

Case Report

A 63-Year-Old Male with AIDS and Diffuse Violaceous Plaques

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Keywords

Kaposi's sarcoma · HIV/AIDS

Abstract

Hyperkeratotic Kaposi's sarcoma (KS) is a rare clinicopathologic variant of AIDS-related KS that typically presents with chronic lymphedema and diffuse hyperkeratotic plaques of the lower extremities. Histopathologically, this variant is defined by epidermal hyperplasia, thickened lymphatic walls, and increased numbers of dermal fibroblasts and vascular spaces. Herein, we report the case of a 63-year-old HIV-positive male who presented with this rare hyperkeratotic variant of AIDS-related KS.

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Published by S. Karger AG, Basel

Introduction

Herein, we present the case of a 63-year-old male with hyperkeratotic Kaposi's sarcoma (KS) in the setting of HIV/AIDS. This case demonstrates an important clinical entity to recognize, the variety of treatment approaches available for diffuse KS, and the extent and morphology of disease that can occur without consistent monitoring and treatment.

Case Report

The patient was first diagnosed with KS in 1999 when he was admitted for workup of an unrelated colitis. Several scattered purple nodules were noticed on his arms and legs, and a skin biopsy obtained from a lesion on his foot confirmed the diagnosis. Subsequent HIV

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antibody testing was positive. Apart from clinical inguinal lymphadenopathy, systemic workup consisting of chest x-ray and colonoscopy did not show any evidence of visceral involvement. His past medical history was notable for hepatitis B and hepatitis C infections. The patient did not engage in sexual activity with his husband who was HIV negative.

The patient was started on antiretroviral therapy (ART) and underwent 12 cycles of liposomal doxorubicin. His response to therapy plateaued so he elected to stop doxorubicin and subsequently was enrolled in various clinical trials over the following years. Treatments he received included: two angiogenesis inhibitors (L-glutamine L-tryptophan [progression of disease] and COL-3 [initial partial response followed by progression of disease]), topical halofuginone (partial response), imatinib (progression of disease), 16 more cycles of doxorubicin, and finally sirolimus (stable disease). He was lost to follow-up in 2010 after sirolimus was discontinued.

The patient was admitted in 2017 following a seven-year absence of medical care. He had discontinued his ART several years prior following the loss of health insurance. He reported experiencing mild anorexia for the past year but denied any chills, malaise, hemoptysis, melena, or bright red blood per rectum. On physical examination, there were approximately 50 smooth violaceous papulonodules located on the trunk and upper extremities (Fig. 1a, b). The bilateral lower extremities had diffuse firm edema and superimposed confluent malodorous hyperkeratotic verrucous plaques (Fig. 1c, d). The patient was wheelchair dependent as a consequence of the restricted range of motion in his knees and hips from diffuse involvement of his disease. He was otherwise hemodynamically stable.

Laboratory evaluation showed an HIV-1 viral load of 11,900 copies/mL, an absolute CD4+ count of 414 cells/ μ L, thrombocytopenia, and macrocytic anemia. Skin scrapings obtained from the left foot and stained with 20% potassium hydroxide solution were negative for hyphae or fungal elements. A mineral oil preparation from skin scrapings did not reveal any mites, eggs, or scybala to suggest scabietic infection. A roentgenograph of the lower extremities demonstrated diffuse soft tissue swelling in the foot and ankle with osteolysis noted in the first and fourth distal phalanges of the left foot, consistent with osteomyelitis. A punch biopsy of a lesion on the right arm was obtained and showed a proliferation of slit-like vascular channels containing erythrocytes that dissect the dermis (Fig. 2). Occasional plasma cells were noted. The tumor exhibited strongly nuclear human herpesvirus 8 (HHV-8) immunostaining, supporting of the diagnosis of KS. Given this history and findings, the lesions on the patient's lower extremities were suspected to be a hyperkeratotic variant of KS, which had led to an elephantiasis nostras verrucosa-like presentation from lymphatic obstruction.

Given the concern for superinfection and while he was awaiting evaluation for lower extremity osteomyelitis, the patient was started on oral levofloxacin and wound care with acetic acid 5% solution and topical metronidazole. In light of his advanced disease, the patient was restarted on ART consisting of tenofovir, alafenamide, emtricitabine, and dolutegravir, and plans were made to start on paclitaxel. However, nine days following admission, the patient suffered acute respiratory failure and passed away.

Discussion

KS is a vascular proliferation associated with HHV-8 infection. Subtypes of KS include: classic (indolent course and typically localized to the lower extremities without mucosal and visceral involvement), endemic (more aggressive form found primarily in sub-Saharan African children who are HIV negative and presents with lymphadenopathy and lymphedema), iatrogenic (most commonly associated with solid-organ transplant recipients on immunosuppressive medications and is positively correlated with the degree of HLA mis-

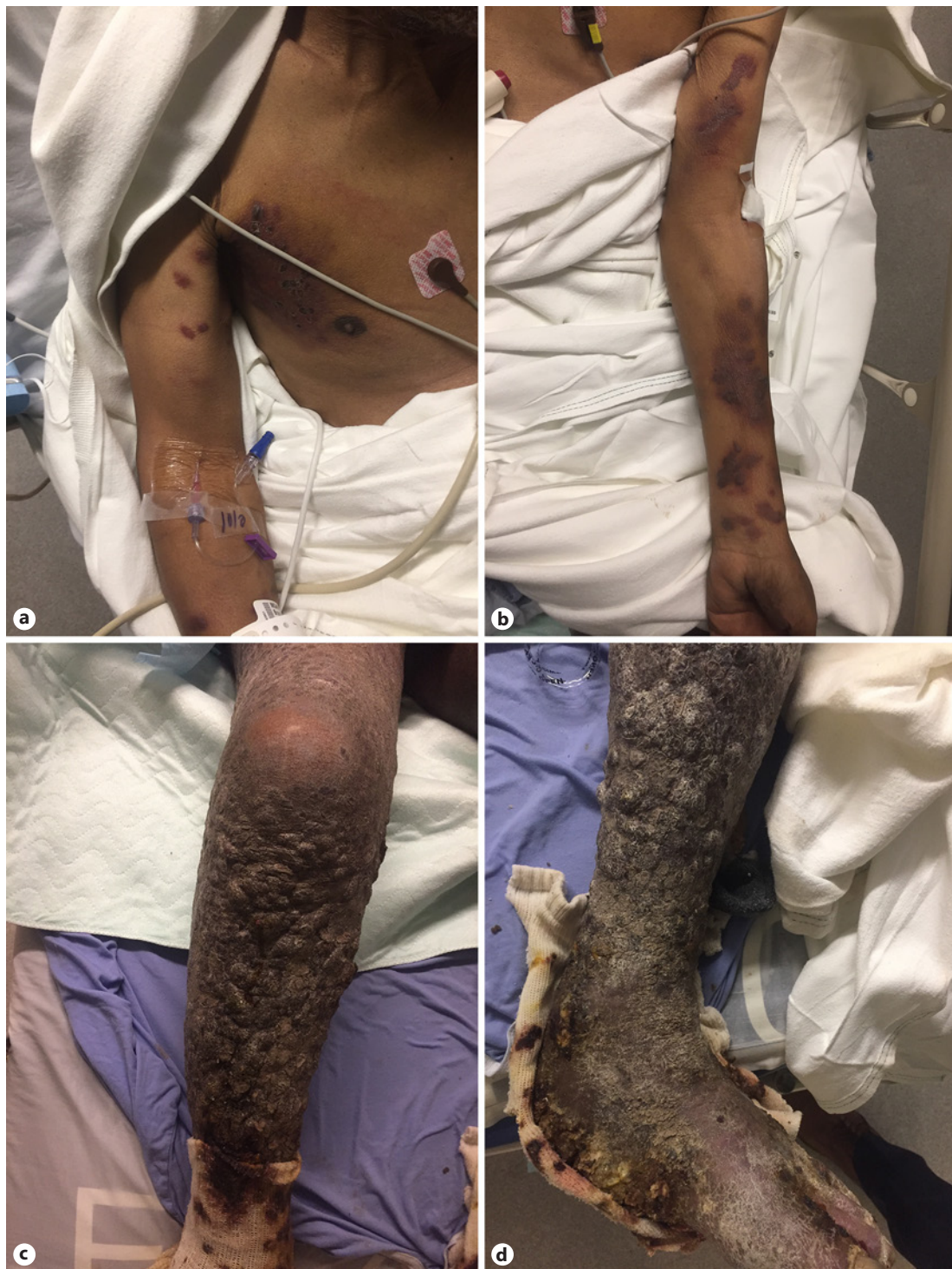


Fig. 1. **a** Numerous violaceous nodules and plaques on the bilateral arms. **b** Numerous violaceous plaques on the bilateral arms. **c, d** Bilateral lower extremities with diffuse firm edema and associated confluent hyperkeratotic verrucous plaques.

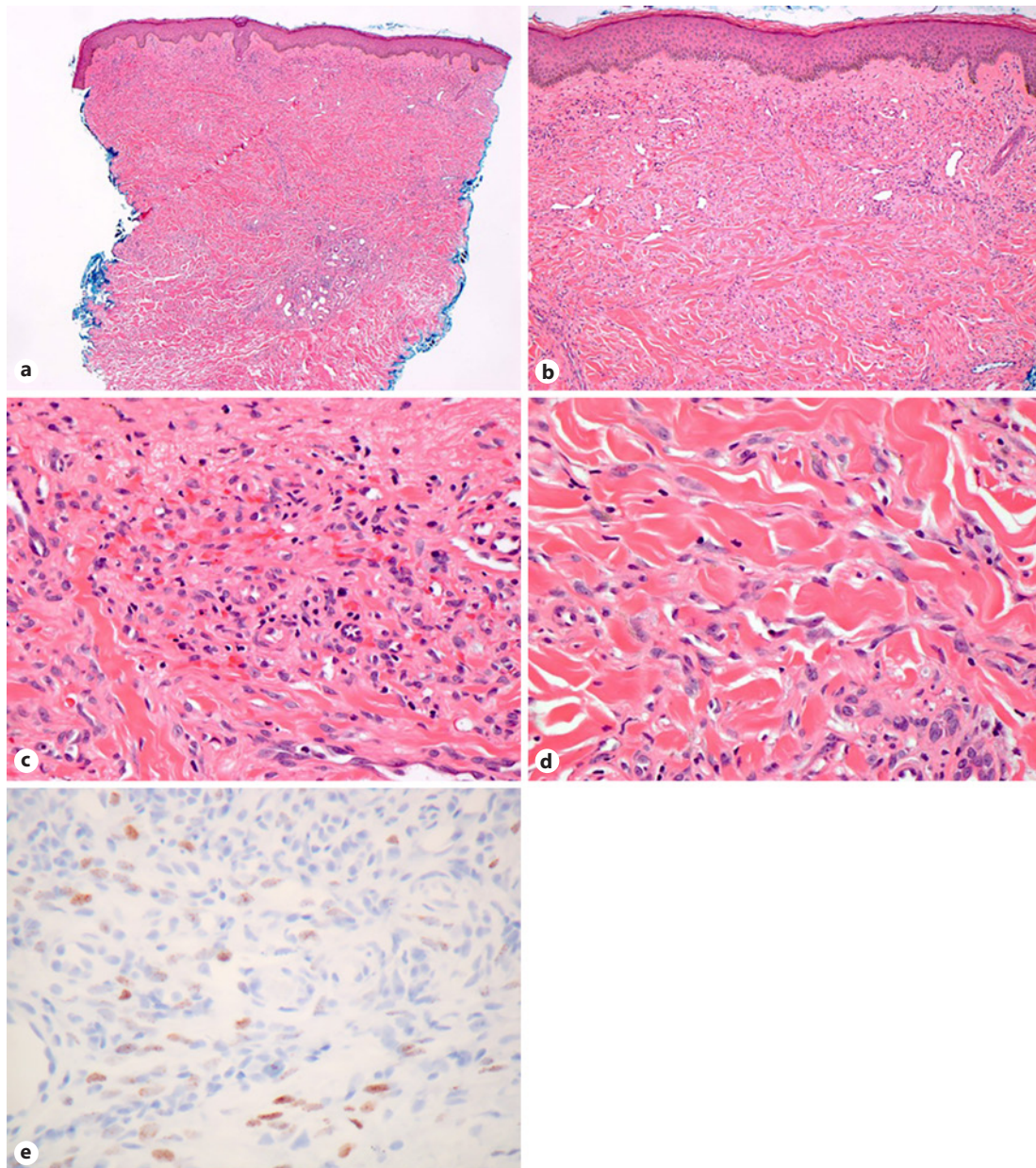


Fig. 2. Punch biopsy of the right arm showing a proliferation of slit-like vascular channels containing erythrocytes that dissect the dermis. Occasional plasma cells were noted.

match of the allogenic graft [1]), and AIDS-related (associated with HIV-1 and, to a lesser degree, HIV-2 [2]).

AIDS-related KS most commonly presents with lesions on the limbs and mucosa. More rarely, visceral involvement can occur. CD4⁺ count is associated with the risk for developing KS, and it also affects the clinical course after diagnosis [1]. In a study of HIV-positive men, CD4⁺ counts of <200, 200–349, and 350–499 cells/ μ L conferred rate ratios of developing KS of 18.9, 3.6, and 4.1, respectively [3]. In resource-rich settings where ART is widely available, the incidence of KS in the HIV-positive population has fallen significantly [4]. Alternatively, it has been hypothesized that a change in prevalence of HHV-8 infection could be responsible

for these changes; however, this has not been supported by population-based studies of HHV-8 seropositivity in HIV-positive men [5]. A low CD4+ count is associated with a more aggressive disease, further supporting the use of ART in the treatment and prevention of KS [1].

Due to the challenge of distinguishing KS from other vascular proliferations in the setting of chronic lymphedema, six clinicopathologic variants of KS in this context were described by Ramdial et al. [6]. The patch variant is described as flat, violaceous lesions with empty vascular spaces and minimal spindle cells. The plaque variant is marked by raised lesions that contain a higher density of all cellular and vascular features of patch lesions, most notably spindle cells. The nodular variant is characterized by palpable violaceous lesions that contain the usual cellular and vascular features but may also harbor hyaline globules. The lymphangioma-like variant is histopathologically similar to patch lesions and marked by irregular, dilated, and interconnected vascular spaces and may present as a bullous lesion clinically. The chronic lymphedema variant presents with verrucous papulonodules and, on histology, shows hyperkeratosis, epidermal hyperplasia, thickened lymphatic walls, and fibroblasts. Finally, the fibroma-like variant is marked by dermal fibrosis with increased collagen and fibroblasts, and it presents clinically as flesh-colored nodules. Our patient first developed KS in the setting of advanced HIV infection which later manifested as the chronic lymphedema variant due to inadequate care and progression of disease.

The pathophysiology behind chronic lymphedema and hyperkeratotic KS is not fully understood. It has been hypothesized that elevated interstitial protein concentrations leading to chronic inflammation and the release of growth factors, such as basic fibroblast growth factor and platelet-derived growth factor, may play a role in tumor development and growth [7]. Levels of basic fibroblast growth factor and vascular endothelial growth factor are increased by HHV-8 infection in the setting of KS, leading to increased angiogenesis and spindle cell proliferation [8]. Additionally, it is hypothesized that spindle cells and fibroblasts produce elevated levels of keratinocyte growth factor contributing to fibrosis and hyperkeratosis [7].

In the case of our patient, the loss of health insurance and inability to access affordable ART in 2010 unfortunately led to a significant progression of his KS. Adherence to ART is crucial in mitigating both the development as well as worsening of KS [9]. Financial cost remains a major barrier to the access of ART for many patients, even in resource-rich areas. One study found that 21% of all patients in a US-based cohort enrolled in a drug assistance program reported that they discontinued their ART following difficulties with the drug assistance program or inability to pay for medication [10]. Accordingly, attention not only to diagnostic and therapeutic decisions but also the socioeconomic factors that affect patient adherence should be considered when this diagnosis is made. The use of a multidisciplinary team that includes licensed clinical social workers is an often necessary approach to caring for these patients and improving their health outcomes.

Statement of Ethics

The authors have no ethical conflicts to disclose. Patient consent is not applicable.

Disclosure Statement

The authors have no conflicts of interest to disclose.

Funding Sources

The authors do not have any funding sources to disclose.

Author Contributions

T.A.B. and P.M.M. wrote the manuscript and performed the literature search. M.P.H. reviewed the images and contributed the histopathology report. D.K. contributed her knowledge and approved the final draft.

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