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COVID-19 CASE

Heart retransplantation following COVID-19 illness in a heart transplant recipient

Jerome Soquet, MD,[a,1] Natacha Rousse, MD,[a,1] Mouhamed Moussa, MD,[b] Celine Goeminne, MD,[b] Delphine Deblauwe, MD,[b] Fanny Vuotto, MD,[c] François Pontana, MD, PhD,[d] Arnaud Lionet, MD,[e] Romain Dubois, MD,[f] Emmanuel Robin, MD, PhD,[b] and Andre Vincentelli, MD, PhD[a]

From the [a]Univ. Lille, CHU Lille, Department of Cardiac Surgery, F-59000 Lille, France; [b]Univ Lille, CHU Lille, Department of Anesthesia and Intensive Care, F-59000 Lille, France; [c]Univ Lille, CHU Lille, Department of Infectious Diseases, F-59000 Lille, France; [d]Univ Lille, CHU Lille, Department of Cardiovascular Imaging, F-59000 Lille, France; [e]Univ Lille, CHU Lille, Department of Nephrology, F-59000 Lille, France; and the [f]Univ Lille, CHU Lille, Department of Pathology, F-59000 Lille, France.

In November 2018, a 22-year-old woman underwent successful heart transplantation (HT) for giant-cell myocarditis and subsequently presented with pericardial constriction and a sub-diaphragmatic mass around the inferior vena cava in December 2019. A pericardectomy was performed. Biopsies of the sub-diaphragmatic mass revealed an Ebstein–Barr virus–induced lymphoma, which was treated with rituximab and reduced immunosuppression (Table 1). In March 2020, during the coronavirus (CoV) disease 2019 (COVID-19) pandemic, the patient was readmitted for abdominal pain and vomiting. Both tracheal and nasal swab polymerase chain reaction (PCR) tests were positive for severe acute respiratory syndrome CoV 2 (SARS-CoV-2) infection. A chest computed tomography scan showed a right-sided pleural effusion. Severe biventricular dysfunction was found, but endomyocardial biopsy ruled out acute humoral rejection. The allograft function continued to deteriorate, and acute rejection was suspected; therefore, methylprednisolone and rabbit anti-thymocyte globulin were administered. Shortly after, computed tomography scan showed the onset of a severe pulmonary COVID-19 infection. Subsequently, an anti-retroviral treatment (lopinavir/ritonavir) was introduced. Despite these therapies, the patient's condition worsened, requiring venoarterial extracorporeal membrane oxygenation support. The patient was extubated 16 days later because the pulmonary insult regressed; however, no cardiac recovery was observed. The patient was, therefore, compassionately registered on the waitlist for an emergent HT. At that time, the nasal swab was still PCR positive.

A heart from a marginal donor was proposed, for which no other recipient was found in France mainly owing to a size mismatch. The graft was managed with the Organ Care System (TransMedics, Andover, MA) because (1) the donor was marginal, (2) the duration of the travel was long (3 hours), and (3) we expected technical difficulties removing the first heart graft owing to the 2 previous sternotomies. The perfusion time under the Organ Care System was 370 minutes. Heart retransplantation was uneventful, and cardiopulmonary bypass was successfully weaned after 199 minutes, with low-dose dobutamine. Hemoadsorption with CytoSorb (CytoSorbents Europe GmbH, Berlin, Germany) was used during cardiopulmonary bypass to modulate cytokine activation. The patient was extubated a week later. She was still SARS-CoV-2 PCR positive on the day of intensive care unit discharge, with a normal chest X-ray. The patient was discharged home after rehabilitation at post-operative Day 44, although she was still PCR positive. Histologic examination of the former graft revealed a chronic rejection process. Of note, the SARS-CoV-2 serology tests were negative during the entire hospital stay. We did not measure direct viral activity or viral loads.

Chen et al[1] reported 3 cases of lung transplantation for SARS-CoV-2–related pulmonary fibrosis but in patients with negative PCR. We present the case of a cardiac transplant in the recovery phase of COVID-19 but with evidence of persistent SARS-CoV-2 positivity on PCR testing. Our team considered the young age of the patient for registration on the waitlist for HT and determined that it was ethical because we chose a donor that would not have been otherwise used.[2] To date, the rationale for the use of an organ from a SARS-CoV-2–positive donor remains controversial.[3,4] The optimal pharmacologic management of HT in recipients with COVID-19 is yet to be defined. At the time of retransplantation, it was decided to avoid induction and use higher doses of immunosuppressive drugs (Table 1). The patient's chronic immunosuppressive status may have given her a better chance by avoiding COVID-19 cytokine storm. However, we suspect that rabbit anti-thymocyte globulin may have triggered the pulmonary form of the CoV infection and resulted in the initial deterioration.

[1]These authors have contributed equally to this work.

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Table 1 Immunosuppression Strategies Used

Treatments	After the first HT (November 2018)	Before readmission (December 2019)	During the treatment of lymphoma (January 2020)	During SARS-CoV-2 infection (March 2020)	After the second HT (May 2020)
Induction/acute rejection treatments					
Antibodies	rATG IV 1.5 mg/kg daily (2 days) 1 mg/kg daily (1 day)	N/A	N/A	rATG IV 1.5 mg/kg daily (3 days)	No induction
Corticosteroids	N/A	N/A	N/A	Methylprednisolone IV 500 mg daily (3 days)	
Maintenance treatments					
Calcineurin inhibitor	Tacrolimus q12h from POD 5 onward (target 8—12 ng/ml)	Tacrolimus q12h (target 8—10 ng/ml)	Tacrolimus q12h (target 5—7 ng/ml)	Tacrolimus q12h (target 6—8 ng/ml)	Cyclosporine IV daily (target 250—300 ng/ml) followed by tacrolimus q12h (target 8—12 ng/ml) from POD 5 onward
Anti-metabolite	MMF 500 mg q8h	MMF 750 mg q12h	MPA 180 mg q12h	MPA 360 mg q12h	MMP 1 g q8h
Corticosteroids	Methylprednisolone IV 2 mg/kg daily POD 1 1 mg/kg daily PODs 2—7 Biopsy-guided tapering of prednisone from POD 8 onward	Prednisone 5 mg daily	Prednisone 5 mg daily	Prednisone 30 mg daily	Methylprednisolone IV 2 mg/kg daily POD 1 1 mg/kg daily PODs 2—7 Slow biopsy-guided tapering of prednisone from POD 8 onward
Other relevant treatments	N/A	N/A	Rituximab (4 cycles) 375 mg/m^2 per cycle	Lopinavir/ritonavir q12h (14 days) ECMO (21 days)	Rituximab on hold

Abbreviations: ECMO, extracorporeal membrane oxygenation; HT, heart transplantation; IV, intravenous; MMF, mycophenolate mofetil; MPA, mycophenolic acid; N/A, not applicable; POD, post-operative day; q8h, every 8 hours; q12h, every 12 hours; rATG, rabbit anti-thymocyte globulin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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