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Case report

HHV-8-associated angiosarcoma like Kaposi sarcoma, presenting in an HIV-negative man

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Abstract

Kaposi sarcoma is an angioproliferative disorder that affects the endothelial cells of the skin and mucous membranes. It is associated with human herpesvirus 8 (HHV-8), which is commonly found in immunocompromised individuals. However, it can also be present in immunocompetent patients. We report a case of Kaposi sarcoma (KS) in an 82-year-old immunocompetent male who is HIV-negative. There were no known risk factors for Kaposi sarcoma, such as a history of HIV or Mediterranean or Central / Eastern European and African ancestry. However, he did have brachytherapy-treated prostate cancer nineteen years ago. Biopsy of the skin lesions revealed vascular proliferation consistent with Kaposi sarcoma, and a diagnosis of an angiosarcoma-like Kaposi sarcoma subtype was made after multidisciplinary consultation. Given that this case shows that KS can develop in immunocompetent people who are HIV-negative, this form of KS may be a unique variation or subtype of classic Kaposi.

Introduction

Kaposi sarcoma is an angioproliferative disorder caused by human herpesvirus 8 (HHV-8), also known as Kaposi sarcoma-associated herpesvirus (KSHV)[1]. It is characterised by lymphadenopathy, pancytopenia, and signs of systemic inflammatory syndrome[2]. Based on clinical and epidemiological characteristics, there are four types: classic, endemic, iatrogenic, and HIV-associated. Although the four types of KS have similar clinical characteristics, they differ in severity[3]. Classic KS (CKS) occurs in older men of Eastern European, Mediterranean, and Middle Eastern descent and presents with cutaneous lesions over the lower extremities and trunk, which grow slowly. Host genetic factors may affect the risk of CKS, at least in part, by influencing the ability to develop antibodies to HHV-8 and, ultimately, control HHV-8 infection. Endemic Kaposi sarcoma, which affects young people in Africa, also presents with ulcerative skin lesions that grow slowly or with soft tissue invasion[4]. Transplant-associated or iatrogenic Kaposi sarcoma presents in people who are on immunosuppressive drugs or recipients of organ transplants[5]. AIDS-related or epidemic Kaposi sarcoma is associated with infections with human immunodeficiency virus (HIV)[6].

Immunosuppression or changes in immunological function, which can be associated with chronic infection, autoimmunity, or malnutrition, are strongly linked to the pathogenesis of KS. Still, the largest association is with HHV-8 infection. The transmission of HHV-8 is primarily via saliva but is also transmitted by sexual contact and blood[7].

Being the most common neoplasm in patients with human immunodeficiency virus (HIV) infection, an increased number of cases of KS have been reported in homosexual men without HIV infection, with some proposing that KS in MSM without HIV should be considered a distinct fifth form of KS[8]. We report a case of an 82-year-old immunocompetent and HIV-negative man presenting with angiosarcoma-like KS.

Case presentation

An 82-year-old man presented with a three-year history of unusual discolouration on his feet, which has increased over time. Despite this, he has remained asymptomatic. In his past, he worked as a professional tap dancer and later as a tour guide. He feels that the condition over the legs may have been aggravated due to the constant time spent on his feet. He believes that his feet have suffered damage over the years, yet he continues to dance at least once a week.

The patient had a history of prostate cancer for which he underwent brachytherapy nineteen years ago. He has no other significant health issues and maintains a healthy lifestyle. He identifies with Scottish and Irish ancestry but has no Mediterranean or Central / Eastern European roots. There is no family history of KS or other skin malignancies. Currently, he is not in

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an active sexual relationship, as his partner lives away, but he has always taken precautions against sexually transmitted infections.

Previously, he was treated with antifungal medications for a suspected fungal skin infection and with topical steroids for suspected dermatitis; however, these treatments did not result in any clinical improvement of the skin lesions on his legs.

On physical examination, his vitals were all normal, and skin examination revealed purplish discolouration over both feet (Figure 1), some taking an annular configuration (Figure 2) and discolouration extending to the dorsum of the third and fourth toes on both sides (Figure 3). He also had discolouration over the shins (Figures 4 & 5).

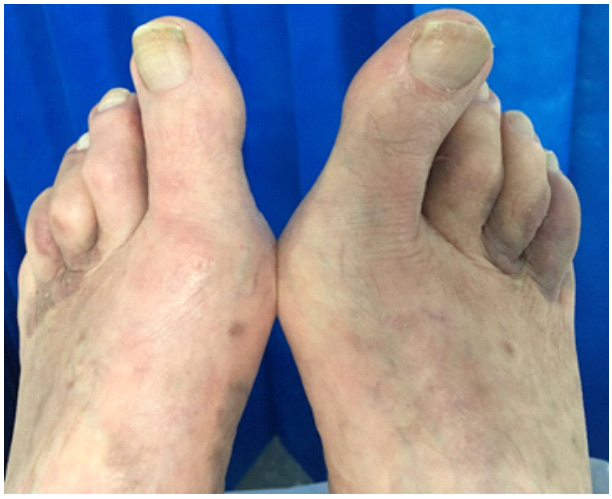

Figure 1. *Purplish discolouration of feet.*

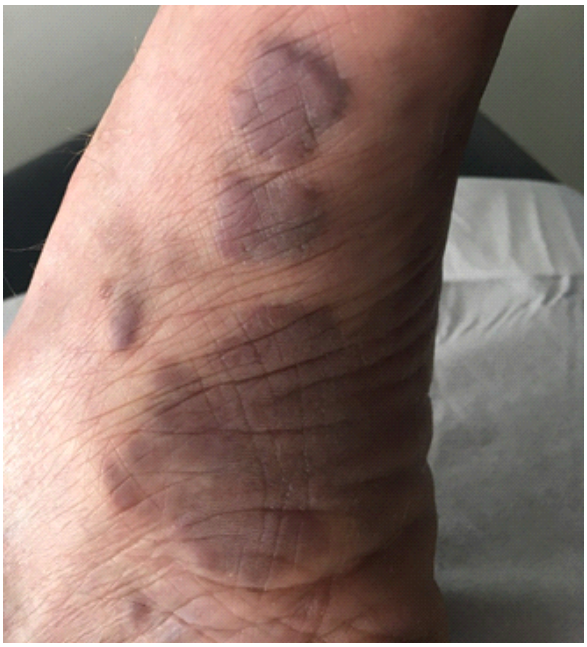

Figure 2. *Lesions of annular configuration.*

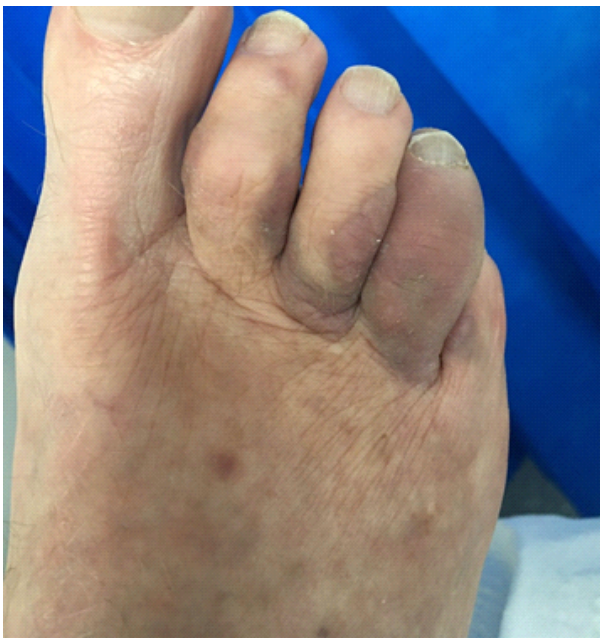

Figure 3. *Discoloration extending to the dorsum of the third and fourth toes.*

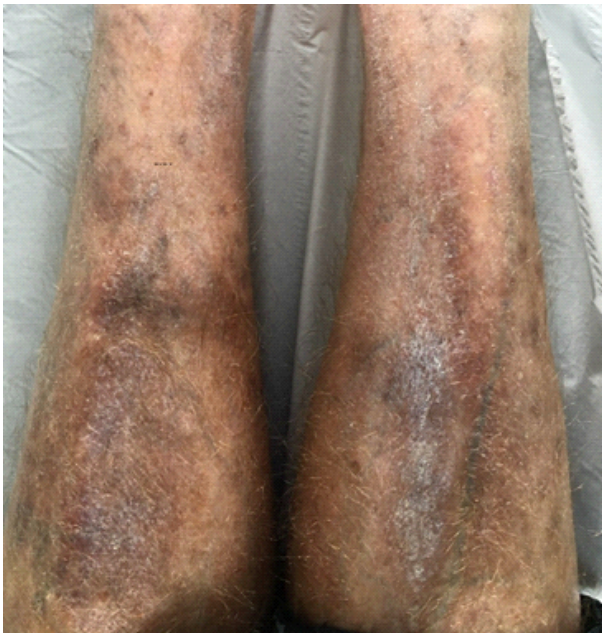

Figure 4. *Discolouration over the shins.*

Laboratory investigations showed normal glycosylated haemoglobin levels. The prostate-specific antigen test was within normal range, and results for human immunodeficiency virus, Epstein-Barr virus, hepatitis C, herpes simplex virus, cytomegalovirus, anti-nuclear antibodies and rheumatoid factors were all negative.

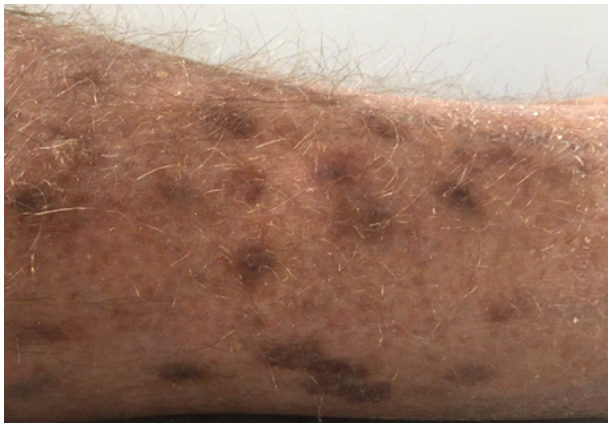

Figure 5. *Discrete discoloured patches over the shin.*

The punch biopsies were taken from his left and right legs, each of which showed a vascular lesion comprising clusters of rounded small to medium-sized vessels (Figure 6). There is a vague network of dilated vascular channels dissecting through dermal collagen (Figure 7). The lining endothelial cells were mildly atypical with hyperchromatic nuclei. The atypical vascular endothelial cells in both biopsies were positive for HHV8 (Figure 8), CD31, and ERG (Figure 9), with MIb-1 positive in vascular endothelial cells (Figure 10). This morphological and immunohistochemical finding of atypical vascular proliferation in the dermis raised the possibility of Kaposi sarcoma. The slides were then discussed in a specialist multidisciplinary meeting, where a second opinion was taken from specialist consultant histopathologists, and it was agreed that the histology fit with new subtype of KS called angiosarcoma-like KS. He was then referred to a specialist tertiary center for further management, where it was decided to take a conservative approach and not to initiate anticancer medications for the time being, as the patient was asymptomatic, with the prospect of starting potential chemotherapy should the disease progress in the future.

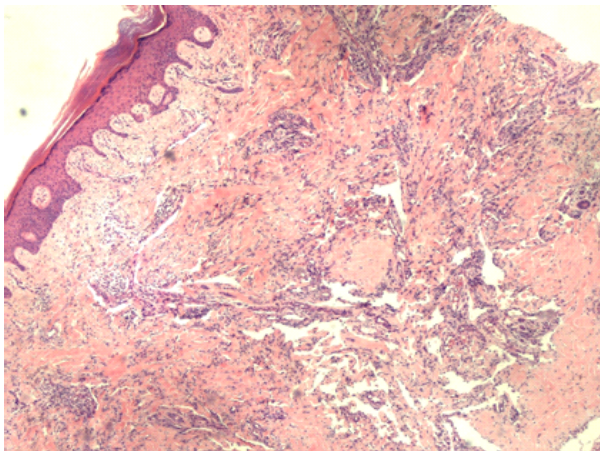

Figure 6. *Vascular lesion consisting of rounded small to medium size vessels.*

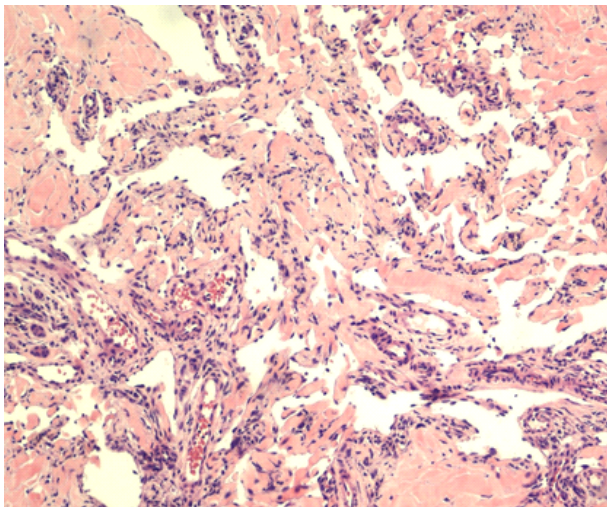

Figure 7. *Dilated vascular channels dissecting through dermal collagen.*

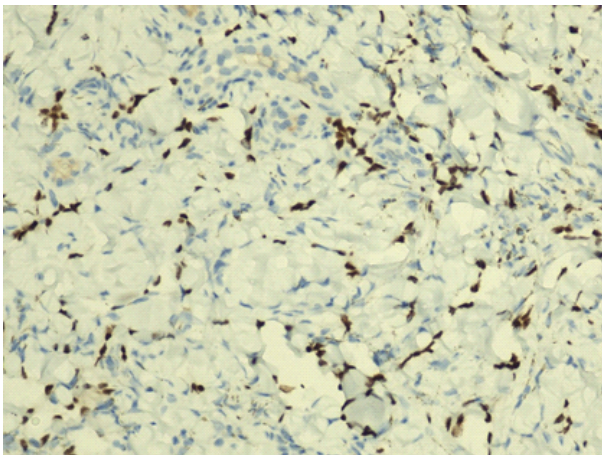

Figure 8. *Tumour positive for HHV8.*

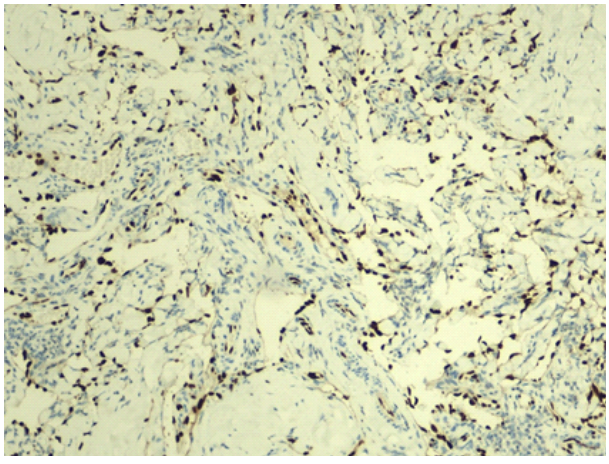

Figure 9. *Endothelial cells diffusely and strongly positive for ERG.*

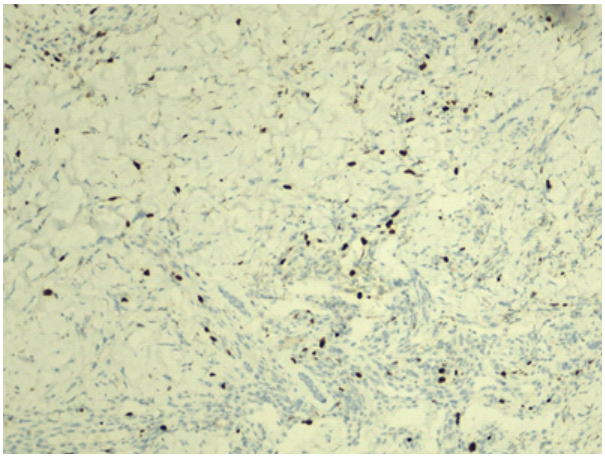

Figure 10. *Low to moderate MIB-1.*

Discussion

KS was first described by a Hungarian dermatologist as a skin sarcoma with idiopathic multiple pigmentation[9]. Based on the cases reported in the literature, it is reasonable to conclude that KS development is generally linked to patients' immunosuppression of many origins, like HIV and/or herpes infections, chemotherapy, and post-transplantation therapy[10-11]. However, KS in HIV-negative patients who are immunocompetent has also been reported[12-13]. We describe a similar case in our report, where an immunocompetent patient developed Kaposi sarcoma. Should this be classified as a fifth type or a subgroup of classic KS, as an increasing number of HIV-negative, HHV8-positive KS cases are now being reported among MSM (men who have sex with men)?

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