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ORIGINAL ARTICLE

Short-term Changes in Gal 3 Circulating Levels After Acute Myocardial Infarction

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Background and Aims. Galectin 3 (Gal 3) is a β-galactoside-binding lectin known to play a part in inflammation, adverse remodeling and fibrosis. Gal 3 seems to be linked to atherogenesis and Coronary Artery Disease (CAD), but less is known about the relationship between Gal 3 and acute myocardial infarction (AMI). The aim of the present study is to assess circulating levels of Gal 3 after AMI and to evaluate short-term changes of the biomarker within 5 days from the acute event.

Methods. Two hundred fifteen confirmed AMI patients (125 STEMI, M/F = 2.8; mean age: 65.4 ± 13.8 years) were enrolled in the present study; two blood samples were collected from each patient: first, within 1 h from admission to the Emergency Area (T1) and then upon discharge (T2).

Results. Kinetics of Gal 3 during AMI show that the marker boosts during the acute event (T1) and then decreases from baseline, being significantly lower at T2 (18 [14.2–25] vs. 16.8 [12.7–23.4]; $p = 0.006$). Gal 3 levels were correlated to hsTnI and eGFR on admission ($r = 0.2$; $p < 0.001$ and $r = -0.25$; $p < 0.001$, respectively). Linear regression analysis confirms an association between Gal 3 and ejection fraction ($r^2 = 0.037$; $p = 0.005$).

Conclusions. Gal 3 is reasonably supposed to be a part of those mechanisms leading to formation, destabilization and rupture of plaque; however, the usefulness of Gal 3 as a biomarker in CAD/AMI is far from being elucidated. © 2016 IMSS. Published by Elsevier Inc.

Key Words: Galectin 3, AMI, Inflammation, Plaque, CAD.

Introduction

Galectins are comprised of 15 lectins with β-galactoside-binding domains. They are divided into three subgroups: prototype, chimera and tandem. Galectin 3 (Gal 3) is the only one belonging to the chimera subgroup (1).

Gal 3 is normally expressed in several cytotypes, e.g., in endothelial cells, epithelial cells, activated microglia, inflammatory cells (mainly macrophages) and various tissues including spleen, stomach, colon, liver, kidney, heart, uterus, ovary and pancreas (2). Gal 3 has been shown to be involved in manifold processes such as cell growth, angiogenesis, carcinogenesis, inflammation, regulation of cell survival during ischemic injury and promotion of cell resistance against nitrogen and oxygen reactive species (3). Under certain conditions such as during hypoxia, Gal 3 is up-regulated in an attempt to regulate and maintain cellular survival (4).

Moreover, Gal 3 is involved in adverse cardiac remodeling and fibrosis and in the modulation of extracellular matrix (5,6). Given its involvement in these processes, Gal 3 has been thoroughly investigated in heart failure (HF) (7,8) and validated as a biomarker with independent prognostic value in patients with both acute and chronic heart failure (9,10).

Many authors (11–13) reported Gal 3 to be linked to atherogenesis and to coronary artery disease (CAD). Indeed, it influences plaque formation, progression and

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destabilization (14–16) via several mechanisms such as sustaining and amplifying inflammation or inducing modified LDL uptake by macrophages (9,17,18). Due to such evidences, Gal 3 has been proposed as a biomarker for progression and destabilization of atherosclerotic plaques (19).

The most common complication of CAD is acute myocardial infarction (AMI), and both CAD and AMI represent the major cause of HF (20). Several authors (9,10,21–24) focused their attention on serum Gal 3 levels in AMI patients; however, less is known about the relationship between Gal 3 and AMI.

The present study aims to assess circulating levels of Gal 3 after AMI and to evaluate short-term changes of the biomarker within 5 days from the acute event.

Materials and Methods

Patient Population

All patients presenting to the Emergency Area of Palermo School of Medicine from July 2015 to March 2016 with a diagnosis of AMI were considered for the study after providing consent to participate. Presenting to the Emergency Area within 2 h from the time of symptom onset was an inclusion criterion. Exclusion criteria were history of recent trauma, recent surgery, myocardial infarction within the last 2 months before starting the study, history of prior heart failure, malignancies, acute or chronic inflammatory diseases, acute and chronic hepatic diseases, end stage kidney disease, autoimmune diseases and immunosuppressive therapy. The remaining 215 STEMI and NSTEMI patients were enrolled.

Demographic characteristics and cardiovascular traditional risk factors are summarized in Table 1. Clinical and laboratory features are summarized in Table 2.

LVEF was measured by echocardiography using biplane Simpson method; echocardiography was performed on average on day 2 after performing pPCI.

Table 1. Demographic and clinical characteristics of patients included in the study

N	**215**
M/F	2.8
Age (years)	65.4 ± 13.8
STEMI, *n* (%)	125 (58.1)
One-vessel disease	119 (55.5)
Two-vessel disease	69 (32)
Three-vessel disease	27 (12.5)
Hypertension, *n* (%)	174 (81)
eGFR, (mL/min)	83 ± 30.4
Diabetes, *n* (%)	81 (37.9)
Hypercholesterolemia, *n* (%)	120 (55.8)
Smoker, *n* (%)	100 (46.5)
Obesity, *n* (%)	55 (25.5)

Note: Variables are expressed as percentage or mean ± standard deviation when appropriate.

Two blood samples were collected from each patient: first, within 1 h from the admission at the Emergency Area (T1) and then on discharge (4.5 ± 0.8 days from admission) (T2). Demographic and clinical characteristics were recorded on admission. The study was approved by the local ethics committee.

Patients were considered diabetic in accordance with the 2016 American Diabetes Association-ADA Guidelines for Diagnosis and Management of Diabetes 2015 (25). Hypertension was defined in accordance with the 2013 European Society of Hypertension-ESH/European Society of Cardiology–ESC Guidelines for the management of arterial hypertension (26). Hypercholesterolemia was defined according to the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Prevention of Primary and Secondary Atherosclerotic Disease (27). Body mass index (BMI) was calculated as weight/height^2. Obesity was defined as BMI ≥ 30. Subjects who reported smoking more than ten cigarettes a day from 6 months before enrollment were defined smokers. Estimated glomerular filtration rate was calculated using CKD-EPI formula.

Laboratory Analysis

Serum Gal 3 and hsTnI were measured by chemiluminescence immunoassay using the Architect i-100 analyzer (Abbott). For hsTnI, imprecision (CV%) at the 99th percentile was $<10\%$.

Statistical Analysis

Categorical data were expressed as percentages and continuous variables as mean ± standard deviation when normally distributed. Non-normally distributed variables were expressed as median and interquartile range. Normality was assessed by Kolmogorov–Smirnov test. Differences between demographic, clinical and biochemical data according to STEMI/NSTEMI were evaluated by ANOVA, Mann-Whitney test or chi square test, when appropriate. Differences between LVEF or hsTnI according to tertiles of Gal 3 were evaluated by Kruskal-Wallis test. Correlation analysis of Gal 3 with hsTnI and LVEF was assessed by the nonparametric Spearman's rank correlation test. Comparison between T1 and T2 Gal 3 serum levels was performed by the Wilcoxon test. LVEF was considered the dependent variable in the model of linear regression analysis; $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS 22.0.

Results

Two hundred fifteen patients with AMI (125 STEMI; M/F = 2.8; mean age: 65.4 ± 13.8) were included in the study. Among all, 69% NSTEMI and 83% STEMI patients