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**SINFUS BRADYCARDIA AS AN EARLY MARKER OF HEART DAMAGE IN A GIRL WITH LYME DISEASE (CASE REPORT AND MINI REVIEW)**  

**Abstract.** Objectives Early clinical markers of Lyme carditis and other life-threatening prognostic factors due to complications of borreli infection are still the beginning of active research by scientists. The literature describes a small number of cases of Lyme carditis with arrhythmias or cardiac conduction disorders. Material and methods We reviewed the case of a 14-year-old girl. LC was diagnosed on the basis of history of disease, physical examination, laboratory examination data (positive anti-borrelia IgM in ELISA with confirmation in immunoblot. The presence of B. burgdorferi s.l. was detected by the method of immunoassay using the Euroimmun AG test systems (Germany). The presence of B. burgdorferi s.l. was detected by the method of immunoassay analysis using the Euroimmun AG test systems (Germany). 2 instrumental methods: (ECG,Echo-cor) were used. Results We described a case of Lyme borreliosis in a 14-year-old girl, accompanied by sinus bradycardia and pericardial fluid (hydropericardium) (passed after a course of antibacterial therapy). Analysis of this case indicates early detection and adequate treatment of Lyme carditis in young people with minimal deviations of the cardiogram. A case of Lyme carditis, in a child was confirmed. Echocardiography of the heart (at the time of admission to the hospital and at the time of discharge from the hospital was made. Conclusions 1. Lyme carditis should be suspected in patients with a history of Lyme disease and minimal Electrocardiographic abnormalities, such as sinus bradycardia. 2. For differential diagnosis of Lyme carditis, it is necessary to make (carry out two-stage serological investigation of blood, especially using antibody screening tests by ELISA with subsequent confirmation by the Western blot assay.  

**Keywords** ELISA, child, COVID-19, Lyme carditis

**List of abbreviations:**  
ASL-O –antistreptolysin-O  
WBC – white blood cells,  
leukocytes APP- Acute-Phase Blood Protein  
LC-Lyme carditis  
LB-Lyme borreliosis  
Borrelia burgdorfery-B.burgdorfery  
Electrocardiography-ECG  

**Background.**  
Lyme disease is the most common disease transmitted by the ixodes ticks. It is endemic in Ukraine. Clinical manifestation of the disease in the early stages often includes erythema migrans and early disseminated infection (multiple erythema migrans lesions, cranial nerve palsy--most commonly VII, aseptic menigitis or acute radiculopathy neurological (Bell's palsy, radiculoneuritis, menigitis) particularly with lymphadenopathy [1,2] or heart (atrioventricular block, myopericarditis, pancarditis) manifestation [3]. In Europe, only 0.3–4 % of all cases of borreliosis manifests itself in myocarditis [4]. Lyme carditis occurs when B. burgdorfery enters directly the heart tissue [5], which can cause conduction disorders. Lyme carditis can cause fainting, shortness of breath, heart palpitations, or chest pain. The most dangerous complication of conduction disorders is the full atrioventricular block of the heart. Its correction requires the use of pacemaker. Other reported serious and even fatal heart complications include heart arrhythmia, myocarditis, heart failure and sudden cardiac arrest [6]. Early LC, defined as signs and symptoms lasting less than 6 months after the tick bite, represent the vast majority of the cases (95%) [5]. The purpose of the work is to describe the peculiarities of the clinical manifestation of Lyme carditis on the basis of clinical, laboratory and instrumental methods of examination and identification of its early clinical markers.  

Materials and methods. Our study was conducted, in Ternopil region (Western Ukraine) and consists of two parts: Study 1. During the first study we analysed case history, anamnesis morbi and in the course of the
second study we performed laboratory and instrumental examination of blood samples of person with lyme carditis. Study 2. Laboratory examination data (CBC, C-reactive protein, (ASL – O), positive anti-borrelia IgM, Ig G in ELISA with confirmation in immunoblot (Euroimmun AG test systems (Germany). According to the manufacturer’s recommendations, the presence of specific IgM antibodies was considered positive, intermediate or negative, depending on the combinations of OspC antigens of the three species of Borrelia (B. afzelii, B. burgdorferi s.s. and B. garinii), p39 and VLS E Bb. At the same time, the presence of IgG was considered to be positive or negative, depending on the combinations of VLS E antigens of the three species of Borrelia (B. afzelii, B. burgdorferi s.s. and B. garinii) and other specific antigens: p18, p19, p20, p21, p58, OspC (p25), p39, p83, Lipid Ba, Lipid Bb. Instrumental methods: (ECG, Echo-cor) were used.

«The authors declare that all the procedures and experiments of this study were conducted according to the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patient included in the study».

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Results.
Case report. We reviewed the case of a 14-year-old girl. She was admitted to the regional hospital because of complaints of general weakness, rapid fatigue and discomfort in the left half of the chest, pain in the left ankle and metatarsal joint. Ankle pain syndrome was unbearable, and did not respond to the action of nonsteroidal anti-inflammatory drugs, flexion was not in full volume. History of present illness: there was an evidence of a tick bite 2 months before, tick bite sign and redness in the area of the joint. At that time mother did not pay attention to symptoms. Thus, the girl was healthy did not receive preventive treatment, and did some in sports. Past medical history: None. A child from the first full-term uncomplicated pregnancy.

Pertinent physical examination: Her mental and physical development corresponds to her age. The skin is pink. The general condition of the patient is moderate severity, body temperature 37.3 °C. Heart rate 56 bpm, the tones were preserved, some arrhythmia is present. Respiratory rate: 20 breaths per 1 minute, auscultatory-vesicular. BP 110/70 mm Hg. SpO2=99 %

Taking into account, that the child before this case was healthy, engaged in sports, the history of tick bite, cardiac clinical symptoms and changes of ECG, the patient was scheduled for following examinations: serological tests for diagnosis of Lyme borreliosis, echocardiography, ECG in the dynamics. The peculiarity of this case was the deterioration of the patient's condition 2 months after tick bite. The treatment with non-steroidal anti-inflammatory drugs did not bring relief. Table I. Laboratory and ultrasound findings in the patient. The patient underwent serological testing for lyme borreliosis. Enzyme immunoassays for specific anti-Borrelia burgdorferi IgM and IgG were positive (176.8 U/ml and 72.2 U/ml respectively. Immunoblot assay identified the presence of several antibodies targeting the OspC Ba (B. afzelii), OspC Bb (B. burgdorferi), OspCBg (B. garinii), P39 Ig M, VlsE B. afzelii (Vls EBa) 34, VlsE B. burgdorferi (VlsE-Bb)33, VlsE B. garinii (VlsE-Bg)33, Lipid B. afzelii (LBa)8, Lipid (B. burgdorferi) (LBb)2, p83 (p83)12, Flagellum (p41)87, BmpA (p39)8, OspC (OspC)27, BB-A34 (p58)1, BB_K53 (p21)4, BB_Q03
Anti-human IgG (IgG) 63 were detected. ECG indicators at the time of admission (Fig. 1, 2):

Heart rate 56 bpn, bradycardia. P 102ms, PQ 136ms, QRS 80ms. QT 398ms, QTc 386ms, QTrel 99%. P 0.8mm 65°, QRS 17.2mm 73°, T 4.2mm 63°. Vertical Axis, Sokolov Index: 29.0mm, Levis Index: -6.4mm, Cornell Index: 4.4mm. Dispersion 12ms Max. 40ms with 8/8 leads. Conclusion: Sinus rhythm, with heart rate 49–60 bpm. Sinus bradyarrhythmia, vertical axis. Early ventricular repolarization syndrome. ECG at the time of discharge from the hospital (Fig. 3, 4):
Conclusion: Sinus correct rhythm 62 bpm. Vertical Axis. Early ventricular repolarization syndrome. Echocardiography of the heart (at the time of admission to the hospital). The chambers of the heart are not dilated. The structure and function of the valves are preserved. Left ventricular contractility is normal. A small echo-free space 4 mm thick (a small amount of fluid in the pericardium) is located behind the posterior wall of the left ventricle. Echocardiography of the heart (at the time of discharge from the hospital).

<table>
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<tr>
<th>Parameter</th>
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<tr>
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<td>62</td>
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</table>

Table 2

The chambers of the heart, the structure and function of the valves are normal. Left ventricular contractility is preserved. Fluid in the pericardium is not determined. During this time, after treatment with antibiotics, the patient's condition became stable. The heart rate was normalized with 62 bpm, BP – 120/80 mmHg. Table 2. Echo-cor Options LA, left atrium; IVS, interventricular septum; PW, posterior wall; EDD, end diastolic distance; EDV, end diastolic volume; RA, right atrium; RV, right ventricle; EF, ejection fraction. Child's treatment. For antibiotic treatment Ceftriaxone 50 mg/kg/day intravenously once daily during 14 days was used. Nonsteroid therapy (ibuprofen) was prescribed. After treatment the patient’s condition improved, signs of arthritis resolved and arthralgias decreased. Discussion. In our case we observed: history of tick bite and erythema migrans in child, signs and symptoms of carditis and arthritis, atrioventricular block or arrhythmia. Lyme disease at the beginning usually presents skin lesions accompanied by fever, flu-
like features – fatigue, low temperature, arthralgia, myalgia and nausea. In many cases, skin lesions can have partial central enlightenment, which looks like "bovine eye"[4,5]. If the infection is not localized, it can spread and affect the whole body [5]. Manifestations of LB. Miocardial presents in many different ways, ranging from mild symptoms to chest pain and palpititation, association with transient ECG changes to life-threatening cardiogenic shock and ventricular arrhythmia [8,9]. In most cases, the clinical expression of myocarditis can be exemplified by 3 main patterns of presentation 1) recent-onset heart failure, 2) arrhythymias and 3) chest pain. Patients may experience bradycardia due to varying degrees of AV block, which often happens to be the only sign of Lyme carditis [10]. Heart symptoms (14 leukocytes/mm² including up to 3) monocytes/mm² with the presence of >7 CD3-positive T lymphocytes/mm². According to some scientific research on autopsy, it was found that the cause of death was diffuse pancarditis with great lymphocytic infiltration and focal interstitial fibrosis [11]. Among the bacterial etiology of carditis: Brucella, Corynebacterium diphteriae, gonococcus, Haemophilus influenzae, Actinomyces, Tropheryma whipplei, Vibrio cholerae, B.burgdorferi, leptospirosis, Rickettsia, Mycoplasma pneumoniae. Most cases of Lyme carditis are clinically asymptomatic. If they are symptomatic, typical signs may be: complaints of fatigue, shortness of breath, heartbeats, fainting, syncope and chest pain [5,6,7,8]. Musculoskeletal manifestations include arthralgia and arthritis. Arthritis typically presents with recurrent brief attacks of joint swelling in 1 or more joints, typically involving the knees [12]. As clinical manifestations of the disseminated form of the disease, the patient may have multiple secondary EM, arthritis of large joints, neurological lesion [13] and heart lesions manifested by the atrophicventricular unit [14]. How long after Borrelia infection can LC symptoms occur? The late-stage infection lasts for months or years after a tick bite and occurs in 60 % of patients who have not received treatment [2]. Such patients may experience periodic bouts of arthritis [9]. Borrelia disseminates from skin to other organs quickly. It replicates, kills host cells, and emerges through the membrane of that cell. Within days to weeks after infection, Borrelia has been recovered from blood, cerebrospinal fluid, myocardium [12,15]. The study was intended to identify changes in blood serum proteins in people infected with B. burgdorferi at the earliest stage [16]. In our study we detected signs of inflammatory activity (leukocytosis with neutrophilic shift to the left, increased ESR, increased C-reactive protein, sialic acids. Analysis of our study shows early LB-associated proteins revealed 1. Increase of acute phase proteins (C-reactive protein) assays for detecting host biomarkers associated with bacterial fevers, such as C-reactive protein (CRP) and are used in hospitals in Europe to differentiate between bacterial and non-bacterial infections [17], (Tab1). Acute phase proteins (C-reactive protein, antistreptolysisin-O (ASL – O), as biomarkers of inflammation, can react within hours after borreliosis penetrate the skin [14]. 2. Borrelia antibody IFA as well as confirmatory IgG and IgM Western Blot were positive. Diagnosis of Lyme disease confirmed by laboratory tests prescribed according to the recommendations of the Centers for Disease Control and Prevention [14]. In response to infection, the host immune response to Borrelia integrates both cell-mediated and humoral mechanisms [15]. That’s why its an importance of the 2 stage tests in the diagnostic of ethioloogy carditis of Lyme disease [14,17]. In Laboratory testing we found antibodies to B. burgdorferi in the serum [15,16]. Although serological testing can initially give false negative results, a second serological study should be conducted within two to six weeks especially in a patient with suspected Lyme carditis [14]. Immunoblot is a highly specific test used to diagnose Lyme disease. In our case Immunoblot assay identified the presence of several antibodies targeting the OspC Ba (B.afzelii), OspC Bb (B.burgdorferi), OspCBg (B.garinii), P39 Ig M, VlsE B.afzelii (Vls E Ba) 34, Vls E B. burgdorferi (VlsE-Bb)33, Vls E B. garinii (VlsE-Bg)33. On the other hand, there is a suggestion the immunobOn the other hand, there is a suggestion the immunoblot assay tests for the presence of antibodies to specific B. burgdorferi antigens, including immunoglobulin (Ig) M antibodies to 3 spirochetal antigens (the 23/24, 39, and 41 kDa polypeptides) and IgG antibodies to 10 spirochetal antigens (the 18, 23/24, 28, 30, 39, 41,45, 60, 66, and 93 kDa polypeptides) [16]. Based on positive results of serological testing, Lyme borreliosis was confirmed. The diagnosis of Lyme carditis is challenging: it is usually made in the presence of other manifestations of Lyme disease—concomitant erythema migrans, arthritis, or neurologic disease, or such cardiac manifestations as ECG findings and congestive heart failure—together with positive serologic testing for B. burgdorferi infection. One should note that positive serologic testing is not by itself diagnostic, nor does negative serologic testing exclude the diagnosis [16]. In our study we estimated ECG Sinus bradyarrhythmia, vertical axis. Early ventricular repolarization syndrome. Echocor. A small echo-free space 4 mm thick (a small amount of fluid in the pericardium) is located behind the posterior wall of the left ventricle. Echocardiography can provide valuable information to assess the presence and stage of heart dysfunction, which is important for the management of these patients [16,17]. According to Nelson CA, SahaS, the 12-lead ECG and Holter can show depression of the ST segment, inversion of T-waves in the chest leads and conduction disorders [16].

The criteria for diagnosis of myocarditis are the following [12, 16]: 1. Standard ECG/Holter Daily Monitoring – AV-block degree I–3 – Blockade of the bunch of Gis – ST/T changes (ST interval inversion), – Paroxysmal tachycardia, – Low voltage (if R in standard leads is less than 5 mm or less than 10 mm in the breast leads. - Frequent extrasystoles. In a previous study, Alida L.P.Caforio et al. [7] electrocardiogram (ECG) is usually abnormal in myocarditis though ECG signs are neither specific nor sensitive. Some ECG
changes are more suggestive of myocarditis than others. For example, ST-T segment elevation in myocarditis is typically concave (rather than convex myocardial ischaemia) and diffuse with out reciprocal changes. AV block in the presence of mild left ventricular dilatation can be due to various causes, but it may also be suggestive of Lyme disease, cardiac sarcoidosis, or giant cell myocarditis. In another recent publication [18], autor said that conduction system involvement is diverse, possibly including but not limited to bundle branch block, intraventricular conduction delay, prolonged QT interval, ventricular and fascicular tachycardias, and complete heart block. The most common LC electrocardiogram (ECG) findings in patients include atrioventricular (AV) conduction abnormalities (first, second, and third degree heart block) [19], atrial fibrillation and a full atrio-ventricular block [20] of a first-second grade type 1. In our study echocardiography of the heart (at the time of admission to the hospital). A small echo-free space 4 mm thick (a small amount of fluid in the pericardium) is located behind the posterior wall of the left ventricle. Echocardiography helps to rule out non-inflammatory cardiac disease such as valve disease and to monitor changes in cardiac chamber size, wall thickness, ventricular function, and pericardial effusions [7]. According to scientific finding, in Echocardiography we found: enlargement of left or right ventricle, thickness of the wall of the left ventricle, pericardial effusion – for no other reason. [18]. The literature describes a number of cases of Lyme carditis with heart rhythm disorders or isolated block of nerve branches or other conduction disorders [21, 22, 23]. Differential diagnosis with other carditis was made. In viral myocarditis, the Coxackie B family of the single-stranded RNA viruses, in particular the plus-strand RNA virus Coxackievirus B3 and Coxackievirus B5 are the most frequent cause [15]. Most studies have reported cases of the involving protozoa, fungi, parasites, allergy, autoimmune disorders are also causes of eosinophilic myocarditis [6]. Other causes of Lyme carditis may be Chagas disease, Kawasaki disease [24]. Acute rheumatic carditis should also be excluded in diagnostic search in patients with violation of AB conduction due to acquired heart disease, especially in pediatric practice. Most cases are reversible AV-blocks of the first or second degree [19]. The mechanisms of development of infectious genesis carditis, are actively studied today, including a completely new infection SARS-CoV-2 [16, 23, 26]. A recent incident reported by Kannangara et al. Diseases (2019) [25] describes manifestations of Lyme carditis (LC) vary from asymptomatic and symptomatic electrocardiographic changes and heart block (HB) reversible with treatment, to sudden death. Tachycardia in the pediatric case of LC. The AV-block in Lyme carditis is usually reversible, and takes place after a course of antibiotics [20, 22].

For diagnosis of carditis it is necessary to make CBC, CRP, ECG, Echo-cor, and which tests are needed for etiological diagnosis of carditis it necessary to make two-stage serological investigation tests of blood are needed. Oral antimicrobial agents are appropriate and effective for most manifestations of disseminated Lyme disease, including multiple erythema migrans and for patients with Lyme carditis treated as outpatients. For patients requiring hospitalization for Lyme carditis (high-grade atrioventricular block), initial therapy usually is parenteral but can be completed with oral therapy for a total course of 14 days (range: 14 to 21 days) [26]. Early clinical markers of LC and other predictors of life-threatening complications of borreliosis infection are still at the beginning of an active study by scientists. Therefore, the case described Lyme borreliosis, accompanied by sinus bradyarrhythmia and pericardial fluid (past after taking an antibacterial therapy course), may target early detection and adequate treatment of Lyme carditis in young people with minimal deviations in cardiogram indicators [27, 28, 29]. Clinicians, pathologists, immunologists, and molecular cardiologists must contribute to the new criteria, which should include clinical presentation, histopathology, immunohistochemistry, viral polymerase chain reaction, cardiac antibody assessment, and imaging results. Finally, it is possible that sinus bradyarrhythmia or other minimal deviations from the normal ECG can be studied Manuscript body Download source file (60.08 kB) as potential early markers of heart lesions not only in Lyme borreliosis, but also in other infectious diseases, including COVID-19.

**Conclusions**

1. Lyme carditis should be suspected in people with a history of Lyme disease and minimal abnormalities in cardiograms, such as sinus bradyarrhythmia.

2. For diagnosis of Lyme carditis, it is necessary to make two-stage serological investigation of blood, especially use of antibody screening tests by ELISA with subsequent confirmation by the Western blot assay.

**References.**


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