Lyme disease and heart transplantation: presentation of a clinical case and a literature review

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Background. Lyme disease, the most common anthropozoonosis, is a transmissible natural focal infection affecting various organs and systems. Also known as Lyme borreliosis, it is caused by Borrelia spirochetes, which are distributed by ticks of the genus Ixodes. Early diagnosis is difficult due to frequent occurrence of atypical symptoms, unnoticed tick bites, the absence of migratory erythematous lesions, and symptoms occurring during the non-tick season. If not diagnosed and treated in time, dissemination of the infection occurs and various complications develop since borrelias damage not only the skin but also the nervous system, joints, and, in rare cases, the heart and eyes.

Materials and methods. This article presents a clinical case of Lyme borreliosis-induced myocarditis, which led to the development of dilated cardiomyopathy and, consequently, urgent cardiac transplantation. According to our data, this is one of the first described cases of this complication in the world.

Results and conclusions. When diagnosed in time and treated properly, the prognosis of Lyme myocarditis is usually good. In most cases, the atrioventricular block disappears within 1–2 weeks of antibiotic treatment and the implantation of a temporary pacemaker is rarely needed. In those rare cases of a chronic Borrelia burgdorferi infection, dilated cardiomyopathy may develop; thus if a sudden atrioventricular block occurs, the physician should be vigilant and perform the necessary tests to exclude the diagnosis of Lyme disease.

Keywords: Lyme myocarditis, atrioventricular block, Lyme disease, dilated cardiomyopathy

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INTRODUCTION

Lyme disease (LD) or Lyme borreliosis is an infectious multisystemic disease caused by bacteria of the *Borrelia* (B) genus of the spirochete family (*B. burgdorferi, B. afzelii, B. garinii*, etc.). Due to natural and climatic conditions, this disease prevails in the temperate zone of the northern hemisphere, especially in Europe and North America and so the risk of infection in these areas is extremely high (1, 2). According to the Lithuanian Centre for Infectious Diseases and AIDS (ULAC), LD affects 2,000-3,000 people in Lithuania annually (3). Although people who are in close contact with nature are at a greater risk of tick bites; ticks are also found in residential yards and lawns. In addition, a nymph’s bite often remains unidentified, unlike that of an adult tick. These factors impede the diagnosis of tick-borne diseases, the most common of which is Lyme disease. No memory of a tick bite and atypical disease symptoms will delay the correct diagnosis, which can lead to very serious consequences. Because no vaccine exists for Lyme borreliosis and infection with the disease does not confer immunity, it is possible to become reinfected. This means that, potentially, anyone can contract LD and so doctors should be very vigilant. This article presents a clinical case of LD-induced myocarditis, which led to the development of dilated cardiomyopathy and, ultimately, urgent cardiac transplantation. According to our data, because the link between LD and advanced dilatative cardiomyopathy has only been established in Europe (4), this is one of the first reported cases of this complication in the world. The purpose of this article is to reveal the course of LD-induced myocarditis and long-term complications as well as to promote medical vigilance. In case of a sudden atrioventricular block of unclear aetiology, dilative cardiomyopathy and heart failure, tests to exclude Lyme Borreliosis need to be conducted.

CASE REPORT

A 45-year-old male in cardiogenic shock was brought to the emergency department by ambulance. At the time of the physical examination, the skin and mucous membranes were pale, the lips appeared to be cyanotic, and the skin was covered with cold sweat. The blood pressure (BP) was unmeasurable, the heart rate (HR) 20 bpm. Vesicular breath sounds with wet basal crackles were audible during the auscultation of the lungs. The anamnesis showed that the patient had been experiencing great weakness and dizziness for the last two months and fainted several times. The patient was taking no medication and had no allergies, history of chronic diseases, or memory of a tick bite. The medical records showed the patient had been treated by a dermatovenerologist for rashes on the inner surfaces of the thighs two years before. The patient was transferred to the Cardiac Intensive Care Unit where a temporary cardiac pacemaker was immediately implanted. Blood test data: white blood cells (WBC) – 8.7 × 10^9/l (norm 4.0–9.8 × 10^9/l), neutrophils (NEU) – 7.47 × 10^9/l (norm 1.5–7.0 × 10^9/l), haemoglobin (HGB) – 141.30 g/l (norm 128–160 g/l), platelets (PLT) – 132.30 × 10^9/l (norm 140–450 × 10^9/l), troponin I – 0.81 ng/l (norm up to 34.2 ng/l), and creatinine – 118 µmol/l (norm 64–104 µmol/l); the electrolyte, glucose, C-reactive protein (CRP), acid-base balance, and the urine test results were normal. The chest X-ray showed venous stasis in the lungs and a left ventricular enlargement. The urgent coronarography showed a catheter-induced spasm in the left coronary artery. The transthoracic echocardiographic examination showed good general and local inotropy, no valve disorder, an ejection fraction (EF) of 50%; the electrocardiogram (ECG) showed a third-degree atrioventricular (AV) block (Fig. 1). An examination failed to reveal the exact cause of the disorder and the AV block was treated with a permanent pacemaker. After his condition improved, the patient was discharged from the hospital.

Three years later, the patient contacted the emergency department due to general weakness and intense chest pain radiating to the left arm. These symptoms lasted for about two weeks. According to the data from the examination performed in the emergency department, vesicular breath sounds without crackles were audible during the auscultation; the heart activity was rhythmic, the heart rate 70 bpm, the arterial blood pressure 130/80 mmHg. The ECG showed effective cardiac pacemaker activity. The blood tests showed an increased mass of creatine kinase isoenzyme MB (CK-MB) – 31.33 µg/l (norm <5.2 µg/l), while troponin I was normal at 0.323 ng/l (norm <34.2 ng/l). Under suspicion of a myocardial infarction, the patient was
hospitalized in the Department of Cardiology. The
departmental blood tests showed a significant rise
in the creatinine kinase (CK) at 1612 U/L (norm
25–195 U/L) and B-type natriuretic peptide (BNP)
at 896.8 ng/l (norm <125 ng/l) but normal values
of the CK-MB, troponin I, complete blood count
(CBC), coagulogram, D-dimers, CRP, electrolytes,
lipidogram, and liver enzymes. The coronary an-
giography performed due to the suspicion of a
myocardial infarction showed no significant con-
strictions of the coronary blood vessels and so the
preliminary diagnosis was rejected. An up to 30%
reduction in EF was observed during cardiac echo-
cardiography as well as a I° mitral regurgitation and
a II° dilation of the left and right atria. A computer
tomography of the resting myocardial perfusion
performed using Technetium (99mTc) tetrofosmin
with electrocardiography synchronization yielded
a scintigraphic image of myocarditis, the ejection
fraction at rest being 24%. The echocardiography
of the dobutamine load performed on the tenth
day of hospitalization showed diffuse contraction
disorders characteristic of a non-ischemic cardi-
omyopathy. During the dobutamine infusion, the
left ventricular EF increased from 26% to 40%, with
significant signs of mechanical intraventricular
asynchronism. After discussing the patient’s con-
dition and the laboratory and radiology tests at a
case conference, myocarditis was diagnosed, but
the cause remained unclear. After excluding many
diseases, LD was suspected and a test for Borrelia
burgdorferi antibodies was performed. Positive
IgG and IgM antibody titres were detected using
an enzyme-linked immunosorbent assay (ELISA)
test. During the detection of the Borrelia antibod-
ies with immunoblot, the IgG titre was found to
be positive. In the presence of positive serological
test results, Lyme borreliosis was diagnosed. After
performing an endomyocardial biopsy, chronic
myocarditis with lymphocyte infiltration was also
diagnosed, the final diagnosis being Lyme myocar-
ditis. The following treatment was applied: Sol. Cef-
triaxoni 1 g twice a day intravenously for 28 days.
The patient’s condition became stable after antibi-
otic treatment. At the time of his discharge from
the hospital, his heart activity was rhythmic, HR
70 bpm, BP 120/80 mmHg, and vesicular breath
sounds without crackles were audible in the lungs
during auscultation. It was recommended that a
cardiologist perform an ultrasound examination
and assess his general condition after the course of
antibiotics. The examination showed the left ven-
tricular EF to be 35% and the overall condition to
have improved.

A year later, the patient’s condition worsened
again and he was hospitalized at the Depart-
ment of Cardiology for severe general weakness.
A transthoracic echocardiographic examination
showed significant disorder of the left and right
ventricular myocardial contraction, dilation of
the left ventricular cavity, a thrombus at the top
of left ventricle, a thrombus on the cardiac pace-
maker cord in the right atrium cavity, II° left and
III° right atrial dilation, III° tricuspid and mitral
regurgitation, right heart cavity overload, system-
ic venous stasis, and an EF of 10% (Fig. 2). Dilated
cardiomyopathy was diagnosed and a biventricular pacemaker implanted. As significant cardiac weakness remained, the patient was added to the list of urgent heart transplant recipients. Three months later, the patient underwent cardiac transplantation.

LITERATURE REVIEW AND DISCUSSION

Lyme disease is a transmissible, natural focal infection that affects various organs and systems. The disease was first described in the US in 1977 (6). In Europe and Asia, Lyme disease is usually caused by the following species of Borrelia spirocheta: *B. garinii* or *B. afzelii*, less often by *B. burgdorferi*, and rarely by *B. spielmani* or *B. bavariensis* (7), in the US, mostly by *B. burgdorferi* and less often by *B. mayonii* (8). The pathogens are spread by ticks of the genus *Ixodes*. A person can be infected by both adult mites and nymphs. After a spirochete enters the human body, Lyme borreliosis occurs in three stages:

- The first, initially localized, stage usually occurs as a migratory erythema along with common signs of a viral infection. Migratory erythema usually occurs seven to 14 days after the bite but the period may vary from three to 30 days (5). The most frequent localization of the erythema is the areas of the armpit, groin, popliteal, and belt. Migratory erythema is hotter when touched; it is not painful, although it may sometimes cause pruritus or a burning sensation (9). In the first stage of the disease, symptoms similar to a viral infection may occur: weakness, fever, muscle and joint pain, headache, and regional lymphadenopathy (10).

- The second, early disseminated, stage starts weeks or months after the tick bite. Organotropism and symptoms of Borrelia damage in the organs occur. Nervous system damage may occur and may include paralysis of the facial nerve, meningitis, radiculopathy, and peripheral neuropathy. Cardiac injury is clinically manifested by an atrioventricular block of varying degree (5). In case of eye damage, iridocyclitis, uveitis, conjunctivitis and optic nerve neuropathy develop (10).

- The third, late disseminated, stage can manifest months or even years after the tick bite. This stage is characterized by intermittent or persistent arthritis of the large joints, especially the knees (12). The following neurological disorders also develop: polynuropathy, radiculopathy, chronic encephalomyelitis, and chronic atrophic acrodermatitis (13, 14).

Lyme disease very rarely manifests in cardiovascular disorders. In Europe, only 0.3–4% of all cases of Lyme borreliosis manifest in myocarditis (15). Damage of the heart tissue occurs three times more often in men than in women (16). Borrelia, which enter the heart through the haematogenous pathway, cause transmural inflammations. The myocardial infiltration with inflammatory cells is mainly composed of lymphocytes (17). Although a spirochete-induced inflammation can affect many cardiac sites, studies with mice have shown that Borrelia are most commonly found in the connective heart tissue, especially around
the aorta, in the upper ventricular and atrial epicardium, and in the myocardial interstitium and the endocardium (18). Acute myocarditis usually occurs with an atrioventricular block. In a review of 105 clinical cases conducted by van der Lind, 49% reported a complete AV block, 16% a second degree block, and 12% a first degree block (16). Myocarditis can also occur with supraventricular and ventricular arrhythmias, pericarditis and, in rare cases, pancarditis (19). Chronic Lyme myocarditis can be defined as chronic heart failure, with positive serological test results and Borrelia in the endomyocardial biopptate (19). In the course of chronic Lyme myocarditis, a very rare complication – dilated cardiomyopathy – may develop, but a link between it and LD has only been established in Europe (4, 20, 21).

Diagnosis of Lyme myocarditis
If Lyme myocarditis is suspected due to a sudden high-grade AV block, we recommend beginning with an evaluation of the likelihood of Lyme myocarditis by calculating the Suspicious Index in Lyme Carditis (SILC) (Table) (22). Our patient’s SILC was retrospectively rated at 5 points: one point for age, male sex and outdoor activity, each, and: two points for constitutional symptoms.

If 0–2 points are collected, the patient is assigned to the low-risk group and other causes of myocarditis are sought. Patients with 3–6 points and 7–12 points (the moderate and high-risk groups, respectively) are subjected to serological tests: using an ELISA test for a search for anti-LD IgM and IgG antibodies and a Western blot test for confirmation (22). The results of the serological tests must be interpreted in the light of the patient’s clinical condition and of the course of the disease (23). A diagnosis of Lyme myocarditis is very complicated and other tests are needed to confirm the final diagnosis:

- Molecular testing for pathogen DNA detection is recommended only in certain situations, such as atypical LD manifestations in the skin or suspected Lyme arthritis (23).
- An electrocardiogram is required: it usually shows a I–III° atrioventricular block, but ST-segment depression and T wave inversion are also possible (16, 24).
- Radiology tests: cardiac echocardiography and magnetic resonance imaging (MRI) are needed. In these imaging examinations, structural changes, such as the pericardial changes found in pericarditis, can be assessed and left ventricular function can be evaluated in the presence of myocarditis, at which point hypokinetic myocardial zones are visible, and the ejection fraction can also be measured. The MRI examination depicts structures in high detail, so any myocardial oedema caused by the inflammatory process and hyperaemia is clearly visible (25). By using intravenous contrast during the MRI, the late contrast accumulation area, which highlights the area affected by the inflammation even more, can be recorded (26).
- An endomyocardial biopsy is the “gold standard” in the diagnostics of myocarditis, especially in complicated cases, such as progressive heart failure or a manifesting left ventricular dilation. Transmural inflammatory infiltration with lymphocytes is seen in biopsy samples. The detection of BB spirochetes in the inflammatory zone, which is mostly located along the collagen fibres, is also possible (17).

| Variable                  | Value | Our patient |
|---------------------------|-------|-------------|
| Age < 50 years            | 1     | 1           |
| Male                      | 1     | 1           |
| Outdoor activity          | 1     | 1           |
| Constitutional symptoms²  | 2     | 2           |
| Tick bite                 | 3     | 0           |
| Erythema migrans          | 4     | 0           |
| Total score               | 12    | 5           |

²Pre-syncope, syncope, fever, malaise, arthralgia, dyspnea.
Treatment of Lyme myocarditis and patient monitoring

In the case of a sudden high-grade AV block and suspected Lyme myocarditis, treatment should be started in accordance with the SILC score (see Fig. 3). Low-risk patients with a high-grade AV block should be treated based on the standard high-grade AV block treatment recommendations (22). Patients with suspected Lyme borreliosis (intermediate and high-risk patients), who have manifested syncope, dyspnoea, or chest pain and with detected second or third-degree AV block or first-degree AV block at a PR interval of more than 300 milliseconds, should be hospitalized, their heart rate monitored, and empirical antibiotic therapy initiated (22, 27). An atrioventricular block may progress in some patients with Lyme myocarditis, so it is recommended to always be prepared to implant a temporary pacemaker (16). Because any complete AV block is temporary and will disappear within a week if properly treated, implantation of a permanent pacemaker should be avoided (28).

The antibiotic therapy for the treatment of Lyme myocarditis is selected depending on the patient's condition. If the patient is haemodynamically stable, the first-line drug is Doxycycline, 100 mg orally twice a day for 21 days. If the patient is haemodynamically unstable, then Ceftriaxone, 1g twice a day for 21 days intravenously, should be administered. It is important to note that Azithromycin should not be given to patients with heart failure because it prolongs the QT interval (29).

CONCLUSIONS

When diagnosed in time and treated properly, the prognosis of Lyme myocarditis is usually good. In most cases, the atrioventricular block disappears within 1–2 weeks of antibiotic treatment and the implantation of a temporary pacemaker is rarely needed. In those rare cases of a chronic Borrelia burgdorferi infection, dilated cardiomyopathy may develop; thus if a sudden atrioventricular block occurs, the physician should be vigilant and perform the necessary tests to exclude the diagnosis of Lyme disease.

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Fig. 3. Diagnosis and management of Lyme carditis and a high-degree atrioventricular block. SILC – Suspicious Index in Lyme Carditis
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LAIMO LIGA IR ŠIRDIES TRANSPLANTACIJA: KLINIKINIO ATVEJO PRISTATymAS IR LITERATŪROS APŽVALGA

Santrauka

Tiksla. Laimo liga – transmisinė židininė infekcinė liga, pažeidžianti įvairius organus ir sistemus. Ši liga dar vadinama Laimo borelioze, pasižymi Borrelia spirochetos, kurias platinaIxodes genties erkės. Tai labiausiai išplitusi antropozoonozė. Anksčiau Laimo ligos diagnostika yra sudėtinga dėl dažnai pasiektų atipinių ligos simptomų, nepastebėto erkės įkandimo, nepasireiškiančios migruojančios eritemos, simptomų atsidaino ne erkių sezonu metu. Laiku ne-diagnozavus ir nepradėjus gydyti, įvyksta užkrato diseminacija, vystosi įvairios sunkios komplikacijos, nes borelijos pažeidžia ne tik odą, bet ir nervų sistemą, sąnarius, retais atvejais – širdį, akis.

Medžiaga ir metodai. Šiame straipsnyje pristatomas klinikinis atvejis apie Laimo borelioze sukeltą miokarditą, lėmusį dilatacinės kardiomiopatijos išsivystymą ir dėl to skubiai atliktą širdies transplantaciją. Mūsų turimais duomenimis, tai vienas pirmųjų aprašomų šios komplikacijos atvejų pasaulyje.

Išvados. Laiku diagnozavus ir paskyrus tinkamą gydymą, Laimo miokardito prognozė dažniausiai yra gera. Daugeliu atvejų, gydant antibiotikais, atrioventrikulino mazgo blokada išnyksta per 1–2 savaites, o laikinojo kardiostimuliatoriaus implantavimo prireikia retai. Retais lėtinės Borelia Burgdorferi infekcijos atvejais gali išsivystyti dilatacinė kardiomiopatija, todėl nustačius staiga atsiradusią atrioventrikulino mazgo blokadą, gydytojai turi būti itin budrūs ir atlikti reikiamus tyrimus Laimo ligos diagnozėi ekskluduoti.

Raktas: Laimo miokarditas, atrioventrikulino mazgo blokada, Laimo liga, dilatacinė kardiomiopatija