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Original article

Clinical and laboratory characteristics in patients with acute myocardial infarction due to occlusive vasospasm

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Summary
Background: The purpose of this study was to determine the clinical and laboratory characteristics in patients with acute myocardial infarction (AMI) associated with coronary vasospasm.
Methods and results: Consecutive 231 patients with documented coronary vasospasm by ergonovine provocation test but with a normal-appearing coronary angiogram were divided into two groups, variant angina pectoris (VAP) patients (group I; $n = 202$, 49.5 ± 11.1 years) and AMI patients (group II; $n = 29$, 47.4 ± 11.2 years). Matched control patients were 84 AMI patients with significant stenosis (>50%) (group III; $n = 84$, 61.2 ± 11.8 years). Although, the incidence of hypertension, diabetes mellitus, and smoking were lower in group I than in group III, there was no difference between group II and III (diabetes, 7.9% vs. 13.8% vs. 29.8%; hypertension, 19.8% vs. 24.1% vs. 41.7%; smoking 48% vs. 48.3% vs. 61.9%; respectively, $p < 0.01$). Measured high-sensitivity C-reactive protein (hsCRP) and fibrinogen level were higher (respectively, $p < 0.001$, $p < 0.001$) in groups II and III (group II, 1.88 ± 2.9 mg/dl, 317.5 ± 51.2 mg/dl; group III, 2.92 ± 3.9 mg/dl, 326.8 ± 107.7 mg/dl) than those in group I (0.68 ± 1.5 mg/dl, 263.2 ± 70.3 mg/dl). A correlation was clearly seen between fibrinogen and hsCRP ($r = 0.472$, $p < 0.001$).
Conclusion: The clinical characteristics of patients with AMI associated with spasm were similar to those with VAP, but laboratory findings were similar to those of AMI in patients with significant stenosis.

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Introduction

Variant angina pectoris (VAP) is a disease by which a transient abrupt marked reduction in the luminal diameter of an epicardial coronary artery leads to myocardial ischemia. This is characterized by spontaneous episodes of angina associated with ST segment elevation on electrocardiogram (ECG) and documented spasm of epicardial coronary artery by coronary angiography (CAG). It was initially described by Prinzmetal in 1959 [1—3]. Generally, patients with VAP responding to vasodilators such as nitrate have a good prognosis, but 7.4% of them progress to acute myocardial infarction with vasospasm (VAMI) [4].

The pathogenesis, predisposing factors, and risk factors for VAMI are not well known. Currently, several contributing factors have been identified. They include thrombin activation and fibrin formation induced by coronary spasm. Impaired fibrinolytic activity, reported in patients with variant angina, suggests that coronary spasm may trigger thrombus formation in coronary arteries and that the reduction in fibrinolytic activity may slow the removal of thrombus, ultimately leading to acute myocardial infarction (AMI) in some patients [5,6]. Fibrinogen, the precursor of fibrin can promote the development of atherosclerosis and thrombosis. Fibrinogen can be a precursor of mural thrombi, which is important in the pathogenesis of acute coronary syndrome [7—13]. Lipoprotein(a) [Lp(a)] plays an important part in the genesis of thrombotic coronary occlusion subsequent to spasm because of a particular feature of its structure that is homology between apolipoprotein (Apo) (a) and plasminogen [13—15]. Apo B/A1 ratio is a good predictor of atherosclerotic cardiovascular disease, more so than low-density lipoprotein (LDL) or high-density lipoprotein (HDL) cholesterol [16,17]. The cause of development and risk factors for VAMI are unknown unlike those for AMI with coronary stenosis (SAMI).

The purpose of this study was to compare the clinical characteristics of SAMI, VAP, and VAMI, and to analyze the laboratory findings such as fibrinogen, Lp(a), Apo B/A1 ratio, and high-sensitivity C-reactive protein (hsCRP).

Materials and methods

All the subjects were selected from patients who were hospitalized for CAG because of suspected VAP or of documented MI during 4 years. We classified these subjects into three groups. Consecutive 231 patients with documented coronary vasospasm with normal-appearing CAG by ergonovine provocation test were divided into two groups, VAP (group I; $n = 202$, 49.5 ± 11.1 years) and VAMI (group II; $n = 29$, 47.4 ± 11.2 years). And, matched control AMI patients with significant stenosis (diameter stenosis > 50%) [group III (SAMI); $n = 84$, 61.2 ± 11.8 years] were selected randomly from patients during the same period. Clearly, the definition of VAP and VAMI were positive result in ergonovine test with normal-appearing coronary angiogram.

AMI was defined by typical chest pain over 20 min on admission, significant ST segment elevation on ECG, or elevation of cardiac enzymes. No patients with hematologic disease, hyperpyrexia (over 38 °C), viral, bacterial, or parasitic infection, sepsis, liver disease, renal failure, malignancy, prosthetic valves, or pacemaker were enrolled. Written informed consent was obtained from all the patients before entering the study.

CAG was performed by insertion of 5 Fr. or 6 Fr. arterial sheath through the right or left femoral or radial artery. Ergonovine provocation test was carried out after discontinuing nitrate, calcium channel blocker, and nicorandil for at least 3 days. Ergonovine, 5 μg, 10 μg, and 30 μg, was injected into the left and right coronary arteries separately in cases without spontaneous spasm at 3-min intervals until there was a positive result. CAG during ergonovine provocation test was performed immediately after each ergonovine injection and 3 min later after the injection. A coronary vasospasm was defined as a focal narrowing above 70% or a diffuse narrowing above 90%, reversible with isosorbide dinitrate, associated with chest pain and ST segment change such as elevation or depression on the ECG. On chest pain, we tried sublingual nitrate tablet or spray.

Venous blood samples for fibrinogen, hsCRP, Lp(a), Apo B/A1, and lipid profiles were withdrawn from the antecubital vein in the supine position without antianginal drugs at admission. Venous samples were obtained in the fasting state when the subjects were free of any acute illness. We used the samples that were obtained at discharge. Fibrinogen (reference value, 180—350 mg/dL) was determined with System CA-6000 Sysmex system (TOA Medical Electronics Co., Kobe, Japan) using thrombin reagent (Dade Behring Inc., Newark, DE, USA). hsCRP was determined with N High Sensitivity hsCRP (Dade Behring Inc.), Lp(a) was done with Behring Nephelometer II (Dade Behring Inc.) using N Latex Lp(a) reagent (Dade Behring Inc.). Reference value of hsCRP was below 0.5 mg/dL and that of Lp(a) was below 30 mg/dL.

Data are expressed as mean ± SD. The SPSS program for Windows package (version 11.0; SPSS Inc., Chicago, IL, USA) was used. Comparisons among the three groups were made using one-way analysis of variance (ANOVA). Turkey HSD was used for odds ratio and multinominal logistic regression analysis for relative risks. Statistical analysis such as multivariate logistic regression was used to evaluate the association between variables and we display as odds ratio with 95% confidence interval (CI). A probability level of $p < 0.05$ was considered to be statistically significant.

Results

The subjects' clinical characteristics including their risk factors for coronary artery disease are shown in Table 1. The patients with VAP and VAMI were younger than the patients with SAMI (mean age: 49.5 ± 11.5 years in VAP; 47.4 ± 11.2 years in VAMI; 61.2 ± 11.8 years in SAMI; $p < 0.001$). With regard to the proportion of males to females, the rate of females is significantly higher in VAP or VAMI than SAMI (male: 133 subjects in VAP (65.8%); 20 (69%) in VAMI; 69 (82.1%) in SAMI; $p = 0.007$). The incidence of diabetes was higher in SAMI than VAP or VAMI (8.7% in VAP and VAMI vs. 29.8% in SAMI, $p < 0.001$). Also, a higher rate of smoking in SAMI than VAP or VAMI was observed (48.1% in VAP and VAMI vs. 61.9% in SAMI, $p = 0.031$), and it was the same with hypertension (20.3% in VAP and VAMI vs. 41.7% in SAMI, $p < 0.001$) and hyperlipidemia (14.7% in VAP and VAMI vs. 40.5% in SAMI, $p < 0.001$). But, there was no statistically significant differ-