Lyme Carditis in the Pediatric Population

Cheyenne M. Beach and Jeffrey M. Vinocur

Abstract

The incidence of Lyme carditis is increasing due to the accompanying increase in incidence of Lyme disease. PR prolongation is the most common manifestation of Lyme carditis in children. An appropriate index of suspicion for Lyme disease and Lyme carditis is needed to initiate timely administration of antibiotic therapy. Temporary transvenous pacing is a successful strategy for patients with high-grade AV block and hemodynamic instability. The great majority of pediatric patients have full recovery of conduction abnormalities (and ventricular dysfunction) in the weeks to months following treatment of Lyme carditis.

Keywords

Lyme carditis • Pediatric • Atrioventricular block • Heart block • Lyme disease

1 Introduction

Lyme disease (LD) and its complications are relatively common in endemic areas and in patients who have traveled to these areas during warmer months. Lyme carditis (LC) is one of the more serious complications of LD and requires an appropriate index of suspicion for its prompt and correct diagnosis. The epidemiology, diagnosis, management, and outcomes of LC in pediatric patients will be discussed.

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2 Epidemiology of Lyme Disease and Lyme Carditis in Children

LD incidence is uncertain in the absence of mandatory reporting infrastructure but may exceed 300,000 cases/year in the United States (US), perhaps approaching 500,000 cases/year. Among the subset of these cases that are voluntarily entered in the US Centers for Disease Control and Prevention passive reporting system, about 20% occur in children. Pediatric cases of LD and LC follow the same geographic distribution that is seen in the adult population. Pediatric and adult cases of early localized and early disseminated LD also have similar seasonality (typically June through October).

LD affects school-aged children and adolescents at a higher rate than younger children, likely due to differences in exposure between these age groups. LC is reported to occur in about 1–4% of pediatric patients with LD, though numerous sources propose that this is an overestimate as the denominator of children with LD is not known (mild outpatient cases being less likely to be reported than severe cases resulting in hospitalization). The prevalence of carditis among pediatric patients hospitalized with LD in US children's hospitals is around 5%, while carditis has been reported in 16% of those hospitalized with the early disseminated stage of the disease [1]. The prevalence of both LD and LC have increased over time in the pediatric population, with the percentage of LD cases affected by carditis remaining steady, suggesting the increase in numbers of LC cases is due to the increase in cases of LD itself rather than by a change in virulence or cardiac tropism [2]. LC is reported to be less common in Europe than in North America, while pediatric data from Europe and Asia, where LD is also endemic in certain areas, have not been clearly studied.

LD occurs more frequently in males than in females throughout pediatric and adult years. Though the reason for this is not known with certainly, it may relate to different exposure rates. As the risk of developing carditis is related to the risk of having LD, males are also more likely to be diagnosed with LC.

Among pediatric patients with LD, older children are more likely to be diagnosed with carditis. This has been consistently reported, with age over 10 years a risk factor for the development of carditis [1].

3 Clinical Manifestations of Lyme Carditis in Children

Importantly, many patients with objective evidence of LC do not have cardiac symptoms. In one cohort, 50% of children with LD and evidence of LC on an ECG did not report any cardiac symptoms at the time of presentation [3]. If LD is appropriately recognized and treated, these children will likely remain free of cardiac symptoms.

Children and adolescents with LC may exhibit other signs and symptoms of LD at the time of presentation. These may include arthritis, myalgias, fever, rash consistent with erythema migrans, headache, neck stiffness, visual disturbance, and

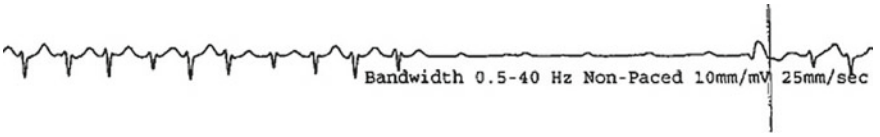

Fig. 1 Ventricular pause in a 17-year-old patient with paroxysmal junctional tachycardia and complete AV block in the setting of LC. There are five non-conducted P waves followed by a ventricular beat and resumption of junctional tachycardia. These pauses are more likely to occur in the setting of increased vagal tone. Reprinted with permission [7]

altered mental status, among others. Lyme meningitis and LC both occur in the early disseminated stage of disease and may therefore co-occur [1, 4].

Atrioventricular block (AVB) is by far the most common manifestation of LC in children. As in adults, conduction system disease is caused by direct invasion of cardiac tissue by the spirochetes that cause LD. A prolonged PR interval (first-degree AV block) is the most common manifestation of LC in children and is seen in about 42% at the time of presentation. Approximately 21% have second-degree AVB, while 5% have complete AVB at the time of presentation [1]. The conduction abnormalities seen in LC may progress rapidly, with complete AVB seen in about 27% of patients at some point during hospitalization [1]. Prolonged ventricular pauses may occur, particularly in the setting of high vagal tone (Fig. 1). Although LC predominantly affects the AV node, often permitting a reasonable junctional escape rhythm, His-Purkinje involvement can occur (reported at 10–20% in adult series and at the case report level in children [5] Fig. 2).

While AV block and associated bradycardia are commonly seen in pediatric patients with LC, other arrhythmias including accelerated junctional rhythm and junctional tachycardia have also been reported [6, 7] (Fig. 1). Other electrocardiogram (ECG) findings in patients with carditis include QT prolongation, ST segment abnormalities, and T wave abnormalities [8]. These repolarization changes are also known to occur in the setting of neurologic abnormalities and in some cases may be related to neurologic manifestations of LD rather than to the presence of carditis.

Pediatric patients with LD can also develop ventricular dysfunction due to myopericarditis. It has been found that 12% of pediatric patients with LC develop ventricular dysfunction [1], with some of these experiencing cardiogenic shock necessitating extracorporeal membrane oxygenation (ECMO) support. In the rare patient undergoing endomyocardial biopsy to assist with diagnosis, “extensive, predominantly lymphocytic infiltrate associated with myocyte damage and necrosis” is seen [1]. Most, but not all, patients with ventricular dysfunction due to LC will also demonstrate AV conduction abnormalities.

Symptoms at the time of presentation with LC are related to the patient’s cardiac abnormalities as well as other symptoms caused by the patient’s underlying LD. Cardiac symptoms may include lightheadedness, syncope, shortness of breath, palpitations, and chest pain. Severity of symptomatology is related to the

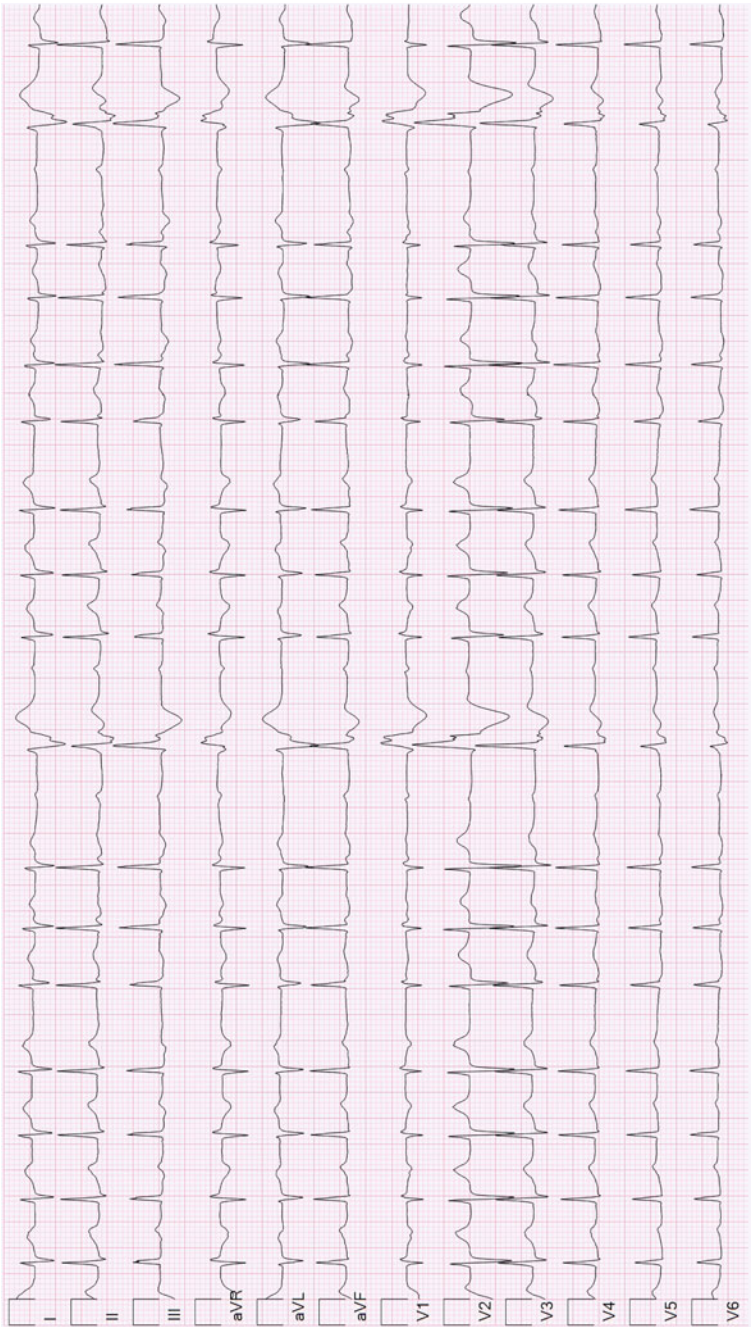

Fig. 2 Erratic AV conduction with left posterior fascicular block and wide-complex beats suggesting phase 4 block of the right bundle or ventricular escape beats in a 14-year-old male with LC who presented with non-exertional syncope two weeks following a viral-like syndrome. Reprinted with permission [5]

degree of AV block, the ventricular rate, and the presence or absence of myopericarditis. Some patients, especially those with relatively mild conduction system involvement resulting in PR prolongation only, may have no cardiac symptoms.

4 Differential Diagnosis of Lyme Carditis in Children

When children present with an ECG finding or arrhythmia suggestive of LC, consideration of the patient's individual risk for tick exposure in a Lyme-endemic area, especially during warmer months, should be made. Recent or current rash consistent with erythema migrans, arthritis, shortness of breath, lightheadedness, palpitations, chest pain, fatigue, and/or neurologic manifestations would increase the suspicion for LD. However, many patients with LC lack a preceding history of tick bite or rash; indeed, these features increase the likelihood of seeking treatment early in the LD course, and so disseminated infection including LC may paradoxically be more likely in those without such clues in the history or physical exam.

Children and adolescents with LC and high-grade AVB typically present with symptoms of bradycardia such as lightheadedness or syncope. Incidentally discovered high-grade AVB without acute symptoms suggests an alternate, chronic diagnosis such as congenital and/or genetic AVB. Notably, patients with distant LD infection may remain antibody seropositive for years, so in endemic areas, patients with non-Lyme causes for AVB will occasionally test positive for Lyme by coincidence.

The behavior of AV conduction at various heart rates can provide insight into the cause of the conduction abnormality. Those with AVB due to LC are expected to have worse AV conduction at higher heart rates; indeed, the first signs of conduction recovery are seen at lower heart rates. In the authors' experience, patients with congenital or genetic causes of AV block tend to have improvement of conduction at higher heart rates. Serial ECGs or use of telemetry and/or Holter monitoring may therefore be very helpful in adjusting a differential diagnosis.

Because LC has particular affinity for the conduction system, it is usually straightforward to distinguish from other causes of myocarditis that tend to have significant ventricular dysfunction and/or tachyarrhythmia by the time heart block is apparent. Selected other pathogens, however, can show LC-like clinical presentation; influenza, for example, has been observed to cause transient AVB as far back as the 1918–1919 pandemic [9].

5 Management and Course of Lyme Carditis in Children

It is imperative to have an appropriate index of suspicion for LD in patients with symptoms suggestive of LC so that they can promptly receive the necessary treatment. It is also important to have an appropriate index of suspicion for LD in patients without carditis to avoid cardiac and other sequelae of the disease.

Patients with early localized LD typically do not need cardiac testing in the absence of cardiopulmonary symptoms, acknowledging that the erythema migrans rash is not exclusive to the early localized stage and can persist into the early disseminated stage. An ECG should be considered for patients with early disseminated LD and is recommended in patients with cardiopulmonary symptoms during any stage of LD. Detailed cardiology evaluation, including echocardiogram, is appropriate for children and adolescents suspected to have LC based on ECG or symptoms. Hospitalization on telemetry is warranted for those with significant first-degree (≥300 ms) or higher-grade AVB, evidence of myocarditis or pericarditis, or concerning cardiopulmonary symptoms, given the risk of progression of conduction system disease and both clinically significant bradyarrhythmias and tachyarrhythmias.

For asymptomatic patients with mild presentations of LC (first-degree AV block and PR interval < 300 ms with no concern for myocarditis or pericarditis), oral antibiotics can be used. Doxycycline (depending on age), amoxicillin, and cefuroxime are commonly used, with specific regimens recommended by the CDC and other groups [10]. Intravenous (IV) antibiotics, typically ceftriaxone, should be used for patients with more severe forms of carditis [10]. In such patients, IV antibiotics should be started as soon as possible without waiting for Lyme testing, which can take days to result at many centers. As improvement can be seen within days, and even hours in some cases, of antibiotic initiation, beginning antibiotic therapy promptly can avert the need for more advanced measures and can reduce hospital length of stay. A typical evolution of AV conduction seen following initiation of antibiotics is shown in Fig. 3.

Placement of a temporary pacemaker should be strongly considered for patients with complete AVB and hemodynamic compromise or evidence of an unreliable escape rhythm. While likely less commonly needed in hospitalized children than in hospitalized adults, temporary pacing is used in up to 20% of pediatric patients hospitalized with LC [11]. Single-chamber ventricular pacing is almost always sufficient; when possible, an active-fixation lead should be placed through an internal jugular or subclavian vein to eliminate the need for bedrest during the recovery process [11]. Pacing is continued until there is an adequate heart rate and hemodynamic stability in the underlying rhythm, most commonly once the patient has recovered some degree of AV conduction. If an externalized permanent generator is used, advanced features such as rate hysteresis can help minimize the pacing burden as conduction begins to return. The duration of temporary pacing in pediatric patients is typically around three to five days [12]. Once AV conduction improves enough to safely remove the pacemaker, it essentially always continues to improve and would not be expected to deteriorate to the point of needing pacing support again.

Avoidance of excessive vagal tone may help to avoid prolonged ventricular pauses. An isoproterenol infusion can be started to increase a patient's ventricular rate, if needed. A dose of 0.02–0.5 mcg/kg/min can be used, with the usual adult range being 2–10 mcg/min. The dose can be titrated to effect, with near immediate onset of action. A good effect is typically seen with doses at the lower end

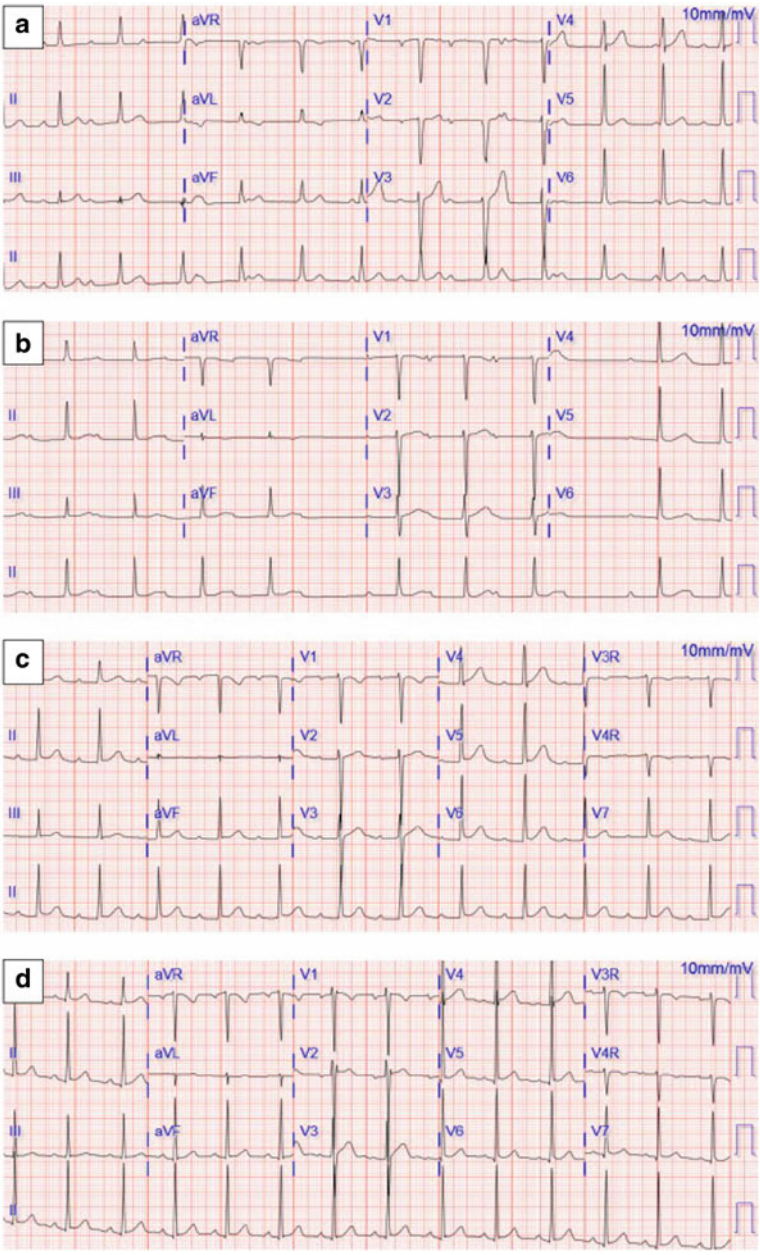

Fig. 3 Typical progression of conduction abnormalities seen in a 12-year-old patient with LC. **a**. ECG at the time of presentation shows sinus rhythm with complete AV block and an accelerated junctional rhythm at 75 bpm. **b**. ECG 2 days after initiation of ceftriaxone shows sinus rhythm with markedly prolonged PR interval of 440 ms and Wenckebach conduction. There has been interval resolution of the accelerated junctional rhythm. **c**. ECG 3 days after initiation of ceftriaxone shows sinus rhythm with prolonged PR interval of 380 ms and 1:1 AV conduction. **d**. ECG 2 months after hospitalization is normal, showing sinus rhythm with a PR interval of 178 ms

of the suggested range, and the high frequency of side effects should be taken into consideration when using this medication. Side effects of chest pain, agitation, restlessness, tremor, nausea, and headache are common and often limit the acceptability of therapy. In the authors' experience, isoproterenol is sometimes used as a bridge to temporary pacemaker placement but is rarely tolerable for prolonged periods. Because of this and concerns about unpredictable tachyphylaxis, temporary pacing is typically instituted within hours of starting isoproterenol.

6 Outcomes of Lyme Carditis in Children

Most patients continue to have some degree of abnormal conduction, typically a prolonged PR interval, at the time of discharge from the hospital. The great majority of pediatric patients have complete normalization of conduction in the weeks to months following treatment, though a small percentage have continued abnormalities. Of the 27 pediatric patients described in one series, 3 (11%) had abnormalities during medium-term follow-up. These abnormalities varied from mild PR prolongation in the initial weeks/months to second-degree AVB up to 2.7 years after treatment [1]. As most pediatric patients with LC are previously healthy, baseline ECGs are rarely available, and it is therefore difficult to be certain that there were not underlying conduction abnormalities in some of these patients.

While some adults require pacemakers at the time of hospital discharge, these patients are more likely than children and adolescents to have underlying cardiac disease contributing to this need. Permanent pacing needs in children with LC have not been described, although it is possible for AVB due to *unrecognized* LC to result in the implantation of a permanent pacemaker for a reversible problem [13]. This unfortunate occurrence can be avoided by maintaining an appropriately high index of suspicion, which includes attention to travel history for those practicing in non-endemic regions.

Deaths in the setting of LC are extremely rare but have been reported. In 2015, Yoon, et al. reported the case of a 17-year-old male who died unexpectedly following a three-week period of viral-like symptoms [14]. A postmortem examination showed diffuse carditis with lymphocyte infiltration, focal interstitial fibrosis, and *B. burgdorferi* in the cardiac tissue and suggested the presence of meningoencephalitis as well.

7 Conclusion

LC occurs in children and adults in similar geographic distributions. School-aged and older children as well as males are more likely to be diagnosed with LD, and, among these, children over 10 years old are more likely to develop LC. A prolonged PR interval is the most common manifestation of LC in children, though higher-grade AVB is seen in a significant number of children as well. An appropriate index of suspicion is required for a timely diagnosis, and antibiotics

should be started expeditiously when LD, and especially when LC, is encountered. Temporary transvenous pacing is a relatively common treatment modality during the recovery period, with the great majority of patients experiencing significant improvement of LC within days and resolution of LC within weeks.

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