Absence of human herpesvirus-8 DNA in Kaposi’s sarcoma following postmastectomy lymphoedema

du Plessis DG, Schneider JW, Treurnicht FK, Engelbrecht S & Janse van Rensburg E

Departments of Anatomical Pathology & Virology, University of Stellenbosch and Tygerberg Hospital, Tygerberg, South Africa

Sir: A variety of tumours, the most common example being angiosarcoma (Stewart–Treves syndrome), have been described in extremities affected by chronic lymphoedema.1 Lymphoedema may follow, coincide or precede classic or HIV-associated Kaposi’s sarcoma (KS).2, 3 However, the development of KS in limbs with primary or secondary chronic lymphoedema in patients with no risk factors for KS is very rare.

Only two cases of KS arising in a chronic lymphoedematous arm following radical mastectomy have been reported.3 We present the clinicopathological features of a third example, including an investigation into the presence of associated human herpesvirus-8 (HHV-8) in this situation. A 67-year-old woman without predisposing factors for KS underwent a radical mastectomy and axillary lymph node resection for infiltrating duct carcinoma of the right breast, followed by a course of local radiotherapy. She remained tumour free with moderate, persistent lymphoedema of the right arm for 16 years until she presented with a small intradermal nodule in the right elbow region. Histology revealed a spindle cell tumour consistent with nodular KS (Figure 1).

![Image](image_url)

Figure 1. The initial biopsy showed nodular KS consisting of short fascicles of spindle cells interrupted by slit-like spaces containing red blood cells (H & E)

Immunohistochemistry showed positive staining of tumour cells for CD34 and CD31 using a routine strepavidin–biotin complex (ABC) method and monoclonal antibodies obtained from Dako. Three years later 'eczematous' lesions were noted in the same area. A biopsy showed features consistent with patch phase KS (Figure 2).
Apart from transient, limited exacerbation during a course of chemotherapy for biopsy-proven metastatic breast carcinoma, the KS lesions have remained static over a 14-years follow-up period, some even showing regression.

Sections from formalin-fixed, paraffin-embedded tissue representative of the original breast carcinoma, normal breast, subsequent metastases, and all biopsies of KS lesions were submitted for the detection of HHV-8 DNA sequences. KS330\textsubscript{233} primers were used to amplify an HHV-8 specific 233-base pair sequence of open reading frame 26. The polymerase chain reaction (PCR) products were subsequently used with nested primers to amplify a 172-base pair sequence. Dilutions of the plasmid KS330Bam were included as positive controls and to determine the number of HHV-8 target molecules present. All the conditions and primers were used as described previously.\textsuperscript{4} HHV-8 specific sequences were not detected in any of the specimens.

Although HHV-8 is strongly associated with KS in systemic immune-suppressed patients, a similar relationship between lymphoedema with regional immune-suppression and HHV-8 remains to be proven. Recently Cerri \textit{et al.} failed to demonstrate HHV-8 DNA in a lymphangiosarcoma of the pubic region that developed in lymphoedematous tissue due to congenital lymphoedema.\textsuperscript{5} The absence of HHV-8 DNA in occasional KS lesions is well documented. This observation may be due to technical factors, incorrect diagnosis, extremely low copy numbers of HHV-8 in the KS lesions, or viral mutations that escape detection by the KS330\textsubscript{233} primer.\textsuperscript{6} However, it remains possible that factors other than HHV-8 may stimulate endothelial cell proliferation and induce anti-apoptotic factors in KS.

Rare cases of localized KS that develop in chronically lymphoedematous limbs of patients who do not have other clinico-epidemiological risk factors for KS, suggest that chronic lymphoedema may be an additional condition predisposing to the development of KS. The demonstration of a reduced delayed type hypersensitivity response in such limbs, has prompted the hypothesis that a regional immune defect limited to areas of localized lymphoedema might also involve the mechanisms of antineoplastic immune surveillance, thereby facilitating the development of certain tumours in those areas.\textsuperscript{2} Additional studies are
necessary to determine whether KS in lymphoedematous tissue is less frequently associated with HHV-8 than other KS variants.

References


