CASE REPORT

HIV Negative Penile Kaposi's Sarcoma in Circumcised Men

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ABSTRACT

Kaposi's sarcoma (KS) is an inflammatory vascular tumor, which can be seen at multiple areas in the body, especially at skin and extremities, mostly in immunosuppressed patients like organ receivers and AIDS patients. It can also be seen in human immune deficiency virus (HIV) negative, heterosexual, circumcised and non-immunosuppressed patients; and the disease course may be very variable. Herein, we present three patients who were referred to our clinic in the last five years and had a rather different course of disease; they were heterosexual, circumcised, non-immunosuppressed, and HIV negative. KS should be kept in mind in nonspecific penile lesions even if the patient is HIV negative. KS has a high recurrence rate even with any kind of treatment. More studies are needed for determining true recurrence rates, treatment plans and any underlying diseases.

Key Words: *Circumcised. HIV-negative. Penile. Kaposi's sarcoma.*

INTRODUCTION

Kaposi's sarcoma (KS) was first described by Moritz Kaposi in 1872. The first case report, which defined glans penis involvement, was published in 1902.[1] KS is an inflammatory vascular tumor, which can be seen at multiple sites in the body, especially at skin and extremities, mostly in immunosuppressed patients like organ receivers and AIDS patients.[2]

Herein, we present three patients who were referred to our clinic in the last five years and had a rather different course of disease; they were heterosexual, circumcised, non-immunosuppressed and human immune deficiency virus (HIV) negative.

CASE REPORT

Case 1: A 63-year male patient who noticed a purple-colored papule on glans penis for the first time in January 2012 was referred to our polyclinic in April 2012 as the lesion became larger. He did not have any suspicious and homosexual intercourse in the past. There was no significant finding in routine hemogram and biochemistry analysis of the patient. HIV and human herpes virus type 8 (HHV8) serology were negative. A purple nodular lesion with dimension of nearly 1x1 cm was observed on glans penis in the physical examination. Wedge resection was done. Vascular capillary proliferation with focal hyper cellularity and mild atypia was observed under squamous epithelium in the histopathological examination (Figure 1). Ki-67 proliferation index had increased despite the significant staining in spindle cells with endothelial marker CD34 and CD31 and weak focal staining with factor 8 in the immunohistochemical staining applied. Specimen was diagnosed as nodular type KS. No systemic findings were observed in the evaluation.

The patient was not given any additional treatment after the operation and was referred to our polyclinic with recurring masses in the penis and chin skin in first postoperative first year (May 2013). Wedge resection was done by plastic surgery clinic on 1x0.5 cm lesion on the chin and by our clinic on 1 cm nodular lesion on glans penis. The pathological examinations were reported as nodular type KS in both specimens (Figure 2). Surgical margins were negative. Systematic treatment was planned by medical oncology due to disseminated recurrence and a total of six cycles were given in every two weeks with doses of 10 mg/m^2 doxorubicin, 1.4 mg/m^2 of vincristine, and 10 mg/m^2 of bleomycin.

The patient was referred to our clinic again because of a 1.5x1 cm, bluish maculopapular lesion on the dorsum of the right foot on fourth year of follow-up (March 2016). The histology of the lesion resected by the plastic surgery department was reported as nodular type KS again (Figures 3 and 4). An 18-month follow-up period was completed after the last surgical operation and no recurrence was detected during this period.

Case 2: A 50-year male patient with a diagnosis of chronic renal failure was referred to our outpatient clinic in March 2016 because of a nodular pink-purple lesion on glans penis, which was first recognised in January 2015 and has grown lately. In his background, there were no suspicious or homosexual relationships. In the patient's routine work-up, creatinine level was 4.72 mg/dL and blood urea nitrogen (BUN) 65 mg/dL. The

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Received: January 18, 2018; Accepted: March 20, 2018.

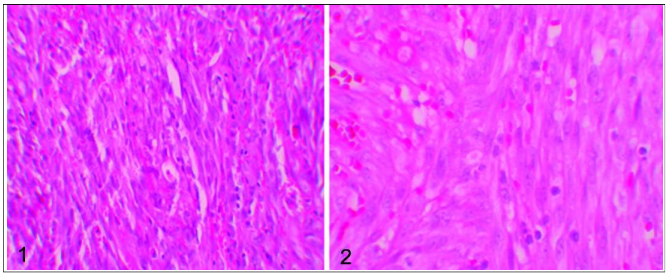

Figure 1 and 2: Glans penis; spindle-celled proliferation forming bunches in the tumor (H&Ex100) and erythrocytes between the proliferous spindle cells on the chin skin (H&EX400).

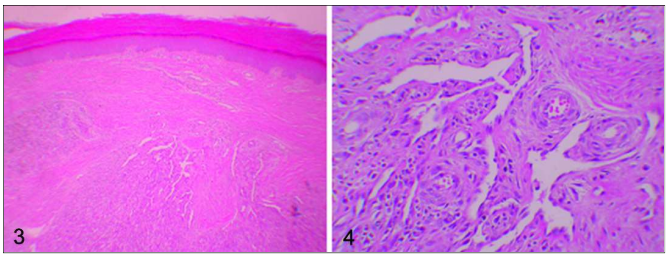

Figure 3 and 4: Right foot dorsum; spindle-celled proliferation below the hyperkeratotic epidermis on the surface (H&Ex40) and the veins protruded inside the new veins (promontory sign) (H&Ex400).

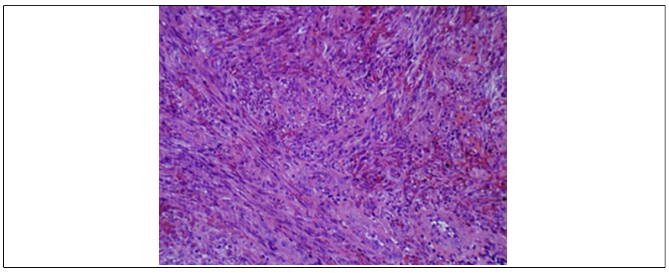

Figure 5: Glans penis; tumor proliferation containing cells with spurred cytoplasmic, spindle nucleate cells forming intercrossing bunches (H&Ex200).

other blood parameters were within normal limits. Serology for HIV was found negative. On physical examination, 1 cm nodular pink-purple lesion at glans penis was detected. Wedge resection was performed. On histopathological examination, slightly atypical vascular capillary proliferation was seen with focal hyper cellularity. The lesion was diagnosed as KS (Figure 5). Moreover, nuclear positive stains were detected with HHV8 on immunohistochemical investigation. Further investigations showed no systemic findings of the disease. The patient was discharged without any additional treatment and is being followed up by urology and dermatology clinics. A follow-up period lasting nearly 18 months was completed and no recurrence was detected.

Case 3: A 61-year male patient was referred to our department due to 1 cm purple nodular lesion with well-defined margins observed in the perineum in June 2017. The patient stated that the lesion was present for the last two months. He was on amlodipine, 10 mg/24h and pramipexole, 2.5 mg/24h due to hypertension and Parkinson's disease. He did not have any suspicious and homosexual intercourse. HIV and HHV8 serology was negative. Resection was done by the orthopedic surgeons due to a 2 cm brown-blue tissue in right leg knee area nearly two years ago (October 2015) and the histology was reported as nodular type KS. The surgical margin was reported as positive in the histological examination. The patient was followed up by Orthopedics and Oncology Departments during this period; and no additional treatment was applied.

We performed resection on the lesion in the perineum with the clinical suspicion of KS recurrence. But the histological diagnosis of the lesion was reported as chronic folliculitis. No recurrence was detected in the patient whose 2-year follow-up period ended after the first diagnosis.

DISCUSSION

Penile KS is rarely seen and generally reported in patients who are infected with HIV. Besides, there are also KS cases with penis involvement in HIV negative patients.[3,4] Immunosupression, homosexuality, multiple partnerships and detection in HIV negative patients are findings that indicate that KS involves another infective agent besides HIV. This argument is corroborated with HIV positive infants who acquire the virus vertically, but do not develop any KS. Latest epidemiologic researches show a strong relationship between HHV8 and KS.[5] HHV8 is a member of herpes virus family and is sexually transmitted. It is especially found in sexual secretions.[6] This feature indicates that penile KS can develop by the direct cytotoxicity of HHV8. Serological test for HHV8 was done in our patients and it was found in one case. Clinic presentation of penile lesions can be solitary, purple colored, well-demarcated lesions or multiple, papillary, nodular and plaque-like lesion. In our cases, solitary, purple and nodular lesions were detected. There were no findings of penile edema or lymphadenopathy.

Nodular type KS, similar to classic type KS, is a benign, slow-growing lesion that can recur in an average of 5-8 years. Venous stasis and lymphedema are the most common complications according to the anatomically involved area. Lesions can increase in numbers and tend to be more nodular. Occasionally, lymph nodes, gastro intertivil system, lungs, liver and other organs can be involved. Rarely, these organ lesions may occur before the skin lesions. These visceral lesions are asymptomatic and commonly found in autopsies. However, gastrointestinal bleeding can be seen. Approximately 90% of the patients die from other reasons such as 37% of the patients developing a second primary cancer and most of them, Non-Hodgkin Lymphoma.

In a very recent case report, a 75-year man presented with paraphimosis and an ulcerated red lesion on the glans penis. Unlike our cases, he was diabetic,

hypertensive; and 3 years ago, he was diagnosed as T cell lymphoma and was treated with chemotherapy.[7] Penis-limited KS in patients with AIDS is found in less than 3% of the patients; and in 20% of the cases, genital lesions are a part of the systematic disease.[8] Lesions on the penis can be at preputium, coronal sulcus, glans and rarely at the shaft.[9] Surgical excision can be curative for early stages of disease in penile lesions as in other areas.

There is no consensus about a standard therapy for the disease due to its rarity. Surgical excision, radiotherapy, laser treatments, intralesional cytotoxic chemotherapy, and systemic chemotherapy have been used in cases that have been reported.[2]

The three patients reported herein, were HIV negative, heterosexual, circumcised and non-immunosuppressed, and their ages were around 50 to 63 years. The histological diagnosis was reported as KS in these three patients. But the clinical course of these patients was quite different. Although the surgical border was negative after complete resection in the first patient, a recurrence was observed in first postoperative year in glans penis and an anatomic area, which was different from literature (chin). Although systemic chemotherapy was applied on this patient, a recurrence was observed in dorsum of the foot on the fourth year after the first diagnosis. Our second patient was rather younger and had renal failure. The HHV8 serology of the patient was positive. But the lesion reached a dimension of 1 cm in quite a long time (14 months) and no recurrence was observed during the follow-up; although, only wedge resection was applied. In the third patient, he had a diagnosis of nodular type KS on lower extremity skin two years ago, a recurrence in the perineal area was suspected. The age of the patient and the macroscopic appearance of the lesion also supported this suspicion but the histological diagnosis did not verify this suspicion. Despite positive surgical margin reported on lower extremity skin, the surgical treatment may be regarded as successful when the 24-month follow-up time is considered.

KS should be kept in mind in nonspecific penile lesions even if the patient is HIV negative. Although, KS has a high recurrence rate even with any kind of treatment, more studies are needed for determining true recurrence rates, treatment plans and any underlying disease.

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