Case Letter

Verrucous Kaposi Sarcoma in an HIV-Positive Man

To the Editor:

Verrucous Kaposi sarcoma (VKS) is an uncommon variant of Kaposi sarcoma (KS) that rarely is seen in clinical practice or reported in the literature. It is strongly associated with lymphedema in patients with AIDS.[1] We present a case of VKS in a human immunodeficiency virus (HIV)–positive man with cutaneous lesions that demonstrated minimal response to treatment with efavirenz-emtricitabine-tenofovir, doxorubicin, paclitaxel, and alitretinoin.

A 48-year-old man with a history of untreated HIV presented with a persistent eruption of heavily scaled, hyperpigmented, nonindurated, thin plaques in an ichthyosiform pattern on the bilateral lower legs and ankles of 4 years' duration (Figure 1). He also had a number of soft, compressible, cystlike plaques without much overlying epidermal change on the lower extremities. He denied any prior episodes of skin breakdown, drainage, or secondary infection. Findings from the physical examination were otherwise unremarkable.

Two punch biopsies were performed on the lower legs, one from a scaly plaque and the other from a cystic area. The epidermis was hyperkeratotic and mildly hyperplastic with slitlike vascular spaces. A dense cellular proliferation of spindle-shaped cells was present in the dermis (Figure 2). Minimal cytologic atypia was noted. Immunohistochemical staining for human herpesvirus 8 (HHV-8) was strongly positive (Figure 3). Histologically, the cutaneous lesions were consistent with VKS.

At the current presentation, the CD4 count was 355 cells/mm^3 and the viral load was 919,223 copies/mL. The CD4 count and viral load initially had been responsive to efavirenz-emtricitabine-tenofovir therapy; 17 months prior to the current presentation, the CD4 count was 692 cells/mm^3 and the viral load was less than 50 copies/mL. However, the cutaneous lesions persisted despite therapy with efavirenz-emtricitabine-tenofovir, alitretinoin gel, and intralesional chemotherapeutic agents such as doxorubicin and paclitaxel.

Kaposi sarcoma, first described by Moritz Kaposi in 1872, represents a group of vascular neoplasms. Multiple subtypes have been described including classic, African endemic, transplant/AIDS associated, anaplastic, lymphedematous, hyperkeratotic/verrucous, keloidal, micronodular, pyogenic granulomalike, ecchymotic, and intravascular.[1-3] Human herpesvirus 8 is associated with all clinical subtypes of KS.[3] Immunohistochemical staining for HHV-8 latent nuclear antigen-1 has been shown in the literature to be highly sensitive and specific for KS and can potentially facilitate the diagnosis of KS among patients with similarly appearing dermatologic conditions, such as angiosarcoma, kaposiform hemangioendothelioma, or verrucous hemangioma.[1,4] Human herpesvirus 8 infects endothelial cells and induces the proliferation of vascular spindle cells via the secretion of basic fibroblast growth factor and vascular endothelial growth

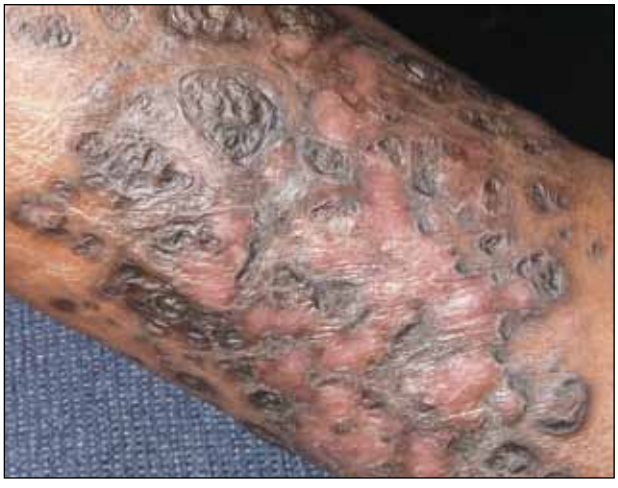

Figure 1. Hyperpigmented, nonindurated, thin plaques in an ichthyosiform pattern, as well as a number of soft, compressible, cystlike plaques on the lower leg.

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The authors report no conflict of interest.

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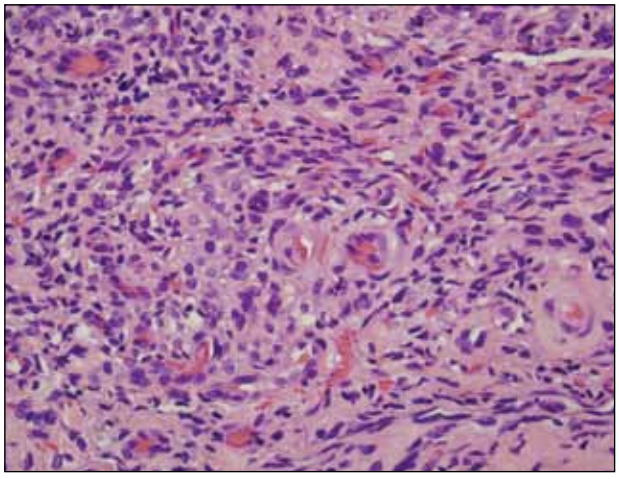

Figure 2. A dense cellular proliferation of spindle-shaped cells was present in the dermis as well as slitlike vascular spaces and minimal cytologic atypia (H&E, original magnification ×40).

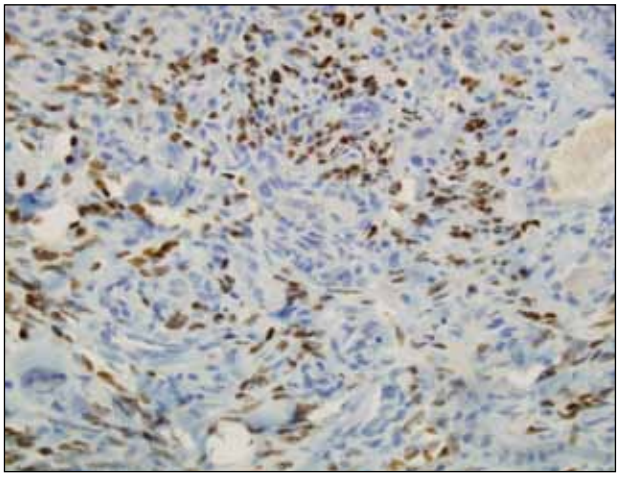

Figure 3. Immunohistochemical staining for human herpesvirus 8 was strongly positive (original magnification ×40).

factor.[5] Human herpesvirus 8 also can lead to lymph vessel obstruction and lymph node enlargement by infecting cells within the lymphatic system. In addition, chronic lymphedema can itself lead to verruciform epidermal hyperplasia and hyperkeratosis, which has a clinical presentation similar to VKS.[1]

AIDS-associated KS typically starts as 1 or more purple-red macules that rapidly progress into papules, nodules, and plaques.[1] These lesions have a predilection for the head, neck, trunk, and mucous membranes. Albeit a rare presentation, VKS is strongly associated with lymphedema in patients with AIDS.[1,3,5] Previously, KS was often the presenting clinical manifestation of HIV infection, but since the use of highly active antiretroviral therapy (HAART) has become the standard of care, the incidence as well as the morbidity and mortality associated with KS has substantially decreased.[1,5-7] Notably, in HIV patients who initially do not have signs or symptoms of KS, HHV-8 positivity is predictive of the development of KS within 2 to 4 years.[6]

In the literature, good prognostic indicators for KS include CD4 count greater than 150 cells/mm^3, only cutaneous involvement, and negative B symptoms (eg, temperature >38°C, night sweats, unintentional weight loss >10% of normal body weight within 6 months).[7] Kaposi sarcoma cannot be completely cured but can be appropriately managed with medical intervention. All KS subtypes are sensitive to radiation therapy; recalcitrant localized lesions can be treated with excision, cryotherapy, alitretinoin gel, laser ablation, or locally injected interferon or chemotherapeutic agents (eg, vincristine, vinblastine, actinomycin D).[5,6] Liposomal anthracyclines (doxorubicin) and paclitaxel are first- and second-line agents for advanced KS, respectively.[6]

In HIV-associated KS, lesions frequently involute with the initiation of HAART; however, the cutaneous lesions in our patient persisted despite initiation of efavirenz-emtricitabine-tenofovir. He also was given intralesional doxorubicin and paclitaxel as well as topical alitretinoin but did not experience complete resolution of the cutaneous lesions. It is possible that patients with VKS are recalcitrant to typical treatment modalities and therefore may require unconventional therapies to achieve maximal clearance of cutaneous lesions.

Verrucous Kaposi sarcoma is a rare presentation of KS that is infrequently seen in clinical practice or reported in the literature.[3] A PubMed search of articles indexed for MEDLINE using the search term *verrucous Kaposi sarcoma* yielded 13 articles, one of which included a case series of 5 patients with AIDS and hyperkeratotic KS in Germany in the 1990s.[5] Four of the articles were written in French, German, or Portuguese.[8-11] The remainder of the articles discussed variants of KS other than VKS.

Although most patients with HIV and KS effectively respond to HAART, it may be possible that VKS is more difficult to treat. In addition, immunohistochemical staining for HHV-8, in particular HHV-8 latent nuclear antigen-1, may be useful to diagnose KS in HIV patients with uncharacteristic or indeterminate cutaneous lesions.

Further research is needed to identify and delineate various efficacious therapeutic options for recalcitrant KS, particularly VKS.

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