original article

Serological Evidence of Chlamydia Pneumoniae in acute MI

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Abstract

Objectives:- Chlamydial infections are being implicated in plaque instability. Human atheromas often contain chlamydial heat shock protein 60(HSP-60), an effect or of activation of macrophages, endothelium and matrix metalloproteinase expression. To establish any association between chronic Chlamydia pneumoniae (CP) infection and acute myocardial infarction.

Methods:- Forty-Four consecutive patients of acute myocardial infarction (AMI)and 23 healthy age- and sex-matched controls were enrolled. Within 24 hours of admission for AMI, blood samples were taken for detecting anti-CP IgG and IgA immunoglobulin levels by using microimmunofluorescence assay. We also tried to assess the relationship between serelogical evidence of chronic CP infection and established major CAD risk factors, viz,. Diabetes, dyslipidemia, hypertension and smoking.

Results:- IgG antibodies were positive in 33 patients (75%) and 10 subjects(43.5%)in the control group, the difference being statistically significant ($p<0.01$). IgA antibodies were positive in 13 cases (30%) and 4 subjects (17%) of the control group, the difference being statistically insignificant ($p>0.01$).Elevated IgG titers were significantly positive in cases compared to controls while the difference in elevated titers of IgA between the two groups was statistically insignificant. Among the major risk factors, only dyslipidemia (total cholesterol>200,mg%) showed a significant correlation with IgG and IgA levels in the study population.

Conclusion:- Study group showed statistically significant association, with IgG and non-significant association with IgA anti C. pneumoniae antibodies. Elevated IgG titers were significantly higher in the patient group compared to the control population.Elevated IgA titers were not significantly higher in the patient group, owing to early fall in the titers.

Hyperlipidemia was significantly associated positive IgG and IgA ANTI c. pneumoniae serology in the study group.

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Introduction

Established cardiovascular risk factor do not completely explain the epidemiological changes and the diverse presentation of coronary heart diseases. This has led to increasing interest in the contribution of certain infectious agents as atherogenic risk factor [1].

The proposed infections implicated are:

1. Chlamydia pneumoniae.
2. Cytomegalovirus infection.
3. H. Pylori.

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Key Word:

Acute MI, Chamydia Pneumoniae

The evidence of Chlamydia pneumoniae as a potential causative agent is strong and is largely based on the findings of

1. Seroepidemological studies.
2. Examination of atherosclerotic plaque specimens.
3. Invitro experiments and animal models
4. Preliminary antichamydial antibiotic intervention studies[1].

Chlamydia pneumonia was first isolated in 1965 in Taiwan. It was subsequently recognized to be a cause of acute respiratory disease giving rise to TWAR (Taiwan acute respiratory) agent. Chlamydia pneumoniae is an obligate, intracellular pathogen. Organism has been found in atherosclerotic tissue and also in stenosed aortic valves, hypothesis. However, in a recent autopsy study Chlamydia pneumoniae was detected using PCR and immuno cytochemistry in a greater proportion of coronary atheromatous lesions and less frequently in other tissues suggesting a predilection by vascular atheromatous lesion [2].

It is hypothesized that macrophages/ monocytes may transport Chlamydia pneumoniae from respiratory tract to the coronary arteries local infection of the coronary vasculature may create a focus for intimal damage and may promote an inflammatory response. Activation of monocytes / macrophages leads to cytokine production and synthesis of acute phase proteins [3] and expression of procoagulant markers such as tissue factor[4] ;

Recent research indicates that the risk of cardiovascular diseases in Chlamydia pnenumoniae infection may be mediated through a simpler process, namely the induction of an atherogenic lipid profile [5].

In order to clarify the role of C. pneumoniae infection in acute myocardial infarction, we conducted a study on patient with acute myocardial infarction and evaluated the prevalence of Chlamydia pneumoniae infection, for comparison the control was also studied for the prevalence of IgG and IgA antichlamydia pneumoniae antibodies.

MATERIAL AND METHODS

This study was conducted in cardiology department of the Sher-i-Kashmir institute of medical sciences Srinagar, forty four consecutive patients admitted with acute myocardial infarction diagnosed on the basis of standard criteria I e , at least two of, the following [6], were included in the study.

1. Recent onset symptoms < 12 hrs, characterized by typical chest pain lasting for > 20 minutes and resistant to nitrates.
2. Typical changes in the electrocardiogram.
3. Raised serum enzymes levels.

Twenty three healthy volunteers of matched age and sex were taken as controls.

Evolution included detailed clinical history, including information about smoking, diabetes mellitus, hypertension and dyslipidemia and detailed physical examination. 12 lead surface electrocardiogram was taken on admission, daily during the course of hospital stay and any time when ever required.

Lipid profile (total cholesterol, HDL cholesterol , LDL cholesterol, VLDL cholesterol and triglycerides) and cardiac enzymes were estimated by standard procedures using multichannel analyser Hitachi 704 troponin T was qualitatively estimated by using a commercially available kit from Boegringer Mannheim, Germany. All the patients received usual standard management for myocardial infarction. The patients were subjected to coronary angiography and managed on merits.

After informed written consent, 5 ml peripheral venous blood sample was taken from each patient within 24 hours of admission with acute myocardial infarction, transferred to serum chemistry tubes. The serum was separated by centrifugation (1500 x 9 /min for 5 minutes) and transferred to the storage tubes and stored at - 60^0 C until analyzed .

The serum was tested for immunoglobulin G (IgG) and immunoglobulin A (IgA) against Chlamydia pneumoniae antigen. IgG titres of > 1:16 and OgA titers of >1:4 were taken as positive (as per the manufacturers instruction on the kit). The analysis was done by microimmunoflourescence assay.

Microimmunoflourescence assay[7-11]

Multiscreen Chlamydia, a microimmunoflouresce test detects, differentiates and measures the levels of type specific antichlamydial antibodies IgG, IgM and IgA against individual Chlamydia agent with similar and / or epidemiological features, thus avoiding false positivity due to the presence of irrelevant antibodies. The assay is based on testing serial dilutions of samples and visualizing the antigen antibody reaction with an indirect immunofluorescence technique. Each kit contains 8 teflon coated slides, antihuman IgG or IgM conjugated with FiTC, positive and negative sera, cover slips, PBS tablets and mountant. Serial dilutions of the test sera are prepared at 1/16, 1/64 and 1/128 dilution and added to each slide containing 18 wells with panels of Chlamydia antigen. The slides are then incubated for 30 minutes at 370 C, washed with PBS for 10 minutes

followed by addition of conjugate to each well. Positive reaction is indicated by the presence of elementary bodies that are evenly distributed with a bright apple green fluorescence.

Statistical Analysis : Data were analyzed by standard statistical procedure Chi square test. AP Value of < 0.05 was taken as statically significant

The study of pathogenesis of coronary heart disease has recently been expanded to include previously unexplored lines of research. It has been suggested that various types of infections may be involved in the development of acute myocardial infarction. Infection was supposed as a cause of atherosclerosis by osler and others at beginning of this century [12] . cytomegalovirus, herpes simplex virus, H pylori and C pneumoniae have been reported as possible co- factor of atherosclerosis and CHD, although the evidence presented so far is controversial [13].

C. pneumoniae involvement has been suggested on the basis of seroepidemiological evidence as well as detection of the agent on the atherosclerotic plaque in arterial specimens by immunocy to chemistry and molecular biological and by culture from the coronary artery of a patient with atherosclerosis[13]. Elevated antibodies to C. Pneumoniae were detected more commonly in patients with acute myocardial infarction and CHD[1] IgG antibody titers rise and decrease slowly as compared to IGA antibodies. Persistence of elevated antibodies titres is generally considered to be a sign of chronic infectious processes. Analysis of IgA titres is not very rewarding. AgA has been implicated in chronical infection but its interpretation and use as a marker of chronicity remains quite different in the face of its high seroprevalance and similarity to IgG protein profile [14] .

The chronic chlamydial infection was shown to be an independent risk factor for coronary events of the classical risk factors of age, smoking, hypertension and total cholesterol and HDL cholesterol ratio. [14]

The present study included 44 patients of acute myocardial infarction and 23 healthy controls. The patients were in the age group of 45-80 yrs (mean 61.7 + 7.9) and the control group in the age ranging from 44-68 yrs (mean 57.9+ 6.5). Of the 44 patients, 33 were male and 11 females respectively 43.17% patients has anterior wall myocardial infarction, 27.27% has non Q myocardial infarction, Rosa Sessa et al [6] studied patients with similar MI patterns.

IgG positively (>1:16) was found in 75% of studied patients with acute myocardial infarction and 43% of the control group, the difference being statistically significant (p<0.01) its presence suggesting chronic chlamydial infection. It was in accordance with the studies conducted by Rosa Sessa et al [6] , P Saikku et al [14]. The elevated titres of IgG were significantly positively in the patient group compared to controls (p<0.05) these findings were consistent with the observations made by P Saikku et al [15] and DH Thomas et al [16] these observations show that chronic Chlamydia pneumoniae infection is more common in patients with myocardial infarction thereby suggesting that C. pneumoniae infection is more common in patients with myocardial infarction thereby suggesting that C pneumoniae may favour atherosclerosis by inducting access into the arterial wall, effect on lipid metabolism and changes in the antithrombotic properties of the vessel wall [6].

IgA serology (> 1:4) was positive in 29.54 % of the patient group compared to 17.4 % of the control group. The difference between two groups being statistically insignificant (p.0.1) these findings are in agreement with Rossa Sessa [6] but not with P Saikku [15] the difference in elevation of IgA titers between two groups was also not significant. It could be explained on the basis of rapid fall of IgA levels as compared to IgG levels, these findings are in accordance with P. Saikku et al [14] who in addition observed that high IgA titres were shown to be significantly associated with the development of coronary heart diseases event.

The major risk factors evaluated were smoking, hypertension and hyperlipidemia. Various studies in the past have shown variable association of major risk factors and chlamdial pneumoniae serology in patients with CHD RossaSessa et al [6] showed a strong association between dyslipidemia and presence of chronic Chlamydia pneumoniae infection in CHD groups, especially higher triglyceride and low HDL cholesterol levels.

Murrary LJ et al [17] showed altered lipid levels association with presence of C Pneumoniae infection in CH. Our results were in accordance with Rossa Sesa[6] and Murrary et al [17] as we could find both IgG and IgA significantly positive in patients with the hypercholesterolemia compared to patients with normal cholesterol. The possible mechanism of this association is not clear, this finding may have substantial public health Implications (Murrary LJ et al)[17] However, Ella linnanmaki et al [18] observed higher levels of total cholesterol in the control group than

among CCHD patients; besides chance the possibility that individuals with CCHD had changed their diet may explain this paradoxical result. Our study did not show significant association between smoking and IgG and IgA serology in the MI patient. Similar observation were made by Rossa Sessa et al [6] and Franceso et al [13] in therefore the result of our study showed that study patients had significantly positive IgG serology while IgA positivity was insignificantly positive. When compared with the control population. Hyperlipidemia has a significant relationship with igG and IgA positive serology in the patient group.

Limitations of the study :

1. The micoroimmunoflourescence antibody test used for diagnosing C. Pneumonia infection is nonstandardised, variable cut offs have been used to determine seropostivvity and anti C. pneumonia antibody titre score is highly dependent on the skill of the microscopist.
2. The second serum sample has not been taken after 4-6 weeks to find the IgG and IgA antibody status after resolution of acute myocardial infarction.
3. Some individuals with asymptomatic or unrecognized coronary disease may been incorrectly classified as controls

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