
【Abstract】

Aim and background: In Okinawa, a subtropical island in southern Japan, many cases of classical type Kaposi’s sarcoma have been reported, although in mainland Japan this tumour is rare, and despite the fact that the mainland statistics include the Okinawa cases. Kaposi’s sarcoma–associated herpesvirus (KSHV) or human herpesvirus 8 (HHV) has been identified in the tumours; detailed sequence analysis has revealed that there are five genotypes of the virus, and geographical differences have been described. In this paper, we analysed the sequences of HHV 8 in classical and AIDS–associated Kaposi’s sarcomas in Okinawa and classified its genotypes.

Materials and Methods: Eight cases of classical Kaposi’s sarcoma (KS), one Of AIDS–associated KS, 5 of granuloma pyogenicum, 2 of inflammatory Pseudotumours, 2 of Castleman disease, one of angiosarcoma and one PEL are used. As a control HHV 8–positive cultured PEL cells (TY–1) were used. Histologic examinations were carried out using H&E staining and immunohistochemical stainings for vascular endothelial growth factor (VEGF／VPF), IL–6, factor V related antigen, estrogen receptor, bFGF and cyclin D1. The presence of HHV 8 sequence is evaluated by PCR method and also in situ hybridization (ISH). The HHV 8 ORF 26, K1, K15 region at right–hand side (RHS)of the genome, gBN, gBC and gHM genes are amplified by PCR. The sequence analysis of the PCR products is performed.

Results: Histology of the Kaposi’s sarcomas varied slightly according to the Clinical stages, but fundamentally they showed the same features. There was No histological difference among KS due to the virus genotypes. HHV 8 was detected from all cases of KS, as well as from one PEL, one granuloma pyogenicum and the control PEL (TY–1), but four cases of granuloma pyogenicum, two inflammatory pseudotumours, two Castleman disease cases and one of angiosarcoma were negative for HHV 8. Interestingly, in the HHV 8 positive granuloma pyogenicum case, Kaposi’s sarcoma–like lesions were found in small areas, and the virus was demonstrated by ISH. Eight cases of classical type KS and one of granuloma pyogenicum 2 were infected with HHV 8 genotype C (K1 region genotype classification) or subtype C (ORF26 region subtype classification) which had a 5 amino acid deletion at K1 VR2 region. On the other hand, an AIDS–associated KS and a PEL were infected with type I／A (K1 region genotype classification) virus, and a Control PEL was infected with I／C virus. The AIDS–associated KS case was considered to have been infected with HIV and HHV 8 in America. The present PEL case has received hemodialysis for
renal failure, but the history of HHV 8 Infection is unclear. In HHV 8 in all cases, eight N–linked glycosylation sites and cystine residues were well conserved. But in Okinawa genotype C\(\div\)C HHV 8 slight Variation were found in K1 gene when compared with the reported sequences.

Conclusion: Classical KS cases in Okinawa were infected with HHV 8 genotype C\(\div\)C which was also classified as subtype C. One granuloma pyogenicum case was also infected with HHV 8 genotype C\(\div\)C. The AIDS– associated KS and PEL were infected with different type of HHV 8 (genotype I\(\div\)A) which was considered to be similar to that frequently found in America. In Okinawa as reported previously, HHV 8 infection is more than 4 times higher than in mainland Japan, and due to HHV 8 genotype C\(\div\)C infection, there are many cases of Kaposi’s sarcoma. On the other hand, the numbers of cases of inflammatory pseudotumours and of Castleman disease in Okinawa are similar to those in the mainland. Further, there is no histological difference among the KS infected with genotype \(\oplus\) and \(\ominus\) viruses.