Protutijelima posredovano odbacivanje srčanog presatka: iskustvo jednog centra

Antibody-mediated rejection in heart transplant patients: a single centre experience

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Dijagnoza protutijelima-posredovanog odbacivanja srčanog presatka (*antibody-mediated rejection*, AMR) temelji se na imunopatološkom nalazu uz potporu kliničkom slikom i dokazom donor-specifičnih protutijela (DSA). AMR je kontinuum od asimptomatske pojave DSA, preko supkliničkog odlaganja komplementa bez histoloških promjena do konačnog popuštanja presatka. Čini se da i supklinička AMR nosi lošiju prognozu. DSA su pokazatelj aloimunizacije i povezana su s popuštanjem, odbacivanjem i vaskulopatijom presatka. Iako nije jasna važnost izoliranog porasta DSA u ranom ili kasnom poslijetransplantacijskom periodu, njihovo liječenje dolazi u obzir.[1,2]

Retrospektivno smo od 2012. godine analizirali 193 transplantirana bolesnika, kada smo postupno uveli imunopatološku analizu bioptata i određivanje DSA u serumu. Kombinirajući različite kriterije (patološki, klinički i serološki, tj. pozitivna DSA), AMR smo dijagnosticirali u 12 bolesnika (6,2%). Četvrtina bolesnika se prezentirala kardiogenim šokom. Kombinacija patološkog i kliničkog kriterija bila je pozitivna u 17%, patološkog i serološkog kriterija u 25%, kliničkog i serološkog u 25%, dok je 33% bolesnika imalo pozitivna sva tri kriterija. Medijan vremena od transplantacije do AMR je iznosio 2,63 godine (0,7-5,9). Medijan dobi bolesnika s AMR je bio 35 (17-62), a 75% su bili muškarci. Svi bolesnici s AMR su bili DSA pozitivni, osim dvoje u kojih se DSA nisu mjerila. 70% ih je imalo klasu I, a 30% obje klase anti-HLA DSA. Najčešći terapijski pristup uključivao je: steroidni puls (92%), plazmaferezu (75%), intravenski imunoglobulin (58%) i rituksimab (58%). Antitimocitni globulin, kao i bortezomib smo dali samo po jednom bolesniku. ECMO (izvantjelesna membranska oksigenacija) je postavljen u bolesnika u kardiogenom šoku. Jednogodišnje preživljenje iznosilo je 83%. Jedan je bolesnik uspješno retransplantiran nakon desenzitizacije. Od 193 bolesnika, DSA smo testirali u njih 97. Pozitivnih je bilo 24%, od kojih je 17% bilo pozitivno na klasu I, 65% na klasu II i 17% na obje klase) (**slika 1**). Premda učestalost AMR u literaturi varira zbog različitih dijagnostičkih kriterija i razlika u načinu probira, naš rezultat je usporediv. Nažalost niti dijagnoza niti terapija AMR nisu dobro standardizirane. Potrebna su veća multicentrična klinička istraživanja da ispitaju različite dijagnostičke i terapijske pristupe.

The diagnosis of antibody-mediated rejection (AMR) is based on immunopathologic features, supported by clinical signs as well as by the presence of donor-specific antibodies (DSA). However, AMR is a continuum with progression from a silent phase of circulating antibodies, followed by subclinical complement deposition without histological alterations, until it becomes symptomatic. Subclinical AMR appears to be associated with poor outcome. DSA are markers of alloimmune activation and are associated with poor graft survival, rejection, and CAV (cardiac allograft vasculopathy). The significance of rising DSA in the early post-transplantation period, as well as their late appearance or increase without pathological changes or clinical manifestations, is unclear, and the treatment may be considered.[1,2]

We retrospectively evaluated 193 transplant (Tx) patients (pts) since 2012, when pathologic analysis for AMR and detection of DSA were gradually introduced. By using different combinations of pathologic, clinical and serologic (i.e. positive DSA) criteria we diagnosed AMR in 12 pts (6.2%). One-quarter of patients with AMR presented with cardiogenic shock. The combination of pathologic and clinical, pathologic and serologic as well as clinical and serologic criteria were present in 17%, 25%, and 25%, respectively. All three criteria were positive in 33%. Median time from Tx to AMR diagnosis was 2.63 yrs (0.7-5.9). The median age was 35 (17-62) and 75% were males. All pts had positive DSA, except 2 pts, in whom testing was unavailable. Seventy percent had class II, and 30% were positive for both class I and class II anti-HLA. The most frequent treatment strategies included: pulse steroid (92%), plasma exchange (75%), intravenous immunoglobulin (58%) and rituximab (58%). Antithymocite globulin, as well as bortezomib, were applied in only one pts. ECMO was implanted in pts with cardiogenic shock. One-year survival is 83%. Among 193 pts, DSA were analyzed in 97 pts. Twenty-four percent were DSA positive (class I in 17%, class II in 65% and both classes in 17%) (**Figure 1**). Although the reported incidence of AMR varies because of different diagnostic criteria and variations in screening schedule, our result is comparable. Both diagnosis and treatment of AMR are not well standardized. We need large prospective multicentric clinical trials to evaluate different strategies.

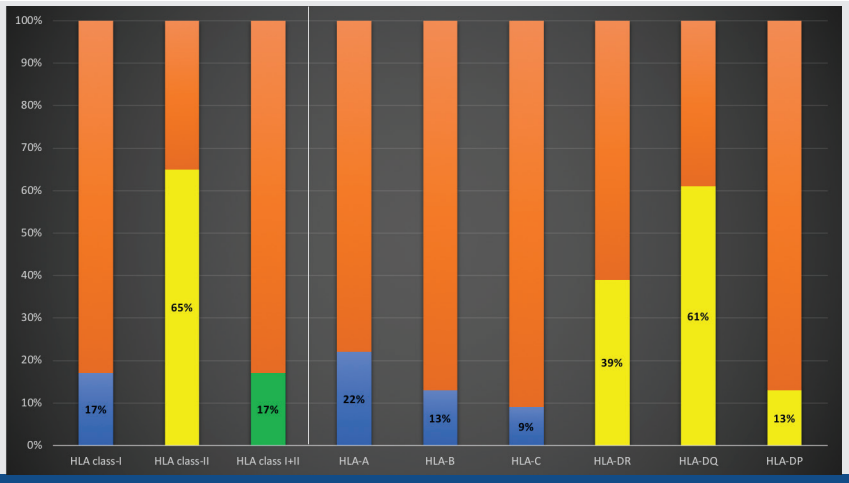

FIGURE 1. The frequency of donor-specific HLA antibodies among tested heart transplant patients.

HLA = human leukocyte antigen

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