

An Evidence against the Effect of Chronic Cytomegalovirus Infection in Unstable Angina Pectoris

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Abstract- Recent reports have suggested that cytomegalovirus (CMV) infection may contribute to risk of cardiovascular disease. However, relationship between CMV infection and unstable angina (UA) is controversial and studies about this subject in Iran and even region are lacking. The aim of this study was to determine whether unstable angina is related to seropositivity to chronic cytomegalovirus infection. We measured serum CMV IgG levels in a case control study participants in CCU in Razi Hospital, Ahwaz, Iran, from 2004 to 2005. Blood samples were drawn during study period from 96 patients (mean age 56 years) with UA according to American Heart Association Criteria and from 96 participants free of cardiovascular disease (mean age 58 years) and stored at -20°C . Blood samples of patients were undertaken for investigating the specific anti CMV-IgG by ELISA method. Data were analyzed in SPSS 11.5 by using chi square test, odds ratios (OR) with 95% confidence intervals (CI). Ninety three percent of patients with unstable angina and 96.7% in the control group presented a positive anti CMV-IgG. Odds ratio was 0.52 with 95% CI: 0.10 to 2.42. There was no significant correlation between CMV-IgG positivity and unstable angina ($P>0.05$). There was also no differences in CMV-IgG positivity in clinical groups of UA ($P>0.05$). The relationship between seropositivity of CMV-IgG and unstable angina has been restituted by the results of this study. However, further population based cohort studies for relationship between CMV infection and coronary artery disease must be conducted.

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Introduction

It's known that common risk factors of atherosclerosis can explain only 50% of its etiology. In only 40% of patients risk factors modification inhibits progression of atherosclerosis.

Therefore, looking for new risk factors of atherosclerosis is necessary (1). Chronic infection has been found to be significantly associated with the development of atherosclerosis and the clinical complications of unstable angina (UA), myocardial infarction and stroke. For the most part, these relationships are still just associations. Failure to confirm initial reports of serologic associations also has been common (2).

Epidemiological studies have suggested an association between some pathogens and atherosclerosis. Two infectious agents, *Chlamydia pneumoniae* (*C*

pneumoniae) and cytomegalovirus (CMV), have been detected in human atherosclerotic lesions. Elevated antibody titers to both *C pneumoniae* and cytomegalovirus conferred a higher risk for premature MI even after adjustment for other risk factors (3). CMV is one of the most common infectious agents in human population and therefore it is suspected as the main infectious pathogen in the coronary disease (1).

It is a hypothesis that, in patients with unstable angina, replication of CMV in coronary atherosclerotic plaques is a major cause of plaque instability (4) but, the possible contribution of CMV to pathogenetic events associated with atherosclerotic lesion establishment and progression is still controversial (5). The aim of this study was to identify a relationship between CMV infection and unstable angina.

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Patients and Methods

In a case control study in Ahvaz a city south west Iran from 2004 to 2005, hospitalized patients with unstable angina in CCU ward of Razi Hospital affiliated to Joundishapour University of Medical Sciences were evaluated for presence of anti CMV-IgG. Ninety six patients enrolled in this study. Inclusion criteria were: 1) Age above 35 years, 2) Clinical criteria (CC) according to American Heart Association Criteria (6): a) Retrosternal pain, b) Duration of pain 2-20 minutes and, c) Pain resolving with sublingual trinitroglycerin (TNG). Exclusion criteria were: 1) Cardiac enzymes rising, 2) EKG changes (q wave in more than 2 pericardial leads, ST elevation in more than 2 pericardial leads), 3) Persistent angina pain, 4) Doubtful CMV- IgG titers.

Ninety six patients with unstable angina were randomly selected out of all the patients who met the inclusion criteria. Patients were divided in 3 groups: TAP (typical angina pectoris, having all 3 CC), AAP (atypical angina pectoris, having 2CC), and NAP (non angina pectoris, having only one CC).

A questionnaire including demographic characteristics and other related variables was fulfilled for each patient. 96 cases whose gender and age individually matched were selected from patients' family members and/or hospital personnel as control group. 5 ml clotted blood was obtained from each subject in patient and control groups for specific anti CMV-IgG by ELISA method with sensitivity of 88%-93% and specificity of 95%-98%.

Commercially available IgG antibody tests for CMV were conducted according to the manufacturer's instructions. Blinded duplicate specimens were included (10%) to assess the reproducibility of the laboratory tests (Serum was frozen in glass vials and stored at -20°C). IgG titer of 30 u/ml or more was considered as positive, 20-30 u/ml was doubtful and lower than 20u/ml as negative. The data were analyzed in SPSS 11.5 by using chi square test and odds ratio with 95% confidence intervals (95% CI).

Results

There were 96 patients with unstable angina (62, 30, 4 cases in TAP, AAP, NAP respectively) in the study group with mean age of 56.48 ± 12.91 years in whom 55% were females.

The control group included 96 persons with mean age of 58.03 ± 11.53 years in whom 52% were females. Ninety (93%) patients with unstable angina and

87(96.7%) in the control group presented a positive anti CMV-IgG. Six of control group because of doubtful results were excluded.

Odds ratio was 0.52 with 95% CI: 0.10 to 2.42. There was no significant relation between CMV-IgG positivity and unstable angina ($P>0.05$). There was also no differences in CMV-IgG positivity in clinical groups of TAP, AAP and NAP ($P>0.05$).

Discussion

The present study revealed no significant relation between chronic cytomegalovirus infection (anti CMV-IgG positivity) and unstable angina pectoris. Our results do not support a role of CMV in promoting the risk of UA ($P>0.05$, OR=0.52).

Several studies have reported associations between chronic CMV infection and UA. (8-11). It is unclear whether infection with CMV is really associated with UA because some of these studies were prone to selection biases, limited by small sample sizes, did not adequately account for possible confounders. It is likely that chance, may explain the positive relation. The present study is similar to recent reports those didn't support a strong relation of CMV with risk of UA. (4, 5). Because of confounding by socioeconomic status relation between CMV and UA is difficult to interpret.

However, our study confirms previous observations of a lack of relation of CMV with unstable angina (4, 5, 12-14).

Against some limitations such as small sample size and study design (low validity of cross sectional versus population-based studies), our research had following advantages: 1) The study sample was included both men and women, who suitable for examining the association of chronic infections with UA. 2) The mean age of the participants was 56.48 ± 12.91 years that decreased the possibility of missing those most susceptible to UA in response to chronic infection with CMV.

Our study was based on IgG testing and was not designed to examine histological or DNA evidence of infection with CMV, accompanying systemic inflammatory responses and rising risk of UA. Controls in our study were hospital personnel and/or family member of patients, high seropositivity may reflex common environmental situation and high exposure to this infectious agent. In conclusion, our study discarded relationship between chronic CMV infection and unstable angina. CMV infections, as evidenced by seropositivity of CMV-IgG, were not associated with increased risk for UA. This finding suggests that further

population based cohort studies for relationship between CMV infection and coronary artery disease must be conducted.

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Conflict of Interest

This study was funded by research deputy of Joundishapoor University and Infectious and Tropical Diseases Research Center and there is no conflict of interest.

Ethical Approval: This work has been approved by the Ethical Committee of Research Council related to Research Deputy of Joundishapoor University.

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