An association between parvovirus B19 infection and the severity of coronary atherosclerosis

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Introduction Besides the well-established risk factors for the development of coronary atherosclerosis, such as sex, hypertension, dyslipidemia, diabetes, and smoking, there have been studies showing a correlation between infections and coronary artery disease (CAD). There is a substantial amount of data suggesting a possible involvement of *Chlamydophila pneumoniae*,[1] herpes simplex virus 2,[2] cytomegalovirus,[3] *Helicobacter pylori*,[4] or *Porphyromonas gingivalis*[5] in the development or exacerbation of atherosclerosis. It is postulated that they might exert an atherogenic effect by causing systemic proinflammatory conditions. Nevertheless, none of the above pathogens targets the human endothelium.[1] One pathogen with direct tropism for human endothelial cells is parvovirus B19, which has been shown not only to infect endothelial cells but also to impair their regeneration.[6] Since atherosclerosis is strongly dependent on endothelial dysfunction, this suggests that parvovirus B19 could be involved in plaque development. Parvovirus B19 infections are common. An epidemiologic study indicated that a parvovirus B19 infection has affected 80% of the Polish population at the age of 40 years.[7] Clinical presentations of the infection range from erythema infectiosum in children to arthropathy or myocarditis in adults, with a suggested involvement in the pathogenesis of rheumatic diseases. However, a parvovirus B19 infection may often be asymptomatic or show influenza-like symptoms only.[8]

The aim of this study was to determine whether there is an association between anti–parvovirus B19 immunoglobulin G (IgG) antibodies and the severity of CAD.

Methods This was an observational study conducted in 2012 at the Department of Cardiovascular Surgery and Transplantology, Institute of Cardiology, Jagiellonian University Medical College (Kraków, Poland). We included 76 consecutive patients referred for coronary artery bypass grafting (CABG) due to stable CAD. The only exclusion criterion was a referral for an urgent procedure. All patients provided written informed consent to participate in the study, and the study was approved by the Jagiellonian University Ethics Committee.

Patients were screened for typical risk factors of atherosclerosis and history of myocardial infarction. Coronary angiograms were analyzed and the Gensini score was used for a quantitative analysis of coronary atherosclerosis.[9]

Parvovirus B19 diagnostics Venous blood was collected before CABG, centrifuged, and the supernatants were stored at a temperature of –80°C. The level of anti–parvovirus B19 IgG antibodies was measured using an enzyme-linked immunosorbent assay (*recom*Well Parvovirus B19 IgG kit; Mikrogen Diagnostik, Neuried, Germany). Based on the results, patients were divided into a group positive for anti–parvovirus B19 IgG antibodies (patients who have suffered the infection) and a group negative for anti–parvovirus B19 IgG antibodies (patients with no evidence of the infection).

Statistical analysis Normal distribution of continuous variables was assessed using the Shapiro–Wilk test. For the association of

nominal variables, the Pearson χ^2 test was used. The Mann–Whitney test was used in the case of one nominal and one continuous variable (no continuous variables showed a normal distribution in any of the groups). A *P* value of less than 0.05 was considered significant.

Results and discussion Of the 76 patients, 63 tested positive for the presence of parvovirus B19 IgG antibodies (82.9%), which is consistent with epidemiologic data.[7] The distribution of risk factors for CAD was typical and did not differ between seropositive and seronegative patients. We found that seropositive patients were more likely to have a history of myocardial infarction (36.5% vs 7.7%, *P* = 0.049). We also observed a larger atherosclerotic burden in the seropositive than in the seronegative group (Gensini score, 98 vs 70, *P* = 0.049). Detailed results are presented in TABLE 1.

Based on the assessed indicators of CAD severity, it seems plausible that a parvovirus B19 infection may influence the development of coronary atherosclerosis. Since one of the first stages and hallmarks of atherosclerosis is endothelial dysfunction, it is possible that infectious agents targeting the endothelium and causing inflammation, such as parvovirus B19, might contribute to the development of atherosclerotic plaques. This hypothesis is in fact supported by published data.[10] Liu et al[11] performed a serology analysis of 565 individuals with CAD and healthy controls and demonstrated that patients with CAD were significantly more often positive for anti–parvovirus B19 IgG antibodies than controls. An interesting study by Niccoli et al[12] showed that the presence of parvovirus B19 DNA on a balloon used to predilate coronary lesions was a predictor of major adverse cardiovascular events defined as a composite of cardiac death, myocardial infarction, and clinically driven target lesion revascularization.

Parvovirus B19 genetic material can be found in cells in a quiescent state, at levels that do not exert an immune response.[13] It has been demonstrated that a simultaneous infection with parvovirus B19 and adenoviruses can augment the expression of parvovirus B19 proteins within endothelial cells.[14] Therefore, it is possible that an isolated parvovirus B19 infection of the endothelium does not have the potency to lead to a clinically relevant effect on atherosclerosis and requires a coinfection with other viruses.

Parvovirus B19 material can be found in around 1% of patients with myocarditis.[15] Still, none of the patients in our group had a history of myocarditis. This might be due to the fact that most parvovirus B19 infections are asymptomatic or display influenza-like symptoms and may have been missed. Since the median age of patients was above 60 years and myocarditis usually affects individuals aged 20 to 40 years old, it is possible that some myocardial infections had occurred in the parvovirus B19–positive group in the distant past and were not diagnosed at the time of presentation.

In conclusion, our results show that patients positive for anti–parvovirus B19 antibodies had a larger atherosclerotic burden measured by the Gensini score and were more likely to have suffered from a myocardial infarction than seronegative patients. However, this was a preliminary study on a small group of patients. Therefore, conclusions must be interpreted with caution and should be confirmed in a larger population. Still, as arterial endothelial cell dysfunction underlies the development of atherosclerosis, it seems that the association between parvovirus B19 infection and CAD is an interesting research field.

TABLE 1 Characteristics of patients with seropositivity and seronegativity for anti–parvovirus B19 immunoglobulin G antibodies

Parameter	Seropositive patients (n = 63)	Seronegative patients (n = 13)	*P* value
Age, y, median (min–max; IQR)	63 (47–80; 14)	62 (51–82; 18)	0.65[a]
Sex, male, n (%)	51 (81.0)	10 (77.0)	0.40[b]
Hypertension, n (%)	50 (79.4)	13 (100.0)	0.40[b]
Dyslipidemia, n (%)	44 (69.8)	11 (84.6)	0.57[b]
Diabetes, n (%)	22 (34.9)	4 (30.8)	0.12[b]
Active smoking, n (%)	38 (60.3)	8 (61.5)	0.84[b]
Preprocedural LVEF, median (min–max; IQR)	52 (35–70; 6)	52 (40–70; 6)	0.91[a]
History of MI, n (%)	23 (36.5)	1 (7.7)	0.049[b]
Gensini score, median (min–max; IQR)	98 (46.5–152.5; 33.5)	70 (45–134; 38)	0.049[a]

a Mann–Whitney test; **b** χ^2 test

Abbreviations: IgG, immunoglobulin G; IQR, interquartile range; max, maximum; MI, myocardial infarction; min, minimum; LVEF, left ventricular ejection fraction

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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