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Letter to the Editor

Human Herpesvirus 8 (HHV8) Infection and Related Diseases in Italian Transplant Cohorts

To the Editor:

We read with interest the latest epidemiological survey by Lebbe et al. (1), assessing the risk of HHV8 transmission after solid organ transplantation in a French cohort of liver, kidney or heart recipients, by applying different serological and molecular tests (i.e. either latent or lytic IFA, and quantitative PCR), as well as providing helpful information on some life-threating cases of HHV8-related diseases. During the last decade, using the same multiple assays, we have similarly performed two multicentric, prospective HHV8 screening studies on previously unreported Italian transplant cohorts (Table 1). The former from the North Italian Transplant (NIT) group and the Gruppo Italiano Trapianto Midollo Osseo (GITMO) enrolled 367 donor/recipient pairs from 2001 to 2003 (referred as NIT-GITMO Study), while the latter from the Regione Emilia-Romagna—Progetto Regione-Università included 525 recipients and 249 donors, enrolled from 2008 to 2012 (referred as RER-PRU Study). Here, we briefly report our data (Table 1) and focus on some main points emerging from recent literature on this topic (1–3).

Although HHV8 seroconversion was not infrequent in HHV8-negative patients receiving HHV8-infected grafts (D+/R− group), seroconversion rates were quite variable, ranging from 21% to 32% in the French cohorts (1,2), showing high frequencies of HHV8 seroreversion and transient seropositivity, to 14% and 19% in our NIT-GITMO and RER-PRU cohorts, respectively (without available data on HHV8 seroreversion). Altogether, these data suggest that the detection of serum anti-HHV8 antibodies may be tricky and highly transient in posttransplant immunosuppressed patients, further exposing the actual lack of a gold-standard serological test. Moreover, this underlines the unmet clinical need for reliable and cost-effective monitoring tools, able to identify posttransplant patients at higher risk to develop HHV8 primary infection and/or HHV8-related diseases (either neoplastic or non-neoplastic). In this view, the recent surveys showed that HHV8 viremia screening by quantitative PCR, while less sensitive than serological tests to identify patients infected after transplantation, seems to become clinically useful when able to reveal the occurrence and evolution of highly-active viremic events, frequently associated with severe HHV8-related complications (1–3). In line with these observations, we found that less than half of seroconverted patients eventually developed at least one positive viremia (HHV8-DNA >100 copies/mL) during our long-term follow-up. Of note, we detected positive HHV8 viremias in 6 out of 16 patients with HHV8-associated diseases, due to primary infections (3/7 cases) or viral reactivations (3/9 cases), yielding a positive predictive value of 20%. In addition to serial HHV8-DNA measurements, an

Table 1: Summary data on HHV8 infection and related diseases, derived from two Italian transplant cohort studies

	NIT-GITMO study			RER-PRU study		
Enrollment period	2001–2003			2008–2012		
Applied HHV8-specific assays[1]	Latent IFA, lytic IFA, lytic EIA, Q-PCR			Latent IFA, lytic IFA, lytic EIA, Q-PCR		
Recipients	Number per organ type		HHV8 seroprevalence	Number per organ type		HHV8 seroprevalence
	Kidney	103	7.7%	Kidney	260	10.4%
	Liver	165	18.1%	Liver	228	20.6%
	BM/PBSC	99	8.1%	Heart	37	8.1%
	Total	367	12.5%	Total	525	15.0%
Donors	Total	363	4.4%	Total	249	4.0%
	HHV8 seroconversion in D+/R− group: 14.3%[2]			HHV8 seroconversion in D+/R− group: 19.0%		
HHV8-related diseases	After primary infection		After reactivation	After primary infection		After reactivation
	4KS		5 KS	1 PEL		3 KS
	1 PEL					1 MCD
	1 BM aplasia					

KS, Kaposi's sarcoma; PEL, primary effusion lymphoma; MCD, multicentric Castleman's disease; BM, bone marrow.
[1]1Patients were considered HHV8-seropositive when samples resulted + with at least two HHV8-specific assays. All recipients and donors were tested once at baseline (pre-transplant) to assess HHV8 seroprevalence in different groups and then, to identify HHV8 seroconversions, the recipients in D+/R− groups were tested at least every 4 months, for 36–48 months or until positive. Seropositive patients were monitored by HHV8 Q-PCR at least monthly.

immunological monitoring of protective HHV8-specific T cells (recently found to be significantly associated with disease control) (4,5) may also provide valuable information for the clinical management of HHV8-seropositive recipients or patients with Kaposi's sarcoma in remission, to guide timely modifications of immunosuppressive treatments. Further investigations are warranted to define the positive predictive value of HHV8 viral loads combined with HHV8-specific T cell enumeration in high-risk HHV8-seropositive posttransplant patients.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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