Disseminated classic Kaposi's sarcoma associated with human herpesvirus 8 infection.

Case report

M. Poljački, V. Đuran, M. Matić, Z. Gajinov, S. Stojanović and N. Vranješ

SUMMARY

Authors report a case of disseminated form of classic Kaposi's sarcoma case, in which presence of DNA sequences of human herpesvirus 8 has been confirmed. Viral DNA was identified with nested PCR method in tissue samples of skin and tumor of left submandibular region. Detected sequences corresponded to amplicone of 160 base pairs. In accordance with previous literature reports, these results confirm the possible etiopathogenetic role of Human herpesvirus 8 in classic Kaposi's sarcoma development.

KEY WORDS

Kaposi's sarcoma, human herpesvirus 8

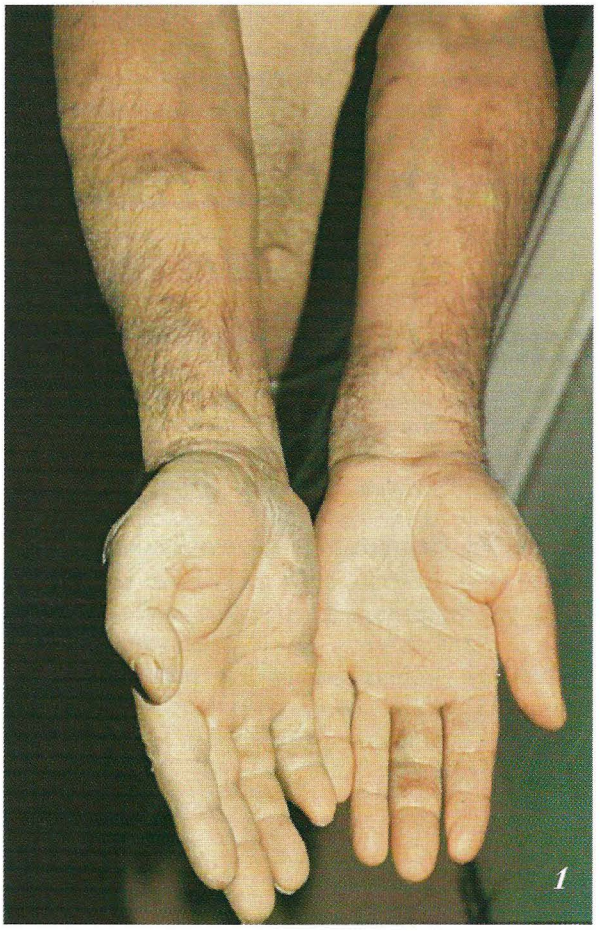
Introduction

Kaposi's sarcoma (KS) is a multicentric malignancy, which apart from skin can affect various internal organs. It became a significant medical and dermatovenerological problem after 1981 when it's association with AIDS was observed. Previously quite rare, tumor was then noted in 35% of AIDS patients in USA (1). Moritz Kaposi described it for the first time in 1872 and named "idiopathic, multiple, pigmented sarcoma" (2). KS is characterized by proliferation of vascular endothelial and lymphoreticular cells; it is rather reactive than neoplastic. The disease is important due to possible multicentric involvement of internal organs that is a cause of death in most cases. On the basis of clinical and epidemiological features, four types of KS can be recognized: *classic, endemic (African), iatrogenic* and *epidemic* (AIDS related). Classic KS with the greatest frequency occurs in Europe and North America, among the elderly male of Mediterranean or Eastern European descent (3).

Etiology and pathogenesis of KS is not clear yet. Recent findings of Human herpesvirus 8 (HHV-8) DNA sequences in tumor lesions and peripheral blood mononuclear cells of patients with all forms of KS, today shed a different light on the possible etiopathogenetic mechanism of the disease (4,5).

Case report

65 years old male patient was refereed to the Clinic for Dermatovenereology of the Clinical Centre of Novi



Sad, because of progression of livid-red nodule on the skin of upper and lower limbs, face, neck, trunk, palms and soles. During the 10 years of disease the patient never consulted a physician. The skin lesions appeared on the right upper arm. Examination revealed numerous nodes, 1 to 10 cm in diameter, distributed mostly on upper and lower limbs, palms and soles (Figures 1, 2). Solitary lesions were present on the face, neck and trunk (Figure 3). On the hard palate mucosa, livid macules were observed, and in the left submandibular region a tumor large as a male fist (Figure 4). All lesions were indolent; except for plantar which were verrucous and accompanied by edema. In his youth he had pulmonary tuberculosis, and in the past 12 years only cardiac medications were taken.

Laboratory examinations were within normal limits for ESR, total blood count, urine analysis, renal and hepatic functions; serology for HIV, Hepatitis B virus, Hepatitis C virus, and Epstein-Barr virus were negative. X-ray examination of the lung and gastrointestinal tract, irigographia and ultrasound examination of hepatobiliary system, spleen, kidneys, urine bladder and prostate were normal, and excluded dissemination of disease. Otorinolaryngologic examination was within normal range. Ultrasound examination of the tumor in left submandibular region revealed infiltration, with hypoechogenic zones within it. Cardiologic examination re-

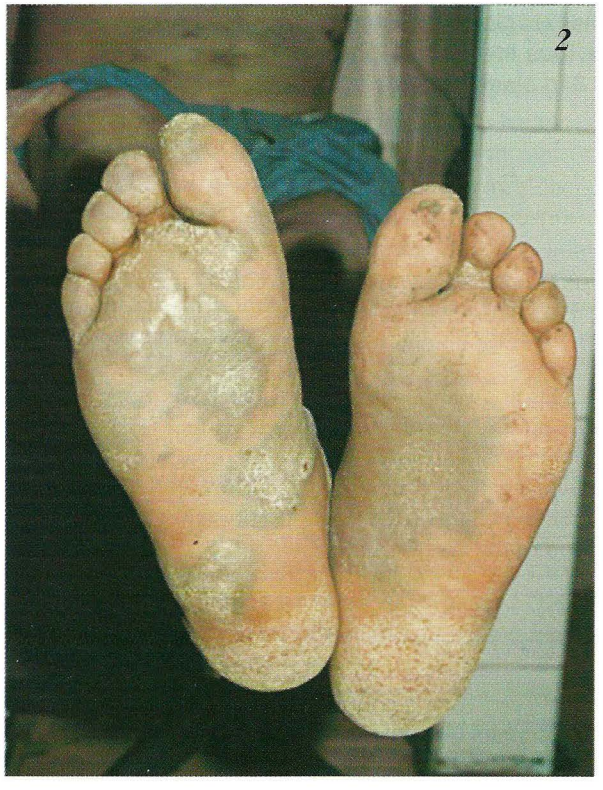
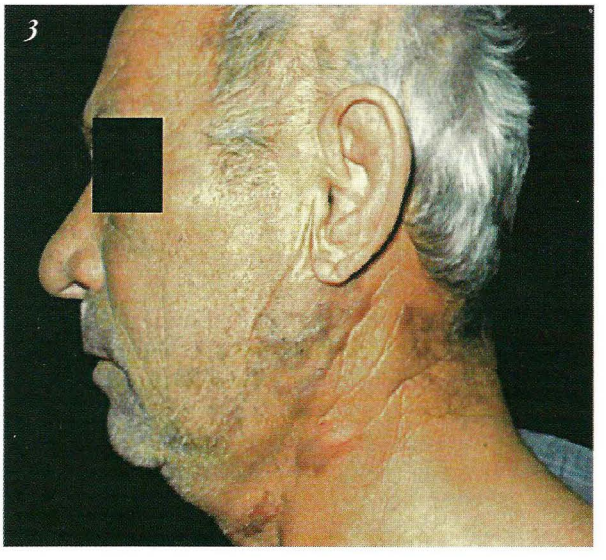


Figure 1. Multiple nodes on upper limbs

Figure 2. Verrucous and nodular lesions on feet

Figure 3. Nodular lesions on head and neck



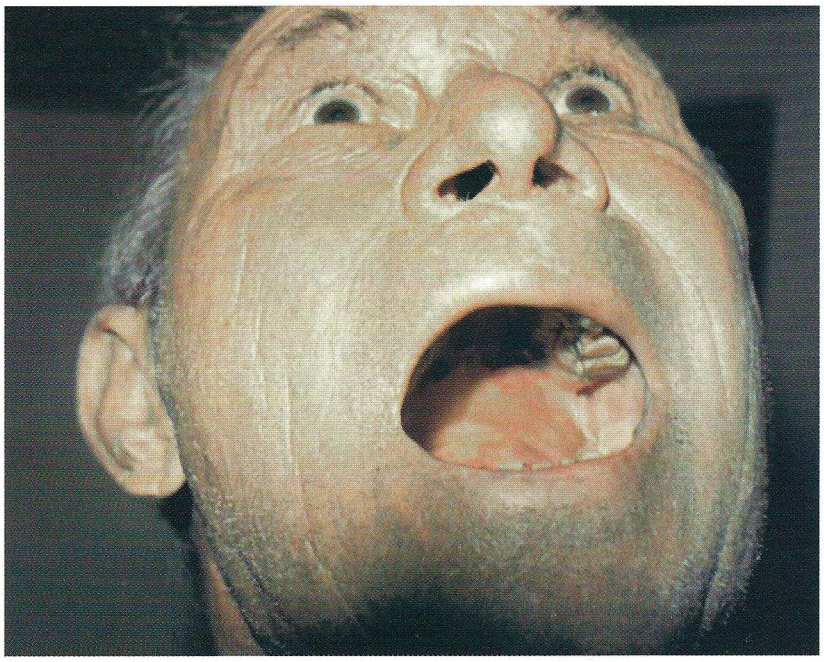
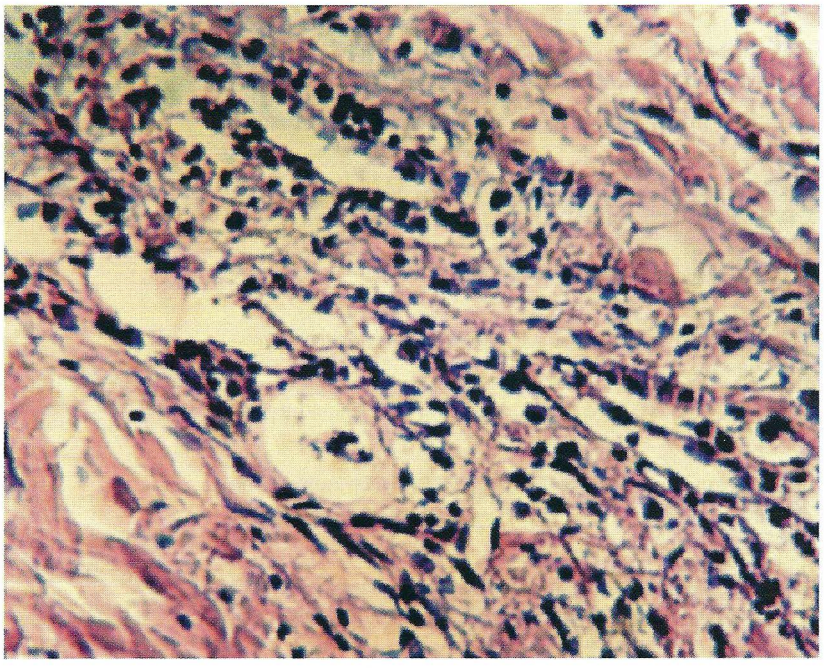


Figure 4. Bluish macules on hard palate

Figure 5. Numerous vascular spaces in middle dermis surrounded with spindle cells and sparse lymphocytes. Dermal collagen and elastin fibers and also fibers between them are homogenized and hyalinized.



vealed a cardiac decompensation. Pathohistology of the skin lesions (2 samples) and the submandibular tumor confirmed the diagnosis of KS (Figure 5). With nested PCR method in all 3 lesions HHV-8 DNA sequences were detected, corresponding to 160 base pairs amplicone (Figure 6). Due to dissemination of lesions the oncologic consultant recommended polychemiotherapy, which should have to be instituted in Clinic for Hematology.

Discussion

Classic KS is a form of disease, which in most cases has a relatively benign course. Usually it is characterized with slow growing benign tumors localized on distal portions of lower limbs. On rare occasions the disease can have aggressive behavior with disseminated skin lesions and involvement of internal organs (6). Dissemination of skin lesions usually follows their unilateral primary localization (2). Changes of oral mucosa are frequent in KS patients, especially on hard palate or in proximity of molar teeth. Rarely it can be the first manifestation of the disease (1,2). Similar to oral mucosa lesions, KS changes can affect pharyngeal, laryngeal of oesophageal mucosa (7). Classic KS can be seen most frequently in Israel, among Jews, Italians, and Greeks but also in people of Eastern-European and Northern-American ancestry (8, 9). Histological features of classic KS are not different from other forms of disease (3, 10). Usually it appears between the fifth and sixth decades of life, in Africans even earlier, in third or fourth decade, more frequently in males (3). Data about male to female ratio are different, several reports claims 10:1 male to female ratio, while others claim a significantly lower number 3:1 (2, 3). Development and course of disease, clinical and histhologic features in our patient led to diagnosis of disseminated form of classic KS, without the involvement of internal organs. Negative HIV serology, normal laboratory findings, and absence of immunosuppressive drugs in patient's history confirmed the diagnosis of classic form of the disease. Coexistence of other malignancies weren't proved in this patient. In the literature reports about possible associations of KS and other tumors, especially lymphoproliferative diseases exist (3, 9, 11). Lymphedema on lower limbs, as a consequence of small lymph vessel obstruction, was observed in our patients too, with predominant localization on feet, with numerous nodes and verrucous lesions. Verrucous aspect of the feet, KS lesions in some cases resembling common warts (1), have been described previously.

Finding of HHV-8 DNA sequences in KS lesions is in accordance with recent reports about viral presence in classic and other forms of disease. Chang et al. in 1994 for the first time, using PCR method, have confirmed DNA viral sequences in tissue samples of HIV associated KS (5). Later studies confirmed Chang's research, and detected HHV-8 DNA sequences in lesions of classic, endemic and iatrogenic form of KS (12, 13, 14, 15, 16). These results assume the possible etiopathogenetic role of this virus in development of all forms of disease, particularly because viral presence was confirmed in other lymphoproliferative disorders, such as body cavities lymphomas or Castelmann disease, which are often, but not obligatory HIV related (16).

Conclusion

Finding of HHV-8 DNA sequences in cutaneous and extracutaneous lesions of classic KS is a further confirmation of the hypothesis suggesting the possible etiopathogenetic role of HHV-8 in KS development, independently from the HIV infection.

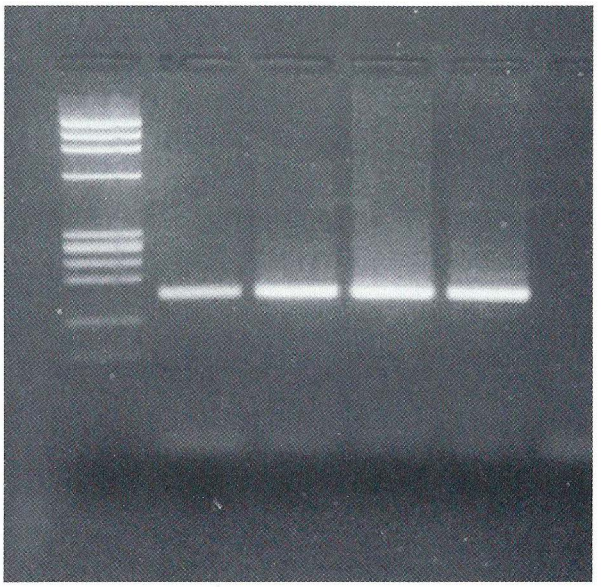


Figure 6. Nested PCR analysis of HHV8 DNA in tissue specimens of classic KS
Column 1: DNA marker O 174; Column 2 and 3: specimen of tumorous skin lesion; Column 4: positive control (DNA extracted from positive specimen); Column 5: specimen from extracutaneous lesion; Column 6: HHV8 negative control (DNA extracted from negative sample); Column 7 and 8: empty laboratory dish.

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A U T H O R S ' A D D R E S S E S

Mirjana Poljaćki, MD, PhD, professor of dermatology, Chairman of the Dept. of Dermatology, Clinical Centre Novi Sad, Hajduk Veljkova 1-3, 21000 Novi Sad, Yugoslavia, e-mail: cojans@eunet.yu
Verica Đuran, MD, PhD, professor of dermatology, same address
Milan Matić, MD, MSc, same address
Zorica Gajinov, MD, MSc, same address
Slobodan Stojanović, MD, PhD, professor of dermatology, same address
Nenad Vranješ, MD, same address