International Journal of Dermatology

WILEY

CLINICAL CORRESPONDENCE

Unusual Presentation of Kaposi Sarcoma in a Virally Suppressed HIV Patient With High CD4 Counts

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Received: 27 September 2025 | **Revised:** 22 December 2025 | **Accepted:** 29 December 2025

Name of the institution(s) at which the research was conducted: Fundação Hospitalar Alfredo da Matta de Dermatologia, Manaus, AM, Brazil.

Keywords: antiretroviral therapy | HIV | kaposi sarcoma | penile neoplasms

Kaposi sarcoma (KS) remains a relevant neoplasm in people living with human immunodeficiency virus (HIV), even under virological control. We report the case of a 57-year-old man, HIV-positive and on continuous antiretroviral therapy (ART), who presented with an eight-month history of progressive, asymptomatic penile lesions. There was no mucocutaneous involvement elsewhere, and the patient denied systemic complaints.

On examination, violaceous nodules and plaques were observed on the glans and shaft (Figure 1). The rest of the tegument, including the oral cavity, was unremarkable. Since his HIV diagnosis in 2015, he has consistently maintained CD4 counts above 500 cells/mm^3 with an undetectable viral load. The only exception occurred in January 2024, when a transient rebound of viral load was detected (48 copies/mL; 1.681 log10 copies/mL). By June 2024, viral suppression was re-established and has remained stable since. Nadir CD4 count was 667 cells/mm^3 (August 2016).

Histopathology of a penile biopsy showed proliferation of spindle cells forming slit-like vascular spaces within the dermis, associated with extravasated erythrocytes and hemosiderin deposits. Immunohistochemistry was positive for CD31 and for nuclear latent antigen-1 of human herpesvirus-8 (HHV-8), confirming the diagnosis of KS (Figure 2). Routine laboratory tests were within normal ranges, except for mild normocytic anemia. Contrast-enhanced chest and abdominal computed tomography (CT) revealed no evidence of active pulmonary or abdominal KS lesions. The patient is receiving pegylated liposomal doxorubicin (20 mg/m^2) every 3 weeks and has completed five of the six planned cycles.

The overall incidence of KS has declined substantially with widespread antiretroviral therapy, yet cases in virologically suppressed individuals are increasingly recognized. In such patients, KS often behaves less aggressively than in viremic, immunosuppressed counterparts, with disease largely limited to the skin, though visceral involvement still occurs [1–3]. The present case, confined exclusively to the penis, illustrates a particularly unusual pattern. Isolated penile KS is rare, even in endemic regions, and recognition may be difficult, especially in patients with preserved CD4 counts and durable viral suppression [4].

This unusual localization presents important diagnostic challenges. Penile KS can be mistaken for infectious balanitis, chronic inflammatory conditions such as lichen planus or Zoon balanitis, vascular proliferations including pyogenic granuloma, or malignancies such as squamous cell carcinoma and melanoma [3]. In the present case, the patient had already been treated empirically with topical antifungals and corticosteroids, without improvement, delaying further investigation. In the context of stable immune status and controlled HIV replication, KS may not be the first diagnostic consideration, which increases the risk of misinterpretation. For this reason, persistent violaceous penile lesions should always prompt histological confirmation.

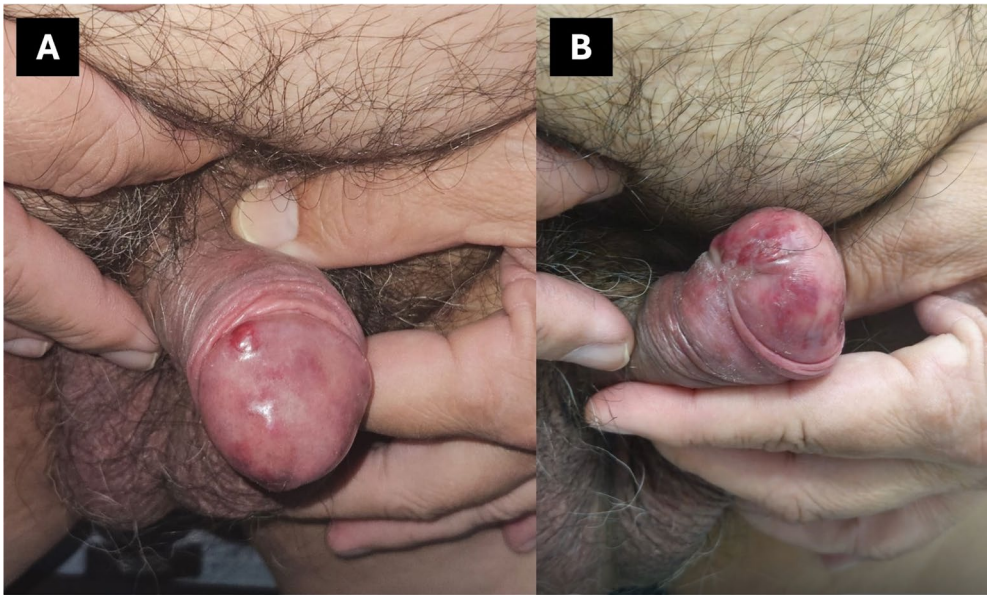

FIGURE 1 | Clinical presentation of Kaposi sarcoma restricted to the penis. (A) Violaceous nodules on the glans. (B) Plaques on the penile shaft.

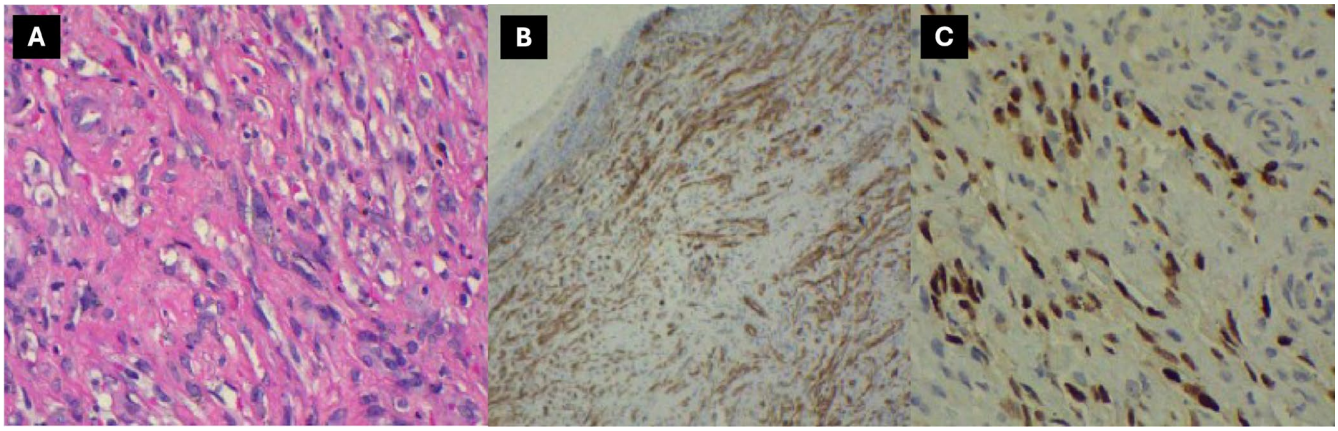

FIGURE 2 | Histopathological and immunohistochemical findings of Kaposi sarcoma. (A) Proliferation of spindle cells forming slit-like vascular spaces, with extravasated erythrocytes and hemosiderin deposits (hematoxylin–eosin, ×200). (B) Diffuse cytoplasmic positivity for CD31 in neoplastic endothelial cells (immunohistochemistry, ×200). (C) Nuclear positivity for HHV-8 latent nuclear antigen in spindle cells (immunohistochemistry, ×200).

The mechanisms underlying KS in patients with long-term viral suppression remain unclear. Persistent immune dysregulation, including features of immunosenescence characterized by expansion of senescent T cells and loss of naïve subsets, has been associated with impaired control of HHV-8 [2, 5]. These subtle changes may allow KS to develop or recur even in patients with robust CD4 counts. This scenario differs from KS associated with immune reconstitution inflammatory syndrome (IRIS), which arises during early ART and is driven by abrupt immune recovery rather than chronic immune imbalance.

In clinical practice, KS under viral suppression is generally indolent and confined to the skin, but systemic therapy may still be necessary. Intensifying ART offers no additional immune benefit, making therapeutic decisions dependent on lesion burden, anatomic site, progression, and patient comorbidities [2, 5]. When disease affects the penis, even limited involvement may cause disproportionate functional and psychosocial consequences, emphasizing the value of early recognition.

In summary, we describe a case of penile-restricted KS in a virologically suppressed patient with persistently high CD4 counts. This report highlights the rarity of penile-only KS, illustrates its potential to mimic diverse inflammatory and neoplastic processes, and highlights the importance of clinicopathological correlation. Vigilance remains essential when evaluating atypical vascular lesions in people living with HIV, regardless of apparent immune stability, and further research into the mechanisms of immune dysfunction underlying KS in this population is warranted.

Funding

This work was supported by Fundação de Amparo à Pesquisa do Estado do Amazonas, 010/2023.

Conflicts of Interest

This study was supported by FAPEAM (Fundação de Amparo à Pesquisa do Estado do Amazonas, Brazil) through "Programa de Apoio à Formação em Ciências Dermatológicas – PRODERM-RH" (grant #010/2023). S.T. is a PVN-II Research Fellow from FAPEAM. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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