Deletion polymorphism of the angiotensin I converting enzyme gene and coronary artery ectasia

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Abstract

Background - Coronary artery ectasia (CAE) is the abnormal enlargement of the coronary artery. The prognosis, treatment, and etiology of this disease remain an enigma. Experimental data suggest that activation of renin angiotensin system may lead to an increased inflammatory response in the vessel wall or to an activation of matrix metalloproteinases. In addition, an insertion/deletion (ID) polymorphism of angiotensin converting enzyme (ACE) has been associated with coronary vascular tone and the development of aneurysm. Patients Results - ACE gene polymorphism had been determined in 34 patients with CAE, 34 patients with IHD, but without evidence of ectasia and 35 patients with normal coronary angiography. Of the CAE group, twenty five patients had CAE with CAD and nine patients had CAE without evidence of obstructive CAD (isolated CAE). Coronary diameter and percent stenosis had been measured by using computerized quantitative angiography in monoplane mode to all the subjects of the study. Smoking was present in 73.5% of ectatic group, 58.8% of IHD group, and 42.86% of normal coronaries group, (P < 0.03). Also, dyslipidemia was found in 52.9% of CAE group and 52.9% of IHD group, (P: 1.0) and both are higher than control group (normal coronaries group) (14.3%) (P 0.001). Obesity was found in 55.9% of CAE group, 52.9% of IHD group, (P 1.0) and both are higher than control group (normal coronaries group) (14.3%) (P 0.001). Also, positive family history of CAD was present in 55.9% of CAE group, 50.0% of IHD group, and 20.0% of normal coronaries group, (P: 0.04 comparing group I vs group III). The incidence of other risk factors (hypertension, diabetes mellitus) was similar in the study populations, (P: 0.1 and 0.2 respectively), while the incidence of diabetes mellitus was statistically higher in the IHD group than the CAE group, (P 0.04), the majority of patients with CAE (44.1%) had type I ectasia while 26.5% of patients had types II IV ectasia and type III ectasia had the lowest incidence (2.9%). The incidence of ectasia was highest in RCA, LAD and CX coronary arteries (67.7%) followed by OM and D arteries (14%) and the least in LM and PDA (2.9%). Diffuse ectasia was seen more in LAD and RCA (52.9%) while localized ectasia was seen more in CX (20.6%). Severe ectasia was common in patients with CAE with obstructive CAD (72%) compared to patients with isolated CAE (66.7%). Coronary artery disease severity was equivalent in CAE group 3.17±2.3 vessels and IHD group 3±2 stenotic vessels (P 0.8). The two groups had a similar incidence of one vessel/two vessels/three vessels and four vessels disease, (P 0.8). There was no difference between ACE genotype in CAE group as regards age, sex, and atherogenic risk factors with tendency to high prevalence of smoking, hypertension, dyslipidemia and positive family history of CAD among the patients showing the DD allele. There was no difference between ACE genotypes in CAE patients regarding angina (both stable exertional angina and unstable angina), (P: 0.77), patients having isolated CAE and CAE with obstructive CAD, (P: 0.58, 0.7 respectively) or a previous treatment with ACEI, (P: 0.25), although DD allele patients had a higher prevalence of a prior history of MI (35.3%) Most of the DD allele patients in the CAE group had type I ectasia (29.4%) of all ectatics and (55.6% of DD allele patients) and type II ectasia (17.6%) of all ectatic patients and (33.3%) of DD allele patients. However, the DD allele patients had the lowest incidence of type III ectasia (5.6%) of DD allele patients. Also, the DD allele patients had their arterial involvement by CAE in the following pattern, CX (77.8%), LAD (70.2%) and RCA (66.7%) while LM and PDA are the least involved (5.6%) of the DD allele patients. Although the DD allele patients had a higher incidence of diffuse CAE (77.8%) however it did not reach a statistically difference with the ID allele patients (81.8%) and the II allele patients (60%) of all ectatic group, (P 0.84). We could not also demonstrate statistically significance difference as regards FS, EF or wall motion score index between ACE genotype in CAE patients (all P 0.5). The overall genotype frequencies for homozygous DD, heterozygous ID and homozygous II polymorphisms were [18 (52.9%)] [11 (32.3%) and 5 (14.7%)] among CAE group, [12 (35.29%)] [15 (44.1%) and 7 (20.6%) among IHD group and [7 (20.1%)] 25 (71.4%) and 3 (8.6%) among normal coronaries group respectively. So, the ACE DD genotype was significantly more frequent in the CAE group than IHD group (52.9%) vs 35.9% (P 0.045)and than normal coronaries group (52.9%) vs 20 % P 0.013). In logistic regression model by comparing DD against ID as a risk factor for development of CAE, it was found that DD is independent risk factor for development of CAE with P value for all other possible risk factors (smoking, dyslipidemia, obesity and positive family history of CAD 0.0002 and for DD as a risk factor for CAE it was found that DD is independent risk factor for development of CAE with P value for all other possible risk factors mentioned before 0.0002 and for DD 0.05 which is statistically significant. Conclusion - CAE is not distinguishable from obstructive CAD in severity of angina, clinical presentation, ECG, mortality or outcome of coronary artery surgery. CAE is not a benign entity since 73.5% of patients presented with a previous history of MI and 56% of them had angina. The majority of patients were males, in the sixth decade with associated obstructive CAD with underlying smoking, obesity, hyperlipidemia and positive family history of CAD. They had no relation to hypertension, diabetes mellitus or hyperuricemia. The incidence of CAE in our series was 1.7% and there is some evidence to suggest that the incidence of ectasia is increasing. RCA, LAD and CX were the most commonly involved vessels and most of the patients had single vessel disease. The DD genotype is the most common ACE gene polymorphism in CAE. On the basis of our data, ACE DD genotype seems to be a potent risk factor for the development of CAE. Understanding of the entity of CAE need to improve and warrants a detailed study on the available management. The possible involvement of the renin-angiotensin system in the genesis of CAE raise the question of whether drugs that modulate activity of ACE and/or component of this system may reduce the risk for CAE.

Keywords

Coronary artery ectasia, Deletion/Insertion, ACE gene polymorphism, Echo scoring system,