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Anti-Cardiolipin Antibody in Acute Myocardial Infarction

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Abstract: Problem statement: Myocardial infarction is the combined result of environmental and personal factors. Data concerning the relation between anti-Phospholipid (aPL) antibodies and myocardial infarction in subjects without evidence of overt autoimmune disease are conflicting. Anticardiolipin antibody is detected in various diseases like rheumatoid arthritis, systemic lupus erythematosus and anti-phospholipid antibody syndrome. The study of Anticardiolipin antibody in Acute Myocardial Infarction (AMI) might shed light on etiologic mechanisms in the pathogenesis of acute coronary syndromes. The purpose of the present study was to determine association of plasma aPL antibodies, namely, anti-Cardiolipin (aCL) antibodies, with AMI. **Approach:** This study recruited 45 patients with the diagnosis of AMI according to WHO criteria in their first 24 h of admission. Thirty six matched individuals were studied as the control group with normal coronary artery angiography. Samples were tested for IgG-class antibodies to cardiolipin by an ELISA and the results were compared. **Results:** There were not significant differences between plasma level of aCLAs IgG in the patients with AMI on admission ant the control group. Also aCLAs IgG was not correlated with hypertension, diabetes mellitus, hyperlipidemia, sex, age and smoking. **Conclusion:** Our findings suggest that aCLAs IgG are not indicative of hypercoagulable state in patients with AMI.

Key words: Anticardiolipin antibody, myocardial infarction

INTRODUCTION

Myocardial Infarction (MI) is the combined result of environmental factors and Personal predispositions (Zimmerman *et al*., 1995). Prothrombotic factors may play a more important role in these patients. Various prothrombotic factors and markers of endothelial damage have been associated with an increased risk of myocardial infarction e.g., fibrinogen (Thompson *et al*., 1995).

In addition to mentioned factors autoantibodies may play a more important role in these patients. Various autoantibodies have been associated with an increased risk of myocardial infarction e.g., antiphosphospholipid antibodies (Hughes, 2010).

Antibodies binding to anionic phospholipids, such as cardiolipin, are associated with a clinical syndrome characterized in particular by venous and arterial thrombosis, recurrent abortion and thrombocytopenia. Although the anti-Phospholipid (aPL) antibody syndrome was first described in patients with Systemic Lupus Erythematosus (SLE), it is now generally accepted that there is a group of patients in whom high titers of aPL antibodies, usually IgG class and thrombotic features occur without clinical manifestations of SLE. On the other hand, aPL antibodies may transiently appear during many infections and in association with several drugs without any association with thrombosis (McNeil *et al*., 1991).

The investigation of anti-Cardiolipin Antibodies (aCLAs) in MI might shed light on hypercoagulability mechanisms in the pathogenesis of acute coronary syndromes. There were a few documents about aPL syndrome in Iranian patients with AMI.

Our goal was to study the plasma level of aCLAs in our patients who developed acute myocardial infarction and healthy control group and to analyze their relationship with traditional cardiovascular risk factors.

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MATERIALS AND METHODS

Subjects: This case-control study recruited 45 consecutive patients with Acute Myocardial Infarction (AMI) including 31 men and 14 women with the mean age of 62.7±13.1 years old who were taken to the emergency room of Peymanieh Hospital of Jahrom, Iran, with the chief complaint of chest pain from Feb. 2007 to May 2008.

We also selected 36 individuals that referred to the emergency room with chest pain with normal coronary angiography as our control group and matched them for age, sex and other CAD risk factors such as Hypertension (HTN), Diabetes Mellitus (DM) and Hyperlipidemia (HLP).

The study protocol was approved by research ethics committee of Jahrom University of Medical Sciences and informed consents were obtained from all participants before enrollment. A questionnaire including information about the past medical and drug history (HTN, HLP, DM, smoking, chronic diseases such as collagen vascular diseases and asthma), family history of Coronary Artery Disease (CAD) and demographic information was completed for each patient.

The exclusion criteria were the presence of severe liver disease, malignancy, recent cardiac surgery, angioplasty, stable or unstable angina, receiving of anticoagulant drugs, hemolysis, pregnancy loss, history of deep vein or arterial thrombosis, inflammatory and rheumatologic diseases such as collagen vascular disease, SLE and APA syndrome.

Definitions: AMI was defined as chest pain lasting more than 30 minutes accompanied by ischemic electrocardiographic changes and was confirmed by the presence of total Creatinine Phosphokinase (CPK) or MB fraction levels of more than twice the upper normal limit (Antman *et al*., 2008). The absence of any narrowing in coronary artery diameter was considered as normal coronary angiography.

Blood pressure was measured two times in sitting position after 5 min of rest using a mercury sphygmomanometer. Hypertension was defined as blood pressure more than 130/85 mmHg or use of any antihypertensive medication (Virella and Lopes-Virella, 2008). DM was defined by a physician's diagnosis, a fasting plasma glucose level of $\geq$126 mg dL^{-1} or use of diabetic medications (Foster and Pitts, 2009). Echocardiography was done for all patients during their hospital stay by one cardiologist. Ejection Fraction (EF) is defined to be normal (>55%), mild (45-54%), moderate (30-44%) and (>30%) severe LV systolic dysfunction (Lang *et al*., 2005).

Laboratory analysis: Fasting levels of plasma total cholesterol, High Density Lipoprotein (HDL) cholesterol, Low Density Lipoprotein Cholesterol (LDL) and Triglycerides (TG) were measured in Research Laboratory of Jahrom Medical University. Total cholesterol and Triglyceride levels were measured by enzymatic techniques using a Selectra E biochromatic analyzer. HDL and LDL cholesterol level was measured after glucose levels were measured by the glucose oxidase method. CPK were measured by an enzymatic method.

Blood samples (5 cc) were obtained by venipuncture from the patients immediately after admission before starting any IV medications by trained staff and for lipid profile and fasting blood sugar at the first 24 h of AMI after 12 h of fasting. In control subjects all blood sample were obtained after 12 h of fasting then plasma was separated and frozen at-70°C for later processing. Level of circulating anti-cardiolipin IgG antibodies were determined by Enzyme Linked Immunosorbent Assay (ELISA) Aeskulisa, REF: 7204, Germany according to manufacturer's recommendations. We consider aCLAs level above 15 ng mL^{-1} and aANVAs level above1.18 ng mL^{-1} as positive results.

Statistical analysis: Statistical analysis was performed by SPSS (version 15; SPSS, Inc., Chicago, IL). Data were expressed as mean ± 1 SD. Continuous variables with little-to-mild skewness were summarized as mean ± SD and compared using Student's t-test. Discrete variables were presented as frequencies and group percentages. Nominal variables were tested with Pearson's 2 test and Binary variables were tested with the chi square test. Generalized Linear Models were used to adjust smoking between two groups. All tests were two-tailed with a 0.05 type I error rate. ANOVA and Kruskal-Wallis test were used to evaluate association of aCLAs with different type of AMI and EF.

RESULTS

The demographic and clinical characteristics as well as laboratory variables of the study groups are shown in Table 1. In patient group 6 cases (14%) had Non-ST Elevation MI (NSTEMI) and 37 (86%) had ST Elevation MI (STEMI). There were no significant differences between the two groups regarding the following variables: age, sex, HTN, DM, LDL, HDL, total cholesterol and TG. Also no significant differences were not found between plasma levels of aCLAs IgG in the patient group ant the control group (Table 1).

Table 1: Demographic and clinical characteristics of the study groups

Variable	Case group n = 45	Control group n = 36	p-value
Age, (years)	62.7±13.1	60.1±11.9	0.38
Male, n (%)	31 (68.9%)	18 (50%)	0.08
Current smoker, n (%)	11 (24.4%)	2 (5.6%)	0.02*
HTN, n (%)	8 (17.8%)	11 (30.6%)	0.18
Type 1 DM, n (%)	2 (4.4%)	4(11.1%)	0.40
Type 2 DM, n (%)	7(5.6%)	4(11.1%)	0.56
Total Cholesterol (mg dL^{-1})	189.2±43.7	176.3±32.3	0.14
LDL-C (mgdL^{-1})	112.8±35.6	106±28.7	0.36
HDL-C (mg dL^{-1})	46.2±11.4	42.3±10	0.11
LDL/HDL ratio	4.23	4.24	0.96
Triglyceride (mg dL^{-1})	146.1±97.6	153±105.5	0.76
aCLAs (ng mL^{-1})	21.7±55.7	13.9±38.1	0.46
Positive aCLAs, n (%)	8(18.6%)	5(13.2%)	0.53

HTN: Hypertension, LDL-C: low density lipoprotein-Cholesterol, HDL-C: High Density Lipoprotein-Cholesterol, aCLAs: anti Cardiolipin Antibodies; Values are presented as mean ± SD or %

We examined the association between plasma aCLAs IgG and selected cardiovascular risk factors. There was not a significant correlation between aCLAs IgG in patients and controls groups. Also, we didn't find a significant association between plasma aCLAs IgG with HTN, Type 1 DM, Type 2 DM, age, sex, LDL, HDL, TG, total cholesterol and adjusted smoking. We didn't find a statically significant association of plasma aCLAs IgG with type of MI, LV systolic Function (EF) and mortality in our cases and with sex and not with age in all subjects.

DISCUSSION

In the present study, no significant differences were not found between the aCL antibody levels in the patients and the control groups.

Thus, the results of our prospective study are in agreement with three earlier researches, (Gaeta *et al*., 1998; Phadke *et al*., 1993; Rebic *et al*., 1993), but they disagree with findings of three other studies of the prevalence of aCL antibodies in patients with myocardial infarction (Yilmaz and Yilmaz, 1994; Ferlazzo *et al*., 1993).

There may be several reasons for these discrepancies. First, there are differences in the study populations. Second, differences in test techniques may be involved. There is evidence that aPL antibodies in patients with SLE are directed against an antigenic complex containing not only anionic phospholipids but also a plasma apolipoprotein H ($ß_2$-glycoprotein I) (McNeil *et al*., 1990). On the other hand, aCL antibodies occurring in infectious diseases appear to bind to pure anionic phospholipids (Hunt *et al*., 1992).

Also, there is accumulating evidence to suggest that infections can play a role in the pathogenesis of coronary heart disease (Lopes-Virella *et al*., 2008). A transient aCL antibody response takes place in a variety of bacterial and viral infections and elevated levels can persist in many chronic infections, notably syphilis (McNeil *et al*., 1991). Thus, it is possible that aCL antibodies in our study subjects reflect some chronic infection, for example, chlamydial infection, which has been associated with coronary heart disease (Saikku *et al*., 1988; 1992; Thom *et al*., 1991). Actually, antibodies against chlamydial lipopolysaccharide may cross-react with anionic phospholipids in ELISA (Vaarala, 1991). We have not excluded infectious cases in two our groups of study.

In accordance with this, Gaeta *et al*. (1998); Vaarala *et al.* (1995); Phadke *et al*. (1993) and Rebic *et al*. (1993) reported no association between elevated levels of aCL antibodies and acute myocardial infarction.

CONCLUSION

This study shows no significant association between anticardiolipin antibody concentrations and acute myocardial infarction. However, according to results our study and previous studies, there are controversial on association of ACLA and AMI. The importance of serum anticardiolipin antibody levels in acute myocardial infarction is still undetermined and remains to be clarified.

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