

23. Rostami Z, Einollahi B, Ghadiani MH. Does living donor hyperoxia have an impact on kidney graft function after transplantation? *Nephrourol Mon.* 2013;5:835-9.
24. Lachenbruch PA, Rosenberg AS, Bonvini E, Cavaille-Coll MW, Colvin RB. Biomarkers and surrogate endpoints in renal transplantation: present status and considerations for clinical trial design. *Am J Transplant.* 2004;4:451-7.
25. Marsden PA. Predicting outcomes after renal transplantation--new tools and old tools. *N Engl J Med.* 2003;349:182-4.
26. Perl J, Dong J, Rose C, Jassal SV, Gill JS. Is dialysis modality a factor in the survival of patients initiating dialysis after kidney transplant failure? *Perit Dial Int.* 2013;33:618-28.
27. Shooshtarizadeh T, Mohammadali A, Ossareh S, Ataipour Y. Relation between pretransplant serum levels of soluble CD30 and acute rejection during the first 6 months after a kidney transplant. *Exp Clin Transplant.* 2013;11:229-33.

Correspondence to:
 Mehrdad Taghipour, MD
 Nephrology and Urology Research Center, Baqiyatallah Hospital,
 Molla Sadra St, Tehran, Iran
 Tel: +98 21 8126 2072
 E-mail: mehrdadtaghipour@gmail.com

Recurrent Cytomegalovirus Infection Prevalence and Risk Factors

Behzad Einollahi, Mohsen Motalebi

Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

See article on page 231

Cytomegalovirus (CMV) is a beta herpes virus that can infect several organs. It is transmitted through infected body secretions, blood, and organ allografts,¹ and is considered as the leading infectious reason of mortality and morbidity in organ transplantation.² It is also the most important cause of infectious disease after kidney transplantation.³ Cytomegalovirus infection is defined according to the American Society of Transplantation's recommendations for use in clinical trials as evidence of CMV replication without any symptoms.⁴ The existence of CMV symptoms, which can be characterized as a viral syndrome (fever, malaise, leukopenia, and thrombocytopenia) or as a tissue invasive disease confirmed the diagnosis of CMV disease.⁴ In addition, recurrent CMV infection is defined as new detection of CMV infection in a patients that has had previously documented CMV infection.⁵

Several studies have evaluated the impact of CMV infection and disease on kidney transplantation outcomes.⁶⁻⁸ Reisching and colleagues⁹ showed that CMV disease was an important risk factor for acute rejection, particularly in the first 12 months after kidney transplantation. Basri and coworkers¹⁰ stated a possible relationship between CMV infection and

graft failure in kidney transplant recipients. Indirect effect of CMV on outcomes of transplantation is enhanced systemic immunosuppression (ie, effect favoring opportunistic infections), increasing risk of posttransplant malignancies (ie, posttransplantation lymphoproliferative diseases),^{3,8} CMV-induced vasculopathy and thrombosis,¹¹ the potential role in allograft rejection (either cellular or antibody mediated),⁸ urologic and gastrointestinal complications, etc.¹¹ It has also shown that CMV infection is an independent risk factor for a high incidence of hyperglycemia¹² and developing new-onset diabetes mellitus, which is an important cause for mortality and morbidity after transplantation.¹³

In the current issue of the *Iranian Journal of Kidney Diseases*, Nafar and colleagues¹⁴ have evaluated the prevalence and risk factors of CMV and its recurrent infection in a sample of 427 kidney transplant recipients. They reported 16% and 4.4% prevalence of CMV infection and recurrent CMV infection, respectively. It means that recurrent CMV infection occurred in 26% of patients after treatment of primary CMV infection. It is similar to the results of a multi-center study of 3065 kidney transplant recipients in Iran.⁷ In this study, the authors showed the incidence of CMV infection

and its recurrent infection was 21.9% and 2.2% of all patients, respectively, and 10.1% of patients with primary CMV infection developed recurrent infection. Moreover, Pourmand and coworkers¹⁵ reported the same prevalence for CMV infection (17.6%) in a single-center study in Iran. Asberg and colleagues¹⁶ reported clinical recurrent CMV in 15.1% and asymptomatic recurrence in 30%, which is consistent with results reported by Nafar and colleagues.¹⁴

Recurrent CMV infection usually occurs in 1 to 3 months after treatment of the primary infection and usually occurs as a mild but serious infection.¹⁷ The present study¹⁴ in the current issue has evaluated the risk of some variables, including age of recipients, recipient sex, immunosuppressive protocol, history of immunosuppression before transplantation and antithymocyte globulin administration on CMV disease and recurrent CMV disease after transplantation and have concluded that the only factor that could be a risk factor for CMV infection was immunosuppressive protocol, which was not confirmed as a risk factor for recurrent CMV infection. Some other risk factors evaluated in different investigations are shorter time since kidney transplantation, kidney allograft failure,⁷ female recipient, young age, second transplantation,¹⁸ and donor-positive-recipient-negative serostatus.⁶

Patients treated with tacrolimus were more likely to develop CMV infection rather than those treated with cyclosporine in Nafar and colleagues' study.¹⁴ Moreover, we found that serum cyclosporine level was significantly higher in patients with CMV infection rather than other non-infected group.⁷ Previous studies demonstrated that potent immunosuppressive regimen could lead to poorer outcomes in organ transplant recipients. It has also been shown that CMV AB-positive patients with azathioprine-based therapy had better outcomes rather than mycophenolic-acid-base therapy⁶; however, a case-control study¹⁹ did not confirm it.

Some important risk factors for recurrent CMV infection are donor-positive-recipient-negative serostatus, acute rejection, and high viral load at first infection episode of CMV. In this regard, Helantera and coworkers demonstrated that delayed graft function and high viral load (> 100 000 copy/mL) at the time of primary CMV infection were the only risk factors for recurrent CMV infection.²⁰ Nafar and colleagues¹⁴ did not

assess these important risk factors in their study, so none of the variables were evaluated by them had impact on recurrent CMV.

In conclusion, although secondary prophylaxis was not approved by some works,⁵ it is suggested for 1 to 3 months after treatment of CMV infection.⁴ However, the benefit of secondary prophylaxis for all patients remained a question. There is not an approved guideline to define criteria for starting secondary prophylaxis, and it seems it needs further multi-center randomized studies for that.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Hjelmsaeth J, Muller F, Jenssen T, Rollag H, Sagedal S, Hartmann A. Is there a link between cytomegalovirus infection and new-onset posttransplantation diabetes mellitus? Potential mechanisms of virus induced beta-cell damage. *Nephrol Dial Transplant*. 2005;20:2311-5.
- Lashini H, Goodarzi Z, Hosseini MJ, Saberfar E. Development of PCR assay for early detection of CMV infection in renal transplant recipients. *Nephrourol Mon*. 2011;03:106-8.
- Nafar M, Firouzan A, Einollahi B. Miliary Tuberculosis and CMV Infection in a Kidney Recipient. *Nephrourol Mon*. 2009;1:153-5.
- Kotton CN, Kumar D, Caliendo AM, et al. International consensus guidelines on the management of cytomegalovirus in solid organ transplantation. *Transplantation*. 2010;89:779-95.
- Helantera I, Lautenschlager I, Koskinen P. The risk of cytomegalovirus recurrence after kidney transplantation. *Transpl Int*. 2011;24:1170-8.
- Nemati E, Taheri S, Pourfarziani V, Einollahi B. Cytomegalovirus disease in renal transplant recipients: an Iranian experience. *Exp Clin Transplant*. 2008;6:132-6.
- Einollahi B. Cytomegalovirus Infection following Kidney Transplantation: a Multicenter Study of 3065 Cases. *Int J Organ Transpl*. 2012;3:74-8.
- Costa C. Cytomegalovirus and acute rejection in kidney transplantation. *Nephrourol Mon*. 2011;3:237-9.
- Reischig T, Jindra P, Svecova M, Kormunda S, Opatrný K Jr, Treska V. The impact of cytomegalovirus disease and asymptomatic infection on acute renal allograft rejection. *J Clin Virol*. 2006;36:146-51.
- Basri N, Abdullah KA, Shaheen FA. Cytomegalovirus disease in renal transplant recipients: a single-center experience. *Exp Clin Transplant*. 2007;5:601-3.
- Ardalan M. Rare Presentations of Cytomegalovirus Infection in Renal Allograft Recipients. *Nephrourol Mon*. 2012;4:431-6.
- Khalili N, Rostami Z, Kalantar E, Einollahi B. Hyperglycemia After Renal Transplantation: Frequency and Risk Factors. *Nephrourol Mon*. 2013;5:753-7.

13. Hjelmsaeth J, Sagedal S, Hartmann A, et al. Asymptomatic cytomegalovirus infection is associated with increased risk of new-onset diabetes mellitus and impaired insulin release after renal transplantation. *Diabetologia*. 2004;47:1550-6.
14. Nafar M, Roshan A, Pour-Reza-Gholi F, et al. Prevalence and risk factors of recurrent cytomegalovirus infection in kidney transplant recipients. *Iran j kidney dis*. 2014;8: 231-5.
15. Pourmand G, Salem S, Mehrsai A, Taherimahmoudi M, Ebrahimi R, Pourmand M. Infectious complications after kidney transplantation: a single-center experience. *Transpl Infect Dis*. 2007;9:302-9.
16. Asberg A, Humar A, Jardine AG, et al. Long-term outcomes of CMV disease treatment with valganciclovir versus IV ganciclovir in solid organ transplant recipients. *Am J Transplant*. 2009;9:1205-13.
17. Helanterä I, Lautenschlager I, Koskinen P. The risk of cytomegalovirus recurrence after kidney transplantation. *Transpl Int*. 2011;24:1170-8.
18. Marker SC, Howard RJ, Simmons RL, et al. Cytomegalovirus infection: a quantitative prospective study of three hundred twenty consecutive renal transplants. *Surgery*. 1981;89:660-71.
19. Sarmiento J, Munn S, Paya C, Velosa J, Nguyen J. Is cytomegalovirus infection related to mycophenolate mofetil after kidney transplantation? a case-control study. *Clin Transplant*. 1998;12:371-4.
20. Helanterä I, Kyllönen L, Lautenschlager I, Salmela K, Koskinen P. Primary CMV infections are common in kidney transplant recipients after 6 months valganciclovir prophylaxis. *Am J Transplant*. 2010;10:2026-32.

Correspondence to:
Mohsen Motalebi, MD
Nephrology and Urology Research Center, Baqiyatallah
University of Medical Sciences, Molla Sadra Ave, Vanak Sq,
Tehran, Iran
Tel: +98 21 8126 2073
Fax: +98 21 8126 2073
E-mail: dr.motalebi@ymail.com