

ANTICARDIOLIPIN ANTIBODIES IN PATIENTS WITH ISCHEMIC EVENTS

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ABSTRACT

To determine the presence of anticardiolipin (aCL) antibodies in patients with ischemic events, we designed a case-control study. We studied 33 patients with unstable angina, 33 male patients with myocardial infarction and 34 control subjects with no evidence of ischemic heart disease. Plasma samples were assessed for IgG anticardiolipin antibodies by enzyme-linked immunosorbent assay (ELISA). The levels of aCL were (mean±SD of optical density multiplied by 1000): 624±319, 486±318, and 239±202 for patients with unstable angina, myocardial infarction and controls, respectively (F=15.74 and $p=0.0000$). High aCL levels were found more often in patients with acute ischemic events.

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INTRODUCTION

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.¹ The presence of antiphospholipid (aPL) antibodies has been reported to be associated with myocardial infarction in young patients with systemic lupus erythematosus or a "lupus-like" disease.^{2,3,4} There have been four studies on myocardial infarction or ischemic heart disease in which the frequency of elevated aCL antibodies was not appreciably higher in patients than in control subjects and such antibodies were not predictive for subsequent cardiovascular complications.^{5,8} However, some individuals may have a propensity to aPL formation,^{6,9} possibly as a response to tissue necrosis. Increased levels of antibodies against oxidized low density lipoprotein (ox-LDL) and cardiolipin at 50 years of age have been shown to correlate positively with the incidence of myocardial infarction and related mortality in other reports.¹⁰

The aim of this study was to determine the presence of aCL in patients with unstable angina and myocardial infarction.

MATERIAL AND METHODS

Patient selection

The patients were classified before the study into 2

groups based on World Health Organization criteria: unstable angina and myocardial infarction. Unstable angina implies anginal pain during the recent 2 months, worsening angina, angina with increased frequency or duration of the pain and resting angina. Myocardial infarction group are patients with anginal pain of more than 30 minutes, electrocardiogram changes and increased serum enzymes. The study included 33 men with unstable angina, 33 men with myocardial infarction and 34 normal control subjects. All patients gave informed consent before participation in the study.

Detection of antibodies to cardiolipin

Antiphospholipid activity was detected by ELISA. Serum was frozen at -20° centigrade and then IgG aCL antibody titer was measured.

Statistical analysis

Results were presented as mean±SD. Differences between the 3 groups regarding autoantibody levels were assessed using the one-way analysis of variance test. For determining the difference between each 2 groups, we used Student's t-test.

RESULTS

Table I shows the basic characteristics of patients.

The mean age of all patients was 52.7 (range 30-60) years. There were no significant differences regarding the average weight, frequency of systemic hypertension, diabetes mellitus, current smoking and history of hypercholesterolemia between the 3 groups.

A comparison between the levels of auto-antibodies in the 3 groups resulted in significant differences in aCL antibodies. The levels of anti-CL were (mean±SD of optical density multiplied by 1000): 624±319, 486±318, and 239±202 for patients with unstable angina, myocardial infarction and control groups respectively. The highest values were found in patients with unstable angina (Figure 1).

DISCUSSION

The aim of this study was to evaluate the ability of the auto-antibodies against cardiolipin to distinguish patients with different manifestations of acute coronary syndrome. The main finding was that men with unstable angina had higher titers of antibodies than did men with acute myocardial infarction and that antibody titers in these 2 groups were higher than normal control subjects.

The results of our study disagree with findings of four other studies on the prevalence of aCL antibodies in patients with myocardial infarction or coronary artery disease.⁵⁻⁸ Anti-CL antibodies are the hallmark of the antiphospholipid syndrome, which is associated with a tendency toward thrombosis.¹² The pathogenic potential of aCL in atherosclerosis has been demonstrated in a mouse model in which immunization with aCL resulted in development of high titers of mouse aCL and increased atherosclerosis compared with controls.¹³ Anti-CL antibodies were found to be increased in patients with ischemic heart disease, with no difference in either level or frequency between patients with stable or unstable angina or myocardial infarction.¹⁴ High levels of aCL antibodies was found to be an independent risk factor for myocardial infarction or cardiac death in middle-aged men,¹⁵ and increased levels of anti-ox-LDL and aCL antibodies at 50 years of age correlated positively with the incidence of myocardial infarction and related mortality.¹⁶ These studies emphasize the association between aCL antibodies and atherosclerotic heart disease and its complications. Association of coronary calcium and aCL antibody with atherosclerosis has been reported in one study.¹⁶ It seems that controversy will continue because another study measuring antibodies against ox-LDL and cardiolipin in coronary heart disease patients showed no major clinical value, although men with myocardial infarction had high titers of these antibodies.¹⁷ Elevated IgG aCL has been reported to carry a 3-fold higher risk of cardiac events¹⁸ and also acute coronary syndrome was shown to be associated with marked immune alterations, primarily elevated levels of circulating immune complexes and aCL.¹⁹

The present study was undertaken to find out whether auto-antibodies against cardiolipin would discriminate patients with different manifestations of acute coronary syndrome. Although elevated levels of aCL has been reported in different manifestations of ischemic heart disease, the reason of higher titers in unstable angina patients than in myocardial infarction patients is not clear and the controversial relationship between aCL antibodies and acute myocardial infarction²⁰ makes further studies necessary.

REFERENCES

1. Hughes GRV: The antiphospholipid syndrome ten years on. *Lancet* 342: 341-344, 1993.
2. Hamsten A, Northerg R, Bjorkholm M, De Faire U, Holm G: Antibodies to cardiolipin in young survivors of myocardial infarction: an association with recurrent cardiovascular events. *Lancet* i: 113-116, 1986.
3. Asherson RA, Mackay IR, Harris EN: Myocardial infarction in a young man with systemic lupus erythematosus,

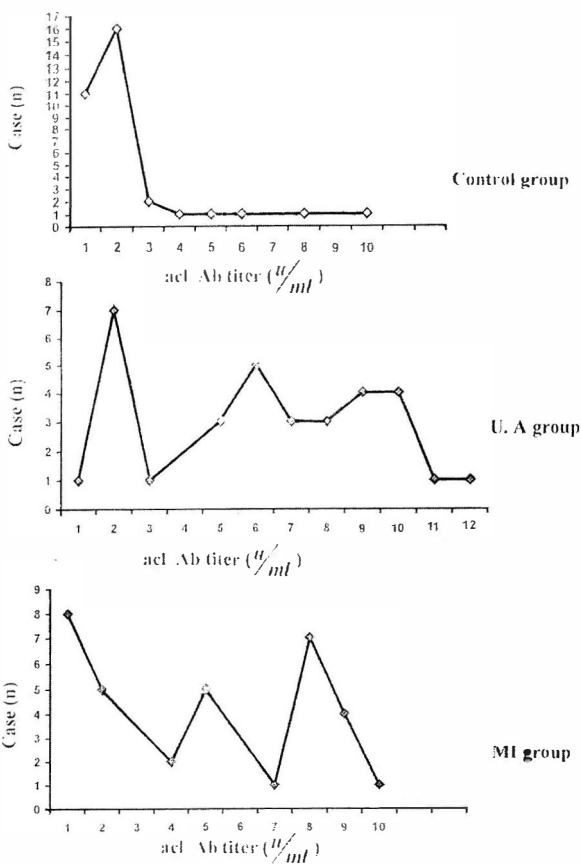


Fig. 2. aCL Ab titers in the study groups.

Table I. Baseline characteristics and risk factors of the study population.

Parameter	Unstable angina (n= 33)	Myocardial infarction (n= 33)	Control subjects (n= 34)
Age (yrs)	50.3	55.4	51.1
Weight (Kg)	77±12	73±10	76±14
Systemic hypertension	21 (64%)	20 (61%)	23 (68%)
Diabetes mellitus	5 (15%)	6 (18%)	4 (12%)
Current smokers	11 (33%)	13 (39%)	9 (26%)
History of hypercholesterolemia	17 (52%)	19 (58%)	15 (44%)

No significant difference was found between the 3 groups regarding any of these parameters (analysis of variance).

- deep vein thrombosis, and antibodies to phospholipid. *Br Heart J* 56: 190-93, 1986.
- Asherson RA, Khamashta MA, Baguley E, Oakley CM, Rowell NR, Hughes GRV: Myocardial infarction and antiphospholipid antibodies in SLE and related disorders. *QJ Med* 73: 1103-15, 1989.
 - De Caterina R, d'Ascanio A, Mazzone A, Gazzetti P, Bernini W, Neri R, et al: Prevalence of anticardiolipin antibodies in coronary artery disease. *Am J Cardiol* 65: 922-923, 1990.
 - Sletnes KE, Smith P, Abdelnoor M, Arnesen H, Wisloff F: Antiphospholipid antibodies after myocardial infarction and their relation to mortality, reinfarction and non-hemorrhagic stroke. *Lancet* 339: 451-453, 1992.
 - Phadke KV, Phillips RA, Clarke DT, Jones M, Naish P, Carson P: Anticardiolipin antibodies in ischemic heart disease: maker or myth? *Br Heart J* 69: 391-394, 1993.
 - Sletnes KE, Larsen EW, Stokland O, Wisloff F: Antiphospholipid antibodies detected in anticephalin and anticardiolipin antibodies in patients with acute myocardial infarction: immunological response to myocardial infarction. *Thromb Res* 59: 675-80, 1990.
 - Morton KE, Gavaghan TP, Krilis SA, et al: Coronary artery bypass graft failure-an autoimmune phenomenon? *Lancet* ii: 1353-57, 1986.
 - Wu R, Nityanand S, Berglund L, Lithell H, Holm G, Lefvert AK: Antibodies against cardiolipin and oxidatively modified LDL in 50-year-old men predict myocardial infarction. *Arterioscler Thromb Vasc Biol* 17: 3159-63, 1997.
 - Bakimer R, Fishman P, Blank M, Stedni B, Djaldetti M, Shoenfeld Y: Induction of primary antiphospholipid syndrome in mice by immunization with a human monoclonal anticardiolipin antibody. *J Clin Invest* 80: 1558-1563, 1992.
 - Sherer Y, Shoenfeld Y: The antiphospholipid (Hughes') syndrome: an entity to be expanded. *Am J Reprod Immunol* 41: 113-16, 1994.
 - George J, Afek A, Gilburd B, Levy Y, Blank M, Kopolov J, Harats D, Shoenfeld Y: Atherosclerosis in LDL-receptor knockout mice is accelerated by immunization with anticardiolipin antibodies. *Lupus* 6: 723-29, 1997.
 - Klemp P, Cooper RC, Strauss FJ, Jordaan ER, Przyboyewski JZ, Nel N: Anti-cardiolipin antibodies in ischemic heart disease. *Clin Exp Immunol* 74: 254-57, 1988.
 - Vaarala O, Manttari M, Manninen V, Tenkanen L, Puurunen M, Ahok Palosuo T: Anti-cardiolipin antibodies and risk of myocardial infarction in a prospective cohort of middle aged men. *Circulation* 91: 23-27, 1995.
 - Sherer Y, Shemesh J, Tenenbaum A, Praprotnic S, Harats D, Fishman E, Blank M, Motro M, Shoenfeld Y: Coronary calcium and anticardiolipin antibody are elevated in patients with typical chest pain. *Am J Cardiol* 86: 1306-1311, 2000.
 - Erkkila A, Narvanen O, Lehto S, Uusitupa M, Yla-Herttuala S: Autoantibodies against oxidized low-density lipoprotein and cardiolipin in patients with coronary heart disease. *Arterioscler Thromb Vasc Biol* 20: 204-209, 2000.
 - Bili A, Moss A, Francis CW, Zareba W, Sanz I: Anticardiolipin antibodies and recurrent coronary events. *Circulation* 102: 1258-1262, 2000.
 - Logacheva IV, Leshchiniskii LA, Zvorigin IA: Immunological characteristics of patients with acute coronary syndrome (unstable angina and myocardial infarction). *Klin Med* 77(4): 23-5, (Abstract), 1999.
 - Gaeta G, Lupoli S, Brancaccio V, Effuso L, Russo V, Boccalane A: Anticardiolipin antibodies and early infarct of the myocardium. *Cardiologia* July 43(7): 731-5 (Abstract), 1998.

