Desensitization procedures in heart transplant recipients: a case series

Mia Dubravčić Došen*,
Petra Mjehović,
Dubravka Šipuš,
Maja Čikeš,
Dora Fabijanovi,
Nina Jakuš,
Hrvoje Jurin,
Daniel Lovrić,
Marijan Pašalić,
Ivo Planinc,
Jure Samardžić,
Marija Burek Kamenarić,
Renata Žunec,
Ines Bojanić,
Sanja Mazić,
Branka Golubić Ćepulić,
Željko Čolak,
Hrvoje Gašparović,
Davor Miličić,
Boško Skorić

University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia

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***ADDRESS FOR CORRESPONDENCE**: Mia Dubravčić Došen, Klinički bolnički centar Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Croatia. / Phone: +385-98-9549-898 / E-mail: dubravcic.mia@gmail.com

ORCID: Mia Dubravčić, https://orcid.org/0000-0003-0441-4772 • Dubravka Šipuš, https://orcid.org/0000-0002-5631-0353
Petra Mjehović, https://orcid.org/0000-0003-4908-4674 • Maja Čikeš, https://orcid.org/0000-0002-4772-5549
Dora Fabijanović, https://orcid.org/0000-0003-2633-3439 • Nina Jakuš, https://orcid.org/0000-0001-7304-1127
Hrvoje Jurin, https://orcid.org/0000-0002-2599-553X • Daniel Lovrić, https://orcid.org/0000-0002-5052-6559
Marijan Pašalić, https://orcid.org/0000-0002-3197-2190 • Ivo Planinc, https://orcid.org/0000-0003-0561-6704
Jure Samardžić, https://orcid.org/0000-0002-9346-6402 • Marija Burek Kamenarić, https://orcid.org/0000-0003-2781-4576
Renata Žunec, https://orcid.org/0000-0003-2607-3059 • Ines Bojanić, https://orcid.org/0000-0002-2985-7847
Sanja Mazić, https://orcid.org/0000-0003-4166-6768 • Branka Golubić Ćepulić, https://orcid.org/0000-0002-3067-0414
Željko Čolak, https://orcid.org/0000-0003-0507-4714 • Hrvoje Gašparović, https://orcid.org/0000-0002-2492-3702
Davor Miličić, https://orcid.org/0000-0001-9101-1570 • Boško Skorić, https://orcid.org/0000-0001-5979-2346

Introduction: Human leukocyte antigen (HLA) sensitization is a barrier for successful heart transplantation (HTx), reduces the chance for compatible donors, prolongs waiting time to HTx, and increases the risk of acute rejection and cardiac allograft vasculopathy. Increasing prevalence of HLA sensitization and limitations of current desensitization strategies represent a great challenge in transplantation cardiology[1,2]. Rather than using pretransplant desensitization, in the last several years we have started peritransplant prophylactic therapy after careful selection of acceptable HLA antigen incompatibility. Therapy includes mechanical removal of antibodies, intravenous immunoglobulins (IVIg), and immunosuppressive drugs targeting antibody production[3]. We present a series of four HLA sensitized patients who underwent successful HTx at University Hospital Center Zagreb.

Case 1: 58-year-old male patient with history of two cardiac surgeries (mitral valve replacement in 1993 and coronary artery bypass graft and mitral valve repair in 2009) underwent HTx in September 2018. Due to positive complement-dependent cytotoxicity (CDC) crossmatch and donor-specific antibodies (DSA, anti-HLA antibodies class I), seven procedures of plasmapheresis followed by intravenous immunoglobulins were conducted, starting on the first postoperative day. Initial endomyocardial biopsy (performed on twenty fourth postoperative day) showed no cellular (CMR) or antibody-mediated (AMR) graft rejection, and DSA showed decline in reaction sensitivity during first 6 post-transplant months. In March 2019 endomyocardial biopsy revealed signs of AMR (without clinical correlate) and three plasmapheresis procedures with intravenous immunoglobulins application were performed. Procedures were suspended due to leukopenia, influenza infection and Cytomegalovirus (CMV) viremia. Follow-up biopsy two months later showed no signs of AMR, with further decline in DSA reaction intensity. Treatment was continued with monthly extracorporeal photopheresis (ECP) procedures (25 cycles over the course of 2,5 years). One year after HTx a coronary angiography with optical coherence tomography imaging was performed and it showed signs of intimal hyperplasia. Due to that finding and continuously positive anti-HLA antibodies, everolimus was introduced as fourth immunosuppressant drug (together with tacrolimus, mycophenolate mofetil and prednisone). Latest patients' check-up was in September 2022, there were no signs of heart failure, CMR or AMR, and DSA are still positive, but with low Luminex median fluorescence intensity (MFI) reactions.

Case 2: 44-year-old female patient with end-stage heart failure due to left ventricular noncompaction cardiomyopathy (LVNC) underwent urgent HTx in December 2019. Due to positive anti-HLA DSA (with negative CDC crossmatch), desensitization protocol was performed (five plasmapheresis procedures, intravenous immunoglobulins and rituximab application). Since initial biopsy, performed one month after HTx, showed CMR (class 1R/2) and AMR, and DSA values showed MFI increase, pulse corticosteroid therapy followed by additional five cycles of plasmapheresis and intravenous immunoglobulins was applied. Control biopsy showed resolution of CMR and AMR. Patient attends regular check-ups (latest in September 2022) in which no signs of CMR or AMR were detected, and DSA are positive, but with low MFI reaction.

Case 3: 60-year-old male patient with ischemic cardiomyopathy underwent HTx in February 2020. Due to positive anti-HLA DSA (with negative CDC crossmatch), desensitization protocol was performed (seven plasmapheresis procedures and intravenous immunoglobulins, followed by anti-CMV immunoglobulin application). Early post-transplantation period was marked with prolonged leukopenia, with no other adverse events. Patient attends regular check-ups (latest in September 2022) in which no signs of CMR or AMR were detected, and DSA remain continuously negative.

Case 4: 54-year-old female patient underwent HTx in August 2022 due to end-stage heart failure caused by ischemic cardiomyopathy. Due to positive virtual crossmatch (but prospective CDC crossmatch negative) and anti-HLA DSA, desensitization protocol was started immediately, with first procedure of immunoadsorption prior to the transplantation. Another eight cycles of immunoadsorption were performed in initial postoperative days, followed by application of intravenous immunoglobulins, without adverse events. First endomyocardial biopsy, one month after transplantation, showed no signs of CMR or AMR, with no anti-HLA DSA in follow-up.

Conclusion: Anti-HLA sensitization among heart transplant candidates is a growing problem with significant risk for posttransplant graft dysfunction and death. Strategy that includes virtual crossmatch and peritransplant desensitization therapies allow us to perform transplantation with good clinical outcome.

LITERATURE

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