Original paper

The clinical significance of anticardiolipin antibody levels in patients with acute myocardial infarction: a regional study

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Postep Kardiol Inter 2013; 9, 4 (34): 328–331
DOI: 10.5114/pwki.2013.38859

Abstract

Introduction: Acute myocardial infarction (AMI) will probably remain the most important cause of death over the next decades. Traditional risk factors of atherosclerosis could not exactly explain the development of acute coronary events such as AMI. Antiphospholipid antibody syndrome is a disorder characterized by the development of arterial and venous thrombosis.

Aim: In this study, we investigated the relations between acute myocardial infarction and anti-phospholipid antibody syndrome in our population representing Aegean Region people characteristics.

Material and methods: One hundred patients with acute myocardial infarction were consecutively included in the study (group I) and one hundred age and sex matched people with similar risk factors were enrolled in the study as a control group (group II). Anticardiolipin antibody (aCL) IgM and IgG levels were measured in the two groups. Levels of aCL IgG ≥ 48 U/ml and/or aCL IgM ≥ 44 U/ml were accepted as positive and significant.

Results: In patients with acute myocardial infarction, 5 patients (5%) had positive IgM levels and 8 patients (8%) were found to have positive IgG levels. All cases in the control group had negative aCL IgM and IgG antibody levels. These results were accepted as significant for both aCL antibodies between patients and controls ($p < 0.001$).

Conclusions: We concluded that aCL antibody levels are also higher in a small proportion of patients with acute myocardial infarction than controls in our region, also, and these results suggest that there may be an immune stimulus in the pathogenesis of acute coronary events.

Key words: acute coronary syndrome, anticardiolipin antibodies, antiphospholipid syndrome, thrombosis.

Introduction

Nowadays, coronary artery disease (CAD) has become the most important cause of death worldwide. The disease causes approximately 30% of all deaths in the world [1]. Despite considerable advances in diagnosis and treatment strategies, acute myocardial infarction (AMI) continues to be a major problem of public health worldwide [2]. Although in-hospital mortality rates of AMI have declined over the past decades with the invention of coronary care units, and fibrinolytic and interventional reperfusion therapies, pre-hospital mortality rates are still higher and the overall mortality rate is about 45% at present [3]. The disease is likely to remain the most important cause of death over the next decades. Traditional risk factors of atherosclerosis such as diabetes, smoking, hypertension and hypercholesterolemia could not explain the development of acute coronary events such as AMI in the course of atherosclerotic coronary artery disease. Some triggering factors initiate coronary plaque fissuring, rupture and concomitant thrombosis. At this point, there are some gray zones that could not be explained completely. Endothelial dysfunction, inflammation, and vasospasm may explain this process in part. Antiphospholipid antibody syndrome is an autoimmune disease characterized by increased tendency of arterial and venous thrombosis, recurrent spontaneous abortions, thrombocytopenia and circulating antiphospholipid antibodies such as anticardiolipin [4]. The association between acute myocardial infarction and antiphospholipid antibody syndrome has drawn attention and has been investigated by some researchers in different populations and regions of the

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Received: 25.03.2013, **accepted:** 10.07.2013.

world. We considered that some regional and racial differences may be seen in this association.

Aim

Therefore, in this study, we investigated the relations between acute myocardial infarction and anti-phospholipid antibody syndrome in our population representing Aegean Region people characteristics.

Material and methods

In this study, because we planned to investigate the prevalence of primary antiphospholipid syndrome in patients with acute myocardial infarction in our region, the case-control study design was selected. The study was conducted in Tepecik Education and Research Hospital in collaboration with the departments of cardiology, Atatürk Education and Training Hospital. The study was approved by the Local Ethics Committee and informed consent was obtained from each patient.

One hundred patients with acute myocardial infarction were consecutively included in the study (group I) and one hundred age and sex matched people having similar risk factors and not having known coronary artery disease, diabetes or hypertension were enrolled in the study as a control group (group II). Patients having signs of infection, autoimmune disease and malignancy or taking any drugs affecting the levels of anticardiolipin (aCL) antibodies (procainamide, quinidine, phenytoin, chlorpromazine, etc.) were excluded from the study. Anticardiolipin antibody levels were measured in two groups. Venous blood samples were drawn from the antecubital vein via a vacuum syringe after the patients were admitted to the coronary care unit with the diagnosis of acute myocardial infarction. Micro-enzyme-linked immunosorbent assay method was used with the device of Tektime 21001 (Organon, IL, USA) to measure anticardiolipin IgG and IgM levels. The levels of anticardiolipin IgG ≥ 48 U/ml and/or anticardiolipin IgM ≥ 44 U/ml were accepted as positive and significant according to the interpretation of the kit manual.

Statistical analysis

The statistical analysis was performed using SPSS for Windows version 15.0 (SPSS Inc Chicago, IL, USA). Continuous variables are expressed as mean ± standard deviation and categorical variables are expressed in number and percentage. Student's *t*-test was used for the comparison of continuous variables and the χ^2 or Fisher exact test was used for comparison of the categorical variables. A p value of < 0.05 was considered as significant.

Results

The characteristics of patients and controls and main results of the study are shown in Table 1. In patients with acute myocardial infarction, the oldest patient was 82 years and the youngest one was 23 years. In the control group, the oldest patient was 79 and the youngest one was 25 years. In patients with acute myocardial infarction, 5 patients (5%) had positive IgM levels, and 8 patients (8%) were found to have positive IgG levels. All cases in the control group had negative aCL IgM antibody and negative aCL IgG antibody levels. These results were accepted significant for both aCL antibodies between patients and controls (p < 0.001). Of the patients with positive aCL IgM antibody levels, 2 were women (40%) and 3 were men (60%). The mean age was 67.00 ±12.1 ranging between 50 and 81. The patients having positive aCL IgM antibody had an average serum aCL IgM antibody level of 56.00 ±7.33 U/ml; the lowest one was 47.00 U/ml and the highest one was 66.00 U/ml. Of the patients with positive aCL IgG antibody levels, 3 were women (37.5%) and 5 were men (62.5%). The mean age was 58.12 ±9.78 ranging between

Table 1. Clinical characteristics of patients and controls and main results

Parameter	Patients		Controls		Value of p
	n	%	n	%	
Age	59.18 ±12.17		57.50 ±10.24		0.645
Gender					0.750
Men	74	74	72	72	
Women	26	26	28	28	
Diabetes	12	12	0	0	< 0.001
Hypertension	31	31	0	0	< 0.001
CAD	18	18	0	0	< 0.001
Hyperlipidemia	49	49	48	48	0.887
Smoking	50	50	32	32	0.010
Family history	40	40	32	32	0.239
Obesity	22	22	32	32	0.111
aCL IgM positivity	5	5	0	0	< 0.001
aCL IgG positivity	8	8	0	0	< 0.001

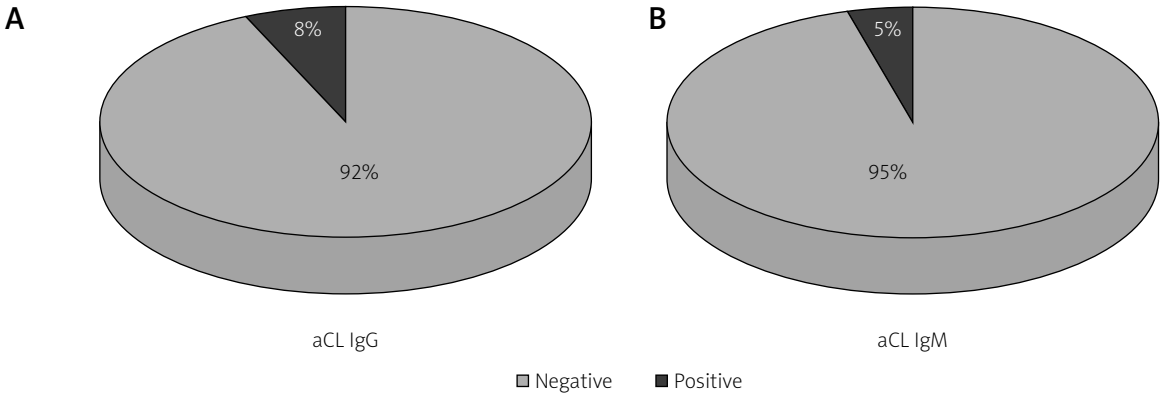

Fig. 1. Distribution of aCL IgG (**A**) and aCL IgM (**B**) positivity in patients with acute myocardial infarction

23 and 80 years. The patients having positive aCL IgG antibody had an average serum IgG level of 58.12 ±9.78 U/ml; the lowest one was 49.00 U/ml and the highest one was 80.00 U/ml.

Discussion

This study reveals that a relatively small percentage of patients with acute myocardial infarction have higher levels of aCL IgM and IgG antibodies than age and sex matched controls with similar risk factors for coronary artery disease in our region, also. In the normal population, seropositivity of aCL antibodies is seen in 0 to 7.5% but it is seen in 6 to 47% of survivors of acute myocardial infarction and prevalence has been increasing with increased age [5, 6]. Anticardiolipin antibodies bind to some cofactors with intrinsic anticoagulant activity such as protein C, protein S, annexin 5 and β_2 glycoprotein-1 and may inhibit their activities [7]. In addition, aCL IgG antibodies increase platelet activation and thromboxane synthesis [8] and activate endothelial cells, which may cause endothelial dysfunction [9]. Therefore aCL antibodies may change anticoagulant system function and cause a tendency to venous and arterial thrombosis and recurrent thrombotic events such as acute myocardial infarction [10]. Transient elevations of aCL antibodies associated with drugs, infections and acute disease are not related to these changes, although chronically high levels of aCL antibodies may be connected with these catastrophic complications. Acute myocardial infarction occurs in 2.8% to 20% of antiphospholipid syndrome patients [11]. However, associations between aCL antibody elevations and recurrent thrombotic events have not been revealed clearly to date. There are many different reports on these associations worldwide, so there may be racial and regional differences influencing these relationships. The association between increased aCL antibodies and arterial and venous thrombosis was reported for the first time in 1983 [12]. In an Italian study, Gaeta *et al*. investigated the relationships between aCL antibodies and acute myocardial infarction in their population, but they found that aCL levels are not elevated in AMI patients, are not associated with in-hospital complications, and do not change the early stage of the disease [13]. Bili *et al*. investigated the association between aCL and recurrent cardiovascular events in a large population of post-infarction patients in the USA and found that elevated IgG aCL and low IgM aCL antibodies are independent risk factors for recurrent cardiac events in 1150 patients [14]. Patients with both elevated IgG aCL and low IgM aCL antibodies have the highest risk for recurrent coronary events [14]. In a Russian study, Logacheva *et al*. also reported that acute coronary syndromes are associated with marked immune alterations primarily with elevated levels of circulating immune complexes and anticardiolipin antibodies, and that these alterations may persist for 3 to 5 weeks after the first event and trigger recurrent coronary events and thrombotic complications after relief of clinical symptoms of an acute coronary event [15]. However, Erkkila *et al*. suggested that the titers of anticardiolipin antibodies did not differ among the patient groups including acute myocardial infarction, acute myocardial ischemia and stable coronary artery disease consisting of coronary artery bypass surgery and balloon angioplasty patients, and that neither of the aCL antibodies was associated with recurrent coronary events in a Finnish study [16]. Hughes and colleagues reported that aCL antibodies are higher in patients with angina and acute myocardial infarction than normal controls in a United Kingdom population [17]. Ranzolin *et al*. reported from Brazil that anticardiolipin antibodies are not independent risk factors for acute myocardial infarction [18]. From Spain, Seijas *et al*. stated that anticardiolipin antibodies are higher (12%) in patients with acute myocardial infarction under 65 years than control cases (5%) but not associated with post-infarction thrombotic events [19]. Phadke *et al*. also reported that there was no significant association between anticardiolipin antibody concentrations and either myocardial infarction or unstable angina in 467 patients [20]. Zuckerman *et al*., however, suggested that the presence of aCL antibody is a marker

for increased risk of subsequent myocardial reinfarction and thromboembolic events after acute MI [21]. Gurlek *et al*. suggested that higher aCL antibody levels were not associated with mortality, reinfarction and the development of intracardiac thrombus but were related to higher rates of restenosis in acute coronary syndrome patients and also pulmonary emboli [22, 23]. As a result, the debate on the associations between increased levels of aCL antibodies and acute cardiac events has been ongoing. Nowadays, aCL antibodies are not used as a marker in coronary risk stratification because of their heterogeneity, measurement differences and insufficiency and mixing of present proofs.

Conclusions

In this study, we concluded that aCL antibody levels are also higher in a small proportion of patients with acute myocardial infarction than controls in our region, and these results suggest that there may be an immune stimulus in the pathogenesis of acute coronary events. Increased aCL antibody levels may trigger new antigenic cascades and these may accelerate acute thrombotic events. In these patients, more intense anti-aggregant and anticoagulant treatment may be required.

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