

ANTICARDIOLIPIN ANTIBODIES IN YOUNG SAUDIS WITH ISCHEMIC STROKE

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Stroke is principally a disease of the elderly and a major source of disability worldwide.¹⁻⁴ In Western countries, more than 70% of stroke cases are above the ages of 65 years.^{1,2,4} Stroke occurring before the age of 45 years is a devastating event because of the consequent economic loss to families and to the nation.² There is evidence to suggest that individuals having anticardiolipin (aCL) antibodies are predisposed to recurrent thromboembolic events, including cerebral ischemia.⁵⁻⁹ The aim of this study was to determine the frequency and features of aCL in young Saudi patients with ischemic strokes.

Subjects and Methods

The study was undertaken at King Khalid University Hospital (KKUH), Riyadh. All Saudi patients below the age of 45 years (range 13-45) presenting to the Neurology clinic, or admitted with the diagnosis of ischemic stroke without evidence of systemic lupus erythematosus (SLE), between January 1993 and December 1995, were consecutively assessed. The patients comprised 41 males and 20 females. The diagnosis was based on a history of sudden neurologic disability which persisted beyond 24 hours without evidence of hemorrhage or features of space-occupying lesions clinically and on brain CT scans. The CT scans were done within 24 hours of the event, and repeated after 72 hours if the initial scans were normal. The presence of low-attenuation lesions in such CT scans located in areas of the brain corresponding to the clinical impression was supportive of the diagnosis.

The data analyzed included age, sex, the mode of onset, distribution of disability, progression, presence of hypertension, diabetes mellitus, cardiac disease, previous transient ischemic events and smoking habits. Investigations included hematologic profile, fasting blood sugar, fasting lipid levels, electrocardiography, transthoracic and transesophageal echocardiography, carotid duplex ultrasonography, and coagulation profile, including protein C, protein S, antithrombin III, brucella

serology, SLE cells, rheumatoid factor, anti-double-stranded DNA, antinuclear factor and venereal disease antigen. The enzyme-linked immunosorbent assay was employed using a commercial kit (Inova, San Diego, CA, USA) for the detection of anticardiolipin antibodies,¹⁰ and was carried out on venous blood obtained within one week of the stroke event. We ascertained that none of the patients was on medications that could give false-positive results. Four-vessel cerebral angiography was performed in all cases to exclude vascular anomalies.

Anticardiolipin antibodies were recorded as positive whenever the immunoglobulin isotope levels, either IgG or IgM, were above the normal range of 6-18 GPL or 6-12 MPL units, respectively, by more than 30%. This yielded a sensitivity of 95% and specificity of 90%.

Hypertension was diagnosed when blood pressure recordings were above 160/90 mm Hg on more than two occasions and/or a history of antihypertensive therapy was obtained. Systolic BP values between 140 and 160 mm Hg were regarded as borderline. Diabetes mellitus was diagnosed when the fasting blood glucose was above 6 mm/L and urine dipstick showed glycosuria. Atrial fibrillation and evidence of ischemic heart disease were diagnosed based on ECG and echocardiographic findings.

The subjects were divided into two groups according to the aCL profiles. The presenting features and other stroke risk factors were compared between the aCL-positive and negative cases. Statistical analysis was done by determining the Fisher's exact probabilities. Probability value below 0.05 was regarded as significant.

Results

Ten cases (16.4%), comprising seven males and three females, were aCL positive. Five had raised IgG isotype, three had raised IgM isotype, and the remaining two cases had both isotypes raised. The antibody titers were 21, 27, 38, 52, and 270 GPL units; 15, 32 and 46 MPL units. One patient had 17 GPL+37MPL units, while the other had 41 GPL+28 MPL units. The presenting features in the aCL positive cases were previous transient ischemic attacks (TIA) and recurrent strokes in six patients, while four cases had had a stroke for the first time. Simple partial motor seizures were documented in three cases associated with stroke. One of the cases had previously experienced

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TABLE 1. Comparison of associated factors according to antiphospholipid antibody (aCL) status.

	aCL pos (n=10)	aCL neg (n=51)	P*
Mean age±SD (in years)	36.7±4.2	33.5±8.8	0.10
Sex ratio (M:F)	7:3	34:17	
Risk factors			
Transient ischemic attacks/ previous stroke	6	11	0.02**
Hypertension	1	11	0.30
Diabetes mellitus	0	7	0.27
Smoking	2	11	0.33
Ischemic heart disease	1	17	0.11
Atrial fibrillation	0	5	0.39
Cholesterol >6.20 mmol/L	1	5	0.42
Triglyceride >2.27 mmol/L	0	2	0.70

*Fisher's exact test; **significant.

recurrent vascular headaches and blindness, while another had a combination of depression, partial seizures and stroke. Only 11 of the 51 (21.6%) aCL-negative cases had previous TIAs, as shown in Table 1. The frequency of previous TIAs was significantly higher in the aCL-positive cases ($P=0.02$). Two of the aCL-positive cases had mitral valve prolapse and intra-ventricular thrombus associated with left ventricular dyskinesia on echocardiography.

Table 1 also shows the frequencies of the various factors assessed, according to the aCL status. All the patients were treated with low-dose aspirin (100 mg/day), and none had a recurrence during the 12 months of follow-up. Although the aCL-negative cases had higher frequencies of ischemic heart disease and arrhythmia compared with the aCL-positive ones, neither factor reached statistical significance. Angiographic abnormalities were documented in six aCL-positive and nine aCL-negative cases. They consisted of stenotic lesions (atheromatous plaque) in 14 cases, and internal carotid artery dissection in one of the aCL-positive cases.

Discussion

Anticardiolipin (aCL) antibodies and the lupus anticoagulant are the two best characterized groups of antiphospholipid antibodies which bind negatively-charged phospholipid moieties, and predispose to thrombotic events.⁸ Cerebrovascular thrombotic events associated with circulating aCL occur in about 10% of stroke cases, which are usually young individuals.¹¹ In this study, the

frequency of aCL was 17%, and is similar to the 18% reported by Nencini et al. in a study in Italy.⁹ A much higher frequency of 43% was reported by Brey et al.¹⁰ The variability of these frequencies could be explained on the basis of differences in patient selection criteria and laboratory assay techniques.

In this study, the aCL status showed no sex predilection, probably because we excluded patients with SLE, although other studies report female preponderance.⁹ The existence of aCL increases the risk for stroke, and is usually independent of other risk factors. The only significant association we found was with previous stroke and transient ischemic attacks, which was also reported by Nencini et al.⁹ Therefore, the study of aCL should be undertaken in young patients with recurrent cerebral ischemia.

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