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Brief Report

Resolution of severe cardiomyopathy in infantile Pompe disease

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Abstract Infantile Pompe disease is a rare inborn error of metabolism characterized by severe hypertrophic cardiomyopathy and generalised hypotonia occurring in infancy. We present a case of an infant with severe hypertrophic cardiomyopathy that resolved after treatment with enzyme replacement therapy.

Keywords: Pompe Disease; cardiomyopathy; enzyme replacement therapy; glycogen storage disease 2; lysosomal acid maltase deficiency; hypertrophic cardiomyopathy

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Infantile Pompe disease is a rare inborn error of metabolism characterised by severe hypertrophic cardiomyopathy and generalised hypotonia occurring in infancy. The prognosis is quite poor, with the median age of death being <9 months of age and the overwhelming majority dying within the first year of life.[1]

Case report

A 3-month-old girl presented to the emergency department with a 2-week history of vomiting and poor weight gain. The mother reported that the patient had previously been diagnosed with an "enlarged heart" at another institution and was started on propranolol but had no further work-up. The mother sought a second opinion because the symptoms were persisting.

Initial work-up included an electrocardiogram revealing diffuse high-voltage QRS complexes and a short PR interval of 90 ms. Echocardiogram on admission showed an obstructive hypertrophic cardiomyopathy with massive concentric left ventricular hypertrophy and moderate left ventricle mid-cavity obstruction with a peak gradient of 46 mmHg. In addition, the patient had diffuse mild hypotonia.

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A metabolic work-up was initiated. Dried blood spot assay revealed reduced acid alpha glucosidase activity suggestive of Pompe disease. Subsequent gene testing confirmed the diagnosis of Pompe disease with three separate heterozygous gene mutations associated with Pompe disease. First, a single nucleotide change was found within the first intron of the GAA gene (c.-32-13 T > G). Second, a single nucleotide change (c.1841 C > A) in exon 13 was noted. Third, there was a single nucleotide change (c.1856 G > A) in exon 13. The patient was started on alpha-glucosidase enzyme replacement therapy in the form of Myozyme™ IV every 2 weeks. Myozyme™ was transitioned to Lumizyme™ at 1 year of age. Propranolol was continued throughout.

At the most recent follow-up, the patient was 18 months old and had been on enzyme replacement therapy for 15 months. There was significant gradual improvement in left ventricular hypertrophy. At presentation, the left ventricle diastolic posterior wall thickness z-score was 6.7 and the interventricular septum diastolic wall thickness z-score was 6.3 (Fig 1). At the most recent follow-up, the left ventricle diastolic posterior wall thickness z-score was 2.9 and the interventricular septum diastolic wall thickness z-score was 1.2, and there was no mid-cavity or left ventricle outflow tract obstruction (Fig 2). The patient now has mild hypotonia but is otherwise asymptomatic with normal neurodevelopment.

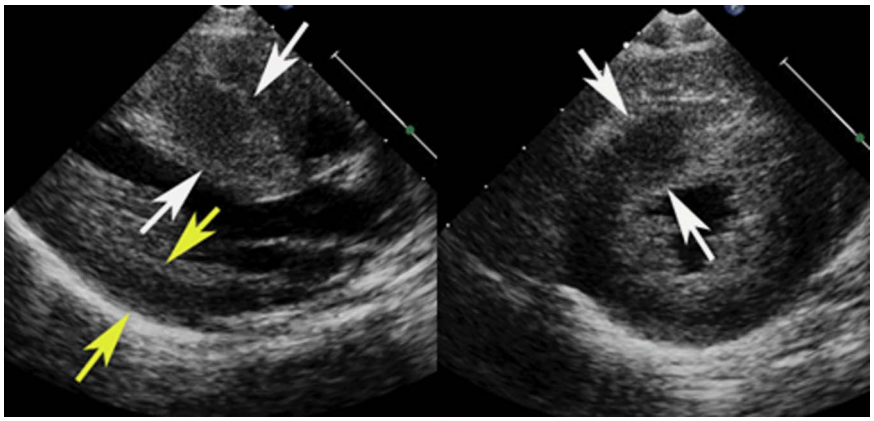

Figure 1.
Echocardiogram at presentation. Left ventricular echocardiographic images (long axis on left and short axis on right) demonstrate dramatic concentric hypertrophy. Note the markedly hypertrophied interventricular septum (white arrows) and posterior left ventricular wall (yellow arrows) during diastole.

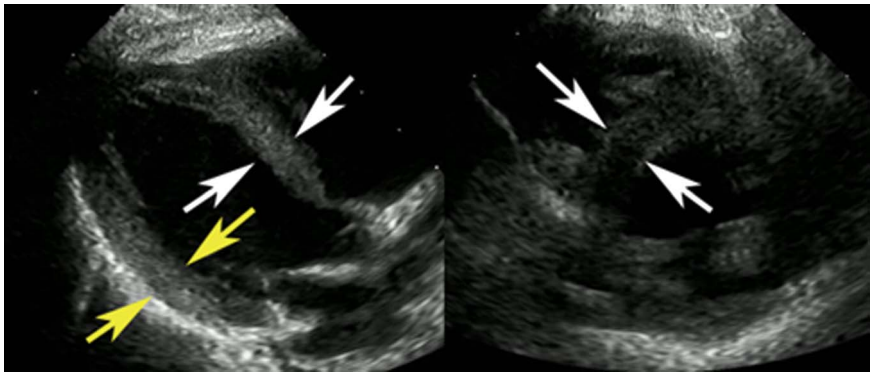

Figure 2.
Echocardiogram after 15 months of enzyme replacement therapy. Left ventricular echocardiographic images (long axis on left and short axis on right) show marked improvement in concentric hypertrophy. Note how much thinner the interventricular septum (white arrows) and posterior left ventricular wall (yellow arrows) are during diastole.

Discussion

Infantile Pompe disease is rapidly progressive, typically resulting in end-stage heart failure secondary to obstructive hypertrophic cardiomyopathy leading to death in the first year of life. This case report presents a patient with severe cardiomyopathy secondary to infantile Pompe disease who showed dramatic improvement on enzyme replacement therapy.

Recent international studies have shown promise with the use of enzyme replacement therapy in infantile Pompe disease; however, very little has been published about this topic in the United States of America.[2–6] Although enzyme replacement therapy is not without risk,[7,8] this case demonstrates that benefit can be obtained in severe infantile Pompe disease, including resolution of severe cardiomyopathy. Continued studies that characterise the risks and benefits of such therapy in infantile Pompe disease are warranted.

Conclusions

Cardiac manifestations can markedly improve in infantile Pompe disease with the use of enzyme replacement therapy. Continued long-term monitoring of these patients is warranted to not only guide treatment, but also to better understand long-term outcomes in patients receiving enzyme replacement therapy beginning in infancy.

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Conflicts of Interest

None.

REFERENCES

1. Kishnani PS, Hwu WL, Mandel H, Nicolino M, Yong F, Corzo D. Infantile-Onset Pompe Disease Natural History Study Group, A retrospective, multinational, multicenter study on the natural history of infantile-onset Pompe disease. J Pediatr 2006; 148: 671–676.
2. Amartino HM, Cavagnari BM. Enzyme replacement therapy in the infantile form of Pompe disease: Argentinean experience in a seven-year follow up case. Arch Argent Pediatr 2012; 110: 323–327.
3. Chakrapani A, Vellodi A, Robinson P, Jones S, Wraith JE. Treatment of infantile Pompe disease with alglucosidase alpha: the UK experience. J Inherit Metab Dis 2010; 33: 747–750.
4. Chen CA, Chien YH, Hwu WL, et al. Left ventricular geometry, global function, and dyssynchrony infants and children with Pompe cardiomyopathy undergoing enzyme replacement therapy. J Card Fail 2011; 17: 930–936.
5. Chen LR, Chen CA, Chiu SN, et al. Reversal of cardiac dysfunction after enzyme replacement in patients with infantile-onset Pompe disease. J Pediatr 2009; 155: 271–275; e2.
6. Klinge L, Straub V, Neudorf U, et al. Safety and efficacy of recombinant acid alpha-glucosidase (rhGAA) in patients with classical infantile Pompe disease: results of a phase II clinical trial. Neuromuscul Disord 2005; 15: 24–31.
7. Case LE, Hanna R, Frush DP, et al. Fractures in children with Pompe disease: a potential long-term complication. Pediatr Radiol 2007; 37: 437–445.
8. McDowell R, Li JS, Benjamin DK Jr, et al. Arrhythmias in patients receiving enzyme replacement therapy for infantile Pompe disease. Genet Med 2008; 10: 758–762.