The Presence of Polyomavirus in Non-Melanoma Skin Cancer in Organ Transplant Recipients Is Rare


TO THE EDITOR

Organ transplant recipients have a 100-fold increased risk of developing cutaneous squamous cell carcinoma (SCC) compared to the general population (Euvrard et al., 1993). Compared to immunocompetent patients, organ transplant recipients often develop more invasive and aggressive SCCs, with increased multiplicity, recurrence, and risk for metastasis. In addition to SCCs, organ transplant recipients develop more keratoacanthomas (KAs), Bowen’s disease, and actinic keratoses. A potential reason for the development of these tumors is that posttransplant immunosuppressive medications result in enhanced susceptibility to infection. Histologically, many of the lesions in these patients demonstrate the hallmarks of viral infection such as the presence of koilocytes and verruciform epidermal hyperplasia (Euvrard et al., 1993; Hsi et al., 1997; Harwood et al., 2006).

Study of viruses in skin tumors of transplant patients has previously focused on human papilloma virus (HPV). PCR assays for epidermodysplasia verruciformis and mucosal serotypes of HPV have revealed that high risk mucosal HPVs are relatively infrequent in these cutaneous tumors. The frequency of epidermodysplasia verruciformis HPV infection ranges from 39-92% in SCCs from transplant patients (Berkhout et al., 1995; Boxman et al., 1997; Hopfl et al., 1997). However, the presence of epidermodysplasia verruciformis HPV can also be found in plucked hairs and forehead swabs from healthy individuals and skin tumors from immunocompetent patients (Boxman et al., 1997; Hsi et al., 1997; McGregor et al., 1997; Hazard et al., 2007). Thus, the exact etiologic role that these viruses play in skin cancer in organ transplant recipients remains unclear. Other viruses may also contribute to tumorigenesis in organ-transplant patients. Recently, the presence of polyomavirus has been detected in 80% of Merkel cell carcinomas (MCCs; Feng et al., 2008). In

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Jürgen C. Becker1, Roland Houben1, Selma Ugurel1, Uwe Trefzer2, Claudia Pfoehler1 and David Schrama1

1Department of Dermatology, University of Würzburg, Würzburg, Germany; 2Department of Dermatology and Allergy, Charité—Universitätsmedizin Berlin, Berlin, Germany and 3Department of Dermatology, The Saarland University Hospital, Homburg/Saar, Germany

E-mail: schrama_d@klinik.uni-wuerzburg.de

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these tumors, two viral genomes, designated MCV339 and MCV350, were identified that are distantly related to the known human polyomaviruses. Polyomavirus infection in immunocompetent individuals is harmless. However, in immunocompromised individuals, BK virus infection most often leads to nephropathy whereas JC polyomavirus infection commonly causes multifocal leukoencephalopathy (Drachenberg et al., 2007; Weiner and Narayan, 1973). MCC is a rare but potentially aggressive primary neuroendocrine carcinoma of the skin that presents most commonly on sun-exposed areas. Increased incidence is associated with immunosuppression, and MCCs are more prevalent in patients with HIV infection, leukemias, and organ transplantation (Miller and Rabkin, 1999; Engels et al., 2002; Kanitakis et al., 2006; Pectasides et al., 2007).

To investigate the potential role of polyomavirus in nonmelanoma skin cancer and actinic keratoses, we used the PCR-based assay described by Feng et al. (2008) to detect the presence of polyomavirus in 156 nonmelanoma skin cancers from organ transplant recipients. The study was approved by the Institutional Review Board of the University of California, San Francisco. The study was conducted according to the Declaration of Helsinki Principles and written consent was obtained from the participants. Genomic DNA was extracted from formalin-fixed paraffin-embedded tumors and the DNA concentration was estimated by Taqman analysis (Ginzinger et al., 2000). A 400 base pair fragment of β-globin was amplified as a positive control to determine the presence of PCR-amplifiable DNA. The PCR assay was validated on a cohort of MCCs and the results showed that 54% (7/13) of tumors were positive for the presence of polyomavirus. Genomic DNA from a MCC was used as a positive control in all subsequent PCR assays. We examined 85 SCCs, 37 KAs, 28 Bowen’s disease, and 6 actinic keratoses for the presence of polyomavirus DNA. Genomic DNA (50 ng) from each tumor was used to amplify for the LT1, LT3, and VP1 genomic DNA of the polyomavirus and the PCR products were separated on 2% agarose gels. Polyomavirus fragments were detected in 1 KA (2.7%). However, the bands were significantly fainter than in MCCs (Figure 1). Sequencing of the polyomavirus PCR products from the KA revealed that the LT3 and VP1 PCR products were identical to the MCV339 virus found in MCC tumors; whereas the sequence of the LT1 PCR product differed by 2 base pairs. With respect to the MCV350 virus, also detected in MCC tumors, the KA-derived LT3 product was identical but the LT1 and VP1 PCR products differed by 5 and 1 base pairs, respectively. The presence of polyomavirus in the KA was not due to contamination because the viral sequence was different to the polyomavirus sequences detected in our cohort of MCC. The pathogenic relevance of polyomavirus in this single KA is unclear.

To conclude, the MCC polyomaviruses are an infrequent finding in nonmelanoma skin cancers of organ transplant patients.

Figure 1. Detection of polyomavirus in a single keratoacanthoma. Genomic DNA (50 ng) from a keratoacanthoma (K) or a Merkel cell carcinoma (MC) were amplified with primers specific for the LT1, LT3, or VP1 genes of polyomavirus associated with Merkel cell carcinomas (MCCs). N, non template negative control; M, low mass DNA ladder (fragment length in base pairs is indicated).

REFERENCES