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Case Report

Primary Classic Kaposi's Sarcoma of the Penis in an HIV-Negative Patient

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Kaposi's sarcoma (KS) is a multifocal hemorrhagic sarcoma that occurs primarily on the extremities. KS limited to the penis is rare and a well-recognized manifestation of acquired immune deficiency syndrome (AIDS). However, KS confined to the penis is extraordinary in human immunodeficiency virus (HIV)-negative patients. We present the case of a 68-year-old man with a dark reddish ulcerated nodule on the penile skin, which was reported as a nodular stage of KS. We detected no evidence of immunosuppression or AIDS or systemic involvements in further evaluations. In his past medical history, the patient had undergone three transurethral resections of bladder tumors due to urothelial cell carcinoma since 2000 and total gastrectomy, splenectomy, and adjuvant fluorouracil/cisplatin chemotherapy for 7 months due to advanced gastric carcinoma in 2005. The patient was circumcised and has had no recurrence for 2 years.

Key Words: *HIV Seronegativity; Kaposi sarcoma; Penile neoplasms*

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Kaposi's sarcoma (KS) was introduced by Moritz Kaposi to describe a malignant neoplasm of the vascular endothelium of multifocal origin that occurs primarily on the extremities. Before the acquired immune deficiency syndrome (AIDS) era, KS was a rare sarcoma that was mainly seen in Mediterranean men. In the early 1980s after the onset of the AIDS epidemic, the incidence of KS increased dramatically throughout the world [1]. Primary presentation on the penis is rare and it is more often observed in AIDS patients, who usually develop an aggressive form and in whom approximately 2-3% of cases show penile KS lesions as the first manifestation of the disease [2]. However, KS limited to the penis is extremely rare in human immunodeficiency virus (HIV)-negative patients. We experienced a case of ulcerated nodular KS confined to the penis that was very rare in Korea. Here, we report our case with a review of the literature.

CASE REPORT

A 68-year-old man with no history of homosexual activity presented with a painless ulcerated dark reddish nodule on the penile shaft noticed 3 months earlier. He had both legs amputated because of a bomb explosion during the Korean War. The patient had undergone three transurethral resections of bladder tumor (TURBTs) due to urothelial cell carcinoma since he visited us with a chief complaint of painless gross hematuria in September 2000. Also, the patient underwent total gastrectomy with splenectomy on account of advanced gastric carcinoma in May 2005 and six treatments of adjuvant fluorouracil (5-FU)/cisplatin chemotherapy from July 2005 to January 2006. On the physical examination, an approximately 1 cm sized nodule with pus-like discharge was evident on the outer layer of the dorsal prepuce and two black discolorations on the glans were obvious. There was no evidence of inguinal lymphadenopathy. The results of routine laboratory investigations and urine examinations were normal. Circumcision including the ulcerated nodule was performed. Purple discoloration and profuse bleeding were evident on the field excised nodule. By histologic examination, the nodule with ulceration was diagnosed as the nodular stage of KS. Histologic findings showed an infiltration composed of spindle cells scattered between collagen bundles and small

vascular proliferation. Slit-like spaces containing red cells with marked nuclear pleomorphism and mitoses were observed. Immunohistochemical investigations revealed a vascular tumor because of reasonable positivity for vas-

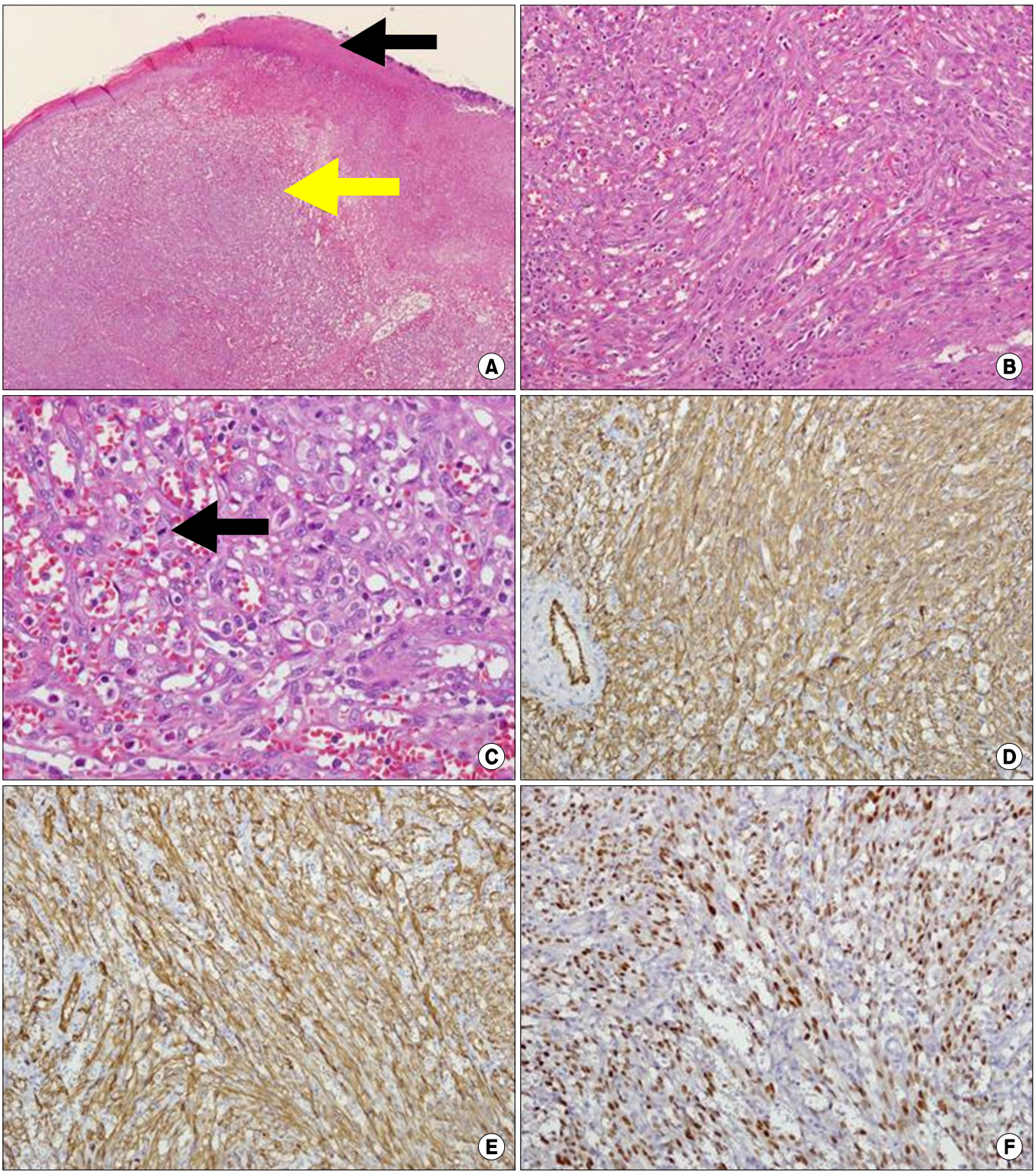

FIG. 1. Histopathologic findings. (A) Ulcerated skin (black arrow) with nodule of spindle cells (yellow arrow) (H&E, x100). (B) Spindle cell proliferation with intracytoplasmic lumina containing red cells (H&E, x200). (C) Spindle cell proliferation with many mitoses (black arrow) (H&E, x400). (D) The neoplastic cells are positive for the vascular marker, CD31 (x200). (E) The neoplastic cells are positive for the vascular marker, CD34 (x200). (F) The neoplastic cells are strongly positive for human herpesvirus type 8 latent nuclear antigen 1 (x200).

cular markers such as CD31 and CD34, and immunohistochemical staining confirmed KS by diffuse nuclear staining of human herpesvirus type 8 (HHV-8) latent nuclear antigen 1 (LNA-1) (Fig. 1).

At the repeat physical examination, we found no other skin lesions. We performed additional local excision of two black discolorations on the glans. However, they were reported as keratosis. Repeated HIV tests (enzyme-linked immunosorbent assay and Western blot) were negative. Computed tomography scanning of the chest, abdominal cavity, and pelvis failed to detect any visceral lesions. A 2-year follow-up did not show any disease progression or recurrence from May 2008 to June 2010.

DISCUSSION

KS is a tumor of the reticuloendothelial system and thus it is vasoformative with endothelial proliferation and spindle cell formation on histologic examination. Usually, it presents as a cutaneous neovascular lesion; a raised, painful, bleeding papule; or ulcer with bluish discoloration. KS is subcategorized as four types: (1) classic KS, which occurs in patients without known immunodeficiency and has an indolent and rarely fatal course; (2) immunosuppressive treatment-related KS, which occurs in a patient receiving immunosuppressive therapy for organ transplantation or other indications and is often reversed with dosage modification of the immunosuppressive agents; (3) African KS, which occurs in young men and may be indolent or aggressive in course; and (4) epidemic or HIV-related KS, which occurs in patients with AIDS [3]. In particular, classic KS primarily affects males of Mediterranean or Eastern European descent over the age of 60 years [4].

In a recent report, localized classic KS of the glans penis was reported to be rare with only 51 cases reported; 38 cases among them were regarded as isolated classic KS without any association with AIDS or immunosuppression [4]. However, the majority of cases of primary penile KS reported before the introduction of HIV testing are difficult to classify [2]. In patients with classic KS, primary penile lesions usually present as a single reddish-purple to bluish nodule, and other clinical presentations are less common. In particular, ulcerative nodules have been described in only two patients. The most frequently involved site is the glans, occasionally in association with swelling and lymphatic edema because of severe involvement. Lesions may also involve the foreskin, the coronal sulcus, or the meatus. However, involvement of the shaft is rare and it is usually associated with lesions located on the glans or coronal sulcus [2]. Histologic characteristics of penile KS are similar to those of KS at other skin sites. In KS, cells that normally line small blood vessels proliferate in an abnormal way, extending outward from what would have been the lining of the vessel to penetrate between and partially surround nearby collagen bundles, thus creating 'stellate' and 'ectatic' blood vessels that are not closed off but rather are open to surrounding tissue [5]. Usually, it includes a sometimes branching, irregular, slit-like vascular space containing erythrocytes in the patch stage and prominent groups or sheets of proliferating spindle cells in the nodular stage [6].

The pathogenesis of KS is uncertain. Recent studies showed an association between all types of KS and infection of human herpesvirus type 8 (HHV-8), known as KS-associated herpes virus (KSHV) [1-4,7-10]. HHV-8 as a potential oncogenic virus is supported by its tight relationships with primary effusion lymphoma (PEL), its homology with two other oncogenic gamma herpesviruses (herpesvirus saimiri and Epstein-Barr virus), and its ability to alter the growth of human endothelial cells in vitro [7]. In addition, AIDS-related multicentric Castleman's disease, multiple myeloma, and lymphoma are other neoplastic disorders in which HHV-8 has been commonly found [8]. Therefore, infection of HHV-8 is a pathogenetic factor in KS considering its potential as an oncogenic virus. It seems that the route of HHV-8 transmission may be both sexual and nonsexual. High HHV-8 seroprevalence in individuals with high-risk sexual activity represents the sexual route, and the detection of HHV-8 antibodies in children without sexual activity suggests the nonsexual route. Zargari reported that saliva could be a potential source of spread of HHV-8 in the general population [7].

In our case, only a single, ulcerated dark reddish nodule at the penile shaft near the coronal sulcus was diagnosed as KS. In that KS occurs on the penile shaft with ulceration, this presentation is unusual and a rare form of primary penile KS in an HIV-negative patient. Our patient had undergone treatment for urothelial cell carcinoma and gastric cancer including chemotherapy. However, he presented with KS about 3 years after his last chemotherapy treatment, and his laboratory findings had been normal since his last chemotherapy. Therefore, the KS of our patient seemed to be the classic type. Histologic examination showed a nodule of spindle cells with intracytoplasmic lumina and many mitoses. Immunohistochemical investigations revealed positivity for CD31, CD34, and HHV-8 LNA-1, which is known as a positive marker for KS. The patient vigorously denied sexual activity since his wife died.

No standard treatment guideline for primary penile KS is available. Treatment includes local surgical excision, radiotherapy, chemotherapy, and laser therapy. Treatment with adjuvant alpha or beta interferon has also been used in some cases. In general, surgical excision is recommended for a small solitary lesion, whereas conservative radiation therapy may be useful for large lesions. Systematic chemotherapy is usually reserved for more advanced cases with visceral involvement or generalized lesions. The clinical course of primary penile KS is variable, and no consistent follow-up data exist. However, local recurrences are rare if the lesion is completely removed. Onset of distant new lesions may be observed after a period of about 1-2 years [2]. Our patient underwent circumcision including the ulcerated nodule and local excision of black dis-

coloration on the glans. No other adjuvant therapy was performed. He has still not presented with any disease progression or new lesions during a 2-year follow-up.

In conclusion, primary penile classic KS in HIV-negative patients is rare and is associated with HHV-8 infection. It should be treated aggressively by surgical excision or laser therapy or radiation therapy or chemotherapy because of an uncommon association with systemic involvement.

Conflicts of Interest

The authors have nothing to disclose.

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