

Antiphospholipid antibodies in forty young patients with stroke

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Summary:

Background: Cerebral ischemia associated with Antiphospholipid Syndrome (APS) is a common arterial manifestation in adults.

Objectives: To look for the frequency of Antiphospholipid Antibodies (aPL), and their relation with other risk factors in young patients with cerebral ischemia.

Patients and methods: A retrospective study of 40 young patients ≤ 50 years with stroke collected from medical and neurological wards of Baghdad Teaching Hospital (BTH) from January - December 2009. All were inquired about the presence of risk factors of stroke, and sent for aPL including Anticardiolipin (ACL) and Lupus Anticoagulant (LA).

Results: Eight (20%) had ACL. Nine (22.5%) had LA. Both were present in 6 (15%). ACL and/or LA were present in 11 (27.5%). Thirty three (82.5) patients had at least one risk factor, 8 of them had aPL, while 7 (17.5%) had no risk factor and only 3 of them had aPL (p 0.1806).

Conclusion: Antiphospholipid Syndrome is a possible risk factor of stroke and any young patient with stroke should be screened for aPL.

Key words: Stroke, Antiphospholipid Syndrome, Antiphospholipid Antibodies.

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Introduction:

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by recurrent thrombo-embolic events, miscarriages and thrombocytopenia etc. ; it is associated with the presence of antiphospholipid antibodies (aPL), which include anticardiolipin (APL) and lupus anticoagulant (LA) (1). Prevalence of aPL in normal population varies, studies report a range of 2-7%(2), and it increases with age(3).

Antiphospholipid antibodies are found in numerous settings, such as systemic lupus erythematosus presented with clinical thrombosis, infectious diseases (syphilis, malaria, HIV), or medications (neuroleptics, quinidine, and procainamide)(4).

A stroke study Group conducted a study to justify stroke and aPL, the authors reported that the risk of cerebral infarction was 2.31 times higher in patients testing positive than in those testing negative(5). In the Framingham study, high serum concentration of aPLs, regardless of other cardiovascular risk factors, were shown to be significantly predictive of the risk of the future stroke and transient ischemic attacks in female but not in male(6).

Brey et al found the risk of stroke to be 1.5 times high in IgG ACL positive patients than those who are The mean age of the clinical manifestation of APS is 31 years: Usual presentation is most commonly with deep vein thrombosis (38.9%),

thrombocytopenia (29.6%), stroke (19.8%), pulmonary embolism (14.1%)(8).

Arterial occlusions are suggestive of APS when they occur in individuals with no identifiable risk factors (Family history, hypertension, hyperlipidemia, diabetes mellitus, etc.)(5).

The mechanism of nervous system involvement in APS is considered primarily thrombotic, there is evidence to suggest that cerebral endothelium is activated by aPL, thereby promoting procoagulant activity (9). There are large and small arterial occlusion as well as lacunar infarcts and venous occlusions(10,4). The high frequency of stroke may reflect selective vulnerability of brain vasculature (2). Patients tend to have high stroke recurrence rate, often with similar manifestations (11).

This study was designed to study the prevalence of aPL and risk factors in young patients with stroke.

Patients and methods:

This retrospective study included 40 consecutive and unselected young patients ≤ 50 years of age, admitted because of stroke, to medical or neurological wards in BTH for the period between January – December 2009.

Full history was taken from the patient or close relative including age, gender, risk factors like family history, history of hypertension, diabetes mellitus, hyperlipidemia. After full examination of the patients consent was taken and they were sent for the following investigations: lipid profile, electrocardiography, echocardiography, computerized

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tomography of the brain, ACL (Antibodies directed against membrane anionic phospholipids, tested by Euroimmune Kit) and LA (tested by Kaolin time, which is the most sensitive test for the detection of circulatory anticoagulants, and it is an activated PTT test without phospholipid), or LA specific APTT.

Statistical analysis: Data were entered into statistical package for social science (SPSS) program for windows version 15. Quantitative variables were summarized by finding mean \pm SD.

Results

Sixty eight patients \leq 50 years were admitted to BTH with stroke for the period between January –December 2009, but only 40 patients were included in the study, as 28 patients didn't finish the investigations requested.

Male patients were 24 (60%), and female were 16 (40%), with M:F ratio of 3:2. Age range 32 –50 years with a median of 38 years.

Anticardiolipin antibodies were present in 8 (20%) patients, while LA were present in 9 (22.5%). Both antibodies were present in 6 (15%), ACL and/or LA were present in 11 (27.5%) (Table1). Prevalence of aPL were more in female 8/16 (50%) than male 3/24 (12.5%) (p 0.007). (table2).

Thirty three (82.5%) patients had at least one risk factor for stroke, 8 (24%) of them had aPL. Seven (17.5%) had no risk factor, 3 (43%) of them had aPL. (p 0.1806). (table 3).

Table1: Prevalence of Antiphospholipid antibodies In 40 patients with stroke

| Antiphospholipid antibody | Positive | | Negative | |
|---------------------------|----------|------|----------|------|
| | No | % | No | % |
| ACL | 8 | 20 | 32 | 80 |
| LA | 9 | 22.5 | 31 | 77.5 |
| ACL & LA | 6 | 15 | 34 | 85 |
| ACL&/or LA | 11 | 27.5 | 29 | 72.5 |

Table 2: Antiphospholipid prevalence in relation to gender

| Gender | Antiphospholipid antibodies | | | | Total | |
|---------|-----------------------------|------|----|------|-------|-----|
| | YES | | NO | | No | % |
| | No | % | No | % | | |
| Male | 3 | 12.5 | 21 | 87.5 | 24 | 60 |
| Female* | 8 | 50 | 8 | 50 | 16 | 40 |
| Total | 14 | 27.5 | 29 | 72.5 | 40 | 100 |

P value for female (0.007)

Table 3: Antiphospholipid antibodies in relation to risk factors

| Risk factor | Antiphospholipid antibodies | | | | Total | |
|-------------|-----------------------------|------|----|------|-------|------|
| | YES | | NO | | No | % |
| | No | % | No | % | | |
| Present | 8 | 24 | 25 | 76 | 33 | 82.5 |
| Absent | 3 | 43 | 4 | 57 | 7 | 17.5 |
| Total | 11 | 27.5 | 29 | 72.5 | 40 | 100 |

P value for risk factor (0.1806)

Discussion

The aetiologic diagnosis of stroke in young adults has changed over time as a result of improvement in the diagnostic workup; today specific causes are identified in the majority of patients. Antiphospholipid syndrome is one of the commonest causes of stroke in young adults (12). The study showed that 8 (20%) of patients had positive ACL, and 9 (22.5%) had positive LA. Both ACL and LA were positive in 6 (15%), and ACL and/or LA were positive in 11 (27.5%). Almost similar results were found by Mishra et al in India; ACL was positive in 6/28 (21.5%) patients, LA in 10/51 (19.6%), 2 had both, and 4 (29.4%) had ACL and/or LA(13).(Table 5). Brey et al in United States found positive ACL in 43/160(29.6%) of patients, 62/320 (18.2%) in the control group (P0.03), LA in 29 (20.9%) and 38(12.8%) in the control group, and ACL and / or AL in 61/160 (38%), while they positive in 27.5% of the control group. They concluded that aPLs are independent risk factor for stroke in young women (7). The study showed that the prevalence of APS in young patients with stroke was27.5% , while it is 6% in Thailand(12), 29.4% in India(13). 18% in Latin America(14) 17% in Taiwan(15), 4.7% in North Sweden(16), 38% in United States(7), and 22.6 % in Euro-phospholipid Cohert(17). Thirty three patient (82.5 %) had at least one risk factor of stroke, 8 (24.2%) had positive aPL, while 7 (17.5%) had no risk factor, 3 (42.8%) of which had positive aPL (p 0.1806). Mishra et al(11) had found 11/28 (39%) had multiple risk factors, 10 (36%) had single risk factor and 7 (25%) had no risk factor. (Table 4). While male constituted 60% of our patients, aPL were significantly more common in female (P 0.007), this compatible with what was found by Nencini et al(18) in Italy.

Table 4: Comparison with other studies

| | Indian % | American % | Current study % |
|---------------|----------|------------|-----------------|
| ACL | 21.5 | 26.9 | 20 |
| LA | 19.6 | 20.9 | 22.5 |
| ACL & LA | 7 | 7 | 15 |
| ACL&/or LA | 29.4 | 42 | 27.5 |
| aPL& RF | 39.2 | NM | 20 |
| NO aPL, NO RF | 25 | NM | 10 |
| Male/Female | 44/7 | 0/160 | 24/16 |

RF = Risk factor, NM = Not mentioned

Conclusion:

There was high incidence of aPL in young patients with stroke, this may suggest that these antibodies are independent risk factor, and while stroke was more common in male but a PLs were more common in female.

Recommendation. Screening for aPLs should be done in young patients with stroke as early diagnosis and treatment may affect the prognosis.

Author's contributions:

Khudhair A. AL- Khalissi : study conception & design

Khudhair A. AL- Khalissi and Mohamed S. Abass: acquisition of data analysis

Ali A. Nabat: data collection

Khudhair A. AL- Khalissi & Ali A. Nabat: interpretation of data

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