Odbacivanje srčanog presatka posredovano protutijelima – prikaz slučaja

Antibody-mediated rejection in heart transplantation: a case presentation

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RECEIVED: October 3, 2016

ACCEPTED: October 10, 2016

KLJUČNE RIJEČI: odbacivanje presatka posredovano protutijelima, transplantacija srca.

KEYWORDS: antibody-mediated rejection, heart transplantation.

CITATION: Cardiol Croat. 2016;11(10-11):403-404. | **DOI:** http://dx.doi.org/10.15836/ccar2016.403

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Prikaz slučaja: Dvije godine nakon presađivanja srca (HTx), 25-godišnjak je hospitaliziran zbog nepodnošenja napora i bolova u epigastriju. Ehokardiografija je pokazala akineziju anterolateralne regije. Nađena je teška vaskulopatija presatka (CAV) s difuznim lezijama lijeve prednje silazne arterije (LAD), okluzijom dijagonalne grane, difuznim stenozama marginalne grane i sporim protokom u dominantnoj desnoj koronarnoj arteriji (RCA). Nije bilo znakova stanično posredovanog odbacivanja (CMR), ali su nabubrene endotelne stanice i imunofluorescencijom dokazani depoziti C3d i C4d u kapilarama potvrdili odbacivanje presatka posredovano protutijelima (AMR). Bolesnik je liječen steroidima, plazmaferezom i intravenskim imunoglobulinima. Kontrolne biopsije (Bx) nisu pokazivale AMR, a sistolička funkcija se oporavila. Treće godine bolesnik je razvio akutni infarkt miokarda s ST-elevacijom inferiorno i učinjena je primarna perkutana koronarna intervencija (PCI) RCA. Više nije bilo difuznih lezija lijevog koronarnog sliva, a žarišna stenoza LAD je elektivno dilatirana. Na Bx nije bilo znakova CMR niti AMR. Četvrte godine koronarografija je pokazala progresiju CAV i učinjena je PCI distalnog debla lijeve koronarne arterije, LAD i intermedijarne grane (RIM) double-kissing crush tehnikom. Pete godine, učinjena je PCI restenoze RCA. Ovaj put smo mogli odrediti donor specifična protutijela (DSA). Iako je Bx bila i dalje negativna na AMR, anti-HLA klase I i II bila su izrazito visoka te smo počeli s fotoferezom. Šeste godine, usprkos redukciji anti-HLA klase I, protutijela klase II ostala su visoka, a bolesnik je razvio kongestivno popuštanje srca. Urađena je angioplastika stenoze RIM balonom koji luči lijek. Nije bilo znakova odbacivanja na Bx. Zbog popuštanja presatka i uznapredovale CAV, odlučili smo bolesnika pripremiti za retransplantaciju. Izračunati PRA (calculated panel reactive antibodies) bio je visok te smo se odlučili za desenzitizaciju (plazmafereza, IVIg, rituksimab, bortezomib) da bi povećali

Case report: On the second year after heart transplantation (HTx), a 25-years-old man was hospitalized for effort intolerance and epigastric pain. Echocardiography showed anterolateral akinesia. Severe cardiac allograft vasculopathy (CAV) with diffuse left anterior descending (LAD) stenoses, occlusion of diagonal branch, diffuse stenoses of obtuse marginal and slow flow in the dominant right coronary artery (RCA) was diagnosed. No signs of cell-mediated rejection (CMR) were present, but swollen endothelial cells as well as positive C3d and C4d capillary staining with immunofluorescence detected antibody-mediated rejection (AMR). The patient was treated with steroids, plasmapheresis and intravenous immunoglobulins. Control biopsies (Bx) were free of AMR and echocardiography showed recovery of systolic function. On the third year he developed inferior ST segment elevation myocardial infarction and primary percutaneous coronary intervention (PCI) of RCA was done. This time left coronary artery was not diffusely ill, and a focal LAD stenosis was electively stented. Neither CMR nor AMR were detected on Bx. On the fourth year, routine angio control revealed CAV progression and we performed PCI of distal left main coronary artery, LAD and intermediate branch (RIM) with double-kissing crush technique. On the fifth year, PCI of RCA restenosis was performed. This time we could measure donor specific antibodies (DSA). Though Bx failed to show AMR, both anti-HLA class I and II were highly elevated and photopheresis was started. On the sixth posttransplant year, despite significant drop in anti-HLA class I, anti-HLA class II antibodies remained high and the patient developed congestive heart failure. An angioplasty with drug-eluting balloon of RIM stenosis was performed. No signs of rejection on Bx were noted. Because of graft failure and advanced CAV, we decided to prepare the patient for re-transplantation. As the calculated panel reactive antibodies (cPRA) were high,

broj mogućih donora (**slika 1**). Kako je cPRA ostao > 50 %, nakon definiranja tzv. zabranjenih HLA antigena, bolesnika smo prijavili na listu za retransplantaciju.

Zaključak: Ovaj slučaj prikazuje složenost liječenja bolesnika s odbacivanjem posredovanim protutijelima.[1] Tek kombiniranjem kliničke slike s patološkim i serološkim nalazima, koji u nedavnoj prošlosti nisu bili dostupni, moguće je rano postaviti dijagnozu i započeti liječenje s ciljem prevencije progresivne disfunkcije presatka.

we opted for desensitization therapy (plasmapheresis, IVIg, rituximab, bortezomib) to increase the number of potential donors (**Figure 1**). Since cPRA remained >50%, we listed the patient for re-transplantation after the definition of unacceptable HLA antigens.

Conclusion: This case presents difficulties in the management of antibody-mediated rejection.[1] Only a combination of clinical with both pathologic and serologic data, that were not readily available in the past, may prove early effective therapy and prevent progressive graft deterioration.

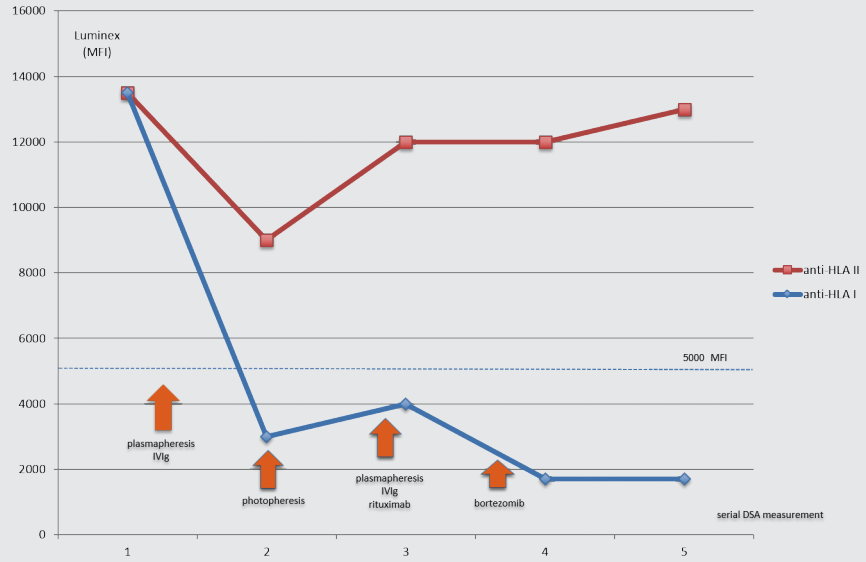

FIGURE 1. The dynamics of donor specific antibodies (DSA) in serum.

LITERATURE

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DOI: http://dx.doi.org/10.1161/CIR.0000000000000093