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Soluble programmed cell death ligand-1 is associated with acute coronary syndrome

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Background

Immune checkpoint by programmed cell death (PD)-1 and its ligand (PD-L1) play crucial role in T cell tolerance toward vascular wall antigens. PD-L1 is widely expressed on a number of cells including immune cells and vascular endothelium. It was reported that increased expression of PD-L1 in dendritic cells implicates upregulated inflammation in atherosclerotic lesions that is associated with plaque instability. Although plaque rupture in coronary atherosclerosis is an important pathogenesis of acute coronary syndrome (ACS), the association between PD-L1 and ACS is still unknown.

Purpose

We hypothesize that circulating PD-L1 might be associated with ACS, reflecting endothelial damage and coronary plaque rupture. To elucidate this hypothesis, we compared serum levels of soluble PD-L1 (sPD-L1) in stable coronary artery disease (CAD) patients with those in ACS patients.

Methods

Serum levels of sPD-L1 were measured by using commercially available ELISA kit (Human PD-L1/B7-H1 DuoSet, R&D Systems) in consecutive patients with CAD admitted to our University Hospital from February 2016 to March 2017. Patients with any malignant disease or severe inflammatory disease were excluded from this study. Serum levels of sPD-L1 and clinical backgrounds were compared between stable-CAD and ACS patients.

Results

In total, 269 patients with CAD were enrolled (28 cases [10.4 %] with ACS and 241 cases [89.6 %] with stable-CAD). PD-L1 had no correlation to C-reactive protein, cardiac troponin, and classical atherosclerotic risks such as age, body mass index, estimated glomerular filtration rate, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol, and hemoglobin A1c. Although age, sex, history of smoking, and the prevalences of hypertension, diabetes mellitus and dyslipidemia were comparable between both groups, the level of LDL-C was significantly higher in patients with ACS compared with those with stable-CAD (94.0 [77.0–112.0] mg/dL vs. 78.5 [65.0–97.0] mg/dL, P=0.008). Also serum level of sPD-L1 was significantly increased in patients with ACS compared with those with stable-CAD (106.1 [60.9–157.7] pg/mL vs. 64.8 [30.9–102.5] pg/mL, P=0.003). Univariate logistic regression analysis identified that serum levels of both sPD-L1 and LDL-C were independently associated with ACS. Moreover, multivariable logistic regression analysis with factors from univariate analysis identified that serum level of sPD-L1 was significantly and independently associated with ACS (odds ratio: 1.006, 95% confidence interval: 1.001–1.012, P=0.03).

Conclusions This is the first study to elucidate that the increased serum levels of sPD-L1 was associated with
ACS. This study suggests that sPD-L1 could be a risk marker and therapeutic target for ACS.