

# Uspješno liječenje kardiogenog šoka uzrokovanog miješanim akutnim stanično- i protutijelima-posredovanim odbacivanjem srčanog presatka

## Successful treatment of cardiogenic shock caused by mixed acute cellular- and antibody-mediated cardiac allograft rejection

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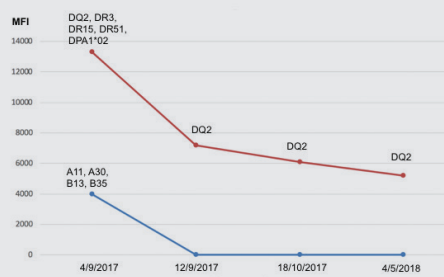
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**Prikaz slučaja:** 18-godišnjakinja je hospitalizirana zbog popuštanja srca tri godine nakon transplantacije srca. Na ehokardiografiji su obje klijetke bile izrazito zadebljanih stijenki i reducirane sistoličke funkcije (ejekcijska frakcija lijeve klijetke, LVEF 30%). Nakon hitne biopsije endomiokarda (Bx) primjeni se pulsna terapija steroidima. Zbog razvoja kardiogenog šoka morali smo postaviti venosko-arterijski ECMO (izvantjelesna membranska oksigenacija). Nalaz Bx pokazao je miješani tip akutnog odbacivanja presatka, tj. protutijelima posredovano odbacivanje stupnja pAMR I (+) i stanično-posredovano odbacivanje stupnja 3R. Luminex® je potvrdio postojanje brojnih donor specifičnih protutijela (DSA) na HLA antigene klase I (A11, A30, B13, B35) i klase II (DR3, DR15, DR51, DQ2, DPA1\*02) s maksimalnim MFI 13000 za anti-DQ2. Odmah je započeto liječenje plazmaferezom, intravenskim imunoglobulinima (IVIg) i antitimocitnim globulinom (ATG). Četvrtog dana na ehokardiografiji su obje klijetke bile normalne debljine stijenki i bolje sistoličke funkcije (LVEF 40%) te je bolesnica uspješno odvojena od ECMO. Krajem drugog tjedna primijenjen je rituksimab. Nakon dva tjedna na kontrolnoj Bx nije bilo stanično-posredovanog odbacivanja, dok je imunohistokemijski nalaz ostao pozitivan. Na koronarografiji su prikazane normalne arterije. Provedeno je još pet ciklusa plazmafereze i ponovljeno

**Case report:** 18-year-old female was hospitalized for acute heart failure three years after a heart transplant. Echocardiography showed thickened walls and reduced systolic function of both ventricles (left ventricular ejection fraction, LVEF 30%). Pulse steroid therapy was started after urgent cardiac biopsy (Bx). Because of the development of cardiogenic shock, a venous-arterial (VA) ECMO (extracorporeal membrane oxygenation) had to be set up. Bx showed a mixed type of acute rejection: antibody-mediated rejection grade pAMR I(+) and cell-mediated rejection grade 3R. Luminex® confirmed the existence of numerous anti-HLA donor specific antibodies (DSA) class I (A11, A30, B13, B35) and class II (DR3, DR15, DR51, DQ2, DPA1\*02) with maximal MFI 13000 for anti-DQ2. Plasmapheresis, intravenous immunoglobulin (IVIg) and antithymocyte globulin (ATG) were immediately initiated. On the fourth day, both ventricles had normal wall thickness and improved systolic function (LVEF 40%). The patient was successfully weaned from ECMO. Rituximab was applied at the end of the second week. Control Bx showed no cell-mediated rejection, while immunohistochemistry remained positive. Coronary angiography was normal. Five additional plasmapheresis cycles were performed and IVIg was administered, whereupon echocardiography showed normal left ventricle size and wall thickness,



**FIGURE 1. Temporal changes of anti-HLA donor-specific antibodies in response to treatment.**

MFI = mean fluorescence intensity; class I = class I anti-HLA donor-specific antibodies; class II = class II anti-HLA donor-specific antibodies

liječenje IVIg-om nakon čega je kontrolna ehokardiografija pokazala lijevu klijetku normalne veličine i funkcije (LVEF 60%) te desnu klijetku normalne veličine i blago reducirane funkcije. Kontrolna Bx ovaj put nije našla znakova niti stanično- niti protutijelima posredovanog odbacivanja. Sedam tjedana od početka liječenja došlo je do negativizacije svih DSA klase I i klase II, osim anti-DQ2 (MFI 6100) (**slika 1**). Bolesnica je nakon 12 mjeseci stabilno, bez znakova odbacivanja i pogoršanja funkcije presatka.

**Zaključak:** Ovaj prikaz ukazuje na važnost primjene mehaničke cirkulacijske potpore u najtežim oblicima popuštanja srca u transplantiranih bolesnika čime „kupujemo“ vrijeme za čekanje na rezultate pretraga i učinak terapije (engl. *bridge-to-decision*, *bridge-to-recovery*). Kombinacijom steroida, plazmafereze, IVIg, ATG i rituksimaba djelovali smo na kompleksne imunološke mehanizme miješanoga, tj. stanično- i protutijelima-posredovanog akutnog odbacivanja srčanog presatka te, u konačnici, omogućili ne samo preživljenje, već i potpuni oporavak bolesnice.<sup>1</sup>

while right ventricle was normal in size but had slightly reduced function. Bx showed no cell- or antibody-mediated rejection. Seven weeks after treatment initiation DSA class I and class II were all negative, except anti-DQ2 (MFI 6100) (**Figure 1**). 12 months later the patient is stable, without signs of rejection or graft function deterioration.

**Conclusion:** This case shows the importance of acute mechanical circulatory support in heart transplant patients with critical heart failure and, therefore, gaining additional time to run tests and wait for therapeutic effects (i.e. bridge-to-decision, bridge-to-recovery). By combining steroids, plasmapheresis, IVIg, ATG and rituximab, we interacted with complex immune mechanisms of mixed cell- and antibody-mediated acute graft rejection, and ultimately provided not only survival, but also the complete recovery of the patient.<sup>1</sup>

#### LITERATURE

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