CASE REPORT

Lyme Borreliosis as a Cause of Myocarditis in Pediatric Age

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Abstract

Lyme borreliosis with myocarditis is rare in pediatrics and diagnosis requires a high index of suspicion. We present an adolescent with myocarditis, depressed left ventricular function, and evidence of Lyme borreliosis infection. Early recognition and treatment of Lyme disease can help to avoid serious complications.

Keywords: Adolescent; Lyme Disease/complications; Lyme Disease/diagnosis; Lyme Disease/drug therapy; Myocarditis/etiology; Myocarditis/drug therapy

Introduction

In Europe, the most prevalent regions with Lyme borreliosis are Central and Eastern Europe but it is also distributed in some parts of northern Mediterranean countries.[1] It is estimated that the average number of patients with Lyme disease in Europe is nearly 65,400 per year.[2]

Lyme carditis was described for the first time in 1980 and represents a less frequent manifestation of Lyme borreliosis. It was reported in 0.3%-4% of the European adult patients with the disease, but the prevalence data in children is still inaccurate.[3-5] Lyme carditis is considered to be less common in Europe than in the United States, partially due to the different prevalence of the strains of bacteria in the two continents and to its relative virulence.[6,7] Cardiac involvement can present as conduction abnormalities, most commonly involving the atrioventricular node, degenerative cardiac valvular disease, endocarditis, myocarditis, pericarditis, pancarditis and dilated cardiomyopathy.[5,8]

Case Report

A 17-year-old male from a rural area in southern Portugal, with a history of recurrent tonsillitis, presented in May to the pediatric emergency department with cervical pain, odynophagia, and fever (39ºC). The physical examination revealed only hyperemia of the oropharynx, and the blood work showed leukocytosis (11,280 x 10^9 cells/L), neutrophilia (8 569 x 10^9 cells/L), and C-reactive protein 23.6 mg/L. Oropharynx antigen screening for group A *Streptococcus* and Epstein-Barr virus serology were negative, and he was discharged with amoxicillin and clavulanic acid for acute bacterial tonsillitis. On the following day (seventh day of disease), he maintained a fever (38.3°C), initiated a pruritic maculopapular rash on the face, trunk, and limbs, with palmoplantar involvement and thoracic pain, that worsened with decubitus. Skin lesions were coalescent, faded to digital pressure without a palpable clearer/darker center or petechial elements. On the blood work revaluation, he presented leukocytosis (14,640 x 10^9 cells/L), neutrophilia (11,040 x 10^9 cells/L), C-reactive protein 142 mg/L, and the erythrocyte sedimentation rate was 22 mm/hour. Chest radiography had broncho-hilar reinforcement, without pleural effusion or cardiomegaly. Electrocardiogram presented sinus rhythm, depressed ST segment in DIII and aVF, inverted T wave from V4-V6, without conduction abnormalities. Due to an episode of tachycardia (200 bpm), cardiac markers were accessed and showed troponin 13,932 pg/mL (reference values < 34.2 pg/mL), creatine kinase 436 U/L. Echocardiography revealed slightly depressed left ventricular function, ejection fraction of 41%, hyperechogenic pericardium without effusion, and the B-type natriuretic peptide was 373 pg/mL (reference values < 100 pg/mL). Admitted under penicillin and clindamycin and started anti-congestive therapy with carvedilol and enalapril. On the 10th day of disease, he tested positive for *Borrelia burgdorferi* (*sensu lato*) immunoglobulin (Ig)

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M antibodies (53 UA/mL), with negative IgG antibodies by enzyme-linked immunosorbent assay (ELISA). Confirmatory test-immunoblot revealed positive IgM (bands OspC Bg, p39, p41). Other probable infectious agents, such as *Bartonella henselae*, *Coxiella burnetii*, *Rickettsia conorii*, *Mycoplasma pneumoniae*, *Treponema pallidum*, *Chlamydia pneumoniae*, *Mycobacterium tuberculosis*, *Leptospira*, *Toxoplasma gondii*, and gastrointestinal and respiratory virus were excluded as well as autoimmune diseases. He was medicated with ceftriaxone 2 g once daily, during and after clinical, analytical, and echocardiographic improvement and completed another seven days with doxycycline, 100 mg twice daily, as monotherapy, in the outpatient setting. He completed a total of two weeks of parental antibiotics and a week of ambulatory oral treatment. On the 20th day of disease, cardiac magnetic resonance showed an active inflammatory process in the myocardium (Figs. 1 and 2), non-dilated ventricles with preserved global systolic function. Progressive improvement of the cardiac markers was noticed and he was discharged on the 24th day asymptomatic with the recovery of ventricular function (ejection fraction 64%). After six months of follow-up, he was asymptomatic, had normal left ventricular dimensions with preserved systolic function, cardiac magnetic resonance without evidence of an active inflammatory process, and two small areas of subepicardial fibrosis in the inferior and inferior-lateral walls of the left ventricle.

Discussion

Lyme borreliosis is a tick-borne infectious disease caused by the spirochetes of the *Borrelia burgdorferi* (*sensu latu*) species. The worldwide distribution of *Borrelia* infection is related to the *Ixodes* ticks and the presence of a competent reservoir host. Involvement of the heart tissue occurs when spirochetes present heart tropism during the early dissemination phase. Cardiac lesions are established by inflammatory cell infiltration, mostly in the conduction system. It is hypothesized that *Borrelia burgdorferi* (*sensu latu*) genetic variations are involved not only in its human virulence but also in its cardiac location.[6,9]

In 2009, Costello et al, proposed to characterize the presentation and clinical course for children with Lyme carditis, and the authors concluded that the spectrum of presentation ranged from asymptomatic first-degree heart block to fulminant myocarditis.[10] In the literature[7], the myocardial involvement of Lyme carditis has been stated to mimic acute coronary syndrome due to its ST-segment deviations, 60% of patients presenting with depression or T-wave inversion, especially in the infero-lateral leads, as in our patient, which disappeared completely with clinical remission.

This diffuse involvement of ST and T changes makes differential diagnosis difficult due to its non-specificity, reflects a diffuse myocardial impairment, can lead to cardiomegaly and left ventricular dysfunction that is identifiable clinically and echocardiographically in 10%-

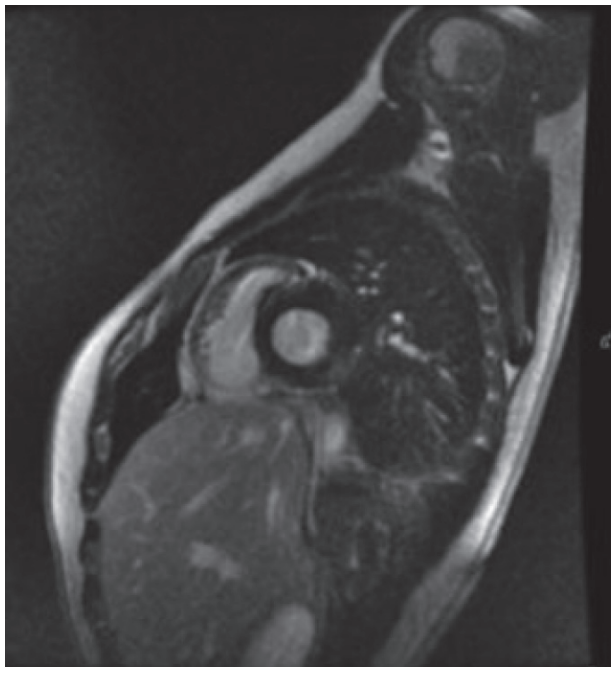

Figure 1. Cardiac magnetic resonance of late gadolinium enhancement. Focal zones of subepicardial enhancement in the left ventricle. Typical pattern of myocarditis.

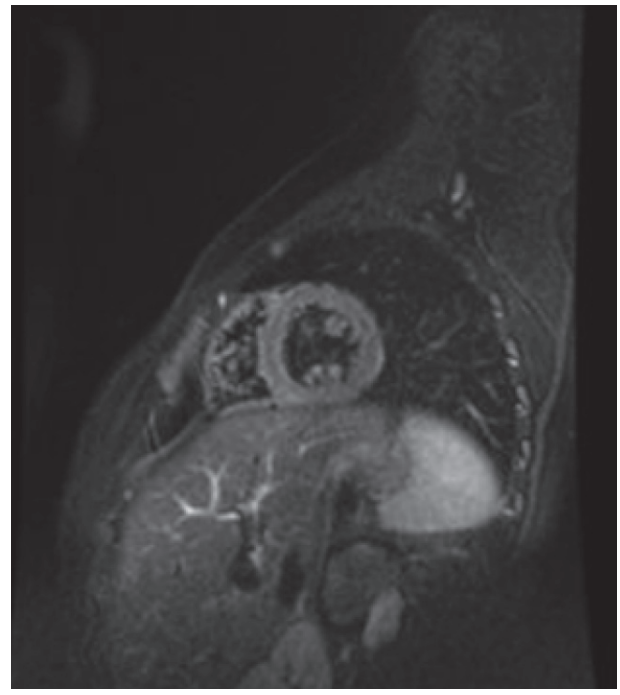

Figure 2. Cardiac magnetic resonance T2-weighted sequence. Slight left ventricular wall edema.

15% of patients with Lyme carditis in the adult population.[11] Several laboratory tests have been developed and adapted to complement the clinical diagnosis of Lyme borreliosis. These tests involve indirect screening for anti-*Borrelia* spp antibodies (immunological methods) and/or direct *Borrelia* deoxyribonucleic acid (DNA) screening by molecular methods. Because of the differences in the regional distributions of *Borrelia* genospecies, the high antigen variability of *Borrelia* and the potential influence of the preferential reactivities of sera from patients with Lyme borreliosis, serological results should always be interpreted in the context of the patient manifestations or the disease progression.[12]

There was a need to simplify the testing algorithm for Lyme borreliosis. Today, the two-step testing procedure uses a sensitive ELISA as an IgM and IgG antibody screening test. Then, positive or borderline results are confirmed using an immunoblot assay.[3] Due to the often-delayed immune response, the results may show a false negative in the early stage of the disease and, consequently, negative serology does not rule out an early infection.[9] Another point to be aware of is that false positive ELISA testing can be observed in patients affected not only by *Borrelia* or spirochetal infections derived from common cross-reactions, but autoimmune diseases can also cause false positive results.[5] As for our case, other probable infectious agents were excluded, and the autoimmune diseases workup came up negative. These data supported even more the fact that the only identified agent, *Borrelia* spp, constituted the true causal agent of the infection underlying the patient clinic, further supporting the initial suspicion raised by the combination of symptoms (cutaneous and cardiac involvement, although not with the typical presentation) and the suggestive epidemiological context.

Currently, cardiac magnetic resonance evolved to be the most useful noninvasive tool for the diagnosis of myocardial inflammation. In addition to all of its functional utilities, it allows for a precise localization of the tissue injury, including edema (using T2-weighted imaging), hyperemia, and fibrosis. Some published data on diagnostic accuracy have been offering substantial evidence for the use of this exam in the diagnosis of myocarditis and it was transported for the assessment Lyme myocarditis, even at a pediatric age.[6,13,14] The patient met the diagnostic criteria (hyperemia, edema, and subepicardial enhancement) suggestive of myocardial inflammation as defined by the International Consensus Group on Cardiovascular Magnetic Resonance Diagnosis of Myocarditis.[14] This exam is especially relevant in patients who have persistent symptoms or, as in our case, that have ventricular dysfunction and a risk of new onset heart failure, anticipating eventual complications. Manifestations of Lyme borreliosis are treated with antibiotics, but the best treatment approach and the duration of therapy is controversial. According to the National Institute for Health and Care Excellence (NICE) guidelines for Lyme borreliosis management, the antibiotic treatment of Lyme carditis in adults or young people (aged 12 and over, as it was our case) included oral doxycycline (100 mg twice per day or 200 mg once per day for 21 days) or intravenous ceftriaxone (2 g once per day for 21 days) and in hemodynamically unstable patients should only comprise intravenous ceftriaxone 2 g once per day for 21 days (when an oral switch is considered, use doxycycline). As to the specificities of the term Lyme carditis it is not referenced and, therefore, it is assumed that these recommendations include all forms of Lyme carditis manifestations (from atrioventricular block, pericarditis, myocarditis, among others). The latest clinical practice guidelines by the Infectious Diseases Society of America[15] and other references in the literature also recommend intravenous ceftriaxone, cefotaxime, or penicillin G for 14 days as the treatment for Lyme carditis, reinforcing the completion of therapy for outpatients with oral regimens such as doxycycline.[3,7,12] Our patient treatment comprised two weeks of parental antibiotics and one week of ambulatory oral treatment. He recovered progressively with clinical and imaging resolution, without any disease complication or adverse drug reaction.

Lyme carditis has an overall good prognosis, particularly if it is identified in the early phase of the disseminated disease and correctly treated, with complete recovery occurring in most patients.[7]

WHAT THIS CASE REPORT ADDS

- Lyme borreliosis with myocarditis is rare in pediatrics and requires a high index of suspicion.
- Lyme borreliosis can occur without the typical rash manifestation.
- Cardiac involvement occurs during the early disseminated phase of the disease.
- Borreliosis should be included in the differential diagnosis of myocarditis of unclear etiology.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Consent for publication

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Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Borreliose de Lyme como Causa de Miocardite em Idade Pediátrica

Resumo

A borreliose de Lyme com miocardite é rara em pediatria e o diagnóstico requer um elevado nível de suspeição. Apresentamos um adolescente com miocardite, disfunção ventricular esquerda e evidência de borreliose de Lyme, bem como a estratégia utilizada que permitiu a sua recuperação. O reconhecimento precoce e o tratamento do envolvimento cardíaco podem evitar complicações graves.

Palavras-Chave: Adolescente; Doença de Lyme/complicações; Doença de Lyme/diagnóstico; Doença de Lyme/tratamento farmacológico; Miocardite/etiologia; Miocardite/tratamento farmacológico