

Carotid Atherosclerosis and Flow Mediated Dilatation in the Brachial Artery in Patients with Antiphospholipid Syndrome: A Case-control Study

Carotid Atherosclerosis in Antiphospholipid Syndrome: Case Control Study

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Abstract- Correlation between Primary Antiphospholipid Syndrome (PAPS) and cardiovascular events is well-known. For this reason it is important to evidence early atherosclerosis to prevent future events.

Aim: to better evaluate Flow Mediated Dilatation (FMD) in a group of subjects affected by PAPS paired with a control group, homogeneous for age, sex and without cardiovascular risk factors.

Subjects and methods: 31 subjects affected by PAPS and 31 healthy controls underwent Echo- Doppler of brachial artery and evaluation of FMD.

Results: PAPS cases perhaps revealed a reduced FMD respect controls. The correlation between age, sex, duration and severity of disease, arterious or venous thrombosis and severity of thrombocythaemia did not influence FMD. Coagulation parameters and presence of IgM and IgG antibodies correlated with FMD alterations.

Conclusions: FMD is reduced in patients with PAPS and it correlates with coagulation parameters and presence of antibodies that can explain the rise of arterious imbalance. FMD evaluation is necessary in PAPS subjects to prevent fatal cardiovascular events.

Keywords- Primary Antiphospholipid Syndrome; Ultrasound; Flow Mediated Dilatation (FMD); Intima-Media Thickness (IMT)

I. INTRODUCTION

Correlation between Primary Antiphospholipid Syndrome (PAPS) and cardiovascular events is well-known. Some authors have recently demonstrated a significantly increased intima-media thickness (IMT) in the carotid artery of patients with primary APS, associated with stroke [1, 2, 3]. Der reported an accelerated atherosclerosis in subjects with APS and suggested that vasoprotective therapy might be beneficial in the treatment of these patients [4].

For this reason it is important to evidence early alteration in order to prevent future disease.

This study was done to verify the presence of a significant difference in terms of endothelial dysfunction among a group of patients with PAPS and a control group, homogeneous for age, sex, weight (BMI) and without cardiovascular risk factors.

II. SUBJECTS AND METHODS

117 subjects with PAPS were examined, diagnosed on the basis of classic clinical and laboratory criteria, i.e. a positive history of deep venous or arterial thrombosis, or miscarriage, and antiphospholipid antibodies positivity in two blood samples obtained two months apart. All individuals were outpatients, recruited during a period of one year (from September 2008 to September 2009). They all were submitted to clinical history, physical examination, 12-lead electrocardiogram and blood test findings to determine the presence of cardiovascular risk factors. The exclusion criteria or diseases correlated with atherosclerosis were: acute myocardial infarction, angina pectoris, TIA, stroke, carotid endarterectomy, arterial vascular disease, aortic aneurysm.

Subjects with autoimmune, thyroid or hemorrhagic diseases, cancer and those taking steroids or contraceptive pills were excluded. Of the 117 cases observed, 86 were excluded based on risk factors for atherosclerosis or already had clinical manifestations of the disease.

The remaining 31 cases were paired with 31 healthy subjects with no common risk factors for atherosclerosis, recruited in our clinic during the same observation period.

In Table I are summarized the baseline characteristics of cases and controls.

All subjects had undergone ultrasound vascular evaluation of carotid arteries (common carotid, carotid bulb, internal and external carotid, both right and left), with determination of Intima-Media Thickness (IMT) using Esaote Technos Toshiba MP High definition, Japan instrument with a 7.5 MHz annular phased array probe. All carotid district arteries were divided into three segments (inferior, medial and superior) with a 60° angle of incidence. In each arterial district the IMT (in mm) and the extent of atherosclerotic lesions were assessed. If present they were expressed as a percentage of stenosis in the vascular lumen [5].

TABLE I BASELINE CHARACTERISTICS OF CASES AND CONTROLS

	Cases	Controls
Sex	13 M; 18 F	13 M; 18 F
Age	47.42 ±12.44 y	48.94 ±31.82 y
BMI	23.59 ± 4.38	24.26 ± 7.42
Heart Rate	74.36 ± 7.51	69.88 ± 4.95

Another parameter considered useful in the early identification of subjects with increased cardiovascular risk is the Flow Mediated Dilation (FMD%). This is measured by changes in artery diameter induced by "shear stress" that allows a good assessment of endothelial function through a non-invasive method. The value of the FMD% in the brachial and in the digital artery of non-dominant arm was considered as an index of endothelial dysfunction, by ultrasound wall tracking [5]. The experimental protocol was designed and performed according to the principles of the Helsinki Declaration and was approved by the Ethical Committee and by Institutions review board of the Padua University Central Hospital. All the patients gave oral informed consent. The same group was also submitted to the autonomic study for another research protocol already published [7].

Excel program was used for data analysis, from Windows operating system. The results were compared using Student's one and two tailed t-test for matched data. Statistical significance was considered for $p < 0.05$.

III. RESULTS

Patients with PAPS showed a reduced FMD and a greater IMT when compared with controls (Table II). The correlation between gender (females versus males), age (<50 years or >50 years), age at onset of the PAPS (<30 years or >30 years), duration of disease (<15 years or >15 years), arterious or venous thrombosis did not influence FMD or IMT.

TABLE II FLOW MEDIATED DILATION (FMD) AND INTIMA –MEDIA THICKNESS(IMT) OF CASES AND CONTROLS

	Cases	Controls	p
FMD%	11.60 ± 7.16	21.95 ± 6.64	< 0.05
IMT mm carotid artery	0.9 ± 2.7	0.7 ± 1.3	< 0.05

The presence of auto-antibodies and alterations of coagulation parameters correlated with reduced FMD in cases (Table III). Subgroups analysis was not possible due to the small number of patients.

TABLE III RELATION BETWEEN FLOW MEDIATED DILATION (FMD) OF CASES WITH 8 IGG ANTIBODIES, PTT-LA, LA1, R<2, R>2 AND CONTROLS.

	FMD %		p
	Cases	Controls	
AgG+	9.28 ± 8.49	22.90 ± 10.70	<0.05
PTT-LA+	10.31 ± 7.04	23.54 ± 6.28	<0.05
LA1+	11.69 ± 6.71	23.46 ± 6.00	<0.05
R<2	12.52 ± 6.34	22.28 ± 4.47	<0.05
R>2	11.66 ± 6.57	24.87 ± 7.53	<0.05

IV. DISCUSSION

In a previous case-control study conducted by our Department, results evidenced that subjects with PAPS presented a greater IMT and a reduced FMD respect a control group. In addition these alterations could be correlated with antiphospholipid antibodies [8].

The study had been performed on 16 subjects and 16 controls. Back then, correlation between coagulation factors and premature atherosclerotic lesions had not been considered.

In this case-control study, previous results were confirmed and a new one was added, by evidence of correlation with coagulation factors.

It is already known that anticardiolipin antibodies also have a role in coagulation alteration and in endothelial changes [8, 9]

and this can well explain our results.

Considering that FMD evaluation is fast, not expensive and could be done during other Echo-Doppler examinations, we recommend to perform FMD study in patients with PAPS, to identify early endothelial dysfunction and in order to prevent future cardiovascular events. Moreover proper therapy for the syndrome can probably reduce the atherosclerotic lesions in these patients.

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