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Uncommon Presentation of Kaposi Sarcoma in an HIV-Negative Patient: A Case Report and Review of the Literature

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Abstract

Kaposi Sarcoma (KS) is a multifocal systemic disease first identified in 1872. It most commonly involves the skin, mucous membranes, lymph nodes, and gastrointestinal tract. There are four clinically distinct subtypes of KS that have been identified: Chronic or classic KS, African endemic KS, KS due to iatrogenic immunosuppression, and AIDS-related epidemic KS. The human herpesvirus 8 (HHV-8) has been implicated in all subtypes of KS. We present a unique case of KS in a 79-year-old male with a widespread distribution of skin lesions on his palms, soles, chest, and back. This case report highlights a novel presentation of classical KS in a patient without typically identified risk factors, which served as a barrier to their diagnosis and treatment.

Keywords

kaposi sarcoma, hhv-8, human herpesvirus 8

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

CASE REPORT

Uncommon Presentation of Kaposi Sarcoma in an HIV-negative Patient: A Case Report and Review of the Literature

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Abstract

Kaposi Sarcoma (KS) is a multifocal systemic disease first identified in 1872. It most commonly involves the skin, mucous membranes, lymph nodes, and gastrointestinal tract. There are four clinically distinct subtypes of KS that have been identified: Chronic or classic KS, African endemic KS, KS due to iatrogenic immunosuppression, and AIDS-related epidemic KS. The human herpesvirus 8 (HHV-8) has been implicated in all subtypes of KS. We present a unique case of KS in a 79-year-old male with a widespread distribution of skin lesions on his palms, soles, chest, and back. This case report highlights a novel presentation of classical KS in a patient without typically identified risk factors, which served as a barrier to their diagnosis and treatment.

Keywords: Kaposi sarcoma, HHV-8, Human herpesvirus 8

1. Introduction

Kaposi Sarcoma (KS) is a low-grade vascular tumor that can invade the skin, mucosa, and viscera. Its most well-known form is in the setting of acquired immunodeficiency syndrome (AIDS) or immunosuppression due to organ transplant.[1] KS is caused by Kaposi's sarcoma herpes virus (KSHV) also known as human herpesvirus 8 (HHV-8).[2] The HHV-8 virus is transmitted predominantly via saliva, and occasionally through blood transfusions or intravenous drug use. The virus attacks endothelial cells, upregulating aberrant angiogenesis via factors such as vascular endothelial growth factor and basic fibroblast growth factor.[1,3]

The virus causes vascular cutaneous lesions characterized as violaceus plaques. The KS lesions have three stages: patch, plaque, and tumor. They first emerge as a macule early in the disease process, then evolve into plaques and eventually into larger nodules/tumors. KS can involve the visceral organs, particularly the respiratory and gastrointestinal tracts.[3]

There are five epidemiological forms of KS, which are epidemic, iatrogenic, endemic, classic and the fifth form presenting in men who have sex with men (MSM) who are HIV negative.[4] The epidemic form, which is also an AIDS-defining illness, presents with multiple cutaneous lesions on the limbs, trunk, and face. Patients with a CD4 cell count <200 cells/μL is a strong risk factor for incident KS.[5] Mucosal lesions are also commonly present. The iatrogenic form affects solid organ transplants and presents as cutaneous lesions, rarely involving the mucous membranes or visceral organs. Endemic form most commonly is seen in sub-Saharan Africa individuals who are HIV negative. The endemic form presents with lymphedema, lower limb lesions, and may have an aggressive involvement of the visceral organs. The classic form, also called sporadic KS, is seen in populations with a high KS herpes virus prevalence, such as Middle East, eastern Europe and the

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Mediterranean areas. It is known to mainly affect men in their sixth decade of life. The classic form presents as a few lesions that are commonly confined to the lower limbs. The MSM population that are HIV negative and not immunocompromised present with few lesions but can erupt anywhere on the skin.[6]

2. Case description

We present a case of a 79-year-old male with a 2-week history of diffuse body rash including the palms and soles who presented to the hospital for an elective transurethral resection of the prostate procedure. The patient is of Mediterranean-descent and is now retired after many years of working in a spaghetti factory. He has diabetes mellitus type I, as well as an extensive cardiac history. The patient's urologist made a decision to postpone due to severity of worsening symptoms on the morning of the procedure. After transfer to the emergency department, the patient described waxing and waning bilateral leg swelling for 7 months, associated with some worsening skin color changes and texture changes on his lower legs and feet. He complained of numerous round or oval-shaped red patches that appeared on his thighs, arms, chest and back over the course of the past 2 weeks, along with pain when walking. The patient's social history is negative for smoking tobacco, alcohol dependence, or illicit drug use.

The physical exam confirmed irregular cardiac rhythm, with signs of exacerbated heart failure, including crackles heard at the lung bases and bilateral lower limb edema. Close skin examination was notable for acral purpura on the fingers, toes and palms, retiform purpura extending proximally to the forearms, upper arms and thighs as well as numerous widespread red/violaceous plaques in the same distribution. Basic workup in the ED included an electrocardiogram which showed atrial fibrillation with preventricular contractions as well as a normal chest Xray.

Dermatology was consulted, after examining the patient, it was determined that the rash was consistent with retiform purpura, which can have various causes related to embolic or thrombotic states (including hypercoagulable state, infection, or inflammation). Therefore, a comprehensive workup was performed to identify the underlying etiology. Rheumatology was consulted at this time for possible antiphospholipid syndrome pending anticardiolipin antibody, lupus anticoagulant, and antibeta 2 glycoproteins. Vasculitis was also considered, therefore antinuclear antibodies, antineutrophilic cytoplasmic antibody, C3 and C4 proteins were ordered, but none returned positive. Infective endocarditis was considered, particularly because the patient developed a rash after cardioversion. Therefore, a transesophageal echocardiogram (TEE) was ordered to evaluate for this possibility. Differential at this time included anti-phospholipid antibody syndrome, disseminated intravascular coagulation, heparin induced thrombocytopenia, thrombocytic thrombocytopenic purpura, endocarditis, angioinvasive infection, calciphylaxis, vasculitis, and warfarin-induced skin necrosis. For a definitive diagnosis, a skin biopsy was done on his right thigh and sent for pathology. In total, the patient had a negative rheumatologic work-up for vasculitis and autoimmune disorders. TEE was negative for embolic etiology. To investigate the possibility of severe atherosclerotic disease as a cause, the patient underwent a CT angiogram (CTA) of the aorta with runoffs, which returned negative for significant atherosclerosis. Vascular surgery was consulted and, due to the presence of pulses and the negative CTA results, it was decided that there was no indication for anklebrachial indices at this time. Skin biopsy revealed vascular damage with marked vascular hemorrhage and massive vascular proliferation, suggestive of diffuse dermal angiomatosis with unclear etiology. An immunohistochemical stain for human herpesvirus 8 was strongly positive in the nuclei of many of the lesional endothelial cells. The positive HHV-8 staining, in combination with the histologic picture of innumerable anastomosing vessels with hemorrhage and hyaline globules, is consistent with a diagnosis of KS.

In the United States, KS is significantly more prevalent in individuals with AIDS, at least 20,000 times higher than in the general population,[7] which is why HIV-1 and HIV-2 antigens and antibodies screen was done, but results were nonreactive. Sexual history was also inquired about the patient as there is a subtype of KS that is prevalent in MSM who are HIV negative. The patient reported history of sexual encounters with women only. After taking into consideration the patient's non-reactive HIV titer, negative sexual history with male partners, ethnic background, and the final biopsy revealing an HHV-8 positive vascular proliferation, diagnosis was felt to be most consistent with Kaposi sarcoma, classic subtype. We discussed the diagnosis of classic KS and its association in older males of Mediterranean or Central/Eastern European ancestry with the patient. Given the patient's widespread cutaneous disease and worsening lymphedema, localized therapy is unlikely to be effective. Therefore, we have discussed the option of systemic treatment with chemotherapy, specifically a single agent Doxil regimen. Treatment with Doxil has been associated with a response rate of

approximately 60 % and may be a viable option for managing the patient's condition.[8]

Regarding the patient's other presenting symptoms, he was effectively managed for heart failure exacerbation as the hospital course progressed, and over the course of his stay, his symptoms improved overall. No other acute issues needed to be addressed during the admission, therefore the patient was discharged and was advised to follow up outpatient with oncology for further management of the KS lesions.

3. Discussion

In summary, this was a unique presentation of Kaposi Sarcoma in an HIV-negative, non-immunosuppressed 79-year-old male patient who was evaluated for a widespread rash and worked up for heart failure. Given the patient's non-reactive HIV titer, his negative sexual history with male partners, his Mediterranean heritage, it is presumed that our patient has the classic form of KS.

There should be an importance placed on early detection of this classic type of KS. Early diagnosis can lead to less complications and less invasive treatment with better outcomes for patients. The typical course for classic KS is indolent in the beginning, but eventually can progress to organ involvement and other complications. In one study involving 87 patients with biopsy-diagnosed classic form KS, 81.6 % were found to have GI lesions on endoscopic exam.[9] In addition to lesional spread onto mucosal surfaces of the body, classic KS has also been found to carry with it an increased risk of other malignancies such as non-Hodgkin lymphoma and cutaneous malignant melanoma.[10] Studies looking at patients with classic KS have found that mortality is typically due to secondary malignancy or other unrelated causes.[9] More research is necessary on this topic, however there could be a possibility that early detection and treatment can not only prevent further organ involvement and damage but also prevent the onset of other diseases as it progresses over time.

Efforts should be made in the public health sphere to spread awareness regarding classic KS to the specific groups it commonly affects, such as those with Mediterranean decent, Eastern European or Jewish heritage. Although it is true that this is a rare form of the disease, it is important to note that early detection leads to better outcomes, according to studies done on the various treatment options of classic KS at varying stages. The stages of KS are separated by either slow tumor evolution indicating stage 1 or rapid tumor evolution indicating stage 2. Stages 3 and 4 are characterized by various disease complications. Patients diagnosed with KS in stages 1 or 2 can see benefit from therapies such as clinical monitoring, surgical excision, radiotherapy, and even elastic stockings for prevention of lymphedema.[11] Patients diagnosed with KS already in later stages require more serious management, typically involving systemic chemotherapy. In the case of our patient, due to his widespread cutaneous disease and the worsening lymphedema, he was unfortunately not able to be treated with localized therapy and will most likely undergo systemic chemotherapy as recommended by oncology.

Conflict of interest

All authors declare that they have no conflicts of interest.

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