CD 28 Gene Polymorphism is not Associated with Susceptibility to Coronary Artery Disease

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Abstract

Background- Coronary artery disease (CAD) is one of the most common health problems facing health care services in all societies. Despite the established significance of the classic risk factors for CAD, a large number of patients present without them. It has recently been identified that elevated inflammatory markers and involved immunological mechanisms are associated with atherosclerosis. CD 28 is the main co-stimulatory receptor for secondary signals delivering for T-cell activation. The aim of this study was to evaluate the polymorphism of CD 28 gene as a probable risk factor for CAD.

Methods- In total, 200 patients were classified into two equal groups: control group including persons with normal coronary arteries and case group who had at least single-vessel coronary disease. CAD was confirmed in the studied patients by coronary angiography. CD 28 genotype was analyzed via polymerase chain reaction (PCR).

Results- The frequencies of C and T alleles were 71% and 29% in the control group and 70.5% and 29.5% in the case group, respectively. There was no significant difference in the allele frequencies between the two groups.

Conclusion- We concluded that CD 28 gene polymorphism was not associated with CAD ***(Iranian Heart Journal 2008; 9 (4):38-41).***

Key words: coronary artery disease ■ genes ■ polymorphis

Coronary artery disease (CAD) is one of the most frequent causes of mortality and morbidity in the world.

More than 250 genes have been identified that may play some role in CAD. Several of the best understood genes are related to LDL-receptor, ApoE, ApoB-100, Apo(a), homocysteine, ApoA1, GpIIb, and IIIa.[1]

For each involved gene, there can be a wide variety of slight changes in the chemical structure of a gene, known as single nucleotide polymorphisms. Some of these changes can increase one's risk for CAD, while others may be protective against the disease, for example a 53 G>A polymorphism identified in the platelet endothelial cell adhesion molecule 1 (PECAM-1) gene is Associated with the progression of atherosclerosis [2] and a monocyte chemoattractant protein 1 (MCP-1) gene polymorphism is associated with occult ischemia.[3]

In this study, we examined the association between CD 28 gene polymorphism and CAD. The association of this polymorphism with other diseases such as diabetes type 1, asthma, SLE, HIV infection, celiac disease, and myasthenia gravis has been investigated before.[4-6]

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CD 28 is a major co-stimulatory molecule for T-cell activation.[5] T-cells cannot be activated by the interaction of the T-cell receptor and the MHC cluster of the antigen-presenting cell alone.

A co-stimulatory signal mediated through CD 28 is essential to T-cell activation. If this co-stimulation does not occur, the T cell resolves in a state of anergy. CD 28 is a membrane-bound molecule that belongs to the immunoglobulin (Ig) super-family. CD 28 binds to its ligands B 7.1 and B 7.2, which are both homodimeric members of the Ig super-family, on antigen presenting cells such as macrophages or dendritic cells.[4]

Methods

This study was a case-control analytic study. We analyzed DNA samples from 100 normal people without CAD, as proven with coronary angiography (control group), and 100 patients with documented CAD (at least single-vessel disease at coronary angiography, case group). DNA extraction was performed via the salting-out method.

The polymorphism was determined by allele-specific PCR using an allele-specific primer for C or T at position IVS3+17 in the CD 28 gene at the 2q33 locus.[5] The primers used to detect T and C alleles were as follows:

5′-CTGGGTAAGAGAAGCAGCAAT-3′ (T primer)
5′-CTGGGTAAGAGAAGCAGCAAC-3′ (C primer)
5′-CTCAATGCCTTCTGGAAATC-3′ (Cm primer) (common primer)

A single-base mismatch was introduced at position 2 from the 3' end of both allele-specific primers (shown by the underline). Each primer combination detected only the primer-specific allele. The PCR products were separated on 3% agarose gel and visualized by ethidium bromide staining.

The differences between the allele or genotype frequencies of the groups were evaluated using the χ^2 analysis.

Results

The case group was comprised of 72 (72%) men and 28 (28%) women, and the control group consisted of 45 (45%) men and 55 (55%) women.

In the case group, 33 (33%) patients had single-vessel disease, 38 (38%) two-vessel disease, and 29 (29%) three-vessel disease.

The allele frequencies in two groups are shown in Figure 1.

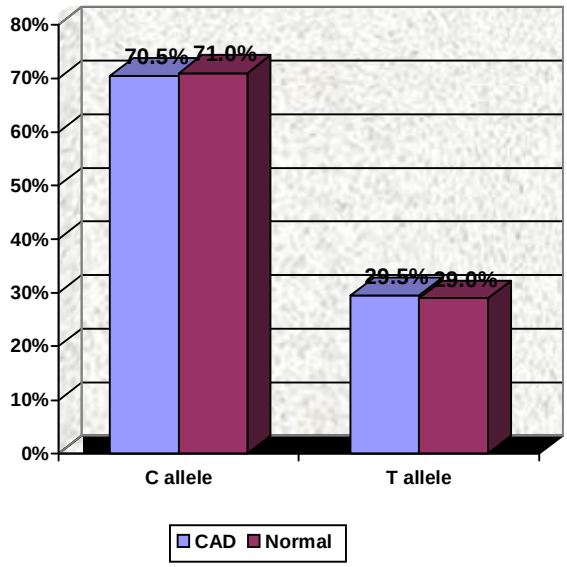

Fig. 1. CD 28 polymorphism allele frequencies in normal persons and CAD patients.

There was no significant difference in alleles C and T frequencies between the two groups. Allele C had a higher frequency in both groups (Table I).

Table I. CD 28 polymorphism genotypes in case and control groups (P>0.05).

	CAD	Normal
CC	41 (41%)	42 (42%)
CT	59 (59%)	58 (58%)
TT	0	0

There were also no significant differences in the genotype frequencies (CC, CT, or TT) between the case and control groups (P>0.05).

Discussion

Atherosclerosis is an inflammatory disease. In fact, the earliest type of lesion, the so-called fatty streak, is a pure inflammatory lesion consisting only of monocyte-derived macrophages and T-lymphocytes.[7]

A large number of epidemiologic studies have reported associations between various inflammatory factors and coronary heart disease. These inflammatory factors include blood levels of fibrinogen, CRP, albumin, leukocyte count, IL-6, serum amyloid A protein, 5-lipoxygenase, and myeloperoxidase.[8-11] Some previous studies have shown an association of some CD molecules with atherosclerosis: CD 14 receptor is a glycoprotein localized on the surface of monocyte/macrophage and neutrophils. CD 14 C (-260) T polymorphism is related to the occurrence of carotid atherosclerosis.[12]

CD 36, which is a member of the scavenger receptor class B family, has some role in the pathogenesis of atherosclerosis.[13]

In this study, we compared the frequency of CD 28 gene polymorphism alleles in 100 persons with normal coronary arteries with 100 CAD patients confirmed by coronary angiography.

The frequency of CD 28 C allele in our study was higher than that reported in the literature for some other populations,[5,14] but we did not find any significant association between CD 28 gene polymorphism and CAD. The allele and genotype frequencies did not differ significantly between the case and control groups. However, in the future it may be possible to identify various potent genetic markers of CAD and tackle these by gene therapy.[15]

On the other hand, the presence of such markers in a person does deserve more intense modification of other known risk factors to prevent the progression of the atherosclerotic process successfully.

Conclusion

In this study, we could not show an association between CD 28 gene polymorphism and CAD. Be that as it may, given the polygenic nature of CAD and the role of inflammation in atherosclerosis, many inflammatory biomarkers remain to be investigated in this way.

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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