EDITORIAL

Lyme carditis and supraventricular arrhythmias: potential pathophysiological mechanisms

Stefan Momčilović[1], Andriana Jovanović[2]

1 Plastic and Reconstructive Surgery Clinic, University Clinical Center Niš, Niš, Serbia
2 Clinic for Nephrology, University Clinical Center Niš, Niš, Serbia

RELATED ARTICLE

by Hasiec et al

Lyme carditis (LC) represents a relatively rare extracutaneous manifestation of Lyme borreliosis and is associated with a nonspecific presentation comprising a broad spectrum of cardiac disorders. In most patients (90%), conduction abnormalities, especially in the form of atrioventricular block (AVB), are the predominant presentation of LC. Moreover, in as many as two-thirds of those patients, high-degree AVB is detected during ECG evaluation and may require continuous cardiac telemetry as well as temporary pacing support.[1] However, in clinical practice, the fact that a large number of physicians are still not familiar with this manifestation of Lyme disease (LD) leads to a number of unnecessary implantations of permanent pacemakers in otherwise healthy young people, which can significantly increase health care costs and prolong hospitalization, while, at the same time, not curing the cause of the arrhythmia.[2] Therefore, caution should be exercised when deciding on the insertion of a permanent pacemaker, especially in young people and those coming from endemic areas for Lyme borreliosis. In order to avoid potential misdiagnosis, a new scoring system, Suspicious Index in LCs, can help clinicians identify LC in patients presenting with high-degree AVB, minimizing the risk of unjustified permanent artificial heart stimulation.[3]

The pathophysiological mechanisms implicated in *Borrelia burgdorferi*–associated cardiac conduction disorders are complex and not yet fully elucidated. To date, there are 3 proposed mechanisms that include high bacterial burden in the myocardium and subsequent increased inflammatory response, autoimmune processes due to molecular mimicry, and immunodeficiency disorders.[2,4] Interestingly, there was also a report of focal inflammation in the immediate vicinity of the atrioventricular node in a patient with high-degree AVB and positive Lyme antibody titers, indicating a possible predilection of *Borrelia burgdorferi* for the certain structures of the heart conduction system. Moreover, the results of previous studies also showed that the heart block most often occurs in the atrioventricular node, a structure that is considered the most vulnerable, which further supports this assumption.[2]

In addition to heart conduction abnormalities, cardiac manifestations of LD may also include endocarditis, degenerative cardiac valvular disease, myocarditis, pericarditis, pancarditis, dilatative cardiomyopathy and congestive heart failure, small- and large-vessel vasculitis, coronary aneurysms, myocardial infarction, cardiogenic shock, and sudden cardiac death due to lymphocytic infiltration of the heart.[2,5]

In this issue of *Polish Archives of Internal Medicine*, Hasiec et al[6] assessed the risk of atrial arrhythmias in patients who tested positive for LD antibodies. This very interesting analysis of 527 individuals showed that the presence of immunoglobulin (Ig) G antibodies against *Borrelia burgdorferi* can increase the risk of atrial fibrillation (AF) and other supraventricular arrhythmias but only in patients with elevated levels of N-terminal pro–B-type natriuretic peptide (NT-proBNP). Indeed, atrial inflammation, as a set of complex, changing responses to *Borrelia burgdorferi* infection, may affect the atrial cardiomyocytes, thus producing subsequent endocardial, myocardial, and interstitial fibrosis that represents an adequate substrate for the development of AF. This is especially possible in patients with past low-grade myocarditis who did not seek health care due to the mild clinical course.[4,7] Likewise, it is interesting to emphasize that, regardless of the etiology, atrial myocarditis occurs concurrently with ventricular myocarditis. Besides, it was shown that, in addition to the morphology and gene expression

Correspondence to:
Stefan Momčilović, MD,
Plastic and Reconstructive
Surgery Clinic, Clinical Center Niš,
Blvd Zorana Djindjica 48, 18000 Niš,
Serbia, phone: +381 605 263 654,
e-mail: m-stefan@mts.rs
Received: May 19, 2022.
Accepted: May 20, 2022.
Published online: May 30, 2022.
Pol Arch Intern Med. 2022;
132 (5): 16265
doi:10.20452/pamw.16265

profile, the amount of collagen also differs between the left and right atria, which may result in a different response to myocarditis. Finally, autoimmune reactions against cardiomyocytes, such as increased local and systemic production of proinflammatory cytokines and increased inflammatory cell infiltration in the atria, may play a potential role in the pathophysiology of AF.[8]

The results of Hasiec et al[6] also demonstrated that the presence of anti–*Borrelia burgdorferi* antibodies in combination with hypertension definitely increased the risk of AF in comparison with patients without such antibodies. To date, the polyreactive nature of some subclasses of IgG and IgM anti–*Borrelia burgdorferi* antibodies has been demonstrated, and they have been shown to be responsible for deleterious autoimmune phenomena due to the immunological cross-reactivity of bacterial epitopes and self-components.[9,10] It is well known that, regardless of the underlying heart disease, at least 4 types of autoantibodies against crucial mediators of atrial electrophysiology, with an emphasis on antimyosin heavy chain that has been proven in LD, have been identified as significantly more prevalent in patients with established AF. These autoantibodies induce inflammation and atrial fibrosis by initiating the production of a secondary messenger.[11] On the other hand, hypertension as a chronic disease can lead to pressure overload and stretching of cardiomyocytes in the heart, including the atrium, which has been shown to promote inflammation.[12]

Despite the multifactorial nature of AF, an imbalance of ventriculovascular homeostatic mechanisms can also lead to the development of this type of arrhythmia by increasing ventricular filling pressures and, consequently, left atrial pressure and stretch. In particular, some specific disturbances in tonometric measures of arterial stiffness, such as higher pulse load and greater apparent wave reflection, have been shown to be significantly associated with an increased risk of AF. Likewise, vasculitis, as an inflammatory process characterized by the presence of inflammation in the walls of blood vessels, subsequent cell necrosis, and ischemia of the end organ, is a possible manifestation of LD which may result in increased arterial stiffness and decreased vascular distensibility. This is especially pronounced in small-vessel diseases that usually contribute to a higher vascular resistance. An increase in afterload may affect the ventricular diastolic function, prolong the duration of systole and, consequently, delay the onset of relaxation. These impairments of the cardiac cycle increase the filling pressure of the left ventricle which is involved in promoting the development of AF. On the other hand, as far as the atria are concerned, the delay in emptying due to impaired diastolic distensibility that increases pressure and wall stretch within these chambers and pulmonary veins represents an important mechanism for altered atrial electrical characteristics that promote the onset of AF.[11]

In patients with LC, vasculitis of small blood vessels often reveals endothelial cell edema in histological examination, while adventitious infiltrates with loose reticulin and increased collagen deposition are found in large vessels.[4] It is important to point out that fibril cross-links and proteoglycan-rich matrix in reticular fibers contribute to mechanical strength and distensibility of blood vessels. Lastly, given the fact that the involvement of coronary blood vessels by LD has also been described, it can be assumed that, due to the motility of the inflammatory mediators and immune cells, inflammatory damage can spread also to the sinus nodal artery and the atrioventricular nodal artery that represent major atrial coronary branches and play a significant role in the pathophysiology of AF and other tachyarrhythmias.[13]

In recent years, NT-proBNP has emerged as a powerful biochemical parameter of cardiac function. This biomarker of wall stretch, in addition to heart failure, acute coronary syndrome, and pulmonary embolism, may also play a role in myocarditis and AF. It has been found that the level of NT-proBNP correlates with that of C-reactive protein, leukocytes, and the neutrophil-to-lymphocyte ratio, indicating inflammation.[14] In patients with preserved cardiac function and AF, NT-proBNP is secreted from the atria due to increased myocardial contraction, volume load, and wall stress caused by this arrhythmia.[15] However, patients with AF and IgG *Borrelia burgdorferi* antibodies represent "an old riddle that's sparked many arguments through the ages: was it the chicken or the egg that came first?" In fact, since these patients had elevated levels of anti-*Borrelia burgdorferi* antibodies and NT-proBNP in serum, there is a possibility that active inflammation was still present in the heart tissue, which, despite the lack of specific clinical symptoms and signs, persisted, most likely due to autoimmunity or untreated disease that has taken a chronic course. In this case, the elevated level of NT-proBNP initially originated from inflammation and cardiomyocyte damage, and then was subsequently stimulated by AF. On the other hand, it is possible that the patient's immune system successfully eradicated the infection, but with concomitant myocardial damage leading to fibrosis and, consequently, AF, which, as already mentioned, may cause an increase in the NT-proBNP level due to atrial dysfunction.

Although LC has attracted increasing attention from the scientific community over the last decade, it still remains an incompletely solved puzzle, especially in a pathophysiological sense. Therefore, additional research and clinical trials that will contribute to a better understanding of the specific mechanisms of this infection are needed.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

HOW TO CITE Momčilović S, Jovanović A. Lyme carditis and supraventricular arrhythmias: potential pathophysiological mechanisms. Pol Arch Intern Med. 2022; 132: 16265. doi:10.20452/pamw.16265

REFERENCES

1 Yeung C, Mendoza I, Echeverria LE, Baranchuk A. Chagas' cardiomyopathy and Lyme carditis: lessons learned from two infectious diseases affecting the heart. Trends Cardiovasc Med. 2021; 31: 233-239.

2 Kostić T, Momčilović S, Perišić ZD, et al. Manifestations of Lyme carditis. Int J Cardiol. 2017; 232: 24-32.

3 Besant G, Wan D, Yeung C, et al. Suspicious index in Lyme carditis: systematic review and proposed new risk score. Clin Cardiol. 2018; 41: 1611-1616.

4 Fish AE, Pride YB, Pinto DS. Lyme carditis. Infect Dis Clin North Am. 2008; 22: 275-288, vi.

5 Nikolić A, Boljević D, Bojić M, et al. Lyme endocarditis as an emerging infectious disease: a review of the literature. Front Microbiol. 2020; 11: 278.

6 Hasiec A, Wolny R, Duda B, et al. Association between the acquisition of antibodies against Lyme disease and the risk of atrial arrhythmias. Pol Arch Intern Med. 2022; 132: 16201.

7 Szymanska A, Platek AE, Dluzniewski M, Szymanski FM. History of Lyme disease as a predictor of atrial fibrillation. Am J Cardiol. 2020; 125: 1651-1654.

8 Begieneman MP, Emmens RW, Rijvers L, et al. Ventricular myocarditis coincides with atrial myocarditis in patients. Cardiovasc Pathol. 2016; 25: 141-148.

9 Raveche ES, Schutzer SE, Fernandes H, et al. Evidence of *Borrelia* autoimmunity-induced component of Lyme carditis and arthritis. J Clin Microbiol. 2005; 43: 850-856.

10 Sulka KB, Strle K, Crowley JT, et al. Correlation of Lyme disease--associated IgG4 autoantibodies with synovial pathology in antibiotic--refractory Lyme arthritis. Arthritis Rheumatol. 2018; 70: 1835-1846.

11 Melduni RM, Cooper LT, Gersh BJ, et al. Association of autoimmune vasculitis and incident atrial fibrillation: a population-based case-control study. J Am Heart Assoc. 2020; 9: e015977.

12 Goldstein DS. Arterial baroreflex sensitivity, plasma catecholamines, and pressor responsiveness in essential hypertension. Circulation. 1983; 68: 234-240.

13 Boppana VS, Castaño A, Avula UMR, et al. Atrial coronary arteries: anatomy and atrial perfusion territories. J Atr Fibrillation. 2011; 4: 375.

14 Moady G, Perlmutter S, Atar S. The prognostic value of natriuretic peptides in stable patients with suspected acute myocarditis: a retrospective study. J Clin Med. 2022; 11: 2472.

15 Meyre PB, Aeschbacher S, Blum S, et al. Biomarkers associated with rhythm status after cardioversion in patients with atrial fibrillation. Sci Rep. 2022; 12: 1680.