Case Report

SUCCESSFUL HEART TRANSPLANTATION IN A PATIENT WITH HIGH LEVELS OF ANTI-HUMAN LEUKOCYTE ANTIGEN (HLA) ANTIBODIES - CASE REPORT

Korina Goluza[1], Sanja Konosic[1,2]

[1] School of Medicine, University of Zagreb, Zagreb, Croatia
[2] Clinic of Anesthesiology and Intensive Care, University Hospital Centre Zagreb, Zagreb, Croatia

Author for correspondence: Korina Goluza korinagoluza@gmail.com

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ABSTRACT

Desensitization plays a key role in improving the outcomes of heart transplantation in sensitized patients, who otherwise face prolonged waiting times and an increased risk of rejection and graft failure. We present the case of a woman who developed severe cardiomyopathy after treatment for breast cancer. As transplantation was initially contraindicated due to recent malignancy, she was maintained on mechanical circulatory support. Following remission, she became eligible for transplantation but was identified as highly sensitized. Following a three-year wait for heart transplantation, the multidisciplinary team approved the initiation of a desensitization protocol, which was subsequently followed by heart transplantation upon allocation of a compatible organ.

The procedure was complicated by early graft dysfunction and bleeding, requiring temporary extracorporeal support. The patient underwent a tailored desensitization protocol, which was applied throughout the perioperative course. Nevertheless, the patient recovered well, with preserved graft function, minimal rejection on biopsy, and remained clinically stable during follow-up. In this case report, we present a highly sensitized patient who underwent successful heart transplantation after an extensive desensitization protocol.

Keywords: *Heart transplantation, anti-HLA antibodies, sensitization, desensitization.*

INTRODUCTION

Heart transplantation (HTx) remains a pivotal therapy for patients with end-stage heart failure, but its success is limited in highly sensitized recipients due to the presence of anti-human leukocyte antigen (HLA) antibodies (1,2).

Sensitization, commonly resulting from previous transfusions, pregnancies, ventricular assist device (VAD) implantation, or earlier transplants, represents a significant therapeutic challenge in the transplantation of all solid organs, including the heart.

Sensitized candidates face lower rates of transplantation, and higher risks of delisting or death while on the waiting list. Finding a compatible donor is more challenging and often leads to adverse outcomes pre-transplant. Postoperatively, these recipients are at increased risk for antibody-mediated rejection, cardiac allograft vasculopathy, graft loss, and mortality (3,4).

The goal of desensitization therapy is to increase the likelihood of a negative crossmatch, expand the pool of acceptable donors, and improve post-transplant outcomes. When successful, desensitization can reduce or eliminate previously strong-binding donor-specific antibodies, thereby lowering the calculated panel reactive antibody (cPRA) and widening donor compatibility (5). However, there is currently no consensus on the optimal desensitization protocol for heart transplant recipients. Most protocols have been adapted from renal transplant experience (5,6).

A standardized measure, cPRA, estimates the percentage of donors to which a recipient has high-risk antibodies. The cPRA highlights that antibodies against common HLA antigens exclude a larger proportion of potential donors compared to antibodies against rare antigens. In analyses of transplant registries, candidates with

cPRA >80% demonstrated nearly 70% lower chance of receiving a transplant and more than twofold increased risk of delisting or death compared to those with cPRA ≤10%. In practice, when cPRA exceeds 50%, desensitization strategies are often considered to lower immunologic risk and expand donor access (7,8).

Desensitization therapies aim at multiple levels of the humoral immune response. Antibodies can be targeted through inactivation with intravenous immune globulin (IVIG), removal using plasmapheresis or immunoadsorption, or suppression of production with agents such as rituximab or bortezomib. Immunoadsorption (IA) and plasmapheresis (PP) are two extracorporeal strategies used in desensitization protocols. IA selectively removes immunoglobulins, particularly IgG, and circulating immune complexes through adsorption columns, while preserving most other plasma proteins such as albumin and coagulation factors; thus, no replacement fluid is usually required. In contrast, PP non-selectively eliminates most plasma proteins, including immunoglobulins and coagulation factors, and therefore necessitates mandatory replacement with colloid solutions or fresh frozen plasma. In summary, IA is more specific and spares plasma proteins, whereas PP is less selective but more widely available. Both techniques effectively reduce pathogenic antibodies and immune complexes, thereby lowering the risk of rejection in sensitized transplant candidates (11).

Other strategies, including the use of tocilizumab and daratumumab, remain more experimental and are currently being investigated in small studies and pilot protocols (9).

This case report highlights the challenges of managing a highly sensitized HTx candidate.

CASE REPORT

A 48-year-old woman with a history of breast carcinoma underwent surgical treatment consisting of left-sided mastectomy with axillary lymphadenectomy. Postoperatively, she received adjuvant chemoradiotherapy and hormonal therapy with tamoxifen.

One year after completion of therapy, she developed symptoms and signs of heart failure. She presented with fatigue, dyspnoea, and peripheral oedema, leading to multiple hospitalizations at a regional centre hospital for acute decompensations. Six months after symptom onset, she was referred to the University Hospital Centre (UHC) for advanced heart failure management.

At the UHC, cardiac evaluation revealed dilated cardiomyopathy characterized by restrictive filling and right ventricular volume overload, with a left ventricular ejection fraction (LVEF) below 40% and NYHA class III symptoms, indicative of end-stage toxic cardiomyopathy (TC). Cardiac magnetic resonance imaging confirmed findings consistent with TC, establishing the final diagnosis.

Cardiotoxicity is a well-recognized complication of systemic cancer therapy and thoracic radiotherapy, with variable incidence, reversibility, and clinical presentation. According to current definitions, it is characterized as a decrease in left ventricular ejection fraction (LVEF) by ≥5% to below 55% in the presence of heart failure symptoms, or an asymptomatic decline of ≥10% to below 55% (10). It represents the second leading cause of morbidity and mortality among breast cancer survivors. This patient was exposed to chemotherapy, radiotherapy, and tamoxifen, placing her at increased risk for late cardiotoxicity.

Given her recent malignancy, HTx was initially contraindicated. Therefore, permanent mechanical circulatory support was indicated, and one year after the onset of TC symptoms, the patient underwent implantation of a left ventricular assist device (LVAD, HeartMate 3) as bridge-to-transplant therapy, combined with replacement of the bicuspid atrioventricular valve with a biological prosthesis. The procedure was complicated by surgical bleeding requiring massive transfusion. She remained on long-term LVAD support for 6.5 years, with regular cardiological follow-up and hemodynamic optimization of LVAD settings.

After five years of oncological remission, she became eligible for transplantation and was placed on the Eurotransplant waiting list. Pre-transplant assessment demonstrated high panel reactive antibody (PRA) levels, and despite three years on the list, no compatible donor was available. Consequently, a desensitization approach was pursued. Initial IA was attempted but discontinued due to adverse reactions, and PP was chosen instead.

Upon identification of a suitable donor with an immunologic mismatch considered to be of acceptable risk and a negative prospective crossmatch, the first cycle of PP was performed as part of the immediate pre-transplant preparation.

For this highly sensitized patient, the pre-transplant strategy included standard immunosuppression combined with seven sessions of PP. Adjunctive therapy consisted of intravenous immunoglobulin (IVIG) and Cytotect® (human cytomegalovirus immunoglobulin). In the event of clinical or histological evidence of rejection, eculizumab, a complement inhibitor, was planned as rescue therapy.

Following the induction protocol, the patient underwent orthotopic HTx. However, the perioperative course was complicated by biventricular graft failure, profuse bleeding, and the need for veno-arterial extracorporeal membrane oxygenation (VA-ECMO). On the same day, after admission to the intensive care unit, surgical revision and haemostasis were required because of profuse drainage necessitating massive transfusion.

VA-ECMO was successfully discontinued on the second postoperative day, and she was weaned from vasoactive and inotropic support (adrenaline, milrinone, argipressin) by day six. After a total of 104 hours of mechanical ventilation, the patient was extubated.

Due to high sensitization, eculizumab was introduced early in the postoperative period in addition to standard immunosuppression. PP was contraindicated because of ongoing bleeding, while IA was initially avoided due to a previous adverse reaction. Once bleeding was controlled, a subsequent rise in donor-specific

antibody (DSA) levels prompted initiation of IA a few days later, with appropriate premedication. A total of nine IA sessions were performed and were well tolerated without adverse reactions. Additional courses of IVIG were administered on multiple occasions. Standard immunosuppressive therapy consisted of tacrolimus, methylprednisolone, mycophenolate mofetil and anti-thymocyte globulin, while eculizumab was given in nine doses as part of the desensitization regimen.

In the late postoperative course, patient developed profuse, predominantly serous drainage, an encapsulated apical pleural effusion, and a left-sided pneumothorax. By discharge, the pneumothorax had resolved and drainage was markedly reduced.

Echocardiography showed preserved LVEF (65%) without contractility defects or valvular abnormalities. She was discharged on the 72nd postoperative day with stable graft function.

DISCUSSION

The patient's high level of sensitization was most likely related to perioperative transfusions during LVAD implantation. This created a significant barrier to transplantation, resulting in a prolonged wait and the need for a carefully planned desensitization strategy.

A key feature of this case is the need to adjust desensitization modalities according to clinical tolerance and evolving postoperative complications. Initial IA could not be continued due to adverse reactions, and PP later became contraindicated because of bleeding, requiring a shift in strategy. The combination of IVIG, complement inhibition, and delayed reintroduction of IA allowed for antibody control during a period of early graft dysfunction.

Despite a complex perioperative course, including severe bleeding and transient VA-ECMO support, the patient achieved stable graft function without significant rejection, underscoring the importance of individualized immunologic management and close monitoring in sensitized recipients.

CONCLUSION

This case highlights that even in highly sensitized patients with initially limited treatment options, heart transplantation can be successfully performed. Careful patient selection, meticulous perioperative management, and the application of multimodal desensitization strategies are essential to achieving favourable outcomes. Although desensitization strategies are essential in overcoming immunologic barriers, there is still no standardized approach for cardiac recipients. Most regimens are adapted from kidney transplantation, highlighting the need for clearer evidence and cardiac-specific protocols (5,6). Further research is needed to define standardized protocols and optimize therapy in this complex subgroup.

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