THE INFLUENCE OF CHLAMYDIA PNEUMONIAE INFECTION ON INTIMA-MEDIA-THICKNESS (IMT) IN COMMON CAROTID ARTERY

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Abstract

INTRODUCTION: Atherosclerosis is a multifactorial disease and the identification and diagnosis of its risk factors can help prevent its complications. Among the recently introduced risk factors is infection with Chlamydia pneumoniae. Atherosclerosis is initially characterized by increased intima-media-thickness (IMT), which can be measured by duplex ultrasonography. This study was designed to assess the role of Chlamydia pneumoniae infection in increasing IMT.

METHODS: Extracranial carotid duplex ultrasound was done in 83 individuals and IMT was measured 1 centimeter proximal to bifurcation of the common carotid arteries. IMT more than 0.9 mm was considered as increased. Forty-four individuals had increased IMT and were included in the case group; 39 individuals with normal IMT were considered as the control group. These two groups were matched for age, sex, smoking, and underlying diseases. Chlamydia pneumoniae IgG (Cp.IgG) and Chlamydia pneumoniae IgA (Cp.IgA) were measured in these 2 groups by using the ELISA method and titers more than 1.10 ISR (Immune Status Ratio) were defined as positive, 0.9-1.09 ISR as borderline, and less than 0.9 ISR as negative. We compared the prevalence of Cp.IgG and Cp.IgA seropositivity and the means of antibody titers in these 2 groups.

RESULTS: There was no significant difference in the prevalence of Cp.IgG and Cp.IgA seropositivity and in the mean titers of these antibodies between the case and control groups.

CONCLUSIONS: Cp.IgG and Cp.IgA do are not valuable predictors of increased IMT.

Keywords: Chlamydia pneumoniae, Intima Media Thickness, Serum Antibody

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Introduction

Atherosclerosis may lead to disabling cerebral complications that are sometimes fatal. Hence diagnosis, identification and control of the risk factors that play a role in its initiation can help in prevention of cerebrovascular events.

Among the recently introduced risk factors are infections, including with Coxsackie's virus,[1,2] Cytomegalovirus,[3-5] Chlamydia pneumoniae,[6-11] and Helicobacter pylori.[12,13] Such studies have conceived the idea that antibiotics may prevent the initiation of atherosclerosis. On the other hand, atherosclerosis is initially characterized by increased arterial wall thickness which is measured as the intima-media-thickness (IMT).[14] One method for assessing cerebral arterial damage in a community population is the measurement of common carotid artery (CCA) wall thickness by using duplex ultrasound. It has been demonstrated that ultrasonic measurement of IMT correlates well with histological measurements.[12]

Some studies indicate that infections and inflammations have a role in increasing IMT such as other risk factors (e.g. hypertension, diabetes mellitus, and hyperlipidemia).[15] If this is true, by diagnosing increased IMT (via duplex ultrasound) and measuring biomarkers of those infections (known as risk factor), we may be able to initiate treatments against these risk factors and thereafter monitor the efficacy of the treatment by serial duplex ultrasound and serological tests.

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This study was designed to assess the association between Chlamydia pneumoniae infection and increase in IMT and thus the initiation of the atherosclerosis; we also aimed to assess the role of Chlamydia pneumoniae serologic markers as predictors of increasing IMT.

Materials and methods

In a cross sectional case-control study conducted between September 2005 and February 2006 in the Department of Neurology of Alzahra Hospital, Isfahan, Iran, 83 individuals who presented to the Duplex Sonography Unit of this department were selected and underwent Doppler ultrasound study that was performed by 2 neurologists using 5.5 MH transducer of ATL duplex ultrasound equipment.

IMT was measured one centimeter proximal to the bifurcation of the right and left common carotid arteries (CCA) by duplex ultrasound. IMT was defined as the distance between the inner echogenic line representing the intima-blood interface and the outer echogenic line representing the adventitia junction.

According to the most recent guidelines of the Joint European Society of Hypertension/European Society of Cardiology, normal IMT was defined as less than 0.9 mm.

Duplex ultrasound of the studied subjects did not show any atherosclerotic plaques in the common carotid artery, external carotid artery, or extracranial portion of the internal carotid artery.

Forty-four patients with increased IMT in at least one common carotid artery were considered as the case group and 39 individuals with normal IMT as the control group. These groups were adjusted for age, sex, hypertension, diabetes mellitus, hyperlipidemia, and smoking. The prevalence of Chlamydia pneumoniae IgG (Cp.IgG) and Chlamydia pneumoniae IgA (Cp.IgA) seropositivity and the means of their titers were compared between these two groups.

Patients with recent pulmonary infection (radiological or clinical) or ischemic heart disease were excluded from the study.

Two milliliters of fasting blood was obtained from every subject and centrifuged after cooling at 4 ºC for 2 hours.

Then serum was separated and stored at -20 ºC for a maximum of 1 week, then at -70 ºC until analysis. Serum samples were tested by one investigator with the ELISA method using Trinity Biotech CapitaTM kit, made in Ireland.

Cp.IgG and Cp.IgA titers were considered negative if they were equal to or lower than 0.90 ISR (Immune Status Ratio), borderline if they were between 0.91 and 1.09 ISR, and positive if they were equal to or higher than 1.10 ISR.

We used Student's t-test to compare antibody titers in the two groups. We used χ^2 (chi-square) test to analyze qualified data. All of the analyses were conducted with SPSS.

Results

There were 44 subjects (24 male, 24 female) in the case group and 39 (24 female, 15 male) in the control group.

The mean age was 67.43 years (SD=8.19) in cases, and 63.86 years (SD=11.43) (P>0.05).

The two groups were adjusted for risk factors such as hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HLP), and smoking (Table 1).

Cp.IgA was reported positive in 9.1% of cases with increased IMT and in 5.1% of controls, with no significant difference (P=0.679) (Table 2).

TABLE 1. Prevalence of the risk factors in case and control groups

		HTN	DM	HLP	Smoking	Total
Increased IMT	n	20	10	12	11	44
		45.5%	22.7%	24.2%	25%	
Normal IMT	n	18	10	12	9	39
		46.1%	25.7%	30.7%	23%	

TABLE 2. Comparing the prevalence of Cp.IgG and Cp.IgA seropositivity in cases with increased IMT and control subjects with normal IMT

	males			Females			total		
	IMT↑	NL IMT	P value	IMT↑	NL IMT	P value	IMT↑	NL IMT	P value
Cp.IgA	12.5%	6.7%	1.000	5.0%	4.2%	1.000	9.1%	5.1%	0.679
N=	3	1		1	1		4	2	
Cp.IgG	12.5%	26.7%	0.396	15.0%	20.8%	0.710	13.6%	23.1%	0.392
N=	3	4		3	5		6	9	

TABLE 3. Comparing the means of Cp.IgG and Cp.IgA titers in cases with increased IMT and control subjects with normal IMT

	Cp.IgA	SD	Cp.IgG	SD
Increased IMT	0.53	0.35	0.63	0.48
Normal IMT	0.55	0.36	0.65	0.62
	P= 0.774		P= 0.860	

Cp.IgG was reported positive in 13.6% of cases and 23.1% of controls, with no significant difference (P=0.392) (Table 2).

The means of Cp.IgA titers in the case and control groups were 0.53 ISR (SD=0.35) and 0.55 ISR (SD=0.36), respectively. Cp.IgG titer was 0.63 ISR (SD=0.48) in the case group and 0.65 ISR (SD=0.62) in the control group. There was no significant difference between the two groups (P=0.774 for Cp.IgA titer and P=0.860 for Cp.IgG titer) (Table 3). Statistical analysis was performed in males and females separately; no significant association was found between antibody titers and increasing IMT in either gender (Tables 2, 3).

Discussion

Atherosclerosis is a multifactorial condition influenced by genetics, hyperlipidemia, hypertension, diabetes mellitus, and smoking. However, some patients do not have any of these risk factors; hence a different theory should be sought to explain atherosclerosis in such individuals.

Recently, infections have been introduced as factors that may contribute to atherosclerotic plaque formation. Some factors such as Coxsackie's virus infection, Cytomegalovirus in transplanted heart, Helicobacter pylori, and Chlamydia pneumoniae have been suggested[1-8,10]

In this study, Cp.IgA and Cp.IgG seropositivity did not have any association with increased IMT one centimeter proximal to CCA bifurcation.

In other studies done by Gerdes VE et al. and Pitirviga VC et al. in 2003, no relationship was found between Cp.IgA and Cp.IgG seropositivity and increased IMT;[9,15] this is in agreement with our study. However, in one study performed by Kato A et al., Cp.IgA (but not Cp.IgG) was found to be associated with increased IMT in multivariate regression analysis.[16]

In another study, Cp.IgG was associated with increased IMT only in linear regression analysis, but no such association was seen in multivariate regression analysis.[10]

In another study conducted only on men, all anti-Chlamydia pneumoniae antibodies (Cp.IgA, IgG and IgM) were predictors of increased IMT.[9]

The existing controversies may be due to several reasons.

Increasing IMT and development of atherosclerosis (atherogenesis) is a multifactorial process, and several different factors may contribute to its initiation and continuation. Although we attempted to match the two groups for other risk factors of atherogenesis, we could not determine the duration of presence and severity of the risk factors and the extent to which they had been controlled. Also, there may be other infections contributing to atherogenesis in different populations. On the other hand, there may be a specific serotype of Chlamydia pneumoniae that contributes as a risk factor to IMT increase and atherogenesis. Hence, more specific antigens and antibodies should be determined by future studies. In summary, Chlamydia pneumoniae infection may contribute to the continuation of atherogenesis, but not its initiation; we recommend another study to evaluate this hypothesis. One such investigation was done by Egle C in 2005; it emphasized the role of inflammation in increasing IMT and starting atherosclerosis.[14]

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