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Case presentation

A case of Kaposi sarcoma in an immunocompetent, heterosexual Irish man: a discussion of etiology and viral transmission

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Abstract

Four types of Kaposi sarcoma (KS) have been described, all of which are caused by human herpesvirus-8 (HHV-8). The incidence of KS in the United States is highest among HIV-positive homosexual men and elderly men of Eastern European, Jewish, or Mediterranean descent. However, few reports describe KS in HIV-negative, immunocompetent heterosexual men in the United States. HHV-8 is transmitted largely via saliva and close sexual contact, whereas there are only a handful of reports of transmission via blood and blood products. We report a case of an HIV-negative, immunocompetent heterosexual man who acquired KS via blood transfusion. A 77-year-old immunocompetent, monogamously heterosexual, HIV-negative Irish man presented with a biopsy-proven KS lesion on the right thigh. Past surgical history included a coronary artery bypass graft, during which he received a blood transfusion from an unknown donor source. His ecchymotic KS lesions progressed while on doxycycline, intralesional vinblastine, and topical anti-angiogenic medications. The patient eventually achieved stabilization of KS lesions with acitretin. Our case report emphasizes the need to characterize the phenotype and transmission route of HHV-8 in heterosexual, immunocompetent patients in geographic regions with low HHV-8 seroprevalence.

Keywords: Kaposi's sarcoma, human herpes virus-8, Kaposi's sarcoma-associated herpesvirus

Introduction

Kaposi sarcoma is a rare, multicentric angioproliferative spindle cell tumor of endothelial origin that frequently presents as multiple cutaneous and mucosal vascular nodules. Before 1981 in the United States, KS was considered to be an uncommon disease affecting older men of Eastern European, Jewish, or Mediterranean descent [1]. The disease became internationally recognized in the early 1980s, when it was found to be present in approximately 40% of homosexual men with AIDS [2]. In the US population KS occurs at a rate of 6 cases per million people each year, whereas the estimated HHV-8 seroprevalence among US blood donors is about 2.8-3.5% [3, 4].

The male predominance, multifocal occurrence, and restricted geographic incidence pointed to an infectious agent as the responsible factor causing KS. In 1994, using a novel technique of polymerase chain reaction (PCR) called representational difference analysis, researchers discovered the presence of new viral DNA sequences in the KS nodules of patients with AIDS [5]. Identified as human herpesvirus-8, the virus shares its homology with gamma-herpesviruses, a group of viruses known for their ability to maintain latency in lymphocytes. Like other herpesviruses, HHV-8 only periodically enters the lytic cycle, at which time it replicates and acquires an infective capacity [5].

Generally, the prevalence of HHV-8 varies between geographic regions from an overall rate of 1%-7% in Western Europe and North America, to 10-20% in Mediterranean countries, and up to about 100% in certain sub-Saharan African countries [6]. HHV-8 is the essential etiological agent for the four commonly described clinical-epidemiological variants of KS: classic (Mediterranean), endemic (African), iatrogenic (post-transplant), and AIDS-associated (epidemic) forms. Some case reports suggest a fifth category of KS occurring among homosexual men without HIV infection [7, 8]. The transmission routes of HHV-8 seem to differ between the endemic and non-endemic countries [6]. Specifically, in the low-prevalence countries including the United States and Western Europe, transmission seems to be mainly from sexual activities among homosexual men, especially in those with concurrent HIV infection [7], from intravenous drug use [9], or from renal transplantation [10]. In the geographic regions with high-prevalence of HHV-8, specifically in countries of the sub-Saharan Africa, evidence suggests that transmission routes may be due to non-sexual transmission among family members and close contacts, mainly through saliva [6]. HHV-8 transmission in the United States tends to occur in higher rates among homosexual men, although HHV-8 acquisition as a result of blood transfusion is exceedingly rare. Dollard et al. reported the transmission risk to be 0.082% per transfused unit of blood, based on a sample of 284 patients who seroconverted after a transfusion [11]. Herein, we present a case of a patient who may have acquired the HHV-8 virus via blood transfusion.

Case synopsis

A 77-year-old man presented to the dermatology clinic with a round, firm, asymptomatic, small dark papule, located on the right posterior thigh. The patient had a past medical history of mild, plaque type psoriasis, rosacea, glaucoma, basal cell carcinoma, hypertension, hyperlipidemia, coronary artery disease status post coronary artery bypass surgery, right acoustic neuroma, and right-sided chronic nephrolithiasis. During his cardiac surgery, he received 6 units of random donor platelets and 2 units of fresh frozen plasma. He had no history of alcohol, tobacco, or illicit drug use. His daily medications consisted of clopidogrel, aspirin, lisinopril, metoprolol, simvastatin, metronidazole, travoprost, and potassium citrate. The patient’s treatment of psoriasis included topical steroids and he denied receiving oral treatment or phototherapy.

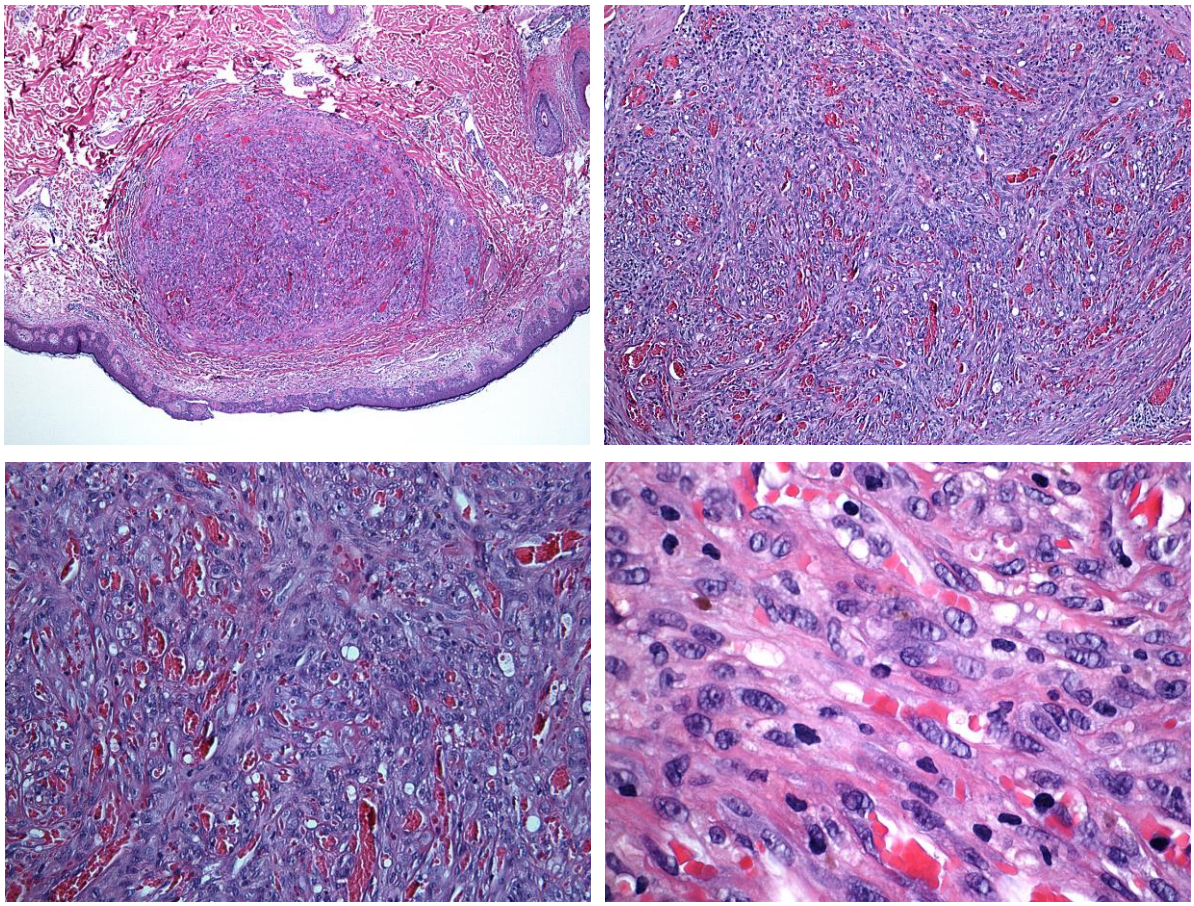

Figure 1. Dermal proliferation of irregular slit-like vascular channels with numerous extravasated erythrocytes. Hematoxylin and eosin stain, magnifications 4x, 10x, 20x, and 40x.

A 4 mm punch biopsy of the lesion on the right posterior thigh revealed a nodular variant of Kaposi sarcoma. Histology showed a dermal proliferation of atypical spindle-shaped cells arranged in a perivascular and interstitial pattern, with surrounding stroma showing fibroplasia with cleft-like spaces filled with erythrocytes. Numerous hemosiderin laden macrophages were noted and the dermis showed a variable, mostly perivascular lymphohistiocytic infiltrate with some plasma cells. There was some involvement of dermal adnexa. Immunochemical analysis showed strong immunopositivity to CD 31, CD 34, and HHV-8.

The patient was found to be negative for HIV with PCR and ELISA testing and he has no history of immunosuppression. The patient grew up in Ireland and moved to the United States at age 17. The patient has had only one monogamous sexual relationship in his life with his wife, whose only sexual partner had been the patient. The patient had not traveled outside of the United States.

Over the next several months, the patient developed several new ecchymotic lesions on the bilateral arms without lymphadenopathy. A second biopsy from the right arm showed Kaposi sarcoma. The patient denied hemoptysis, hematochezia, melena, weight loss, anorexia, night sweats, chills, fevers, or bone pain. Laboratory workup and imaging were within normal limits with exception of hyperglycemia. We treated the patient with intralesional vinblastine and daily applications of calcipotriene, triamcinolone, tretinoin, and imiquimod. The treated lesions showed reduced color intensity and induration. However, new blue-violet patches and plaques continued to develop on the bilateral upper and lower extremities. Adjunctive therapy with alitretinoin 0.1% gel twice daily and oral doxycycline 100mg twice daily for four months did not result in significant improvement. Workup by the oncology service did not reveal metastatic KS. We discontinued doxycycline after 4 months of unsuccessful treatment and began 35 mg oral acitretin daily and 500 mg of vitamin C twice daily. The patient appeared to have achieved stabilization of KS with oral acitretin and vitamin C, with no internal organ involvement.

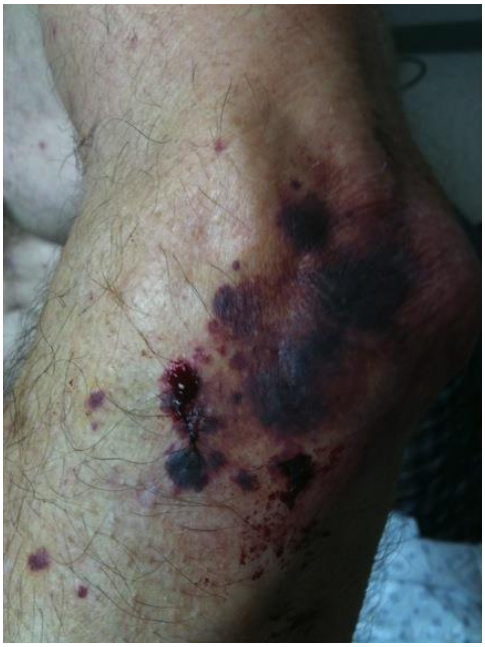

Figure 2. Gross picture of the ecchymotic patch located on the patient's arm.

Discussion

HHV-8, the etiologic agent for KS, is typically transmitted through saliva or sexual contact [1]. Recent studies have found evidence of rare HHV-8 transmission via blood transfusion [11, 12, 13]. One case report showed that HHV-8 recovered from blood donation can be infectious because the reverse transcription PCR detected HHV-8 RNA in the inoculated target cells [12]. Interestingly, there has only been one report that suggested actual transmission of HHV-8 via blood components in the United States [11]. This study randomly selected 406 cardiac surgery patients, primarily receiving coronary artery bypass, and collected serum specimens immediately before and six months after their surgeries. The study identified two patients with possible transmission of HHV-8 by blood transfusion, as was evidenced by their seroconversion. However, because linked donor specimens were not available, it was possible that seroconversion may have occurred owing to an outside source [11]. In 2006, a seminal study published in the New England Journal of Medicine by Hladik and colleagues provided strong evidence that HHV-8 is transmitted by blood transfusion in Uganda [13]. Specifically, Hladik et al. showed that transfusion of fresh, non-leukoreduced blood from a donor population with a high rate of HHV-8 infection resulted in a small increment of seroconversion among blood transfusion recipients (2.8%, $p<0.05$) [13].

Cannon et al. conducted the largest study in the US on HHV-8 infection among transfusion recipients and their linked donors in the 1970s [14]. They performed serologic testing among 1023 blood donors, 1350 transfusion recipients, and 599 surgical controls who did not receive blood recipients, and found that the risk to current transfusion recipients was very low, although it could not be ruled out [14]. The question remains why the transfusion risk was shown to be higher in Uganda than in United States. Some hypothesize that it may be related to lack of leukoreduction, or to shorter storage of blood samples in Uganda, allowing the virus to remain viable for longer period of time [6].

Although the concern over transmission via transfusion was raised more than two decades ago when Chang et al. discovered HHV-8, the debate continues to be addressed for several reasons. One of the issues with screening blood samples is that the assays for HHV-8 antibody detection require standardization as they often have variable sensitivity and variability [15]. Furthermore, HHV-8 antibody tests are difficult to interpret in healthy donors with latent infections, in whom antibody titers are low and viremia is generally undetectable [15]. Additionally, PCR methodology has technical deficits that may generate false-

positive results [15]. Yet another reason is that identifying appropriate populations in which to conduct large-scale linked donor-recipient transmission studies a remains to be a challenge [14].

Conclusion

Despite many studies, there is still no clear data to establish or disprove transmissibility of HHV-8 by blood. Clinicians need to be aware that KS may occur in patients without known risk factors for this angioproliferative disorder. Our case report emphasizes the need to characterize the transmission route of HHV-8 in heterosexual, immunocompetent patients in geographic regions with low HHV-8 seroprevalence such as the United States.

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