

Seroprevalence of Human Herpesvirus 8 in Kidney Transplant Recipients in a Single-Center Study From Tunisia

Hella Lahlaoui, Hbiba Niija, Mohamed Ben Moussa

Laboratoire de Microbiologie,
Hôpital Militaire de Tunis,
Tunisia

Keywords. human herpesvirus
8, Kaposi sarcoma, kidney
transplantation, Tunisia

Human herpesvirus 8 (HHV8) is a herpesvirus that is always associated with Kaposi sarcoma. An enzyme-linked immunoenzymatic assay was used to detect antibodies to the latent nuclear antigen of HHV8 in kidney transplant patients and kidney transplant candidates from Tunisia. A significantly high HHV8 seroprevalence was documented; 17% of kidney transplant patients and 23% in kidney transplant candidates were seropositive. This is a first report of HHV8 in Tunisia.

IJKD 2012;6:14-6
www.ijkd.org

Human herpesvirus 8 (HHV8) is a member of the *Herpesviridae* family, *Gammaherpesvirinae* subfamily¹ and was identified for the first time in 1994.² Emerging evidence suggests that HHV8 may be transmitted through sexual contact, saliva, and blood transfusion.³⁻⁵ Many people infected with HHV8 never develop the disease, suggesting that some form of equilibrium usually exists between the virus and the immune system.^{6,7} Immunocompromised individuals, such as people infected with human immunodeficiency virus or transplant recipients, may develop Kaposi sarcoma (KS). The prevalence of KS after kidney transplantation varies significantly in different geographic areas, supporting the theory of racial or environmental factors in its pathogenesis.⁸ In fact, posttransplantation KS mainly affects patients with Mediterranean, black African, or Caribbean origins.

Given the increased risk of KS in immunosuppressed organ transplant patients, we investigated the seroprevalence of HHV8 in kidney transplant recipients and kidney transplant candidates from Tunisia. This is the first report of HHV8 in kidney transplant recipients and dialysis patients from Tunisia. The study population consisted of 127 participants, including 60 healthy Tunisians recruited from dentistry clinics (control group), 26 hemodialysis patients, and 41 kidney

transplant recipients evaluated between may 2008 and April 2010 at the military hospital of Tunisia. Follow-up visits were scheduled every month during the first year after transplantation and every 3 months subsequently, and the main inclusion criterion for participation in this study was that patients should have reached the clinically stable stage following kidney transplant surgery after 3 postoperative months. The dose, duration, and timing of immunosuppressive therapy were carefully adjusted as necessitated by the clinical status of each patient. Serum samples were collected from all study participants and was stored at -20°C. All the samples were tested for HHV8 antibodies with the use of an enzyme-linked immunoassay (HHV8 immunoglobulin G immunoenzymatic assay, Biotrin International, Dublin, Ireland), according to the manufacturer's instructions. Demographic information, including gender and age, are shown in the Table.

The data showed that the association of HHV8 seropositivity was higher in kidney transplant recipients (17%) and in kidney transplant candidates (23%) when compared with HHV8 seropositivity in the healthy individuals (5%). The observed HHV8 seropositivity in end-stage renal disease patients was higher compared to those in North America and Europe. In fact, this seroprevalence in kidney transplant recipients is 0.6% in Spain, 2.1% in France,

Demographic and Clinical Data of Participants

Parameter	Healthy Individuals (n = 60)	Kidney Transplant Patients (n = 26)	Kidney Transplant Candidates (n = 41)
Sex			
Male	26	22	23
Female	34	4	18
Age range, y	7 to 67	12 to 60	10 to 67
Mean age, y	39	40	29
Anti-HHV8*	5	17	23
Kaposi sarcoma	0	0	0

*P = .001

4% in Greece, 14.8% in Italy, 7, 6% in Belgium, and more than 1% in Canada.¹⁰⁻¹⁴ The Middle East is reported to be a highly prevalent region for the incidence of posttransplant KS.¹⁵ Reports from Saudi Arabia, Egypt, and Turkey indicate a high incidence of this disease.¹⁶⁻¹⁸ Based on seropositivity for HHV8, 3 areas have been defined in the world¹⁹: those regions with seroprevalence rates less than 5%, like North America and northern parts of Europe; regions with intermediate seroprevalence, ranging from of 5% to 20%, like the Mediterranean and the Middle East; and regions with high seroprevalence rates more than 50%, such as Africa and Amazon. The low rate of HHV8 (5%) in the control group of this study suggest that Tunisia is classified into the low-prevalence region group.

Human herpesvirus 8 is an etiological factor associated with KS, one of the most common tumors to occur in kidney transplant recipients.²⁰ The risk of posttransplantation KS is 23% to 28% among seropositive patients compared with 0.7% among seronegative patients. Since 1993, of 162 patients who have received a kidney transplant at our hospital only 1 **patient** has developed KS (0.6%). This patient was a male aged 41 years, transplanted in 1993 with a kidney from a cadaveric donor and developed KS after 6 years in 1999. Reduction of immunosuppressive therapy in this patient led to KS regression. The reported incidence of posttransplant KS ranges from 0.5% to 5%, depending on the patients, country of origin, and the type of organ received, mainly after kidney transplantation.¹⁰ Previous studies showed a prevalence of 0.3% in Belgium, 25% in Italy, 0.5% in Spain, 0.7 % in Greece, and 4% in Iran.¹⁹⁻²³ Therefore, even if after the transplantation, the seroprevalence of HHV8 is increased, the main risk factor is the infection

before transplantation.²⁴ There is some evidence that KS can regress when the immunosuppressive therapy stops.²⁵ A study from Italy of 1844 kidney transplant patients showed a 113-fold increased risk for KS.²⁶

In conclusion, our results indicate that HHV8 antibody prevalence is low in the general population of Tunisia. In contrast, this prevalence is increased in kidney transplant recipients and kidney transplant candidates. If immune suppression increases the rate of HHV8 antibody positivity as a result of increased viral replication in infected individuals, it may be possible that current serological assays underestimate the true prevalence of HHV8 in the nonimmunocompromised general population (control group). Thus, the establishment of a policy of systematic screening of donors and recipients is necessary for prevention of the development of HHV8-associated posttransplant complications.

ACKNOWLEDGEMENTS

This work was funded by grants from the Military Hospital of Tunisia.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Moore PS. The emergence of Kaposi's sarcoma-associated herpesvirus (human herpesvirus 8). *N Engl J Med*. 2000;343:1411-3.
- Chang Y, Cesarman E, Pessin MS, et al. Identification of herpesvirus-like DNA sequences in AIDS-associated Kaposi's sarcoma. *Science*. 1994;266:1865-9.
- Engels EA, Atkinson JO, Graubard BI, et al. Risk factors for human herpesvirus 8 infection among adults in the United States and evidence for sexual transmission. *J Infect Dis*. 2007;196:199-207.
- Pauk J, Huang ML, Brodie SJ, et al. Mucosal shedding of human herpesvirus 8 in men. *N Engl J Med*. 2000;343:1369-77.
- Dollard SC, Nelson KE, Ness PM, et al. Possible transmission of human herpesvirus-8 by blood transfusion in a historical United States cohort. *Transfusion*. 2005;45:500-3.
- Pellet PE, Wright DJ, Engels EA, et al. Multicenter comparison of serologic assays and estimation of human herpesvirus 8 seroprevalence among US blood donors. *Transfusion*. 2003;43:1260-8.
- Gazouli M, Zavos G, Papaconstantinou I, et al. The interleukin-6-174 promoter polymorphism is associated with a risk of development of Kaposi's sarcoma in renal transplant recipients. *Anticancer Res*. 2004;24:1311-4.

8. Firoozan A, Hosseini Moghaddam SM, Einollahi B, et al. Outcome of Kaposi's sarcoma and graft following discontinuation of immunosuppressive drugs in renal transplant recipients. *Transplant Proc.* 2005;37:3061-4.
9. Lebbe C, Legendre C, Frances C. Kaposi sarcoma in transplantation. *Transplant Rev (Orlando).* 2008;22:252-61.
10. Marcelin AG, Calvez V, Dussaix E. KSHV after an organ transplant: should we screen? *Curr Top Microbiol Immunol.* 2007;312:245-62.
11. Panayiotakopoulos GD, Papaconstantinou I, Mavroyianni D, Kostakis A, Kordossis T. Pretransplantation prevalence of human herpes virus 8 antibodies in kidney donors and recipients in Athens, Greece. *Transplant Proc.* 2005;37:4180-2.
12. Cattani P, Capuano M, Graffeo R, et al. Kaposi's sarcoma associated with previous human herpesvirus 8 infection in kidney transplant recipients. *J Clin Microbiol.* 2001;39:506-8.
13. Sheldon J, Henry S, Mourad M, et al. Human herpes virus 8 infection in kidney transplant patients in Belgium. *Nephrol Dial Transplant.* 2000;15:1443-5.
14. Delorme S, Houde I, Deschenes L. Seroprevalence of antibodies against human herpesvirus 8 in a population of renal transplant recipients at Hotel-Dieu de Quebec Hospital. *J Clin Microbiol.* 2003;41:5207-8.
15. Einollahi B. Kaposi sarcoma after kidney transplantation. *Iran J Kidney Dis.* 2007;1:2-11.
16. Qunibi W, Akhtar M, Sheth K, et al. Kaposi's sarcoma: the most common tumor after renal transplantation in Saudi Arabia. *Am J Med.* 1988;84:225-32.
17. El-Agroudy AE, El-Baz MA, Ismail AM, Ali-EI-Dein B, El-Dein AB, Ghoneim MA. Clinical features and course of Kaposi's sarcoma in Egyptian kidney transplant recipients. *Am J Transplant.* 2003;3:1595-9.
18. Duman S, Toz H, Asci G, et al. Successful treatment of post-transplant Kaposi's sarcoma by reduction of immunosuppression. *Nephrol Dial Transplant.* 2002;17:892-6.
19. Ahmadpoor P, Ilkhanizadeh B, Sharifzadeh P, et al. Seroprevalence of human herpes virus-8 in renal transplant recipients: a single center study from Iran. *Transplant Proc.* 2007;39:1000-2.
20. Einollahi B, Lessan-Pezeshki M, Nourbala MH, et al. Kaposi's sarcoma following living donor kidney transplantation: review of 7,939 recipients. *Int Urol Nephrol.* 2009;41:679-85.
21. Bergallo M, Costa C, Margio S, et al. Human herpes virus 8 infection in kidney transplant patients from an area of northwestern Italy (Piemonte region). *Nephrol Dial Transplant.* 2007;22:1757-61.
22. Garcia-Astudillo LA, Leyva-Cobian F. Human herpesvirus-8 infection and Kaposi's sarcoma after liver and kidney transplantation in different geographical areas of Spain. *Transpl Immunol.* 2006;17:65-9.
23. Panayiotakopoulos GD, Papaconstantinou I, Mavroyianni D, Kostakis A, Kordossis T. Pretransplantation prevalence of human herpes virus 8 antibodies in kidney donors and recipients in Athens, Greece. *Transplant Proc.* 2005;37:4180-2.
24. Schwartz RA. Kaposi's sarcoma: an update. *J Surg Oncol.* 2004;87:146-51.
25. Haverkos HW. Multifactorial etiology of Kaposi' sarcoma: a hypothesis. *J Biosci.* 2008;33:643-51.
26. Serraino D, Piselli P, Angeletti C, et al. Risk of Kaposi's sarcoma and of other cancers in Italian renal transplant patients. *Br J Cancer.* 2005;92:572-5.

Correspondence to:

Hella Lahlaoui
Laboratoire de Microbiologie, Hôpital Militaire de Tunis, 1089
Monfleury, Tunisia
Tel : +216 5077 8984
E-mail: hella_lahlaoui@yahoo.fr

Received June 2011
Revised October 2011
Accepted October 2011