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The Journal of Heart and Lung Transplantation

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Case Anecdotes, Comments and Opinions

Sotrovimab in pediatric cardiac transplant recipients with SARS-CoV2 infection

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Cardiac transplant recipients infected with SARS-CoV2 represent a high-risk cohort for a severe and potentially life-threatening course of coronavirus disease 2019 (COVID-19). Conway et al. have recently shown that 21% among all pediatric SARS-CoV2-infected post-heart transplantation patients were hospitalized, 7% required intensive care, and 1% were mechanically ventilated.[1] However, data on potential treatment options in pediatric COVID-19 patients are still sparse. Recently, the National Institutes of Health (NIH) recommended the use of SARS-CoV2 antibody therapy in immunocompromised patients with mild to moderate COVID-19. An additional pediatric consensus statement advocated the use of SARS-CoV2 monoclonal antibody (mAB) therapy in order to avoid severe illness in infected adolescents ≥ 12 years.[2] Among the available mABs, sotrovimab is a newly developed immunoglobulin G-1 (IgG-1kappa) mAB which provides sufficient passive immunization against SARS-CoV2, including the B.1.1.529 (omicron) variant, and recently received emergency authorization by regulatory authorities.[3]

We herein report on 9 pediatric cardiac transplant recipients infected with SARS-CoV2 who received treatment with sotrovimab (Table 1). In all patients, infections were confirmed by quantitative polymerase chain reaction (qPCR). Children ≥ 20 kg received the full dose of sotrovimab recommended for adults (500 mg) intravenously[4] and children < 20 kg received 250 mg. Sotrovimab was administered to all nonhospitalized patients over a period of 30 to 60 minutes in the pediatric emergency department. After an additional surveillance period of 4 hours under close monitoring patients were allowed to go home.[5] Of note, sotrovimab treatment was initiated within the first 72 hours after the onset of symptoms in all of our patients.

Six out of 9 patients were younger than 12 years and thus received sotrovimab off-label after informed consent had been obtained from their parents/legal caregiver. Six patients were vaccinated prior to their SARS-CoV2 infection (all Comirnaty, Biontech/Pfizer, Germany). Only 1 patient required hospitalization for 4 days. The patient received sotrovimab upon admission and was hospitalized for surveillance due to moderate respiratory symptoms (cough and mild dyspnea) without the need for oxygen or noninvasive respiratory support. Five other patients had only mild respiratory symptoms (cough, common cold-like symptoms, fatigue, no dyspnea) and 3 patients were only minimally symptomatic (rhinitis). Of note, results of routine cardiac examinations (troponin T, echocardiogram, electrocardiogram) provided stable results in all patients, indicating the absence of any cardiac involvement during SARS-CoV2 infection. None of the patients experienced any adverse reactions or side effects, such as allergic symptoms or anaphylaxis,[4,5] and all patients showed full recovery within 3 weeks.

While in our cohort only 1 out of 9 patients was hospitalized (~11% as compared to the previously reported 21%),[1] conclusions regarding potential efficacy of sotrovimab in pediatric cardiac transplant recipients cannot yet be drawn due to the following reasons: First, our small observational cohort lacks an appropriate control group. Second, changes in hospitalization rates may become evident over time as providers gain more experience with SARS-CoV2-infected pediatric heart transplant patients. In addition, viral variants likely affect efficacy of different mAB treatments.

In conclusion, this is the first report that indicates feasibility and safety of sotrovimab application within the first 72 hours after the onset of symptoms in SARS-CoV2-infected pediatric cardiac transplant recipients, including those <12 years. However, further systematic investigations

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Abbreviations: COVID-19, coronavirus disease 2019; Mab, monoclonal antibody; NIH, National Institutes of Health; qPCR, quantitative polymerase chain reaction

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https://doi.org/10.1016/j.healun.2022.05.003

Table 1 Clinical Characteristics of Pediatric Cardiac Transplant Recipients Treated With Sotrovimab for SARS-CoV2 Infection

Patient #	Age	Age at HTx	Diagnosis leading to HTx	Immunosuppressive medication	Sars-CoV2 vaccination	SARS-CoV2 symptoms	Hospitalized	Therapy
1	15	8	LQTS (CACNA1C)	Tac 3.7 ng/mL Eve 7.7 ng/mL	2x	Mild respiratory symptoms	No	Sotrovimab 500 mg
2	17	13	d-TGA, Mustard	Tac 3.2 ng/mL Eve 6.3 ng/mL	2x	Moderate respiratory symptoms	Yes, 4 days, no respiratory support	Sotrovimab 500 mg
3	11	2	DCM	Tac 3.7 ng/mL Eve 4.7 ng/mL	2x	Mild respiratory symptoms	No	Sotrovimab 250 mg
4	7	6	DCM	Tac 5.8 ng/mL MMF	None	Mild respiratory symptoms	No	Sotrovimab 250 mg
5	6	1	ccTGA, VSD hypo-plastic aortic arch	Tac 9.1 ng/mL Eve 7.6 ng/mL	None (prior COVID-19 infection)	Minimal respiratory symptoms	No	Sotrovimab 250 mg
6	4	0	DCM	Eve 7.6 ng/mL Ciclo 108 ng/mL	1x	Mild respiratory symptoms	No	Sotrovimab 250 mg
7	9	6	DCM	Eve 6.9 ng/mL Ciclo 84 ng/mL	3x	Minimal respiratory symptoms	No	Sotrovimab 500 mg
8	12	7	DCM	Eve 6.1 ng/mL Ciclo 88 ng/mL	3x	Minimal respiratory symptoms	No	Sotrovimab 500 mg
9	11	4	LVOTO/AoVS/EFE	Tac 6.1 ng/mL Eve 6.1 ng/mL	None	Mild respiratory symptoms	No	Sotrovimab 500 mg

Abbrevations: AoVS, aortic valve stenosis; CACNA1C, calcium voltage-gated channel subunit alpha1 C; ccTGA, congenitally corrected transposition of the great arteries; Ciclo, ciclosporin A; DCM, dilative cardiomyopathy; d-TGA, dextroposition of the great arteries; EFE, endocardial fibroelastosis; Eve, everolimus; HTx, heart transplantation; LQTS, long QT-syndrome; LVOTO, left ventricular outflow tract obstruction; MMF, mycophenolate mofetil; mustard, mustard operation; Tac, tacrolimus; VSD, ventricular septal defect.

in multi-institutional cohorts are warranted in order to establish safety and efficacy of sotrovimab treatment in immunocompromised pediatric patients after heart transplantation.

Author contribution

Collection and analysis of data (all authors). Preparation of the manuscript (HS, SCW, FD). Review for important intellectual content and approval of the final manuscript (all authors).

Disclosure statement

All authors declare that do not have any conflicts of interest to disclose. There is no funding for this study.

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A modified heterotopic heart transplant technique to bridge patients with "fixed" pulmonary hypertension: A case report

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Advanced heart failure (AHF) management includes heart transplantation (HT), ventricular assist devices, and palliative care.[1,2] Heart transplantation is the gold standard therapy for most of these patients. However, some specific situations preclude a patient with AHF from successfully undergoing orthotopic HT. Pulmonary hypertension (PH) is one of these conditions due to the higher incidence of right ventricle (RV) failure after HT in patients with "fixed" PH. Left ventricular assist device (LVAD) implantation is the current approach for these patients worldwide.[3,4] Nevertheless, the high cost of the devices could limit their use. Heterotopic HT (HHT) is an alternative for treating patients with PH with limited results.[5] Copeland et al[6] described a new technique for HHT: a biological left ventricular assist transplant (bio-LVA). Recently, we have reported a new 2-stage approach to assist the left ventricle (LV) by introducing a modification to Copeland's HHT technique.[7] The aim of this report is to describe the first case of modified bio-LVA in a patient with AHF and PH. The study was approved by the local Ethics Committee (CAAE: 20026018.6.0000.0068).

A 53-year-old man with ischemic cardiomyopathy due to an extensive anterior wall infarction was referred for HT evaluation. After the acute coronary event (16 months earlier), patient was hospitalized with acute decompensated heart failure. At admission, clinical signs of hypervolemia and hypoperfusion were detected, a B-type natriuretic peptide level of 1486 pg/ml, and negative high-sensitive troponin. Echocardiogram showed LV ejection fraction of 30% and moderate RV dysfunction. Patient was initially treated with intravenous diuretics, nitroprusside, and dobutamine. No other organ dysfunctions were detected. Table 1 shows pulmonary arterial pressure (PAP) parameters at baseline and after optimized hemodynamic and volume management.

Considering a "fixed" PH, despite intensive inotropic support and decongestion, orthotopic HT was contraindicated. Because LVAD is not available at public health services in our country, HHT as a bio-LVA was proposed.

The procedure was performed using standard sternotomy. After aortic cross clamping, custodial cardioplegia was infused. The donor heart was prepared by closing the inferior vena cava and the 2 right pulmonary veins. The first stage started with the anastomosis between both left atria, using standard running sutures. Donor's aorta was anastomosed with the recipient's ascending aorta in a "lateral to end" fashion, and then anastomosis from the donor's pulmonary trunk and recipient's right atrium was performed. The aortic cross clamp was removed, and the superior vena cava (SVC) was anastomosed with the recipient's SVC in an "end to end" fashion. Surgery had no complications with an ischemic time of 170 minutes. Patient received dobutamine 10 mcg/kg/min, milrinone 0.3 mcg/kg/min, and intra-aortic balloon pump to wean from bypass. Recovery in the intensive care unit lasted