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SARS-CoV-2 Antibody Serology Testing in a 3-Month-Old Organ Donor: A Case Report and Review of Available Literature

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a highly prevalent infectious disease. Currently, organs are not being transplanted from donors who are SARS-CoV-2 positive. It remains unclear as to how to differentiate active from recovered patients. We report our recent experience of a 3-month-old deceased organ donor who died as the result of an anoxic brain injury after a cardiopulmonary arrest (presumed sudden infant death syndrome). The child was born to a mother presumed to have coronavirus disease 2019. The donor tested negative for SARS-CoV-2 reverse transcriptase–polymerase chain reaction and positive for SARS-CoV-2 immunoglobulin A antibodies. We suspect this is the first known report of its kind and noteworthy for the organ donation and transplantation community.

WE report the circumstances of a 3-month-old, 5.1 kg African American male deceased organ donor in Texas. The child was born in early February 2020 and died in May 2020. The donor was admitted after a cardiorespiratory arrest, initially presumed to be sudden infant death syndrome. On the morning of admission, the donor experienced an unknown duration of downtime and approximately 1 hour of cardiopulmonary resuscitation until return of circulation. The donor's adoptive mother reported the child had been well the previous evening with the exception of emesis 30 minutes after an evening feeding. On the morning of admission, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcriptase–polymerase chain reaction (RT-PCR) testing was performed on nasopharyngeal and oropharyngeal swabs, which were negative. However, the sample was positive for human rhinovirus. The chest radiograph from the day of admission demonstrated patchy airspace disease in bilateral upper lobes. A computed tomography scan of the abdomen and pelvis included visualization of the lower lobes of the lungs and the radiologist appreciated bilateral lower lobe atelectasis, left greater than right. The donor progressed to brain death and was declared brain dead by clinical examination, including apnea examination and electroencephalogram, on hospital day 3. Authorization for organ and tissue donation was obtained from the donor's adoptive mother after brain death declaration.

PRESENTING CONCERN AND CLINICAL FINDINGS

The donor medical history was notable only for prematurity of 36 weeks' gestation requiring a 1-month neonatal intensive care unit admission without identifiable sequela. On the day of birth, the donor's birth mother was admitted to the hospital complaining of respiratory distress and was considered a person under investigation for coronavirus disease 2019 (COVID-19), but confirmatory SARS-CoV-2 testing was not performed because of a lack of available testing at that time. The donor had been adopted at birth and had remained in the care of the adoptive mother after neonatal intensive care unit discharge. The adoptive mother provided the medical and social history interview at time of organ donation. The interview also revealed that the donor's birth mother had a history of homelessness and illicit drug use, including during pregnancy. The donor did not receive breast milk from the birth mother nor any other source at any time. No other medical or social information was available for the donor's birth mother or biological father, and neither could be contacted to obtain additional information; for this reason, the donor was categorized as Public Health Service Increased Risk. During a subsequent interview, the donor's

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adoptive mother reported that while the donor was in her care, she was fostering 2 other children, a 1-year-old and a 3-year-old who were siblings. During the month of March, when the donor was 1 month old, the 1-year-old had diarrhea and a fever, and the 3-year-old had vomiting, cough, and a fever. Both children were treated for ear infections and responded well. The adoptive mother reports that she felt tired and congested during this same time period, but this was thought to be related to her own immunosuppressive disorder as well as caring for 3 young children. None of the members of the household were under investigation or tested for SARS-CoV-2.

Standard donor serology and nucleic acid testing was performed with cytomegalovirus total antibody and Epstein-Barr virus immunoglobulin (Ig) G antibody positivity. SARS-CoV-2 RT-PCR testing, having been performed on hospital day 1, was not repeated. Given that the donor's birth mother had been reported to be a person under investigation for COVID-19 at the time of the donor's birth 3 months earlier, the decision was made to perform SARS-CoV-2 IgA/IgG/IgM antibody testing on donor blood. SARS-CoV-2 IgA was performed on the EUROIMMUN (Lübeck, Germany) enzyme-linked immunosorbent assay and SARS-CoV-2 IgG/IgM testing was performed on the Gold Standard Diagnostics (Davis, Calif, United States) enzyme-linked immunosorbent assay.

Donor management and organ evaluation were initiated after authorization for organ and tissue donation on hospital day 3. Echocardiogram, chest radiography, and bronchoscopy were performed.

The donor had 2 echocardiograms, the first with an ejection fraction of 57% and the second with an ejection fraction of 69%. The other chambers showed normal function and morphology. The heart was successfully transplanted into a 4-month-old male.

The donor's chest radiograph showed increased right upper and left lower atelectasis. Oxygenation was adequate with a partial pressure of oxygen of 98 mm Hg on 40% fractional inspired oxygen. The bronchoscopy revealed normal anatomy and mildly inflamed bronchus lining. A gram stain showed many white blood cells, no squamous epithelial cells, and no organisms seen. After recruitment, the partial pressure of oxygen improved to 378 mm Hg on 100% fractional inspired oxygen and a repeat radiograph showed some improvements. Despite the improvement of the donor's lung function over the course of donor management, the lungs were declined for the only 3 candidates appearing on the lung match run.

Donor liver function tests were initially elevated but decreased quickly. Despite this improvement in function, the liver was declined by all recipient centers.

Donor kidney function was affected by hypoxemia as a result of the donor's significant downtime and cardiopulmonary resuscitation with an admission creatinine of 0.65 mg/dL and urine output of 40 cc/h. Creatinine peaked at 1.27 mg/dL on hospital day 3 and decreased to 0.77 mg/dL before organ recovery on hospital day 5. Urine output remained within normal limits throughout the hospitalization. The kidneys were transplanted en bloc into an adult (male) candidate.

ORGAN TRANSPLANT RECIPIENT CONDITION AND OUTCOMES

The heart recipient was a 4-month-old, 6-kg (0.85:1 donor weight matching) child with a diagnosis of idiopathic dilated cardiomyopathy and end-stage heart failure requiring high-dose (0.5 mcg/kg/min) milrinone therapy. The total cardiac ischemic time was 95 minutes, the crossmatch was negative by flow cytometry testing, and his postoperative echocardiogram showed normal biventricular systolic function. He underwent induction of immunosuppression using antithymocyte globulin and received a total dose of 6 mg/kg over the span of 7 days using CD3 (T-cell) counts as a dosing guide. He transitioned without event to a chronic immunosuppression regimen consisting of tacrolimus, mycophenolate mofetil, and 3 months of low-dose oral prednisone. He experienced no symptoms throughout his posttransplant course to suggest SARS-CoV-2 infection, and he was discharged without any posttransplant complications 14 days posttransplant. Over the initial 9 months of his transplant course, he has maintained normal cardiac function and has been void of any infectious complications of any kind despite development of valgancyclovir-associated leukopenia that has since resolved.

The kidney recipient is a 71-year-old man with type I diabetes mellitus. He was on dialysis at the time of transplant. He received induction with antithymocyte globulin to a total of 4.5 mg/dL. He received a standard steroid taper with a target dose of 5 mg of prednisone daily at 1 month. He was also started on mycophenolic acid at 720 mg twice daily and tacrolimus starting day 3 posttransplant. He experienced some slow graft function early on but did not require posttransplant dialysis. He was discharged on postoperative day 6. His estimated glomerular filtration rate at the time was 12 mL/min. This improved over the course of the next 3 months to an estimated glomerular filtration rate of 57 mL/min. The recipient developed no symptoms to suggest transmission of SARS-CoV-2. He was tested several times for SARS-CoV-2 via PCR testing and was negative. These tests were performed on day of admission to the hospital for transplant. They were also performed several times throughout the first 9 months posttransplant for either symptomatic rule-out or before procedures. The PCR tests were all negative. Almost 9 months posttransplant the patient had a SARS-CoV-2 IgG antibody test, and those results were also negative.

DISCUSSION

In this case report, the absence of SARS-CoV-2 virus was determined through a negative RT-PCR test and negative IgG and IgM antibodies. However, IgA antibodies were detected, resulting in the decline of organs by some transplant programs. Other programs were more confident and ultimately accepted these organs, resulting in transplantation of the donor's heart and kidneys.

As with all areas of health care, the COVID-19 pandemic has had significant impact on organ donation and transplantation. Deceased donor testing for SARS-CoV-2 has enabled organs to

be safely transplanted due to transplant centers being reassured of minimal risk to infectious spread of the virus.

As the number of people reportedly infected with SARS-CoV-2 has increased to over 30 million in the United States, organ procurement organizations are evaluating potential donors to exclude those with active infection and to consider those who are at different stages of recovery. In those cases whereby the donor or immediate companion is known to have tested positive for SARS-CoV-2, organ procurement organizations and transplant centers may consider the use of organs from these donors. As described in a recent article reviewing 6 organ donors with a history of COVID-19 infection, from which 13 organs were transplanted, there are no reports of transmission of COVID-19 from donor to recipient to date, and organs from donors who have recovered from COVID-19 should be considered for transplant [1]. SARS-CoV-2 antibody testing of the donor, in addition to RT-PCR testing, may provide additional information regarding stage of recovery from the infection. This information may enable transplant programs to weigh the risk of transmission and accept those organs for the candidates awaiting transplantation at their centers.

The donor, having tested positive for SARS-CoV-2 IgA antibody, although having been tested negative for SARS-CoV-2 IgM and IgG antibodies and negative for SARS-CoV-2 by RT-PCR testing, initially led us to believe that the donor must have had some maternal-fetal antibody transfer vs a primary exposure event.

IgA antibodies are produced as a response to infection and can be found as a first line of defense in mucosal secretions and as a second line of defense in serum [2]. As it pertains to SARS-CoV-2, IgA acts as an immune barrier and can neutralize the virus before it binds to the epithelial cells [3].

IgG antibodies can be transferred across the placenta to fetus to provide protection to the infant, but IgM and IgA are thought to not be able to cross the placenta [4]. In this case, the donor did have evidence serum IgA specific to SARS-CoV-2, likely representing infectious exposure that led to an immune response, as opposed to passive spread of protective antibody.

Zeng et al [5] performed IgG and IgM antibody testing on 6 infants born to mothers with COVID-19 pneumonia. However, the authors did not test the infants for the presence of IgA antibody. They found IgG and IgM antibody levels in the infants that correlated with the level of IgG and IgM antibodies in the mothers [5].

It is likely that this particular donor had a primary exposure and cleared the virus. Moreover, the updated clinical history in the corresponding recipients demonstrates that the use of organs from a pediatric donor with evidence of previous SARS-CoV-2 infection may be safe for transplant.

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