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Successful heart transplantation from a donor with Ullrich congenital muscular dystrophy

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Abstract

Heart transplantation is the most effective therapy for children with end-stage heart disease; however, its use is limited by the number of donor organs available. This shortage may be further compounded by concerns about organ quality, leading to refusal of potential donor organ offers. We report on the successful transplantation and 5 year follow-up of a heart from a donor with Ullrich congenital muscular dystrophy (UCMD). The candidate was critically ill at the time of the transplant and the donor organ was declined repeatedly on the match run list due to concerns about organ quality, despite having normal cardiac function by echocardiography on minimal inotropic support. We believe the diagnosis of “muscular dystrophy” in the donor combined with a lack of understanding about the specifics of the diagnosis of UCMD enabled our candidate to receive a primary offer for this organ. We are unaware of any previous reports of the use of a heart from a donor with UCMD for orthotopic heart transplantation in adults or children.

Keywords

pediatric; heart; transplant; donor selection; donor evaluation; organ shortage

Case report

A 5 year-old, 16 kg male with a history of idiopathic dilated cardiomyopathy and nonsustained ventricular tachycardia was admitted to our institution with fatigue, decreased oral intake, and poor output. The day after admission he decompensated further and he was intubated, placed onto inotropic support, and listed for urgent heart transplantation. A Levitronix® CentriMag biventricular assist device (BiVAD) was placed the next day and the patient's clinical status improved. The BiVAD was removed 12 days post-implantation after marked improvement was noted in ventricular function and the patient's clinical condition. However, over the next 10 days the patient had worsening clinical status with return of severe biventricular dysfunction culminating in ventricular fibrillation arrest. CPR and direct current shock therapy were utilized and the patient was placed onto extracorporeal

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membrane oxygenation. In the hours preceding his cardiopulmonary arrest and placement onto ECMO, a donor heart became available.

The donor was a 7-year old, 27 kg male with a diagnosis of UCMD. He used nighttime ventilator support at home and suffered respiratory distress with resultant cardiorespiratory arrest with one hour of reported cardiopulmonary resuscitation. Echocardiogram performed as part of the donor evaluation process showed a structurally normal heart with left ventricular ejection fraction of 61% and shortening fraction of 32% on dopamine 2 mcg/kg/min and T4 infusion. Troponin I was 0.03mg/mL and ECG was normal. Our candidate was third in the match run for this donor; however the two candidates ahead of him turned down the organ citing the refusal code 830 - "donor age or quality." Of the 25 candidates on the match run, there were only 2 other provisional acceptances and 13 refusals citing code 830. Because of the paucity of literature on cardiac involvement in UCMD, we urgently contacted an expert on this rare condition who confirmed that long-term follow-up of a cohort of cases of UCMD (some into the fourth decade of life), including serial echocardiographic evaluation, had not identified cases of clinical cardiomyopathy (personal communication, Professor Francesco Muntoni, Director of the Dubowitz Neuromuscular Centre, UCL Institute of Child Health and Great Ormond Street NHS Trust). Based on this information, the donor organ was accepted for transplantation.

The patient underwent successful transplantation and did not require mechanical circulatory support post-transplantation. Intra-operative echocardiogram showed good systolic ventricular function, as did all follow-up studies. The immediate post-transplant course was complicated by a peri-transplant stroke, posterior reversible encephalopathy syndrome, systemic hypertension, pancreatitis, renal tubular acidosis, and gross motor debilitation; however the patient was discharged to rehabilitation 4 weeks after transplant and subsequently to home. His initial catheterization on day 14 showed a mildly elevated right atrial pressure of 8 mmHg with cardiac index of 4.1 L/min/m² and mixed venous saturation of 70%.

At most recent follow-up, approximately 5 years after transplant, the patient was doing well, living at home and attending school at appropriate grade level for age. He is clinically well with no concern for dysrhythmias or heart failure. He has a benign rejection history and no known chronic allograft vasculopathy. All echocardiograms have shown normal left ventricular shortening fraction with qualitatively normal right ventricular systolic function. Most recent hemodynamics show a mean right atrial pressure of 4 mmHg with a pulmonary capillary wedge pressure of 8 mmHg and cardiac index of 3.9 L/min/m².

Discussion

The use of heart transplantation is limited by the number of donor organs available [1]. Many strategies have been tried in an effort to expand the donor pool including the use of marginal donors, donation after cardiac death, and warm blood preservation [2-5]. One common reason for refusal of a potential organ is concern about the quality of the organ [6]. Whereas muscular dystrophies typically do not spare the heart, Ullrich congenital muscular dystrophy (UCMD) is a rare genetic disorder caused by mutations in genes encoding subunits of collagen VI and characterized by contractures of the proximal joints, hyperlaxity of the distal joints, generalized weakness, kyphoscoliosis, and respiratory failure [7, 8]. Patients generally present from birth to 12 months of age and respiratory function often declines after 6 years of age [9]. To date no cases of UCMD with cardiac involvement have been reported [9, 10] However, due to UCMD's rarity, relatively few studies of the disease have been performed. In a review of the literature, we found 11 case series describing the clinical and genetic findings of UCMD patients, with between 5 and 15 patients (average

age 12.4 years) in each report [7,8,11-19]. Nine of these specifically commented on cardiac status and reported no abnormalities. In another case series of 49 patients with either UCMD or Bethlem myopathy (another collagen VI myopathy), there was no mention of cardiac involvement [20].

On first pass we believe it was reasonable to be wary of accepting a heart from a donor with a diagnosis of “muscular dystrophy.” However, because our patient was critically ill at the time of this organ offer and the donor assessment revealed normal cardiac function on minimal inotropic support, we felt compelled to learn more about the diagnosis of UCMD. Fortunately we were quickly able to review literature and consult a world's expert on UCMD to determine that the potential benefits of transplantation in this setting likely outweighed the risks. By taking these steps to further investigate UCMD, we were able to comprehensively assess the quality of this donor heart and provide a much needed treatment for our patient.

We believe this case is the first to document the successful transplantation of a donor organ with UCMD. More importantly, this case highlights the importance of gathering complete knowledge about the donor, including information about chronic conditions that may initially cause concern for organ acceptance, prior to making a decision about organ acceptance. This may be especially important in the pediatric population where unusual genetic syndromes are more prevalent. Given the shortage of donor organs and the high waitlist mortality in pediatric candidates, an aggressive and proactive approach to evaluation of donor organs is required, especially when the donor carries a rare diagnosis of uncertain significance for the organ donation process. In this case, consultation with an international expert on a very rare diagnosis led to successful use of a donor organ, which might otherwise have been discarded as unsuitable for transplantation.

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References

1. Johnson MR, Meyer KH, Haft J, Kinder D, Webber SA, Dyke DB. Heart Transplantation in the United States, 1999-2008. *American Journal of Transplantation*. 2010; 10:1035–1046. [PubMed: 20420651]
2. Chen JM, Russo MJ, Hammond KM, Mancini DM, Kherani AR, Fal JM, Mazzeo PA, Pinney SP, Edwards NM, Naka Y. Alternate Waiting List Strategies for Heart Transplantation Maximize Donor Organ Utilization. *Ann Thorac Surg*. 2005; 80:224–8. [PubMed: 15975371]
3. Bruschi G, Colombo T, Oliva F, Morici N, Botta L, Cannata A, Frigerio M, Martinelli L. Orthotopic heart transplantation with donors greater than or equal to 60 years of age: a single-center experience. *European Journal of Cardio-thoracic Surgery*. 2011; 40:e55–e61. [PubMed: 21450480]
4. Boucek MM, Mashburn C, Dunn SM, Frizell R, Edwards L, Pietra B, Campbell D. Pediatric Heart Transplantation after Declaration of Cardiocirculatory Death. *N Engl J Med*. 2008; 359:709–14. [PubMed: 18703473]
5. Marasco SF, Kras A, Schulberg E, Vale M, Lee GA. Impact of Warm Ischemia Time on Survival After Heart Transplantation. *Transplantation Proceedings*. 2012; 44(5):1385–1389. [PubMed: 22664020]
6. Gridelli B, Remuzzi G. Strategies for making more organs available for transplantation. *N Engl J Med*. 2000; 343:404–410. [PubMed: 10933740]

7. Nadeau A, Kinali M, Main M, Jimenez-Mallebrera C, Aloysius A, Clement E, North B, Manzur AY, Robb SA, Mercuri E, Muntoni F. Natural history of Ullrich congenital muscular dystrophy. *Neurology*. 2009; 73(1):25–31. [PubMed: 19564581]
8. Giusti B, Lucarini L, Pietroni V, Lucioi S, Bandinelli B, Sabatelli P, Squarzoni S, Petrini S, Gartioux C, Talim B, Roeleins F, Merlini L, Topaloglu H, Bertini E, Guicheney P, Pepe G. Dominant and Recessive COL6A1 Mutations in Ullrich Scleroatonic Muscular Dystrophy. *Ann Neurol*. 2005; 58:400–410. [PubMed: 16130093]
9. Lampe AK, Bushby KMD. Collagen VI related muscle disorders. *J Med Genet*. 2005; 45:673–685. [PubMed: 16141002]
10. Finisterer J, Ramaciotti C, Wang CH, Wahbi K, Rosenthal D, Duboc D, Melacini P. Cardiac Findings in Congenital Muscular Dystrophies. *Pediatrics*. 2010; 126:538. [PubMed: 20679303]
11. Nalini A, Gayathri N, Santosh V. Ullrich congenital muscular dystrophy: Report of nine cases from India. *Neurol India*. 2009; 57:41–5. [PubMed: 19305075]
12. Demir E, Ferreiro A, Sabatelli P, Allamand V, Makri S, Echenne B, Maraldi M, Merlini L, Topaloglu H, Guicheney P. Collagen VI status and clinical severity in Ullrich congenital muscular dystrophy: phenotype analysis of 11 families linked to the COL6 loci. *Neuropediatrics*. 2004; 35(2):103–12. [PubMed: 15127309]
13. Jimenez-Mallebrera C, Maioli MA, Kim J, et al. A comparative analysis of collagen VI production in muscle, skin and fibroblasts from 14 Ullrich congenital muscular dystrophy patients with dominant and recessive COL6A mutations. *Neuromuscul Disord*. 2006; 16(9–10):571–582. [PubMed: 16935502]
14. Mercuri E, Yuva Y, Brown SC, Brockington M, Kinali M, Jungbluth H, Feng L, Sewry CA, Muntoni F. Collagen VI involvement in Ullrich syndrome: a clinical, genetic, and immunohistochemical study. *Neurology*. 2002; 58(9):1354–9. [PubMed: 12011280]
15. Nonaka I, Une Y, Ishihara T, Miyoshino S, Nakashima T, Sugita H. clinical and histological study of Ullrich's disease (congenital atonic-sclerotic muscular dystrophy). *Neuropediatrics*. 1981; 12(3): 197–208. [PubMed: 7290342]
16. Kim J, Jimenez-Mallebrera C, Foley AR, Fernandez-Fuente M, Brown SC, Torelli S, Feng L, Sewry CA, Muntoni F. Flow cytometry analysis: a quantitative method for collagen VI deficiency screening. *Neuromuscul Disord*. 2012 Feb; 22(2):139–48. [PubMed: 22075033]
17. Lampe AK, Zou Y, Sudano D, O'Brien KK, Hicks D, Laval SH, Charlton R, Jimenez-Mallebrera C, Zhang RZ, Finkel RS, Tennekoon G, Schreiber G, van der Knaap MS, Marks H, Straub V, Flanigan KM, Chu ML, Muntoni F, Bushby KM, Bönnemann CG. Exon skipping mutations in collagen VI are common and are predictive for severity and inheritance. *Hum Mutat*. 200829(6): 809–22. [PubMed: 18366090]
18. Baker NL, Mörgelin M, Peat R, Goemans N, North KN, Bateman JF, Lamandé SR. Dominant collagen VI mutations are a common cause of Ullrich congenital muscular dystrophy. *Hum Mol Genet*. 2005; 14(2):279–93. [PubMed: 15563506]
19. Demir E, Sabatelli P, Allamand V, Ferreiro A, Moghadaszadeh B, Makrelouf M, Topaloglu H, Echenne B, Merlini L, Guicheney P. Mutations in COL6A3 cause severe and mild phenotypes of Ullrich congenital muscular dystrophy. *Am J Hum Genet*. 2002; 70(6):1446–58. [PubMed: 11992252]
20. Briñas L, Richard P, Allamand V, et al. Early onset collagen VI myopathies: Genetic and clinical correlations. *Ann Neurol*. 2010; 68(4):511–20. [PubMed: 20976770]

Abbreviations

BiVAD	biventricular assist device
UCMD	Ullrich's congenital muscular dystrophy