiolipin antibodies in our antinuclear antibody positive patients was 50% and was similar to that found in patients with a negative antinuclear antibody test. A lack of correlation between a positive antinuclear antibody test and anticardiolipin antibodies has been found also in other autoimmune disorders.

It should be noted that all patients with high titre IgG anticardiolipin antibodies had a raised
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erythrocyte sedimentation rate. This finding might suggest that these antibodies are present in high titre only in patients with active disease; no correlation was found between antcardioli

prevalence antibdies and erythrocyte sedimentation rate or disease activity defined on clinical grounds, however.

The presence of antcardiolipin antibodies is often associated with circulating anticoagulant activity and with distinctive clinical features, including deep vein and arterial thromboses, autoimmune cytopenia, cutaneous necroses, and neurological disease; this clinical picture is currently defined as 'antcardiolipin syndrome'. This syndrome has been reported more often in patients with IgG antcardiolipin antibodies and high antibody titres and has been found also in children. We found no association between antcardiolipin antibodies and either abnormal clotting tests or specific clinical features in our patients with JCA, however, despite a large number of cases with high titre IgG antcardiolipin antibodies. This is in accordance with the general view that the clinical and biological significance of these antibodies may be different in different conditions.

In conclusion, our study showed a high prevalence of antcardiolipin antibodies in JCA. The prevalence and the titre of antcardiolipin antibodies in patients with JCA were much higher than those found in adult rheumatoid arthritis. No correlations were found between antcardiolipin antibodies and specific clinical and laboratory features. Further studies are needed to clarify the significance of these antibodies in JCA and their possible usefulness in further defining the heterogeneity of this condition.

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