Citomegalovirusna infekcija nakon transplantacije srca

Cytomegalovirus infection after heart transplantation

Jana Ljubas Maček*,
Boško Skorić,
Marijan Pašalić,
Daniel Lovrić,
Jure Samardžić,
Maja Čikeš,
Hrvoje Jurin,
Ivo Planinc,
Nina Jakuš,
Dora Fabijanović,
Hrvoje Gašparović,
Davor Miličić

Medicinski fakultet Sveučilišta u Zagrebu, Klinički bolnički centar Zagreb, Zagreb, Hrvatska

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

KLJUČNE RIJEČI: transplantacija srca, citomegalovirusna infekcija, vaskulopatija srčanog presatka.

KEYWORDS: heart transplantation, cytomegalovirus infection, cardiac allograft vasculopathy.

CITATION: Cardiol Croat. 2018;13(11-12):363. | https://doi.org/10.15836/ccar2018.363

***ADDRESS FOR CORRESPONDENCE**: Jana Ljubas Maček, Klinički bolnički centar Zagreb, Kišpatićeva 12, HR-10000 Zagreb, Hrvatska / Phone: +385-98-577-707 / E-mail: janaljubas@yahoo.com

ORCID: Jana Ljubas Maček, https://orcid.org/0000-0001-7171-2206 • Boško Skorić, https://orcid.org/0000-0001-5979-2346
Marijan Pašalić, https://orcid.org/0000-0002-3197-2190 • Daniel Lovrić, https://orcid.org/0000-0002-5052-6559
Jure Samardžić, https://orcid.org/0000-0002-9346-6402 • Maja Čikeš, https://orcid.org/0000-0002-4772-5549
Hrvoje Jurin, https://orcid.org/0000-0002-2599-553X • Ivo Planinc, https://orcid.org/0000-0003-0561-6704
Nina Jakuš, https://orcid.org/0000-0001-7304-1127 • Dora Fabijanović, https://orcid.org/0000-0003-2633-3439
Hrvoje Gašparović, https://orcid.org/0000-0002-2492-3702 • Davor Miličić, https://orcid.org/0000-0001-9101-1570

Uvod: Citomegalovirusna (CMV) infekcija poznat je vanjski okidač nastanka vaskulopatije srčanog presatka (CAV - eng. *cardiac allograft vasculopathy*), zbog mehanizama kojima potiče pojačanu imunogenost presatka.[1,2] Cilj studije je bio istražiti različite aspekte CMV infekcije te njihov utjecaj na nastanak CAV-a i staničnog odbacivanja (SO) nakon transplantacije srca (HTx).

Bolesnici i metode: Uključena su 123 bolesnika nakon HTx učinjene od 2005. do 2016. godine, kojima je praćena CMV viremija PCR metodom (određivanjem broja virusnih kopija). Vrijeme praćenja iznosilo je 3 godine (IQR 2-6 godina). Pojavnost CAV-a evaluirana je koronarografijama i analizirana s obzirom na prijetransplantacijsku imunizaciju (IgG pozitivnost) te prisutnost i oblik CMV infekcije, vrijeme infekcije (rana infekcija, koja je trajno izliječena unutar 6 mjeseci nakon HTx ili kasna – perzistiranje viremije ili reaktivacija virusa nakon isteka prvih 6 mjeseci). Svi bolesnici su primali CMV profilaksu kroz tri mjeseca.

Rezultati: CMV infekcija je dokazana je u 31,7% bolesnika, od kojih je 64% imalo asimptomatsku viremiju, 25% pneumonitis, 10% enterokolitis i 2.5% miokarditis. Nije nađeno razlike u CMV-seropozitivnosti (91% bolesnika) u odnosu na kasniji razvoj CAV-a (p=0,551) te nije imala utjecaja na smanjenje pojave CMV infekcije nakon HTx (p=0,485). Značajno veća pojavnost CAV-a bila je vezana uz višu prevalenciju CMV infekcije (p=0,013), međutim rana CMV infekcija je imala manju prevalenciju CAV-a od kasne. Broj kopija virusnih čestica nije pokazao korelaciju s incidencijom CAV-a. Bolesnici s CMV infekcijom nisu imali kraće preživljavanje od CMV-negativnih bolesnika (p=0,384) niti veću učestalost značajnog SO presatka.

Zaključak: Prijetransplantacijska seropozitivnost nije utjecala na konačan broj CMV infekcija. CMV infekcija dokazani je okidač razvoja CAV-a, ali nije uzrok povišene smrtnosti. Visina broj kopija virusa nije imala značaja u predikciji incidencije CAV-a, no kasna CMV infekcija pokazala je veći značaj u nastanku CAV-a od rane CMV infekcije. Unatoč visokoj prevalenciji CMV infekcije u naših bolesnika (32%), nije dokazana veća incidencija CAV-a, moguće dijelom i zbog učinkovite profilakse i time kratkog trajanja viremije. CMV infekcija se nije pokazala kao uzrok češćeg SO presatka.

Introduction: Cytomegalovirus (CMV) infection is known as an external trigger for cardiac allograft vasculopathy (CAV), due to the mechanisms that stimulate graft immunogenicity.[1,2] The aim of the study was to investigate different aspects of CMV infection and their effect on the development of CAV and cellular rejection (CS) after heart transplantation (HTx).

Patients and methods: 123 patients after HTx performed in the period from 2005 to 2016 were included, with regular CMV monitoring by PCR method. Follow-up was 3 years (IQR 2-6 years). The presence of CAV was evaluated by coronary angiography and analyzed with respect to pretransplant CMV-immunization and the presence and form of CMV infection, time of the infection (early infection, which was permanently cured within 6 months after HTx, or late with persistence of viremia or viral reactivation after the first 6 months). All patients received CMV-prophylaxis for three months.

Results: CMV infection was detected in 31.7% of patients, of which 64% had asymptomatic viremia, 25% pneumonitis, 10% enterocolitis and 2.5% myocarditis. There was no difference in CMV seropositivity (91% of patients) compared to later CAV development (p = 0.551) and no effect on reduction of CMV infection after HTx (p=0.485). Significantly higher CAV incidence was associated with higher prevalence of CMV infection (p = 0.013), however early CMV infection had a lower prevalence of CAV than late. The number of viral copies by PCR did not correlate with CAV incidence. Patients with CMV infection did not have a shorter survival rate than CMV-negative patients (p = 0.384) or higher frequency of significant cellular rejection.

Conclusion: Pretransplant CMV-seropositivity did not affect the ultimate number of CMV infections. CMV infection was confirmed as the trigger for later development of CAV, but it was not related to increased mortality. The number of viral copies was not significant in predicting CAV incidence, but late CMV infection showed higher importance in CAV development than early CMV infection. Despite the high prevalence of CMV infection in our patients (32%), no higher incidence of CAV has been demonstrated, possibly due to effective prophylaxis and thus shorter duration of viremia. The CMV infection did not prove to be the cause of the more frequent cellular graft rejection.

RECEIVED:
October 21, 2018

ACCEPTED:
November 5, 2018

LITERATURE

1. Vassalli G, Gallino A, Weis M, von Scheidt W, Kappenberger L, von Segesser LK, et al; Working Group Microcirculation of the Eurpean Society of Cardiology. Alloimmunity and nonimmunologic risk factors in cardiac allograft vasculopathy. Eur Heart J. 2003 Jul;24(13):1180-8. https://doi.org/10.1016/S0195-668X(03)00237-9
2. Delgado JF, Reyne AG, de Dios S, López-Medrano F, Jurado A, Juan RS, et al. Influence of cytomegalovirus infection in the development of cardiac allograft vasculopathy after heart transplantation. J Heart Lung Transplant. 2015 Aug;34(8):1112-9. https://doi.org/10.1016/j.healun.2015.03.015