DOI: 10.3315/jdcr.2011.1067

Journal of Dermatological Case Reports

Isolated Kaposi Sarcoma in two HIV negative patients

Iman Seleit[1], Abdalla Attia[1], Alaa Maraee[1], Rehab Samaka[2], Ola Bakry[1], Emad Eid[3]

1. Department of Dermatology, Andrology and S.T.Ds, Faculty of Medicine, Menoufiya University, Egypt.
2. Department of Pathology, Faculty of Medicine, Menoufiya University, Egypt.
3. Department of Microbiology, Faculty of Medicine, Menoufiya University, Egypt.

Corresponding author:

Ola Bakry

Department of Dermatology, Andrology and S.T.Ds

Faculty of Medicine, Menoufiya University

Egypt

E-mail: *drola_2007@yahoo.com*

Key words:

face, HIV, Kaposi sarcoma, nodule, penis, tumor

Abstract

Background: Kaposi sarcoma (KS) is a neoplasm of the endothelial cells. It often manifests with multiple vascular nodules on the skin and other organs. It is a systemic, malignant and multifactorial disease and has a variable course. There are four types: classic, endemic, iatrogenic and HIV-associated. The primary presentation on the penis and face is uncommon and is mainly observed in HIV-positive patients. Multiple treatment modalities are used including surgery, cryotherapy, electrosurgery, laser and radiation therapy.

Main observation: The authors present two cases of isolated Kaposi sarcoma in HIV negative, human herpes virus 8 (HHV-8) positive non immunocompromised patients. One case with facial KS and the other one with penile KS. Both were treated surgically with no recurrence in the following 6 months of the follow up period.

Conclusions: Kaposi sarcoma is rare in HIV negative patients and is associated with HHV-8 infection. Lesions are usually solitary and can be treated surgically. It should be included in the differential diagnoses of penile and facial lesions that are clinically suspecious and resistent to therapy. (*J Dermatol Case Rep.* 2011; 5(2): 24-26.)

Introduction

Kaposi's sarcoma is a vascular neoplasm, described by Morris Kaposi in 1872.[1] Although true metastases appear to occur, a multifocal origin is the most common.[2] The pattern of Kaposi sarcoma is variable, with a course ranging from indolent with only skin manifestations to fulminant with extensive visceral involvement.[3]

It occurs most frequently in mucocutaneous sites, typically the skin of the lower extremities, face, trunk, genitalia and oropharyngeal mucosa. KS also commonly involves lymph nodes and visceral organs, most notably the respiratory and gastrointestinal tracts.[4] The tumor is categorized into classic form, African endemic form, transplantation associated form and AIDS related epidemic form.[5] Cutaneous KS rarely may be infiltrative or exophytic. Exophytic KS may erode downward into bone.[4]

The exact nature of the disease is not clear. It remains controversial whether the endothelial cells are of vascular origin, lymphatic origin or both.[6] Current data support the notion that KS is a vascular hyperplasia with a tight link to HHV-8 infection. The virus was first identified in KS cells of a patient with AIDS but later, it had been linked convincingly with all 4 types of KS, an association that is necessary, but not sufficient to develop KS. Therefore, other factors also are important. At this point, immunosuppression appears to be the most significant cofactor.[7] HHV-8 contains homologues of cellular genes that can stimulate cell proliferation, inflammation and angiogenesis and perhaps inhibit apoptosis.[8] The host immune response and cytokines particularly fibroblast growth factor released by virally infected cells may further support tumor growth in an autocrine and paracrine manner.[7]

Case Reports

CASE 1

A 42-year-old male with a violaceous firm facial nodule. The nodule was (1x1 cm) and surrounded by erythematous halo on the right cheek. The lesion was not tender or painful

and enlarged gradually from the time of appearance over a period of 4 weeks. There was no bleeding, no enlarged regional lymph nodes. No other skin or mucosal lesions were detected on patient's physical examination. Patient was generally well with no history of immunosuppressive drug intake, systemic illness or organ transplantation. Patient is heterosexual with no history of sexually transmitted diseases or relations with prostitutes. Routine blood tests, urine analysis, liver and renal function tests were within normal limits.

CASE 2

A case of 34-year-old circumcised male who developed a bluish firm penile nodule. The nodule was (1x1 cm) in size, on the glans penis lateral to urethral meatus (Fig. 1). The lesion was not tender or painful and enlarged gradually from the time of appearance over a period of 6 months. There was no urethral discharge or enlarged inguinal lymph nodes. Patient was generally well with no history of immunosuppressive drug intake, systemic illness or organ transplantation. There was no other skin lesions and no mucosal affection. The patient medical history was completely insignificant. The extended laboratory investigations including routine blood tests, urine analysis, liver and renal function tests showed no abnormal findings and particularly no clue to haematologic or immunological diseases. The patient is heterosexual with no past history of sexually transmitted diseases.

Figure 1

Violaceous nodule on glans penis.

Excisional biopsy was taken from each lesion for histopathological examination. Hematoxylin and eosin stained sections revealed blood filled slit like spaces and spindle shaped cells with prominent atypia and frequent mitoses scattered between collagen bundles. Inflammatory infiltrate composed of lymphocytes and plasma cells as well as dilated blood vessels were also seen (Fig. 2A,C). So the diagnosis of KS was made for both cases. Confirmatory immunohistochemical staining for CD 34 antibody was done and revealed positive staining for endothelial cells and malignant spindle shaped cells in both cases (Fig. 2B,D).

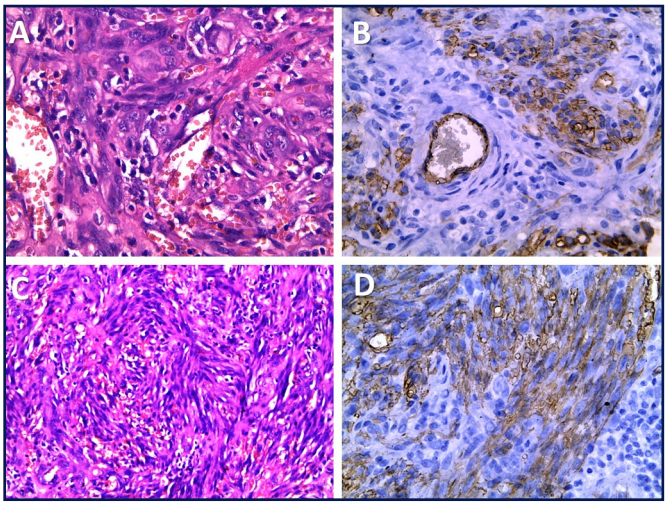

Figure 2

A) Blood filled slits like spaces, spindle shaped cells with prominent pleomorphism, extravasated RBCs and cellular infiltrate made of plasma cells and lymphocytes (hematoxylin and eosin X200). B) Positive immune reactivity for CD 34 in endothelial cells and neoplastic cells (immunoperoxidase X200). C) Slit like spaces and proliferating pleomorphic spindle shaped cells (hematoxylin and eosin X100). D) Positive immune reactivity for CD 34 in endothelial cells and neoplastic cells (immunoperoxidase X100).

Testing for HIV antibody by ELISA yields negative results for both patients. Testing for HHV-8 by polymerase chain reaction yields positive results for both patients.

Chest X ray, abdominal and pelvic ultrasonography didn't detect any additional visceral lesion in both cases.

No recurrence was detected for both lesions (facial and penile) in the following 6 months of the follow up period.

Discussion

Kaposi's sarcoma can be classified into four distinct forms: classic, endemic, iatrogenic and AIDS-associated.[1,2] The classic form is frequently observed in elderly male patients of Mediterranean origin and Ashkenazi Jews, presenting as an indolent disease, with nodular lesions on the skin, and affecting more often the lower limbs and feet and rarely presenting visceral involvement.[3] The primary presentation on the face is rarely described in the HIV-negative and non-immunosuppressed individual.[9] The primary presentation on the penis is also rare and it is more common in HIV-positive patients, especially among those who are homosexual in whom it has an aggressive behavior.[2]

Although primary facial and penile Kaposi sarcoma is uncommon in HIV negative men, one should consider this possibility when treating nonspecific penile and facial lesions.[10,11]

A minimal lesion with non distinctive clinical features may

be the exclusive manifestation of Kaposi sarcoma. In addition, it may appear as a skin-colored, violaceous or erythematous papule, nodule or plaque.[12,13] Most patients presented by a single or few lesions, however multiple lesions were also reported. In most cases lesions are asymptomatic.[1]

The sites more often involved on the penis are glans penis (more common), foreskin, coronal sulcus, frenulum and urethral meatus.[12] Increased penile volume and lymphatic edema due to massive involvement were described in some cases.[14] However, involvement of the shaft is rare and it is usually associated with lesions located on the glans or coronal sulcus.[10]

The differential diagnoses for facial lesion include pyogenic granuloma, histiocytoma, hemangioma and angiosarcoma.[9] While the differential diagnoses for penile lesion include pyogenic granuloma, condyloma acuminata, glomus tumor and molluscum contagiosum.[10] Biopsy is diagnostic and histopathological findings are the same as KS in other body sites. Those are, blood filled slit like spaces, pleomorphic spindle cells with frequent mitoses, extravasated erythrocytes, hemosidrin laden macrophages and may be cellular infiltrate by lymphocytes and plasma cells.[13,15] 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.[14] Immunohistochemical staining may be done for CD34 antibody. It yields positive results for endothelial lining of slit like spaces and for spindle cells.[2]

The pathogenesis of KS is uncertain. Recent studies showed an association between all types of KS and infection with HHV-8, known as KS-associated herpes virus (KSHV).[12] 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 and nuns 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.[16]

There are multiple treatment modalities described in literature including, local surgical excision, cryotherapy, electrosurgery, chemotherapy, laser therapy and radiation therapy, besides adjuvant treatment with intralesional or systemic injections with cytostatic agents, alpha- and beta-interferon, photodynamic therapy and topical therapy in form of nitrogen mustard or imiquamod.[17] For small and single lesions, surgical excision may be recommended.[10] Local recurrence is rare after complete excision of the primary lesion. When present, relapse occurs from six months to two years after the procedure.[13,17]

Conclusions

We describe two cases of isolated Kaposi sarcoma in HIV negative, HHV-8 positive, heterosexual patients. Face and penile Kaposi's sarcoma are rare in immunocompetent individuals and are associated with HHV-8 infection but must be included in the differential diagnoses of suspecious facial and penile lesions. Lesions are usually not associated with systemic involvement and can be treated with surgical excision.

References

1. Mukai MM, Chaves T, Caldas L, Neto JF, Santamaría JR. Primary Kaposi's sarcoma of the penis. *An Bras Dermatol.* 2009; 84(5): 524-526. PMID: 20098857.
2. Borkovic SP, Schwartz RA. Kaposi's sarcoma. *Am Fam Physician.* 1982; 26(4): 133-137. PMID: 7124577.
3. Schwartz RA, Micali G, Nasca MR, Scuderi L. Kaposi sarcoma: a continuing conundrum. *J Am Acad Dermatol.* 2008; 59(2): 179-206. PMID: 18638627.
4. Mitsuyasu RT. Clinical variants and staging of Kaposi's sarcoma. *Semin Oncol.* 1987; 14(2 Suppl 3): 13-18. PMID: 3603056.
5. Dupin N, Grange PA. Looking for the target cell of Kaposi's sarcoma-associated herpesvirus. *J Invest Dermatol.* 2006; 126(3): 545-547. PMID: 16482196.
6. Patel RM, Goldblum JR, Hsi ED. Immunohistochemical detection of human herpes virus-8 latent nuclear antigen-1 is useful in the diagnosis of Kaposi sarcoma. *Mod Pathol.* 2004; 17(4): 456-460. PMID: 14990970.
7. Moore PS, Chang Y. Kaposi's sarcoma-associated herpesvirus immunoevasion and tumorigenesis: two sides of the same coin? *Annu Rev Microbiol.* 2003; 57: 609-639. PMID: 14527293.
8. Santarelli R, De Marco R, Masala MV, Angeloni A, Uccini S, Pacchiarotti R, Montesu MA, Satta R, Cerimele D, Faggioni A, Cottoni F. Direct correlation between human herpesvirus-8 seroprevalence and classic Kaposi's sarcoma incidence in Northern Sardinia. *J Med Virol.* 2001; 65(2): 368-372. PMID: 11536246.
9. Wang X, Wang X, Liang D, Lan K, Guo W, Ren G. Classic Kaposi's sarcoma in Han Chinese and useful tools for differential diagnosis. *Oral Oncol.* 2010; 46(9): 654-656. PMID: 20656545.
10. Micali G, Nasca MR, De Pasquale R, Innocenzi D. Primary classic Kaposi's sarcoma of the penis: report of a case and review. *J Eur Acad Dermatol Venereol.* 2003; 17: 320-323. PMID: 12702076.
11. Bayne D, Wise GJ. Kaposi sarcoma of penis and genitalia: a disease of our times. *Urology.* 1988; 31: 22-25. PMID: 3336923.
12. Gönen M, Cenker A, Kiyici H, Kalkan M. Penile Kaposi's sarcomas in a circumcised and HIV-seronegative patient. *Int J Urol*. 2006; 13: 318-320. PMID: 16643638.
13. Balle JR, Hasselager T. Kaposi's sarcoma interpreted as haematoma. *Ugeskr Laeger*. 2010; 172: 2388-2389. PMID: 20825744.
14. Schwartz RA, Cohen JB, Watson RA, Gascón P, Ahkami RN, Ruszczak Z, Halpern J, Lambert WC. Penile Kaposi's sarcoma preceded by chronic penile lymphoedema. *Br J Dermatol.* 2000; 142: 153-156. PMID: 10651713.
15. Grayson W, Pantanowitz L. Histological variants of cutaneous Kaposi sarcoma. *Diagn Pathol.* 2008; 3: 31-39. PMID: 18655700.
16. Zargari O. Exclusive penile Kaposi's sarcoma: report of an HIV-negative man successfully treated with radiotherapy. *J Eur Acad Dermatol Venereol.* 2006; 20: 318-320. PMID: 16503896.
17. Soufiane M, Fadl TM, Nawfel M, Ouafae M, Kawtar Z, Afaf L, Jamal el FM, Hassan FM. Kaposi's sarcoma: HIV-negative man with isolated penile localization. *Indian J Pathol Microbiol.* 2010; 53: 535-536. PMID: 20699519.