ELSEVIER

CrossMark

Archives of Medical Research

Archives of Medical Research 45 (2014) 478–483

ORIGINAL ARTICLE

Evaluation and Analysis of Plasma Soluble Adhesion Molecules in Patients With Coronary Ectasia and Atherosclerotic Coronary Artery Disease

Maria Elena Soto,[a] Martha Abigail Reyes-Villatoro,[b] Ricardo Márquez,[a] Guillermo Cardoso,[c] Rosalinda Posadas-Sánchez,[c] and Luis Eduardo Juárez-Orozco[d]

[a]*Department of Immunology, Instituto Nacional de Cardiología "Ignacio Chávez", Mexico City, Mexico*
[b]*Department of Electrophysiology, Instituto Nacional de Cardiología "Ignacio Chávez", Mexico City, Mexico*
[c]*Department of Endocrinology, Instituto Nacional de Cardiología "Ignacio Chávez", Mexico City, Mexico*
[d]*Department of Nuclear Cardiology, Instituto Nacional de Cardiología "Ignacio Chávez", Mexico City, Mexico*

Received for publication January 27, 2014; accepted June 27, 2014 (ARCMED-D-14-00060).

Background and Aims. The pathogenesis of coronary artery ectasia (CE) is poorly understood. An underlying inflammatory process is suspected; current therapy aims to prevent thrombotic events. Presently, there is no evidence to support an anti-inflammatory approach for CE patients. We undertook this study to determine the presence and levels of adhesion molecules as well as other inflammation-related markers and evaluate their invasive angiography findings to compare between patients with CE or atherosclerotic coronary artery disease (CAD).

Methods. We included 23 patients with CE alone and 23 patients with CAD alone reported by diagnostic angiography. The two groups were paired according to gender and age. Clinical variables, angiographic findings (STEMI, NSTEMI, previous coronary stenting and previous CABG), serum VCAM, ICAM, C-reactive protein (CRP), IL-6 and adiponectin were compared between groups.

Results. In patients with CE, median for serum VCAM was 1700 ng/mL with a range from 900–4050 and for serum ICAM was 550 ng/mL (370–1530); in contrast to the obstructive lesions group where we found a median for VCAM of 1150 ng/mL (650–2000) and for ICAM of 370 ng/mL (150–480). Both measurements achieved statistical significance with a p value = 0.0001. There was no important variation between patients measured at different times from diagnosis.

Conclusion. Plasma soluble adhesion molecules in CE are elevated in comparison to CAD. The presence of high levels of these molecules, along with not uncommon multivessel and extensive coronary affection suggest the participation of subclinical inflammation, which may have an important role in the development of CE. © 2014 IMSS. Published by Elsevier Inc.

Key Words: Coronary ectasia, Adhesion molecules, VCAM, ICAM, CRP.

Introduction

Coronary artery ectasia (CE) represents a common diagnosis with a poorly understood pathogenesis. The coexistence of CE and atherosclerotic coronary artery disease (CAD) has been considered by some a base to suggest that the former could be a variant of the latter. CE is defined, according to its angiographic characteristics, as an increment of the vessel segmental diameter of at least 1.5 times the diameter of the healthy adjacent vessel. Recently, inflammation has been proposed as an important contributing factor for obstructive CAD and CE as a part of the natural history of subjacent atherosclerosis (1–3).

The inflammatory process has numerous contributing stimuli that induce the liberation of endogenous proinflammatory mediators which promote endothelial activation. Activated endothelium synthesizes de novo and increases numerous adhesion molecules such as E and

Address reprint requests to: Martha Abigail Reyes-Villatoro, M.D., Juan Badiano #1. 14080 México, D.F., Mexico: Phone: (+52) (55) 56552924; FAX: (+52) (55) 5573-0994; E-mail: martyreyes@hotmail.com

http://dx.doi.org/10.1016/j.arcmed.2014.07.002

P selectins, vascular cell adhesion molecule 1 (VCAM-1) and intercellular adhesion molecule 1 (ICAM-1). These molecules can be found both in the cellular surface or the serum in a soluble form. Soluble molecules arise from proteolytic rupture of cellular membranes with adhesion molecules expressed in them. These can serve as plasmatic markers for endothelial activation and vascular inflammation. Therefore, their measurement has been evaluated in several clinical scenarios in which inflammation has been suspected as a causal contributor. Moreover, activated endothelium releases chemotactic factors that directly affect synthesis of pro-coagulant molecules and lower apoptotic threshold. Endogenous factors that induce endothelial activation are synthesized mainly by macrophages such as the tumor necrosis factor alpha (TNF-α), interleukin 1 (IL-1) and interferon gamma (IFN-γ). TNF constitutes the main stimulus for activated endothelium expression of adhesion molecules. IL-6, a secondary pro-inflammatory cytokine stimulates expression of acute phase proteins such as C-reactive protein (CRP) and fibrinogen in the liver. Nowadays IL-6 and CRP are commonly used as inflammation biomarkers (4).

Adiponectin, a molecule secreted by the adipose tissue, has direct effect over insulin resistance and an anti-inflammatory and anti-atherogenic profile. Therefore, it modulates inflammatory reactions by inhibiting monocyte adhesion to endothelial cells and suppressing the transformation of monocytes to foam cells. In contrast to inflammatory markers, adiponectin concentrations have been found decreased in chronic inflammatory and cardiovascular diseases (5).

CE represents an important problem in the clinical setting since it increases the likelihood of thrombus formation and consequently, of acute coronary events. Moreover, is has been associated to aortic aneurisms, coronary spasm, spontaneous coronary dissection and sudden death. Longitudinal studies in these groups of patients have reported a mortality rate of 19% after a 2-year follow-up (6). These results are similar to the mortality found in patients in trivascular CAD who received conservative treatment. In a 5-year follow-up this rate increased to 29.1% (7).

The association of plasma soluble adhesion molecules as viable markers for endothelial activation and their behavior over time in patients with isolated CE and obstructive CAD has been studied in several populations (1).

Measurements of serum VCAM, ICAM, CRP, IL-6 and adiponectin have been addressed in reproducibility studies to evaluate their possible inflammatory contribution in both conditions.

CE is not a benign pathological entity. We consider crucial to evaluate the presence of adhesion molecules possibly related to its pathogenesis and prognosis.

The present study aimed to determine the presence and levels of soluble adhesion molecules and other inflammatory markers and compare them between patients with CE and patients with atherosclerotic CAD determined by their invasive angiography findings. An assessment of these markers may be able to guide research towards analyzing the influence of inflammation in the physiopathology of both entities.

Materials and Methods

This is a paired group comparative ambispective study. We included selected patients from the National Heart Institute in Mexico City between 2010 and 2013.

Patients

We included 23 patients with a previous angiography report, which documented CE without CAD (isolated CE) and 23 patients with CAD but without ectasia. These were selected from the angiographic procedural archives. All patients had undergone invasive angiography as an approach for suspected acute coronary syndrome. The groups were paired according to gender and age. Patients were contacted and agreed to attend the institute for routine laboratory testing for their follow-up. We carefully excluded patients with an angiographic report of coexisting CE and CAD as well as those who did not wish to participate in the protocol. Each patient voluntarily signed an informed consent for the study according to the established policies by the Declaration of Helsinki. The clinical archives for each patient were analyzed to evaluate their clinical variables and reported angiographic findings. The study was approved by the institute's board of research and ethics with the authorization number 13−826.

Samples and Processing

After the report and description of the angiographic results, samples were obtained from the antecubital portion with a 19-gauge catheter. All samples were obtained with at least 8 h fasting. Samples were immediately centrifuged at 3000 rpm for 15 min and stored at 7°C for later assay.

ICAM, VCAM, CRP, IL-6 and adiponectin were measured. Samples were blinded for the chemist and biologist who performed the technical measurements.

ICAM, VCAM and adiponectin were assessed with the commercially available ELISA kit (eBioscience and R&D Systems) according to the standard recommendations in 96-well high protein binding capacity microplates. Reference curve was specified and the plates were read by ELISA standard at 450 nm.

CRP was measured through polarization fluorescent immunoassay (Abbott Laboratories, Abbott Park, IL). Each sample was analyzed with high sensitivity (0.05 mg/dL) and low range (0−6.5 mg/dL) protocols. Samples that exceeded the aforementioned were reanalyzed with low sensitivity (1.5 mg/dL) and high range (0−26 mg/dL) protocols. IL-6 was measured with sequential immunometric assay (Immulyte Analyzer, Diagnostic Products