

Isolated left bundle branch block progressing to complete heart block and asystole: A novel presentation of a desmin mutation



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Introduction

Isolated left bundle branch block (LBBB) is a conduction abnormality found in some healthy adults, but it is rare in the pediatric population.^{1,2} Electrocardiographic analysis of large cohorts of healthy children has failed to identify this entity.³ This discrepancy may be due to the fact that adults are predisposed to age-related degeneration of the conduction system or may have undetected ischemic or valvular heart disease or cardiomyopathy.¹ Chiu and colleagues⁴ studied cardiac conduction disturbances in 432,166 children (age group 6–20 years) and mentioned 1 case with isolated LBBB. Agrawal and colleagues⁵ reported a 2-year-old, healthy African-American female subject who was incidentally discovered to have isolated LBBB that persisted in a follow-up of 3 years with no clinical sequelae. However, no genetic testing was performed.

In this case report, we discuss an 11-year-old Caucasian female subject who presented with chest tightness and dizziness and was discovered to have an LBBB. She subsequently presented 6 months later with complete heart block and asystole. Genetic testing revealed a heterozygous mutation in the *DES* gene, which encodes a protein essential for the structural integrity and mechanosignaling of skeletal, cardiac, and smooth muscle.⁶

Case report

An 11-year-old Caucasian female patient with a history of asthma presented to our cardiology clinic with chest tightness and dizziness. Her initial electrocardiography (ECG) showed an LBBB (Figure 1). Her family history was negative for sudden cardiac death or metabolic diseases. Initial testing, including troponins, complete blood count, and complete metabolic panel, was unremarkable. Her echocardiogram was normal with no evidence of a restrictive

or dilated cardiomyopathy. A cardiopulmonary stress test demonstrated good exercise tolerance with mild chest tightness at peak exercise. Pre- and post-stress ECGs demonstrated findings of LBBB consistent with her initial ECG. A 24-hour Holter monitor, followed by a 30-day continuous ambulatory cardiac telemetry monitor, exhibited normal atrioventricular (AV) conduction with interventricular conduction delay.

Six months later, the father found the patient in her bed pulseless and unconscious. The father resuscitated the patient. The initial rhythm strip in the emergency room revealed complete heart block with a slow underlying escape rhythm at 20 beats per minute (Figure 2). A temporary pacing lead was placed, followed by a transvenous dual-chamber pacemaker. An electrophysiology study was considered to map the location of the block but ultimately was not performed. In her critically ill state, the risks of an electrophysiology study were felt to outweigh the benefit. Subsequent follow-up visits in clinic revealed complete dependency on the pacemaker with no underlying escape rhythm. Whole exome gene sequencing unveiled that the patient harbored a R454W mutation in the *DES* gene. Negative samples from both parents led to the conclusion that this was a de novo mutation. Cardiac magnetic resonance imaging (MRI) was not performed because an incompatible pacemaker was selected and placed under emergent conditions prior to the discovery of her diagnosis. However, serial echocardiograms continue to show no evidence of a developing cardiomyopathy.

Discussion

An isolated LBBB without evidence of a cardiomyopathy on imaging is rare but, when present, can be associated with a desminopathy. Pathologic mutations in the *DES* gene resulting in a myofibrillar myopathy are coined “desminopathy.” The classic patient presents with lower-extremity skeletal muscle weakness that ascends proximally, with eventual cardiac involvement. However, as in our case and as many as 22% of cases, patients present with an isolated cardiomyopathy or conduction disturbance without skeletal muscle involvement.⁶ Cardiac conduction defects are seen in 39% of asymptomatic carriers, but typically occur in patients

KEYWORDS Left bundle branch block; Complete heart block; Desminopathy; Syncope; Pacemaker
(Heart Rhythm Case Reports 2018;4:184–186)

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KEY TEACHING POINTS

- An isolated left bundle branch block is a rare conduction abnormality in the pediatric population and when present is typically pathologic.
- Desminopathies are genetic mutations that encode a protein essential for the structural integrity of skeletal, cardiac, and smooth muscle. Clinically, desminopathies present with a wide range of variability and severity, with almost a quarter of cases presenting with an isolated cardiomyopathy or conduction disturbance without skeletal muscle involvement.
- The main cause of death in all desminopathies is a cardiac arrhythmia.
- The 2012 updated guidelines for device-based therapy for cardiac rhythm abnormalities from the American Heart Association, Heart Rhythm Society, and American College of Cardiology suggest the consideration of permanent pacemaker placement for neuromuscular diseases with any degree of atrioventricular block, with or without symptoms, due to the progressive nature of the disease.
- The clinician should have a high index of suspicion for a genetic defect associated with conduction abnormalities and order an appropriate genetic workup early on because recognition of certain mutations, such as a desminopathy, may sway the provider to place a pacemaker sooner.
- When placing a pacemaker, the clinician should select a magnetic resonance imaging (MRI)-compatible device, as this is the imaging modality most sensitive for detecting disease progression. If the patient already has an MRI-incompatible pacemaker, echocardiography may be used for surveillance.

already diagnosed with a cardiomyopathy or skeletal myopathy.⁶ Patients with LBBB and right bundle branch block can progress to develop complete heart block, but the rate at which this occurs is variable.⁷ In these cases, as was the case in our patient, a junctional or ventricular escape rhythm may emerge but cannot always be relied upon.

More than 50 different *DES* mutations have been discovered.⁶ The type of *DES* mutation and the inheritance pattern affect the clinical manifestations and disease course.⁶ Our patient had a de novo R454W mutation. The rare published cases of the R454W mutation have an autosomal dominant inheritance pattern. A notable case is a father, son, and daughter who developed total AV block at ages 19, 17, and

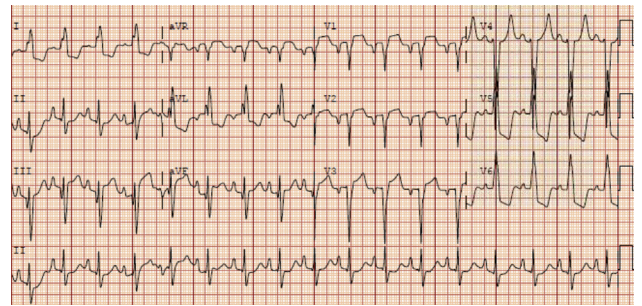


Figure 1 Initial electrocardiogram (ECG) from emergency department visit for evaluation of syncope. ECG shows sinus rhythm, left bundle branch block, possible biatrial enlargement, and nonspecific ST-segment changes.

9, respectively. All 3 died of cardiac complications while in their 20s and 30s; only 1 had skeletal manifestations.⁸ Subsequent analysis found that the R454W mutation had a more detrimental effect on the architecture of intercalated disks than other *DES* mutations, potentially explaining this mutation's more severe course.⁹ Determining our patient's prognosis proves difficult, because of the limited cases of R454W mutations and wide range of phenotypes even within the same family.⁹ Two meta-analyses cited disparate mortality rates at 26% at 49 ± 9.3 years and 17.8% at 58.0 ± 6.5 years.^{6,7} However, neither stratified by mutations or inheritance patterns.

The main cause of death for all desminopathies is cardiac.⁶ Therefore, the clinician should consider ordering a genetic workup early, as placement of a pacemaker is lifesaving. Treatment is geared toward early diagnosis and prevention of cardiac arrest. Our patient suffered a cardiac arrest and qualified for a pacemaker. The 2012 updated guidelines for device-based therapy for cardiac rhythm abnormalities from the American Heart Association, Heart Rhythm Society, and American College of Cardiology suggest the consideration of permanent pacemaker placement for neuromuscular diseases with any degree of AV block, with or without symptoms, due to the progressive nature of the disease.¹⁰ Consensus in the literature is to select an MRI-compatible pacemaker, as cardiac MRI is the most sensitive imaging modality for monitoring disease progression.⁹ In cases in which the patient has an MRI-incompatible pacemaker, serial echocardiograms are recommended for surveillance of disease progression.

Conclusion

Mutations in the *DES* gene are important to include in the differential diagnosis for an isolated LBBB with an otherwise

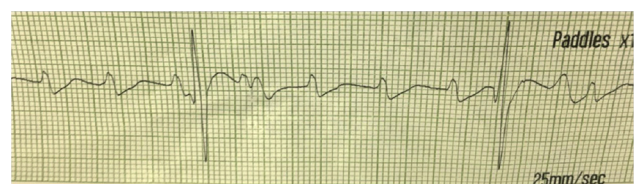


Figure 2 A rhythm strip obtained after sudden cardiac arrest. Rhythm strip shows complete heart block with a slow underlying escape rhythm at 20 beats per minute.

negative workup because of the potential for associated conduction disturbances to rapidly progress to complete heart block and asystole. Early recognition of a genetic defect associated with conduction abnormalities, such as a desminopathy, may lead the provider to the lifesaving intervention of inserting a pacemaker sooner.

Acknowledgments

The authors thank the patient and her parents for all their continued support. They were an invaluable source of information.

References

1. Rabkin SW, Mathewson FA, Tate RB. Natural history of left bundle-branch block. *Br Heart J* 1980;43:164–169.
2. Hardarson T, Arnason A, Eliasson GJ, Palsson K, Eyjolfsson K, Sigfusson N. Left bundle branch block: prevalence, incidence, follow-up and outcome. *Eur Heart J* 1987;8:1075–1079.
3. Niwa K, Warita N, Sunami Y, Shimura A, Tateno S, Sugita K. Prevalence of arrhythmias and conduction disturbances in large population-based samples of children. *Cardiol Young* 2004;14:68–74.
4. Chiu SN, Wang JK, Wu MH, Chang CW, Chen CA, Lin MT, Wu ET, Hua YC, Lue HC. Cardiac conduction disturbance detected in a pediatric population. *J Pediatr* 2008;152:85–89.
5. Agrawal H, Zimmerman F, Naheed Z. Isolated left bundle branch block in a toddler. *Case Rep Cardiol* 2014;2014:464–467.
6. Van Spaendonck-Zwarts KY, Van Hessem L, Jongbloed JDH, Jongloed JD, de Walle HE, Capatanaki Y, van der Kooij AJ, van Langen IM, van den Berg MP, van Tintelen JP. Desmin-related myopathy. *Clin Genet* 2011;80:354–366.
7. Wahbi K, Béhin A, Charron P, Dunand M, Richard P, Meune C, Vicart P, Laforet P, Stokjkovic T, Becane HM, Kuntzer T, Duboc D. High cardiovascular morbidity and mortality in myofibrillar myopathies due to DES gene mutations: a 10-year longitudinal study. *Neuromuscul Disord* 2012;22:211–218.
8. Otten E, Asimaki A, Maass A, van Langen IM, van der Wai A, de Jonge N, van den Berg MP, Saffiz JE, Wilde AA, Jongbloed JD, van Tintelen JP. Desmin mutations as a cause of right ventricular heart failure affect the intercalated disks. *Heart Rhythm* 2010;7:1058–1064.
9. Strach K, Sommer T, Grohé C, et al. Clinical, genetic, and cardiac magnetic resonance imaging findings in primary desminopathies. *Neuromuscul Disord* 2008;18:475–482.
10. Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Thorac Cardiovasc Surg* 2012;144:e127–e145.