Becker muscular dystrophy associated with sarcomeric hypertrophic cardiomyopathy in a paediatric patient: a case report

Paola Dolader 1, Ella Field1,2, Anna Sarkozy3, and Juan Pablo Kaski 1,2*

1Centre for Inherited Cardiovascular Diseases, Great Ormond Street Hospital, Great Ormond Street, London WC1N 3JH, UK; 2Institute of Cardiovascular Science, University College London, London WC1N 1EH, UK; and 3The Dubowitz Neuromuscular Centre, Department of Neuropathology, Great Ormond Street Hospital, Great Ormond Street, London WC1N3JH, UK

Received 8 November 2018; first decision 14 January 2019; accepted 28 June 2019; online publish-ahead-of-print 13 July 2019

Background

Becker muscular dystrophy (BMD) is a neuromuscular disorder associated with myocardial involvement. The most frequent presentation is dilated cardiomyopathy. There have been isolated reports of hypertrophic cardiomyopathy (HCM) in association with BMD, but it is unclear whether these patients had an additional aetiology.

Case summary

A 10-year-old boy was diagnosed with BMD having presented with a history of muscular pain during exercise and elevated serum creatine kinase levels. A cardiac screening was arranged and the echocardiogram confirmed an asymmetric septal hypertrophy. Given the unusual finding of HCM in this patient with BMD, we performed genetic testing for HCM-causing mutations and identified a likely pathogenic variant in heterozygosis in the beta-myosin heavy chain gene.

Discussion

This case highlights the importance of considering additional aetiologies of cardiac disease in the presence of infrequent phenotypic expressions in neuromuscular disorders.

Keywords

Cardiomyopathy • Hypertrophic • Muscular dystrophy • Sarcomere • Phenotype • Genetics • Case report

Learning point

• This case highlights the importance of considering additional aetiologies of cardiac disease in the presence of infrequent phenotypic expressions in neuromuscular disorders.

Introduction

Becker muscular dystrophy (BMD) is an X-linked neuromuscular disorder caused by mutations in the dystrophin gene and characterized by progressive muscle weakness. Myocardial involvement is less frequent among patients with BMD than in those with Duchenne muscular dystrophy, and most commonly takes the form of a dilated cardiomyopathy. There have also been isolated reports of hypertrophic cardiomyopathy (HCM) in association with BMD, but it is unclear whether these patients had an...
additional aetiology for the observed left ventricular hypertrophy.1–3 Here, we report a case of a child with BMD coexisting with sarcomeric HCM.

**Timeline**

| Time         | Events                                                                 |
|--------------|------------------------------------------------------------------------|
| June 2016    | Suspected neuromuscular disorder due to a history of high serum creatine kinase and muscular pain during exercise. |
| August 2016  | Genetic testing confirmed an in-frame deletion of exon 45–48 of the dystrophin gene |
| September 2016 | The echocardiogram showed hypertrophic cardiomyopathy                   |
| March 2017   | Genetic testing identified a likely pathogenic variant in the beta-myosin heavy chain gene |

**Case presentation**

A 10-year-old boy was diagnosed with BMD having presented to the neuromuscular clinic with a history of muscular pain during exercise and elevated serum creatine kinase levels (2495 U/L). Targeted neuromuscular examination revealed bilateral calf hypertrophy, decreased ankle joint range, and very mild weakness in hip abduction and adduction (Medical Research Council (MRC) scale power Grade 4), with preserved muscle strength in all other muscle group. He was asymptomatic from a cardiovascular point of view and his cardiovascular examination was unremarkable. Genetic testing confirmed an in-frame deletion of exon 45–48 of the dystrophin gene (DMD c.6439-72951_7098 + 1309del; p.Glu2147_Lys2366del hemizygosis). Following the diagnosis, cardiac screening was arranged as per the standards of care.4–6 A 12-lead electrocardiogram showed sinus rhythm with normal PR interval for his age, normal QRS axis, voltage criteria for biventricular hypertrophy with pathological Q waves inferolaterally (Figure 1). The echocardiogram showed asymmetric septal hypertrophy affecting primarily the anteroseptal wall and extending more distally towards the apex. Maximal left ventricular wall thickness was 18 mm at the mid-septum. The left ventricular cavity was relatively small and globally hyperdynamic. Left ventricular diastolic performance was normal and left atrial dimensions were also normal. There was no systolic anterior motion of the mitral valve or left ventricular outflow tract obstruction at rest (Figure 2). A cardiac magnetic resonance imaging was performed, confirming an asymmetric septal hypertrophy affecting primarily the basal and mid septum with a maximal left ventricular wall thickness of 18 mm and no left ventricular outflow tract obstruction (Figure 3A). There was patchy late gadolinium enhancement of the hypertrophied myocardium (Figure 3B).

Given the unusual finding of HCM in this patient with BMD, we explored the possibility of an additional aetiology for the left ventricular hypertrophy. Genetic testing for HCM-causing mutations was performed on a 104-gene panel, including the sarcomere protein gene, and identified likely pathogenic variants in heterozygosis in the beta-myosin heavy chain gene (MYH7).
Family screening for this mutation has been recommended but has not been undertaken to date. The only family member with a history of cardiac disease was the maternal grandfather, who was reported to have undergone a heart transplant due to cardiac sarcoidosis and had died in his forties as a result of subsequent rejection. There was no history of premature cardiac disease or sudden cardiac death in any other family members.

Figure 2 The echocardiogram showed asymmetric septal hypertrophy affecting primarily the anteroseptal wall and extending more distally towards the apex. Maximal left ventricular wall thickness was 18 mm at the mid-septum.

Figure 3 (A) Cardiac magnetic resonance imaging showing an asymmetric septal hypertrophy affecting primarily the basal and mid septum with a maximal left ventricular wall thickness of 18 mm. (B) Patchy gadolinium enhancement of the hypertrophied myocardium.

The patient remains asymptomatic from a cardiac point of view without treatment, with no progression of his wall thickness on his follow-up echocardiograms at 1 year. As the concomitant diagnosis of BMD and sarcomeric HCM has not been previously reported in childhood, it is unclear how and whether this combination will affect his prognosis, but he will require regular cardiac follow-up.
Conclusion

We present a patient with BMD and sarcomeric HCM, representing the first report of a paediatric patient affected with BMD and with sarcomeric HCM. His neuromuscular presentation is in keeping with BMD with no features suggestive of MHY7 gene-related congenital myopathy.

The combination of neuromuscular symptoms and left ventricular hypertrophy should prompt a search for alternative differential diagnoses, including inborn errors of metabolism such as glycogen storage diseases or, in an adult, Fabry disease. This case, however, highlights the importance of considering additional aetiologies of cardiac disease in the presence of infrequent phenotypic expressions in neuromuscular disorders. Although isolated cases of HCM have been previously described in patients with BMD, the present case suggests that this is likely to be a concomitant disorder rather than a cardiac manifestation of BMD.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Acknowledgements

All contributors meet the criteria for authorship.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

References

1. Hayashi Y, Ikeda U, Ogawa T, Miyashita H, Sekiguchi H, Arahata K, Shimada K. Becker-type muscular dystrophy associated with hypertrophic cardiomyopathy. Am Heart J 1994;128:1264.
2. Park OY, Ahn Y, Park WS, Lim JH, Park HW, Kim JH, Hong YJ, Kim W, Jeong MH, Cho JG, Park JC, Lee MC, Kang JC. Rapid progression from hypertrophic cardiomyopathy to heart failure in a patient with Becker’s muscular dystrophy. Eur J Heart Fail 2005;7:684–688.
3. Tandon A, Taylor MD, Cripe LH. Co-occurring Duchenne muscular dystrophy and hypertrophic cardiomyopathy in an adult with atypical cardiac phenotype. Cardiol Young 2015;25:355–357.
4. Bushby K, Finkel R, Binkirrant EJ, Case LE, Clemens PR, Cripe L, Kaul A, Kinnett K, McDonald C, Pandya S, Payshy J, Shapiro F, Tomeszko J, Constantin C; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77–93.
5. Finsterer J, Stollberger C. Cardiac involvement in Becker muscular dystrophy. Can J Cardiol 2008;24:786–792.
6. Yilmaz A, Sechtem U. Cardiac involvement in muscular dystrophy: advances in diagnosis and therapy. Heart 2012;98:420–429.

Lead author biography

After finishing paediatric residency, Paola Dolader completed Paediatric Cardiology training at Vall d’Hebron Hospital in Barcelona. She was always been interested in inherited cardiovascular diseases and currently performing a clinical fellowship in the Inherited Cardiovascular Diseases Centre at Great Osmond Street Hospital in London.