Scrotal Kaposi’s Sarcoma in HIV-negative Patient: A Case Report and Review of the Literature.

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Abstract
Background: Kaposi’s sarcoma (KS) is an indolent angio-proliferative tumor proliferation with spindle cells originating from endothelial and immune cells infected with human herpes virus type 8. (HHV-8: also known as Kaposi sarcoma herpes virus [KSHV]). HHV-8 was identified as the causative agent of KS. This virus is present in 95-98% of cases with KS. Kaposi’s sarcoma was first described by a Hungarian dermatologist 1872 named Moritz Kaposi.[1]

The lesions are characterized by the proliferation of spindle cells of endothelial origin, which present different degrees of abnormal vascularization, inflammatory infiltrates, and fibrosis. Kaposi’s Sarcoma (KS) is a malignancy that generally affects the skin, and can be systemic with internal organ involvement. It originates from the vascular endothelium. KS’s relationship with human immunodeficiency virus (HIV) infection is well known.

In this article, we will present a 73-year-old male patient with 3 purple scrotal lesions up to 0.5 cm in size.

Conclusion: Kaposi’s sarcoma of the scrotum in a negative patient is a rare pathology. However, in cases of scrotal lesions that last over time, a differential diagnosis should be made and Kaposi’s sarcoma should be taken into consideration. Also, a screening for other accompanying lesions, especially a detailed examination of the gastrointestinal tract is important in cases of Kaposi’s sarcoma of the scrotum.

Keywords: Kaposi’s Sarcoma, Human herpes virus, HIV, Scrotal Kaposi

Introduction
Kaposi’s sarcoma (KS) is an indolent angio-proliferative tumor proliferation with spindle cells originating from endothelial and immune cells infected with human herpes virus type 8. (HHV-8: also known as Kaposi sarcoma herpes virus [KSHV]). HHV-8 was identified as the causative agent of KS. This virus is present in 95-98% of cases with KS. Kaposi’s sarcoma was first described by a Hungarian dermatologist in 1872 named Moritz Kaposi.[1]

The lesions are characterized by the proliferation of spindle cells of endothelial origin, which present different degrees of abnormal vascularization, inflammatory infiltrates and fibrosis. Red blood cells and hemosiderin deposits give the lesions their purplish appearance. Spindle
cells are infected with HHV-8. HHV-8 encodes for a number of genes that induce proliferation, cytokine production and angiogenesis thus contributing to tumor pathogenesis. Kaposi’s sarcoma has a variable clinic from minimal mucocutaneous lesions to extensive organ involvement. The skin lesions are classically characterized by macules, plaques and nodules that are of a purple, red, blue, dark brown or black appearance. Penile KS is relatively common, while isolated scrotal KS has rarely been seen.[2] In this article, we will present a 73-year-old male patient with 3 purple scrotal lesions up to 0.5 cm in size.

Case report

In this case report we will address a 73-year-old male with 3 dark-colored nodular scrotal lesions with a diameter of 0.3, 0.5 and 0.4 cm (Figure 1). The lesions appeared 2 years ago and during this period they were treated several times...
by a dermatologist with local agents but without results. The patient is diagnosed with diabetes mellitus type 2, hypertension and also with rheumatoid arthritis for which has being treated with immunosuppressors (Methotrexate). No other similar lesions were seen in other part of the body. Routine laboratory tests were all normal. After the failure of treatment with conservative methods, surgical excision of the lesions was performed. The excision of the lesions was performed with spinal anesthesia and the material is sent for histopathological examination. In the Hematoxylin – Eosin staining the lesion make it easier to see different parts of the cell under a microscope.

Also, the immunohistopathological examination are performed and the lesions are: HHV8 (+++), D2-40 (+++), CD34 (+--), Ki67 20 %, MelanA (--), S100 (---). (Figure 3). In this way the diagnosis of Kaposi Sarcoma is established. The patient underwent a total body CT and also a gastric endoscopy. The results of these examination are normal and no regional lymphadenopathy was observed. The serological tests for HIV, HbsAg, anit-HCV, TPHA and VDRL were negative.

After surgery the patient was follow - up for any recurrence. No local recurrence or systemic lesions was observed during last year of follow up.

**Discussion**

Kaposi’s sarcoma is caused by an uncontrolled proliferation of spindle cells which are thought to originate from endothelial cells. Regardless of their heterogeneity, the tumor consists of HHV-8 genetic material with immunohistochemical markers of endothelial, spindle and lymphoid cells. [3]

Previous molecular studies suggested that Kaposi’s Sarcoma originated from a single clonal cell rather than a multifocal origin. However, a current study with data from 98 patients with primary cutaneous Kaposi’s Sarcoma analyzing HHV-8 viral DNA in tumors showed that approximately 80% of tumors originate from multiple cell-independent tumors.[4]

Kaposi sarcoma may be caused by HHV-8 (KSHV) with stimulation by autocrine and paracrine growth factors secreted by the spindle cells themselves as well as the supporting network of mononuclear and endothelial cells. Coinfection with HIV may create a more aggressive course, which is mitigated by effective antiretroviral therapies. Indeed, the risk of Kaposi sarcoma development is amplified 500-10,000 times in patients coinfected with KSHV and HIV. [5]

In summary, complex immune dysregulation is the center theme for the pathogenesis of Kaposi sarcoma. This includes cellular immunity defects, [6, 7] humoral immunity defects and abnormalities of vascular endothelial growth factor. Apparent overlapping mechanisms for upregulation of multiple pathways produce the malignant phenotype.

Kaposi Sarcoma is characterized by few or widespread multifocal, brown-violescent or dark red patches and papules, plaques and/or deep nodular skin lesions. Its classical form is often seen in older male patients of Mediterranean or Ashkenazi descent and it is localized in the mucocutaneous tissues, more commonly affecting the lower extremities and feet with its nodular lesions and presents as a clinical entity rarely showing visceral involvement. [8] In the genital region, cases of penile involvement are more frequent, while Kaposi’s sarcoma of the scrotal region in HIV negative patients is very rare and only a few cases have been reported in the literature. From our search in the English literature, it appears that the first case of Kaposi’s sarcoma in the scrotal region was first described by Vyas S et al. in 1976 [9].


This means that our case is the sixth case of scrotal Kaposi’s Sarcoma in HIV negative patient reported in English literature.

Cases of involvement in the organs of the gastrointestinal tract, according to a Greek study, are high in Kaposi’s Sarcoma cases, therefore screening with endoscopic examination is recommended. [14].

The diagnosis of Kaposi’s sarcoma is an immunohistopathological diagnosis, therefore the role of the pathologist is very important. Kaposi’s sarcoma goes through several stages: 1. Patch stage, 2. Plaque stage, 3. Tumor (nodular) stage. [15, 16].

In the examination with immunohistochemistry, Kaposi’s Sarcoma is positive for: HHV8, CD34, CD31, D2-40 and negative for: SMA, Desmin, Cytokeratins, S100, MelanA, HMB45.

The differential diagnosis should include: angiosarcoma, hobnail hemangioma, spindle cell hemangioma, Kaposi form hemangioendothelioma, which are HHV8 negative. [17, 18, 19].

**Conclusion**

Kaposi’s sarcoma of the scrotum in a negative patient is a rare pathology. However, in cases of scrotal lesions that last over time, a differential diagnosis should be made and Kaposi’s sarcoma should be taken into consideration. Also, a screening for other accompanying lesions, especially a detailed examination of the gastrointestinal tract is important in cases of Kaposi’s sarcoma of the scrotum.

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