Inflammatory response in patients with coronary artery ectasia and coronary artery disease

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Introduction Coronary artery ectasia (CAE) is a dilation of the artery to the diameter of 1.5-fold or more of the largest native coronary vessel.[1] The incidence of CAE varies from 0.15% to 5.3% among coronary angiographies of patients diagnosed with coronary artery disease (CAD).[2] The etiology of CAE has not been fully established yet. Lenihana et al[3] observed that coronary aneurysms in adults younger than 33 years of age are typically congenital, resulting from a defect of an internal elastic membrane and fibrillar proteins of the connective tissue. At an older age, secondary causes of CAE were predominant, such as atherosclerosis, vasculitis, or angiogenic disorders. The underlying mechanism is probably based on the enlargement of the artery lumen at the site of atherosclerotic lesions, compensating for atheromatous plaque buildup. One of the pathophysiologic factors is an immune–inflammatory response to endothelial injury.[2,4] Endocan, a proteoglycan secreted by the endothelium in response to inflammatory cytokines, plays a crucial role in regulating major physiologic and pathophysiologic processes, such as cell adhesion, inflammation, and tumor progression.[4] Additionally, several readily available inflammatory and metabolic parameters have been shown to be promising and were validated in other cardiac diseases, especially in ischemic heart disease. They include mean platelet volume (MPV),[5] neutrophil-to-lymphocyte ratio,[6] platelet-to-lymphocyte ratio,[7] and the ratio of triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C).[8]

In this study, we sought to assess the severity of inflammation and metabolic disorders in patients with CAE compared with patients with and without significant atherosclerosis, using endocan and simple inflammatory and metabolic markers.

Methods In this study, we consecutively enrolled 27 patients with CAE (CAE group) out of patients who underwent coronary angiography for suspected CAD. The diagnosis of CAE was based on the conventional definition of a coronary artery dilation to a diameter of 1.5 times or more of the adjacent normal segment. The second group included 27 age- and sex-matched patients with coronary artery stenosis greater than 70% and without CAE (CAD group). Finally, the third group included 27 age- and sex-matched participants with normal coronary arteries (control group). We excluded patients with acute inflammatory disorders (high-sensitivity C-reactive protein >10 mg/l), active neoplastic disease, connective tissue diseases, thrombotic and plasmatic diathesis, acute and chronic renal failure with a glomerular filtration rate of less than 30 ml/min, or allergy to iodinated contrast medium.

Blood samples were obtained 1 day after coronary angiography. For blood serum collection, standard tubes with chemically neutral coagulation activator (silicon dioxide as the main component) were used. Serum samples were obtained to determine routine laboratory parameters. Additionally, the ratios of monocyte to HDL-C, TG to HDL-C, and low-density lipoprotein cholesterol (LDL-C) to HDL-C were assessed. The remaining serum was aliquoted, frozen, and stored at a temperature of –80°C.

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Endocan was measured using Human Endothelial cell-specific Molecule 1 (ECSM1/ENDOCAN) ELISA Kit (DRG MedTek, Springfield, New Jersey, United States). The analysis was performed in the laboratory of the Department of Clinical Pharmacology at Poznan University of Medical Sciences (Poznań, Poland).

Statistical analysis was performed with the STATISTICA 12.0 software (StatSoft, Tulsa, Oklahoma, United States). The normality of variable distribution was tested with the Shapiro–Wilk test. Descriptive analysis, Kruskal–Wallis test, analysis of variance, and Mann–Whitney test were used for comparisons between groups. Differences with a *P* value of less than 0.05 were considered significant.

Results and discussion The baseline characteristics of the study groups are presented in TABLE 1. The prevalence of cardiovascular risk factors such as age, sex, hypertension, or diabetes did not differ between groups. Ectasias were most often located in the right coronary artery and left anterior descending artery (53.5% and 48.8%, respectively). Diffuse ectasias were significantly more frequent than localized aneurysms (60.5% and 33.4%, respectively). Significant stenosis of the coronary arteries was diagnosed in 60.5% of patients with CAE. The level of endocan did not differ significantly between groups. However, we found significantly elevated MPV both in the CAE and CAD groups compared with the control group. Similarly, metabolic disorders such as reduced HDL-C, higher TG/HDL-C ratio, and monocyte/HDL-C ratio were more pronounced in the CAE and CAD groups than in the control group. The LDL-C/HDL-C ratio was significantly higher in patients with CAE than in those with CAD (Supplementary material, *Table S1*).

TABLE 1 Clinical characteristics of the study groups

Parameter	CAE group (n = 27)	CAD group (n = 27)	Control group (n = 27)	*P* value[a]
Male sex	20 (74.1)	20 (74.1)	20 (74.1)	1
Age, y	64 (59–68)	67 (63–70)	64 (58–69)	0.19
BMI, kg/m^2	29.7 (27.4–32.4)	28.7 (27–30.4)	27.7 (23.6–33.3)	0.56
Hypertension	23 (85.2)	20 (74.1)	19 (70.4)	0.55
Hyperlipidemia	17 (63)	13 (48.1)	14 (51.8)	0.69
Diabetes	8 (30)	13 (48.1)	8 (29.6)	0.18
Previous MI	12 (44.4)	11 (40.7)	5 (18.5)	0.1
Smoking	5 (18.5)	1 (4)	5 (18.5)	0.07
Antiplatelet therapy	24 (89)	24 (89)	20 (74.1)	0.36
ACEIs	22 (81.5)	20 (74.1)	19 (70.4)	0.63
β-blockers	22 (81.5)	20 (74.1)	20 (74.1)	0.76
Statins	25 (93)	25 (93)	22 (81.5)	0.78

Data are presented as median (interquartile range) or number (percentage) of patients.

a *P* <0.05 for all comparisons (analysis of variance)

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index; CAD, coronary artery disease; CAE, coronary artery ectasia; MI, myocardial infarction

The above inflammatory markers are readily available and promising parameters that have been validated in cardiac diseases. Elevated MPV levels are related to increased platelet activation and, in consequence, a higher risk of thrombotic disorders and myocardial infarction, especially myocardial infarction with ST-segment elevation.[5] Chen et al[9] found elevated MPV levels also in patients with coronary aneurysms in the course of Kawasaki disease. Interestingly, Şarlı et al[10] revealed significantly higher MPV levels only in patients with CAE coexisting with CAD. Isolated CAE was not associated with elevated MPV levels as compared with the control group.

The above results suggest that inflammation contributes to atherogenesis and, consequently, to aneurysms. Another interesting finding was a significantly lower HDL-C level and higher TG/HDL-C ratio in the CAE and CAD groups, as compared with controls. An increase in the TG/HDL-C ratio reflects an unfavorable alteration in lipid profile, which has also been linked to insulin resistance and incidents of ischemic heart disease.[8] Sudhir et al[11] demonstrated an increased prevalence of CAE in patients with heterozygous familial hypercholesterolemia and a strong correlation between low HDL-C levels and a more frequent incidence of ectasias. Our analysis also revealed a higher monocyte/HDL-C ratio in patients with coronary aneurysms compared with controls. Yildirim et al[12] reported a significant increase in the adhesion of monocyte and lymphocyte in the CAE group in comparison with CAD and control groups. This finding may reflect an increased intensity of inflammation and oxidative stress in CAE compared with CAD.

Coronary artery ectasia is a rare phenomenon; therefore, the number of patients in our study is limited. Due to the relatively small study group and potentially complex etiology of CAEs, further research is needed to confirm our findings.

In conclusion, the majority of aneurysms in adults coexist with significant atherosclerosis. Almost all of the studied parameters were elevated in patients with CAE and CAD compared with controls. This is most likely due to the atherosclerotic etiology of most aneurysms. Therefore, there is still a need to investigate additional risk factors for the formation of CAEs.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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