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LETTER TO THE EDITOR

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HHV-8 is associated with recurrent Kaposi's sarcoma in a renal transplant recipient

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Sir: We have recently described how renal transplantation exposes patients with previous Kaposi's sarcoma (KS) to a high risk of recurrence [2]. The cause of this phenomenon is unclear. Recently, a new herpes virus (HHV-8), initially identified by Chang et al. [1] in AIDS-associated KS, has been described in classic and endemic KS, as well as in KS occurring in immunosuppressed patients [3, 4, 6–9]. This virus is suspected of being a widespread, latent virus that may be reactivated in certain conditions, such as immunosuppression, causing various tumors, in particular KS. We present here evidence that recurrence of KS after renal transplantation is associated with the presence of reactivated HHV-8 in KS lesions.

In October 1988, a 32-year-old woman underwent a first cadaveric kidney transplantation for end-stage nephroangiosclerosis. Immunosuppression consisted of azathioprine (AZA), prednisolone (PRED), and cyclosporin A (CyA). At the end of the 5th post-transplant month, she developed multiple KS cutaneous lesions on her limbs and right breast. Skin biopsy confirmed the diagnosis of KS. There was no visceral involvement and antibodies against the HIV were absent. CyA was discontinued. Nevertheless, skin lesions progressed rapidly, leading to discontinuation of AZA. An acute rejection episode resulted in transplant loss in April 1989, but KS was found in an inguinal lymph node harvested during allograft nephrectomy. The skin nodules disappeared within 2 months after initiation of dialysis, and histological examination of an iliac lymph node 2 years later revealed no signs of KS. The patient was retransplanted in December 1993 under CyA, AZA, and PRED. Three months later, skin and then visceral (stomach) recurrence of KS were clearly demonstrated by histological examination. A reduction in immunosuppression resulted in complete regression of KS but also in allograft loss requiring nephrectomy in July 1994. The patient remains in clinical remission of KS 1.5 years later.

We retrospectively searched for evidence of HHV-8 using the nested PCR method with KS 330–233 primers on all of the paraffin-embedded specimens obtained from this patient [1]. The virus was detected in initial and recurrent KS biopsy specimens (cutaneous and visceral). In contrast, using the same PCR conditions, no HHV-8 DNA could be detected in the lymph node harvested during KS clinical remission when the patient was off all immunosuppression (Fig. 1).

These data strongly suggest that, firstly, KS recurrence after renal retransplantation is associated with HHV-8 and, secondly, that discontinuation of immunosuppression induces KS regression, apparently in parallel with a reduction in the number of viral copies, leading to a lack of detection by PCR. Thus, reintroduction of immunosuppression in the setting of renal retransplantation may induce HHV-8 reactivation, leading to clinical KS recurrence.

Naturally, these findings must be viewed with caution because recent data suggest that HHV-8 is frequently present in otherwise healthy males [5]. However, as the detection of HHV-8 in peripheral blood cells seems to predict the subsequent appearance of KS [10], it could be useful for transplantation centers to screen their patients for this virus.

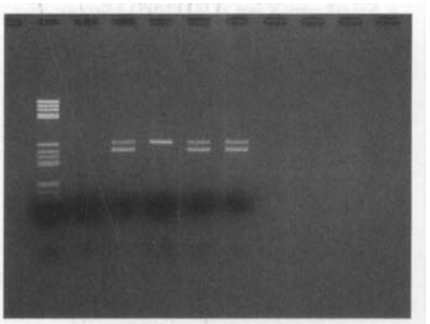

Fig. 1 Agarose gel electrophoresis of products amplified using K 330–233 primers for HHV-8. The numbers in the ordinate refer to base pairs. *Lane 1*: Molecular DNA weight marker VPBR 322-DNA-HAE III; *Lane 2*: Negative control; *Lane 3*: Visceral (lymph node), HHV-8-positive after the first transplantation episode; *Lane 4*: Lymph node harvested when patient was in clinical remission, free of immunosuppression; no HHV-8 could be detected; *Lanes 5 and 6*: Cutaneous and gastric KS lesions that develop after the second transplantation. Both lesions are HHV-8-positive; The 233 bp fragment corresponds to specific HHV-8 DNA sequences and the 268 bp product to β-globin gene

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