Kaposi's Sarcoma and Herpesvirus 8: A Word of Caution

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Key Words

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Recent clinical, histological and epidemiological data strongly suggest that a new herpesvirus (HHV-8) is involved in the pathogenesis of various forms of Kaposi's sarcoma (KS) [1, 2]. Still numerous conflicting data have previously been reported on the identification of various other causative agents in KS. To clarify this issue, we compared biopsies of KS at different stages with cell cultures from these biopsies for the occurrence of HHV-8.

Skin lesions of KS were biopsied from 7 HIV-infected patients. Routine microscopic examination on formalin-fixed paraffin-embedded samples revealed 3 early and 4 late stages [2]. The fresh remaining tissue was divided into two parts, which were either immediately stored at -70 °C for subsequent DNA extraction, or immediately processed for culture, similarly as previously described [3]. The

experiments presented here were performed on cultures from the second to the seventh passage. Cells isolated from these cultures were characterized as KS cells morphologically and immunohistochemically (spindle-shaped morphology and irregular expression of factor VIII, positivity for laminin, vimentin, collagen IV, but not for keratin, ELAM-1, or VCAM-1). Moreover, Northern blot analysis showed the basal expression of collagenase-IV by these cells, suggesting that they have an invasive potential. The DNA was extracted from the biopsies and from their derived cell cultures, and was amplified by nested PCR. A 233-bp-sized HHV-8 sequence was amplified using the primers KS4 and KS5 described by Boshoff et al. [4] as external primers and the primers KS 1 and KS2 [1] as internal primers. For human herpesvirus 6 (HHV-6) DNA detection, a nested PCR was used according to Dewhurst et al. [5].

We observed the HHV-8 sequences in all 7 biopsies from AIDS-associated KS lesions, independently of their stage, and the HHV-6 genome in no early stages but in 3 of the 4 late stages.

Confirming previous studies [6, 7], we found no HHV-8 or HHV-6 in the spindle-like cell cultures derived from these biopsies. This may suggest that the studied cultured spindle-like cells are not the recipient cells of these viruses.

One can also speculate that these conflicting results between the in vivo lesions and their derived cell culture are due to differences in the environment of the cells studied. HIV-infected homosexuals are known to have increased levels of inflammatory cytokines which may play a critical role in the progression of KS. Since the same cytokines can upregulate virus expression, it is possible that they are involved in both KS induction and HHV-8 or -6 expression. This could explain the viral coinfections in KS reported here and previously [8].

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272 *Dermatology* 1996;193:269–272

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