Seroprevalence of Cytomegalovirus in Patients with and without Coronary Artery Diseases at Madani Heart Center, Iran

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Abstract- Inflammation plays a major role in coronary artery disease (CAD). Currently, it is unclear, whether Cytomegalovirus (CMV) infection is associated with the risk of the atherosclerosis. The aim of this study was to determine the prevalence of anti- CMV antibodies in CAD and non CAD patients undergoing artery bypass surgery. Sera from 157 patients who underwent coronary angiography were tested for CMV by enzyme linked immunosorbent assay (ELISA) at Madani Heart Hospital, Tabriz University of Medical Sciences, Iran. Our study population was 58.6% male and 41.4% female, with an age range of 38 to 86 years. The prevalence of CMV positivity tended to be higher in coronary artery diseases patients than in those without non coronary artery diseases (83.2% versus 63.6%) (*P*= 0.01). This analysis demonstrated that CMV seropositivity may be a risk factor for CAD in the present study population.

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Key words: Coronary artery diseases; cytomegalovirus; infection

Introduction

Coronary artery disease (CAD) is the leading cause of death for both men and women. CAD is usually caused by atherosclerosis (1). Risk factors for atherosclerosis include age, sex, smoking, diabetes mellitus, hypercholesterolemia, hypertension, family history and elevated CRP levels (2, 3). Inflammation plays a central role in CAD (4). Epidemiological studies indicate that infective agents may predispose to atherosclerosis and adverse clinical events. Infections have been associated with an increased risk of atherosclerosis (2-12). At the beginning of the 1970s, the monoclonal hypothesis was first proposed, suggesting a potential role for viral inflammation in the atherosclerotic process (13). Several experimental studies have suggested that immune mechanisms have important roles in the pathogenesis of atherosclerosis. Since some pathogens have been identified in atherosclerosis plaques, it has been hypothesized that it may precipitate vascular inflammation by either persistent infection or by immunity related injury (14). Recently, the association of atherosclerosis and cytomegalovirus (CMV) infection has been reported (15-18). Acute CMV infections in immunocompetent patients are common worldwide, with seroprevalence rates of 40%–100%, depending on the country, socioeconomic conditions, and the patient's age. Infection is most often asymptomatic, but acute cytomegalovirus infection is occasionally revealed by prolonged fever, cervical lymphadenitis, and arthralgia (19). CMV infection of endothelial cells may increase cellular proliferation and inhibit apoptosis of infected smooth-muscle cells, thereby contributing to an increase in the mass of arteriosclerotic lesions. Furthermore, individuals infected with CMV have impaired endothelium- mediated coronary vasodilator responses (20). The aim of the present research was to evaluate the association between the CMV infection and the risk of atherosclerosis in the northwest of Iran.

Materials and Methods

A total of 157 individuals entered the study. The study consisted of consecutive subjects who were referred for coronary angiography because of chest pain or non-invasive testing compatible with myocardial ischemia at Madani Heart Center, Tabriz, Iran. Coronary angiography was performed in a cardiac catheterization laboratory.

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Table 1. Comparision of traditional risk Factors between the patients with and without coronary artery diseases

Variables	CAD(+)n=113	CAD(-)n=44	P
Male	73 (65.21%)	15 (34.78%)	0.01
Female	29 (25.79%)	32 (73.27%)	
Hyperlipidemia	90 (79.64%)	24 (54%)	0.02
CRP	89 (76.76%)	11 (25%)	0.001
Hypertension	79 (70%)	10 (22.2%)	0.045
Diabetes	61 (54.14%)	20 (45.85%)	0.37
Smoking	69 (61%)	16 (36.3%)	0.031
CMV	94 (83.2%)	28 (63.6%)	0.01

CRP: C - reactive protein, CMV: Cytomegalovirus

ECG electrodes were placed on the patient's chest and an intravenous line was inserted. A local anesthetic was injected into the site where the catheter was to be inserted. The cardiologist inserted a catheter into a blood vessel and guided it into the heart. A contrast dye was then injected to make the heart visible on x-ray cinematography. One experienced cardiologists blinded for laboratory data reviewed the films. Venous blood samples were collected under standardized conditions after an overnight fast and centrifuged within 15 minutes (3000 g for 10 minutes). CMV antibodies were determined by enzyme- linked immunosorbent assay (CITOMEGALOVIRUS Ig G- EIA WELL, Radium, Italy). CRP was determined by an immunoradiometric assay (range: 0.05–10 mg/l).

Results for normally distributed continuous variables are expressed as mean ± S.D. Statistical analysis was performed using ANOVA or by the unpaired t-test in case of continuous variables between different groups, the chi-square test or proportional comparison in case of dichotomous variables and also univariate and multivariate logistic regression analyses using SPSS software, version 14. Statistical significance was considered as rejection of the null hypothesis with 95% confidence (*P*-values <0.05 were considered significant).

Results

Total of 157 sera submitted for CMV screening in Madani Heart Center, Tabriz University of Medical Sciences. Of one hundred fifty seven cases 92 were male and 65 were females and mean age of the patients was 49 ± 10. All serum samples used in this study were tested for anti-CMV antibody using ELISA kit. Of the 157 patients 122 (77.7%) had anti- CMV Ig G antibodies. The traditional risk factors, CRP levels and anti-CMV antibodies were compared between the patients with and without CAD (Table 1). CAD prevalence was 83.2% in CMV-seropositive and 63.6% in CMV-seronegative patients (*P* =0.01). Mean high sensitive CRP value among CAD patients was 10.8 ± 5.2 and in normal angiography population group was 5.01 ± 4.1 (*P*= 0.001).

Discussion

In recent years, atherosclerosis has come to be recognized as active and inflammatory, rather than simply a passive process of lipid infiltration. Inflammation occurs in response to vascular oxidative stress and injury through known and unknown stimuli. Inflammatory triggers undoubtedly include oxidized and glycosylated products (eg, modified lipoproteins). Given their association with inflammation, infectious agents also are being explored as potential stimulator of vascular inflammation and promoters of atherosclerosis (17). Atherosclerosis appears to be of multifactorial etiology (5). Results of large epidemiological studies have established the concept of traditional risk factors, such as hypercholesterolemia, arterial hypertension, diabetes mellitus, smoking and a family history of vascular diseases. In addition, several studies have reported an association between atherosclerosis and certain persistent bacterial and viral pathogens (8). Many patients with CAD lack conventional risk factors, suggesting that there are additional unidentified factors contributing to vascular injury (2, 4). However, one of the most interesting developments in recent years has been the idea that infective agents may induce a pro-inflammatory effect and play a basic role in atherosclerosis (2-12).

In this study, we were found association between CMV infection and coronary atherosclerosis. Seroepidemiological studies of the role of CMV in the development of coronary arteriosclerosis have yielded

controversial results. Several authors found an association (1, 15-18, 21), whereas others did not (8, 22-26). Differences in study design, frequency of individuals with chronic CMV infection, and regional differences may explain the differing results studies.

Since serologic markers of CMV infection provide tools to follow the natural course of disease and hither to, there was no concrete evidence supporting the infection of CMV in endothelial cells. In our study, were examined just one widely used a serologic marker instead of more sensitive CMV-DNA detection with the hypothesis that circulating CMV-associated antigens might be the risk factors for atherosclerosis. Thus, we could not fully include the effects of CMV infections on the risk of atherosclerosis, the link between CMV-DNA positivity and atherosclerosis should be clarified at a large population in future studies. We conclude that there is association between CMV infection and the atherosclerosis in this population. Screening for CMV is may be useful in preventing atherosclerotic disease.

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