SCIENTIFIC LETTER

No association between anti-Borrelia immunoglobulin G and cardiac disorders: results from a population based sample

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Lyme disease is a systemic disorder caused by *Borrelia burgdorferi*. While acute cardiac manifestations of borrelioses are not doubted, chronic cardiac consequences are currently under investigation. The aim of this study was to explore associations between anti-Borrelia immunoglobulin G (IgG) antibodies and the risk of cardiac disorders.

METHODS

The Study of Health in Pomerania is a cross sectional study in North East Germany. A random sample from the population aged 20–79 years was drawn. The study population comprised 4310 subjects. All participants gave informed written consent. The study was approved by the local ethics committee.

Sociodemographic and clinical characteristics were assessed and medication was classified according to the anatomic, therapeutic, and chemical code. Anti-Borrelia IgG were determined by enzyme linked immunosorbent assay (ELISA) (Virion, Rüschlikon, Switzerland). A titre of $>$ 5 IU/ml was considered elevated and a titre of $>$ 10 IU/ml was considered positive. Of the 4310 subjects, 36 refused to have blood withdrawn or had missing data on Borrelia serology. In all, 4274 individuals (2174 women) were available for the present analysis.

Twelve lead ECGs were processed by the modular ECG analysis system (MEANS). For this study, P, PR and QRS duration and data on definite left bundle branch block (LBBB), right bundle branch block (RBBB), incomplete RBBB, left anterior fascicular block (LAFB), and left posterior fascicular block (LPFB) were analysed. Atrioventricular block (AVB) I°was defined as PR duration >200 ms. ECG data of 3690 individuals were available. Echocardiography was performed in participants $\geqslant$ 45 years. M mode images of the left ventricle were recorded at papillary level. Left ventricular end diastolic diameter (LVEDD) was measured, and left ventricular mass (LVM) and fractional shortening (FS) were calculated. Data on LVM and FS were available from 1807 subjects. Aortic and mitral valves were scanned from different views. An abnormal thickening and discrete to moderate focal increase of the echogenicity of the leaflets or the annulus was defined as moderate sclerosis, and a notably increased echo with reduced valvar opening was defined as severe sclerosis. There were 2330 aortic and 2314 mitral valve findings available.

Participants were divided into three groups: (1) absence of Borrelia IgG; (2) presence of elevated anti-Borrelia IgG; (3) positive anti-Borrelia IgG. Multivariable comparisons were made using general linear model and logistic regression. A probability value of $p < 0.05$ was considered significant.

RESULTS

The sera of 385 participants (9.0%) were found to contain elevated titres of anti-Borrelia IgG and the sera of 131 individuals (3.1%) tested positive. There was an age related trend towards increased seroprevalence in older individuals, but there was no sex related difference except in the 60–69 year decade in which men had elevated anti-Borrelia IgG more often than women ($p < 0.05$).

As regards ECG characteristics, subjects with elevated as well as those with positive anti-Borrelia IgG exhibited values for P, PQ and QRS duration that were similar to those of seronegative individuals (table 1). Anti-Borrelia IgG was not associated with any of the conduction abnormalities investigated (table 1). Further adjustment for antiarrhythmic drugs did not affect this general result. Subjects with low, elevated, or positive anti-Borrelia IgG did not differ with respect to left ventricular parameters and cardiac valve disorders (table 1). Analyses which were repeated in hypertensive individuals, as well as in participants who were symptomatic for exercise induced dyspnoea, yielded similar results.

DISCUSSION

Possible associations between anti-Borrelia IgG and the risk for cardiac disorders were systematically studied using different end points. Our study found no such associations. To the best of our knowledge, this is the first study to investigate the association between anti-Borrelia IgG and cardiac end points in this detailed manner.

While conduction disturbances are detected during the first weeks and months after infection with *B burgdorferi*, our study did not reveal an association between seropositivity for anti-Borrelia IgG and ECG changes. This is in agreement with results from another population based study[1] which could exclude such associations in individuals with previous treatment for Lyme disease. Also, in concordance with a case–control study[2] which did not find an increased seroprevalence in patients with end stage heart failure, our analyses did not reveal an association between anti-Borrelia IgG and left ventricular characteristics. Recently, findings from one study[3] suspected borrelioses to cause chronic heart failure, but in this study[3] the selection of patients was clinically based and controls were not well matched to the cases according to age. At present, there is little information regarding the involvement of cardiac valves in the course of

Abbreviations: AVB, atrioventricular block; ELISA, enzyme linked immunosorbent assay; FS, fractional shortening; IgG, immunoglobulin G; LAFB, left anterior fascicular block; LBBB, left bundle branch block; LPFB, left posterior fascicular block; LVEDD, left ventricular end diastolic diameter; LVM, left ventricular mass; MEANS, modular ECG analysis system; RBBB, right bundle branch block

Table 1 ECG and echocardiographic characteristics in individuals without (<5 IU/ml), with elevated (>5 IU/ml), and with positive (>10 IU/ml) anti-Borrelia IgG antibodies

	Interval data	Seronegatives	Elevated anti-Borrelia IgG	Positive anti-Borrelia IgG	Nominal data	Seronegatives (reference)	Elevated anti-Borrelia IgG	Positive anti-Borrelia IgG
ECG		n = 3345	n = 345	n = 119		n = 3345	n = 345	n = 119
	P duration (ms)	113.9 (0.2)	114.3 (0.6)	114.2 (1.1)	AVB I°	1.0	1.19 (0.77 to 1.84)	1.13 (0.57 to 2.25)
	PQ duration (ms)	159.4 (0.4)	160.4 (1.2)	158.7 (2.1)	*LBBB	1.0		
	QRS duration (ms)	99.8 (0.2)	99.0 (0.8)	100.2 (1.3)	LAFB	1.0	0.89 (0.46 to 1.64)	1.15 (0.48 to 2.76)
					LPFB	1.0	3.49 (0.20 to 60.1)	8.32 (0.51 to 137.2)
					RBBB	1.0	1.19 (0.60 to 2.36)	2.05 (0.88 to 4.76)
					*Incomplete RBBB	1.0	0.70 (0.16 to 3.0)	
Echo		n = 1621	n = 186	n = 72		n = 2058	n = 272	n = 100
	LVM (g)	190.8 (1.3)	195.4 (3.8)	193.7 (6.0)	Moderate aortic valve sclerosis	1.0	1.22 (0.90 to 1.65)	1.54 (0.96 to 2.45)
	LVEDD (mm)	51.2 (0.13)	51.5 (0.39)	51.0 (0.62)	Severe aortic valve sclerosis	1.0	0.97 (0.58 to 1.63)	1.07 (0.48 to 2.42)
	FS	0.371 (0.002)	0.374 (0.007)	0.372 (0.012)		n = 2042	n = 272	n = 100
					Moderate mitral sclerosis	1.0	0.63 (0.30 to 1.35)	0.41 (0.10 to 1.71)
					Severe mitral sclerosis	1.0	1.14 (0.63 to 2.07)	1.04 (0.40 to 2.70)

*No subject with elevated or positive anti-Borrelia IgG had LBBB and no subject with positive anti-Borrelia IgG had incomplete RBBB.
All data are adjusted for sex and age; in both the general linear model (interval data) and logistic regression (nominal data) no differences attained significance. Data are given as adjusted mean (standard error) and as odds ratio (95% confidence interval) as indicated.

Lyme disease. Our study did not reveal an increased prevalence of valve disorders in individuals with seropositivity for anti-Borrelia IgG, suggesting that even asymptomatic involvement of heart valves during borrelioses does not cause later valve sclerosis.

Our study has some limitations. Firstly, no information was gathered regarding the time and acuteness of infection, symptoms experienced, treatment received, and individual host related conditions at the time of infection. Secondly, it would have been useful to investigate end points defined by tissue Doppler analysis and serological markers to further exclude an association between anti-Borrelia IgG and subclinical cardiac disorders. Thirdly, without further diagnostic information, seropositivity to anti-Borrelia IgG represents a serum scar after prior exposure to *B burgdorferi* rather than an indication of chronic Lyme disease. A pathological role of Borrelia in chronic cardiac disorders can therefore not be fully excluded. Fourthly, serological tests for anti-Borrelia IgG may yield false negative and false positive results.[4] Although efforts were made to improve the specificity of the test by considering positive antibody titres, it is possible that an association between seropositivity to anti-Borrelia IgG and cardiac disorders could have been missed. Western blot analysis, however, was not practical for this population based study. Finally, there is limited comparability of Lyme disease serology and, therefore, a strong need for international standardisation.[4]

We conclude that there is no association between seropositivity to anti-Borrelia IgG and ECG characteristics, LVM and function, and aortic and mitral valve sclerosis.

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