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Case report

Penile Kaposi Sarcoma as an initial manifestation of HIV infection: A case report and literature review

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ABSTRACT

Kaposi Sarcoma (KS) is most commonly associated with Acquired Immunodeficiency Syndrome (AIDS). Kaposi sarcoma herpesvirus is thought to play a huge role in the pathogenesis of KS. The diagnosis and management of KS can be quite challenging, and Physicians need high index of suspicion to diagnose KS as it can be mistaken for other skin pathologies. We present a case of a young male who developed KS on the penis as the initial manifestation of human immunodeficiency virus infection (HIV) and AIDS. Initially, he presented with a painful non-resolving ulcer on the glans penis for 2 weeks. He tested positive for HIV and his HIV viral load was more than 200,000 copies with CD4 count being only 8 per microliter. Histopathological examination of the lesion along with immunohistological staining were positive for KS. The patient was not adherent to his antiretroviral therapy (ART), and his condition deteriorated. Literature review showed only 16 cases of HIV positive patients presenting with KS involving the penile area, with only 4 of them being the initial manifestation of HIV and AIDS. A combination of systemic chemotherapy and ART is often needed for visceral or metastatic KS. There is a huge need to increase awareness about HIV and related complications among health care providers and the general population.

Introduction

More than a century ago, Kaposi sarcoma (KS) was described by the Hungarian dermatologist Moritz Kaposi as idiopathic pigmented sarcomas in the skin [1]. KS is an angioproliferative tumor derived from vascular endothelial cells [2]. Human herpesvirus 8 (HHV-8) infection, also called Kaposi sarcoma herpesvirus (KSHV), plays a major role in the pathogenesis [3]. Four clinical types have been identified for this disease. The classic variant affects older men of Mediterranean, Eastern European and Middle Eastern origin. Endemic or Africa variant presents in young adults living in Equatorial region. Immunosuppression related KS affects mainly transplant patients and those receiving immunosuppressive medications. Finally, the most common variant is the Acquired Immunodeficiency Syndrome (AIDS)-associated KS [2,4].

KS is considered an AIDS-defining illness and the most common malignancy observed in those patients [5,6]. It usually presents as violaceous macules, papules, or plaques on the face, trunk, or oral mucosa [5,6]. Penile KS is rare, and patients presenting with penile KS as the initial skin lesion account for only 3% [7]. Here we describe a young patient who presented with KS on the penis as the primary manifestation of HIV and AIDS.

Case report

A 35-year-old single male, with no prior history of chronic illnesses, presented to the emergency department with painful penile swelling for 2 weeks. It was associated with dysuria and urinary retention. The lesion started as an itchy papule over the glans penis and progressed into an

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ulcer. There was an unintentional weight loss of 25 kg over 2 years. He also reported subjective fever, loss of appetite and night sweats. On examination, there was a large tender dry ulcer on the glans penis. The penile shaft was otherwise unremarkable and there was no inguinal lymphadenopathy.

Because of urinary retention and the extension of the ulcer to the urethral meatus, he was placed on a suprapubic catheter. Upon hospitalization, the ulcer was believed to be caused by a sexually transmitted infection (STI) like Neisseria gonorrhea, Haemophilus ducrei, Chlamydia trachomatis or Klebsiella granulomatis. Hence, he was started empirically on a single dose of 1000 mg Ceftriaxone Intramuscular injection, a single dose of 1000 mg oral Azithromycin and 100 mg Doxycycline twice daily.

Investigations were positive for treponemal antibodies and HIV. However, other STI workup was negative including NAAT for Chlamydia trachomatis, Neisseria gonorrhea and urine culture. HIV viral load was more than 200,000 copies and lymphocyte subset analysis revealed advanced immunosuppression with only 8 CD4 counts per microliter. For the HIV infection, he was started on a 4-drug co-formulated single-tablet regimen of Elvitegravir, Cobicistat, Emtricitabine and Tenofovir diproxil fumarate. Radiologic screening of opportunistic illnesses was negative.

One week after hospitalization, the penile ulcer did not show any improvement. Chronic atypical infections and malignancies were suspected and a decision was made to proceed with a biopsy of the ulcer. The patient declined any further testing and interventions and was discharged home on Doxycycline to complete 21 days.

He lost follow-up and presented 5-months later with virologic failure due to non-adherence to ARVs. The lesion became harder in consistency, darker in color and has enlarged and reached the distal part of the penile shaft. In the Operating theatre, he underwent partial penectomy because of extensive involvement and destruction of the urethra (Fig. 1).

Histopathological examination of the lesion showed extensive dermal proliferation by atypical vascular channels of mostly spindle cells with nuclear irregularities in a slit-like pattern (Fig. 2). Also, immunohistological staining showed a positive reaction for HHV8, CD31 and CD34 which confirm the diagnosis of KS (Fig. 3). The sample was negative for bacteria, mycobacterial and fungal infections. The excised margin was positive.

He was then referred to the radiation oncology team after the urology team did not think a further penectomy to achieve a negative margin was feasible. The radiation oncology team have offered him radical radiotherapy to the margin but the patient declined.

Screening for visceral involvement of KS revealed a left upper lung lobe mass-like consolidation in the chest CT scan which was concerning. CT-guided core biopsy of the lung mass showed metastatic focally necrotic KS with HHV-8 immunostain positive in 70–80% of the tumor cells (Fig. 4). The oncology team then opted to start him on systemic liposomal Doxorubicin at a dose of 20 every 3 weeks. He tolerated the first three cycles well with minimal toxicity. However, again, he unfortunately lost follow-up again and was not adherent to his ART. He presented 7 months later with more advanced HIV and KS. His performance status was poor, and was no longer fit for chemotherapy. His condition rapidly deteriorated and he passed away.

Discussion

English language literature review was done using PubMed database searching for previously reported cases of HIV positive patients presenting with KS involving the penile area. From 1985–2020, 16 cases have been identified (Table 1). The mean age of the patients was 41.1. Most of the cases presented as violaceous papules or plaques that occurred mainly on the glans penis, similar to our patient, with some of them progressing to ulcerative or necrotic lesions, and others involving the urethral meatus causing urinary symptoms. Only in four previous cases penile KS was reported as the first presentation of HIV and AIDS.

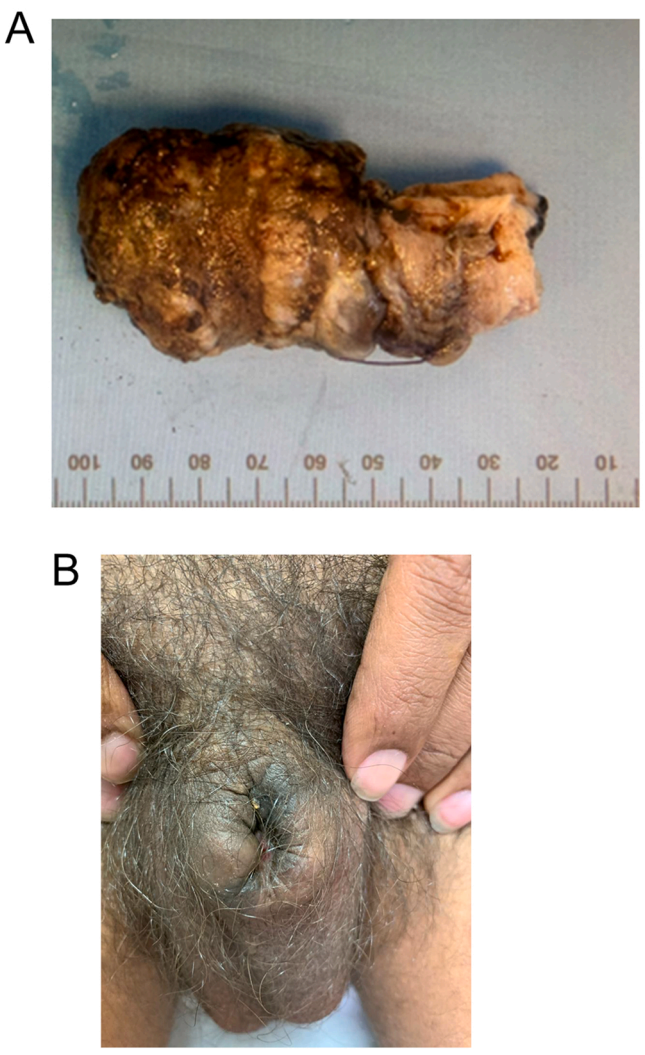

Fig. 1. A: Gross image of the ulcer post partial penectomy, B. Post partial penectomy of the ulcer.

Seven of all patients were mentioned to be homosexual which increases the risk of KS by 5–10 times compared to those with other high-risk behaviors [8]. Furthermore, homosexuality is most likely under reported since most of the studies were in the 90′s and 80′s. A low CD4 count is associated with high risk for KS. surprisingly, there have been reported cases of patients developing KS with normal CD4 count [5,9]. Out of all reported cases, five patients died after being diagnosed with penile KS and before discovery of potent combination of ART. Eight patients improved, and three of them had resolution of the lesion by only HAART treatment. In fact, only six cases were reported after discovery of HAART medications.

KSHV is a DNA virus of the Herpesviridae family that can be transmitted vertically as well as through sex, blood transfusions, and solid organ transplantation [2–4]. HIV and KSHV play a combined action in the pathogenesis of KS. HIV causes chronic inflammatory state and release of vascular endothelial growth factors, and KSHV induces the secretion of inflammatory cytokines and increase in expression of viral genome that is directly involved in angiogenesis [22–26].

Physicians need high index of suspicion to diagnose KS, especially in immunocompromised patients. Evaluation starts with a detailed history and a complete physical examination including the skin and mucosal membranes. A biopsy of the skin lesion is needed to confirm the diagnosis [27]. KS features on histopathology include: mononuclear inflammatory and spindle cells, ill-defined vascular channels with

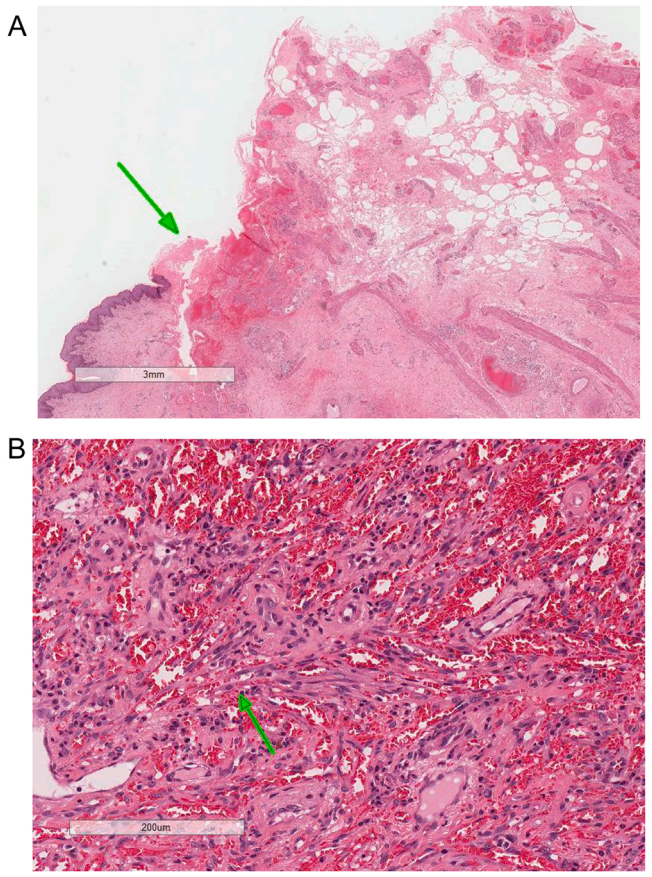

Fig. 2. (A) (H&E stain). Microscopic image of the tumor's hemorrhagic ulcer site (arrow). The ulcer is characterized by a discontinuation of the epidermal surface by the underlying vascular tumor, (B) The tumor is characterized by an extensive dermal proliferation by atypical vascular channels of mostly spindle cells with nuclear irregularities in a slit-like pattern (arrow) along with extravasated red blood cells.

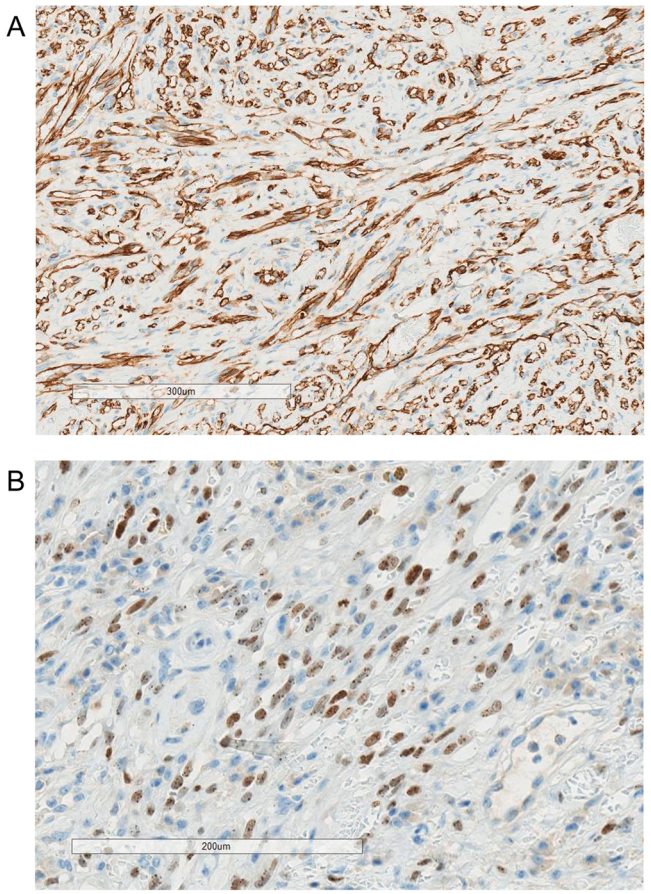

Fig. 3. (A) The tumor's vascular differentiation was further confirmed with the CD31 immunostain. (B) The tumor's positivity for the HHV-8 immunostaining with a nuclear "dot-like" pattern is essentially consistent with the diagnosis of Kaposi sarcoma.

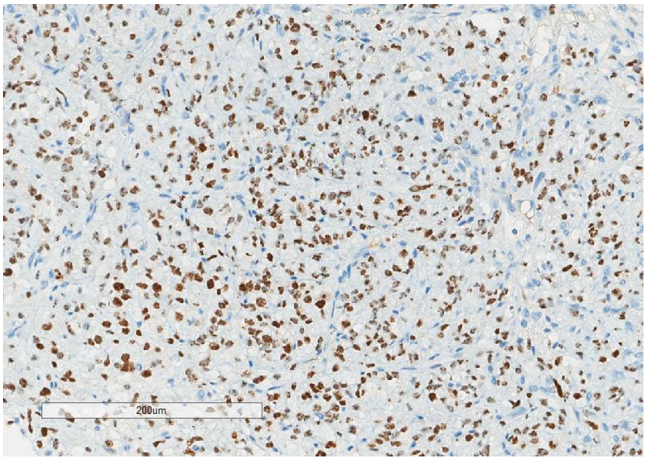

Fig. 4. The metastatic tumor's positivity for the HHV-8 immunostaining with the nuclear "dot-like" pattern is consistent with the diagnosis of metastatic Kaposi sarcoma to the lung.

hemorrhage [25,28]. AIDS-KS may involve the internal organs in more than 50% of the patients, and usually involves the Gastrointestinal or respiratory systems [8,29–31]. When visceral involvement is suspected, endoscopy or bronchoscopy may be indicated [27].

Combined ART alone is less effective in patients with HIV related KS with visceral involvement or metastatic KS. Combination with systemic chemotherapy is frequently needed. Objective response rates (partial & complete responses) ranged between 20% and 39% in patients on combined ART alone, with a significant improvement in response rates when combined with systemic chemotherapy [32,33]. Pegylated liposomal doxorubicin, and paclitaxel are both acceptable, and preferred first line options for advanced or rapidly progressive KS [34]. Discussion between the medical oncologist and the infectious disease specialist is essential when choosing appropriate combination therapy (of ART and systemic chemotherapy) due to risk of overlapping toxicity, drug-drug interactions, and other factors.

Unfortunately, we report the first case in which a patient with penile KS deteriorates after the discovery of potent combination of ART. In Saudi Arabia, awareness of HIV among the general population and health care providers needs further improvement. A study showed a poor knowledge of HIV and high stigmatization among health care providers in Saudi Arabia [35]. This pattern is also observed in a study among university students in Saudi Arabia [36]. In a study of 276 Saudi males with HIV, 33% had AIDS as the first presentation which is considered higher than the international figures. Also, the mean age of diagnosis of HIV in heterosexual males was around 38 years [37]. Strategies to fill gaps in knowledge and attitudes are highly needed to significantly influence the quality of HIV-related health care in Saudi Arabia.

Penile KS is a very rare subset of KS. In general, penile KS in a young patient is most likely secondary to HIV infection, while in older patients it is mostly primary. A study included 19 HIV negative patients with penile KS. The mean age of patients was 57 years while in our study it

Table 1
Summary of Previous Similar Reports.

Report	Age	Presentation	CD4 #	Viral load	KS as initial presentation of HIV	Adherence to ART	Extracutaneous involvement	Urinary symptoms	Outcome
2020. Sacks, et al. [10].	49	Multiple slow-growing, violaceous, ulcerated lesions on the glans penis and external urethral meatus	48	n/a	no	no	no	n/a	improved
2016. farshidpour, et al.[11]	34	several small violaceous macules ranged from 2 mm to 1 cm were observed on the glans and shaft of the penis	79	395,722	no	yes	yes	no	n/a
2014. Lebari, et al.[5].	40	Solitary violaceous pedunculated lesion on the penis	437	undetectable	no	yes	no	n/a	improved
2013. Ruocco, et al.[12].	35	Round, violaceous, firm nodule exactly located on the HZ-affected dermatome	100	n/a	no	no	n/a	n/a	improved, only mentioned that lesion disapear
2011. Almeida, et al.[6].	47	Violaceous confluent nodules with a smooth lobular surface, with multiple skin-colored verrucous papules, were distributed over the foreskin and glans	69	16,034	yes	n/a	no	n/a	improved
2011. Waiters, et al.[13].	56	Numerous yellow-green and white indurated plaques on the glans penis, coronal sulcus, and penile shaft	< 15	122,000	no	no	n/a	n/a	improved
1996. John, et al. [14].	n/a	Meatal obstruction caused by Kaposi-sarcoma	n/a	n/a	n/a	n/a	n/a	n/a	n/a
1995. KLEIN, et al.[15].	47	Massive KS lesions involving the penis, scrotum, and lower extremities. The glans was mummified with blackened eschar	n/a	n/a	no	n/a	n/a	n/a	died
	34	Significant swelling of the glans and shaft. with massive exophytic and necrotic KS involving the scrotum, base of the penis, and groin. An area of gangrene was note midshaft with black eschar	n/a	n/a	no	n/a	n/a	n/a	died
1993. SWIERZEWSKI, et al.[16].	36	Purplish lesion involving the entire glans penis and meatus	n/a	n/a	no	–	n/a	yes	died
1993. Cerdá, et al. [17].	40	A purpura-type lesion with inflammatory features appeared in the foreskin of the penis	n/a	n/a	n/a	n/a	n/a	n/a	n/a
1991. Angulo, et al.[18].	28	Rapidly growing red-purple nodule on glans penis	n/a	n/a	yes	n/a	n/a	n/a	improved
	26	Multiple cutaneous lesions in the penis, scrotum, right calf and leg	n/a	n/a	yes	n/a	n/a	n/a	died
1988. Bayne, et al.[19]	30	Engorged hypervascular penis	n/a	n/a	n/a	n/a	no	n/a	survived 5 years
1988. Wishnow, et al.[20].	42	Purplish nodule on the glans penis adjacent to the urethral meatus and a small, bluish, vascular-like lesion within the fossa navicularis	n/a	n/a	no	n/a	n/a	yes	improved
1986. SEFTEL, et al.[21].	54	Two Purplish lesions, one was on the shaft of the penis and the other was on the glans penis, extending onto the meatus	n/a	n/a	no	n/a	n/a	yes	died

n/a: unknown or not applicable.

was 41. Also, their study showed good prognosis for patients and low recurrence rate in comparison to our study findings [38].

Conclusion

We report a rare case of penile KS as the first presentation of HIV infection and AIDS in a young patient. This report showed the importance of early detection and treatment of HIV patients to prevent the development of complications such as AIDS and KS even in low prevalence areas. Also, an unusual genital lesion in a previously healthy patient that is resistant to treatment should raise the suspicion of KS and AIDS, as early detection will result in early treatment with ART and a better prognosis. Also, developing interventions to increase awareness and decrease stigmata of HIV among health care providers and general population are crucial to early detection of HIV positive people.

Ethical approval

The study was approved by the institutional review board of King Abdullah international medical research center (KAIMRC).

CRediT authorship contribution statement

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing, others, who have contributed in other ways should be listed as contributors.

Declaration of Competing Interest

None.

Acknowledgments

Not applicable.

Ethical consideration

All procedures in this study involving human participants were in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Informed consent

Written informed consent was obtained from the patient's next of kin (his father) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

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