Received: 9 May 2019 | Revised: 24 June 2019 | Accepted: 26 August 2019

DOI: 10.1111/petr.13585

CASE REPORT

WILEY

Pediatric heart transplant from an incompletely treated influenza A-positive donor

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Abstract

There is a shortage of pediatric donor hearts for waitlisted children, and yet nearly 50% of organs offered are not transplanted. Donor quality is often cited as a reason for declining organs offered from donors infected with influenza, presumably due to concern about disease transmission at transplant leading to severe disease. We previously described an excellent outcome after heart transplant from a donor infected with influenza B that had been treated with a complete course of oseltamivir. In this report, we describe a similar outcome after transplantation of an organ from an influenza A-positive donor with symptomatic disease incompletely treated with oseltamivir. Due to the availability of effective antiviral treatment, we suggest that influenza A is also a manageable donor infection that need not preclude heart placement.

KEYWORDS
heart transplant, influenza, oseltamivir, pediatric

1 | CASE

Our patient was a 13-month-old male baby at the time of transplant. He was born with hypoplastic left heart syndrome and underwent staged palliation with a Norwood procedure with Sano modification followed by a bidirectional Glenn procedure at 5 months of age. His Norwood procedure was complicated by bilateral vocal cord paresis requiring tracheostomy. He remained hospitalized until his Glenn procedure and was discharged on a home ventilator from which he was subsequently weaned. He developed clinical heart failure from moderate-to-severe tricuspid insufficiency with associated ventricular dysfunction several months after his Glenn procedure that resulted in the initiation of an aggressive medical regimen including spironolactone, furosemide, enalapril, and carvedilol, with doses being optimized for weight gain. Over the following months, he required several hospitalizations for viral infections, each leading to worsening of congestion but never requiring inotropic support. He was fully immunized, including having received 2 doses of the inactivated influenza vaccine at 10 and 12 months of age in accordance with current national guidelines. He additionally received monthly injections of palivizumab. One month prior to transplant, he developed severe congestion with poor perfusion, anuria, and reduced responsiveness. This resulted in admission to the critical care unit, where a milrinone infusion was started along with reinstitution of positive pressure ventilation via his tracheostomy. Due to this episode of decompensation without an obvious precipitating event, he was evaluated for transplant and listed status 1A. His blood type was O with elevated anti-A and anti-B isohemagglutinin titers, so he was listed for ABO compatible transplant. He remained hospitalized through transplant for resistant congestion despite his milrinone infusion and enteral heart failure regimen. After one month on the waitlist, a heart became available. Our patient developed fever on the day of the organ offer with the only additional symptom being nasal congestion. A respiratory viral panel obtained with the fever was reported the next day to be positive for coronavirus and rhino/enterovirus.

The organ match run initially included our patient at sequence 5. Four prior institutions declined the organ for "organ quality" using code 830. The donor had presented after a respiratory arrest following a short illness with a cough. As part of the evaluation for the respiratory arrest, the donor's nasopharyngeal secretions exhibited influenza A positivity by polymerase chain reaction testing. Chest

radiograph demonstrated diffuse pulmonary interstitial markings consistent with pneumonitis or edema, and a bronchoscopy demonstrated purulent secretions with mixed gram-negative and gram-positive organisms, but no pathologic organisms were found. Cardiac structure and function were normal by echo. The donor progressed to brain death over the next 36 hours, during which time 3 doses of oseltamivir were administered. When our center accepted the organ, a dose of oseltamivir was administered to our recipient, and twice-daily dosing was continued for 10 days post-transplant. Graft function was excellent immediately after transplant, and an endomyocardial biopsy on post-transplant day 14 revealed no rejection. Respiratory viral panels on our recipient were positive for coronavirus and rhino/enterovirus but negative for influenza on post-transplant days 5 and 10 and negative for all viruses on post-transplant day 15. He never developed symptoms of a respiratory infection and was discharged from the hospital on post-transplant day 15. His immunosuppression was not modified in response to his potential donor influenza exposure, including 1 day of solumedrol 10 mg/kg, 5 days of 1.5 mg/kg/dose thymoglobulin and solumedrol 3 mg/kg/d, 60 mg/kg/dose mycophenylate twice daily, and tacrolimus twice daily starting on post-transplant day 5 with a target range of 10-12. Additional immunosuppression consisted of 2 g/kg of intravenous immunoglobulin for a positive T- and B-cell crossmatch on post-operative day 1.

2 | DISCUSSION

The perception remains that the nearly 20% pediatric heart transplant waitlist mortality is largely due to donor organ shortage despite the fact that nearly 50% of available organs are declined and not placed.[1,2] Expansion of what is considered an acceptable organ is likely to be the most efficient way to address this problem.[3] A significant number of donor hearts declined by pediatric transplant centers due to donor quality issues are subsequently transplanted at other centers with outcomes comparable to organs not previously declined for donor quality, suggesting our ability to identify quality donor organs should be refined.[4] Furthermore, over 15% of waitlisted patients that decline an organ offer that is subsequently placed do not receive another organ offer before expiring or being removed from the waitlist for deterioration.[4] This led Davies et al to conclude that some in the pediatric heart transplant community may be waiting for the "perfect" organ rather than taking one that is "good enough," and that this negatively impacts waitlist outcomes.

Donor infectious disease impacts organ acceptance practices for donation due to concern for transmission to an immunocompromised host at the time of transplant. This reluctance does not extend to either cytomegalovirus or Epstein-Barr virus status as these are both common and, at least for cytomegalovirus, there is effective medical therapy. Organ donation from hepatitis C-positive donors to hepatitis C-negative recipients is increasingly utilized in adult transplantation due to the recent development of highly effective antiviral agents, which can then be used to treat the recipient.[5] Given the expanded repertoire of anti-infectious agents against viruses and other microorganisms, infections previously thought to render a donor heart unacceptable for transplantation are being reconsidered.

Influenza is one such disease. Influenza caused over 100 childhood deaths in the United States yearly in the period 2010-2015, all potential organ donors.[6] Although severe infection in a kidney recipient from an influenza-positive donor has been reported, such reports are rare.[7] A recent survey of the American Society of Transplantation Infectious Disease Community of Practice demonstrated that more than 90% of practitioners would recommend accepting non-lung organs from influenza-positive donors.[8] Multiple adult centers have reported positive outcomes with transplants from influenza-positive donors, but uncertainty remains regarding the duration of donor and recipient antiviral therapy necessary to prevent disease transmission.[9]

We recently published the first case report of a pediatric patient receiving a heart transplant from a donor with symptomatic influenza B disease. The donor had received a full course of oseltamivir and was documented to have tested negative for influenza B before organ harvest.[10] Our recipient received a 10-day course of oseltamivir therapy, and disease transmission did not occur. The present case documents that the use of oseltamivir in donor and recipient, even without a complete course in the donor, may be adequate to mitigate the risk of influenza A transmission. There has been uncertainty in cases in which donors are positive for influenza as to need for and duration of therapy of both the donor and recipient.[9] In 2010, the American Society for Transplantation, The Transplantation Society, and Canadian Society of Transplantation endorsed recommendations that influenza-positive donors be considered for non-lymphoid solid organ transplant, and, while acknowledging inadequate supporting data, suggested a full course of antiviral therapy be used prior to organ procurement whenever possible.[11] It is also of note that the Center for Disease Control maintains updated information in regard to specific antiviral resistances reported, which may play a role in antiviral therapy choice.[12] However, in 2009, one United Kingdom group reported success with 13 solid organ transplants from H1N1-positive donors, of which three had not completed therapy, and only seven of the recipients received any antiviral therapy. They reported no cases of influenza A viral transmission, and our experience also supports this approach in pediatric heart transplant.[13] This suggests that an inability to completely treat a donor with a full oseltamivir course may not be a contraindication to transplant, and using organs of incompletely treated hosts may expand the pool of donor organs.

AUTHORS' CONTRIBUTIONS

All authors have participated sufficiently in this work to be listed as such. No unlisted persons were involved directly with the writing of this manuscript, and the manuscript is not being submitted to or published by any other publication.

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How to cite this article: Smith CJ, McCulloch MD, Shirley D-A, L'Ecuyer TJ. Pediatric heart transplant from an incompletely treated influenza A-positive donor. *Pediatr Transplant*. 2019;23:e13585. https://doi.org/10.1111/petr.13585