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Original Article

Classic Kaposi's Sarcoma (Non-Hiv-Associated) of oral cavity: a case report

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Kaposi's sarcoma (KS) is a locally aggressive multicentric mucocutaneous malignant neoplasm. The aim of this article is to report and discuss the immunohistochemical profile of a rare case of classic primary Oral Kaposi's sarcoma presenting on the hard palate of a female patient which was non-HIV and was not immunocompromised.

Keywords: Kaposi's Sarcoma. Oral Cavity. Classic Kaposi's Sarcoma.

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Introduction

Kaposi's sarcoma (KS) is a locally aggressive multicentric mucocutaneous malignant neoplasm which belongs to the group of intermediate type of vascular/ endothelial origin and may also involve mucosal sites, lymph nodes and visceral organs. KS may appear in four main clinical forms as, respectively, (a) classic or Mediterranean which occurs among elderly men of Ashkenazic Jewish and East European origin, (b) epidemic or acquired immunodeficiency syndrome (AIDS)-associated, (c) iatrogenic or post-transplant seen in patients undergoing immunosuppressive therapy, (d) and endemic or African which involves children, adolescents, and adults with a high frequency of extracutaneous manifestations[1-4]. Currently, there is strong evidence that all types of KS are caused by the human herpesvirus (HHV-8) infection, known as Kaposi's sarcoma-associated herpesvirus (KSHV)[1,2,4-8].

The epidemic KS is the variant which most commonly affect the oral cavity, however, the classic form of KS may also but rarely occur in the oral cavity (OKS) and, the initial oral involvement existing as the sole presentation of the condition, is an even rarer occurrence with only a few previously reported cases[3,8-13]. Clinically, OKS most often affects the hard and soft palate, gingiva and dorsal tongue with plaques or tumors of coloration ranging from non-pigmented to brownish-red or violaceous. Early lesions may appear as erythematous or ecchymotic patches which progress to papular, nodular, and exophytic forms. It could invade bone and create tooth mobility and morbidity may be associated with pain, bleeding, and functional interferences[3,8,9,14].

The aim of this article is to report and briefly discuss the immunohistochemical profile of a rare case of classic primary OKS presenting on the hard palate of a female patient which was HIV-negative and wasn't immunosuppressed.

Clinical Case

A Brazilian female patient with 63 years old, with distant Polish descent, searched treatment due to an asymptomatic increase of volume on had palate with two months of evolution. The main complain was the increase of volume itself and occasional bleeding. Clinical evaluation evidenced an ulcerated soft nodular lesion red-purplish (Figure 1). Blood cells count test showed to be within the normal parameters. An incisional biopsy was recommended. The hematoxylin and eosin stain (H&E) showed a hypercellular tumoral mass being composed of bland-appearing spindle cells, ill defined or atypical vascular channels, and extravasated red blood cells (figures 2). Due to its unspecific H&E pattern a immunohistochemical study was required and included: HHV-8 (clone LN53), positive (figure 3); CD31 (clone (JC/70A), positive; CD34 (clone QBEnd10), positive; Cytokeratin 40,48, 50 and 50.6 kDa (clone AE1/AE3), negative; Desmin (clone D33), negative; S-100 protein (policlonal), negative; ERG ETS Family (clone EP111), positive. The lesion immunohistochemistry profile is summarized in table 1. Based on the clinical, histopathological and immunohistochemical findings it was possible to reach the diagnosis of OKS. Due to a low suspicion for OKS, the anti-HIV test was performed just after the final diagnosis and showed to be negative. The patient underwent to careful medical screening searching any undiagnosed additional disease or condition which may induce to an immunological deficit and none has been found.

Table 1. Oral cavity Kaposis's sarcoma immunohistochemistry profile.

Antibody / Clone	Reactivity
HHV-8 (clone LN53)	Positive
CD31 (clone (JC/70A)	Positive
CD34 (clone QBEnd10)	Positive
ERG ETS Family (clone EP111)	Positive
Cytokeratin 40,48, 50 and 50.6 kDa (clone AE1/AE3)	Negative
Desmin (clone D33)	Negative
negative; S-100 protein (policlonal)	Negative

The intra-oral lesion was treated through a conservative oral surgery including a five millimeters free margin from visible lesion and the area was left to second intention healing. The patient was also referred for additional radiotherapy; however, since intra-oral cone radiation therapy was not available, the patient refuted this additional treatment. The patient is clinically disease free for seventeen months and maintains periodic monitoring (Figure 4).

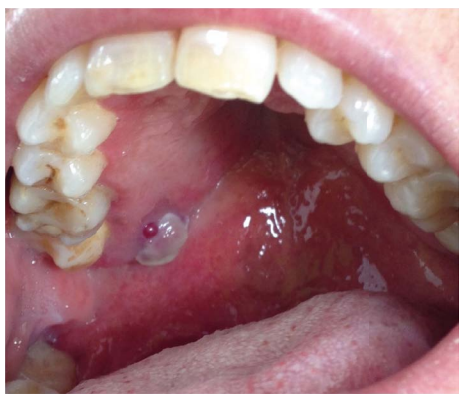

Figure 1. Oral Kaposi's Sarcoma at hard palate.

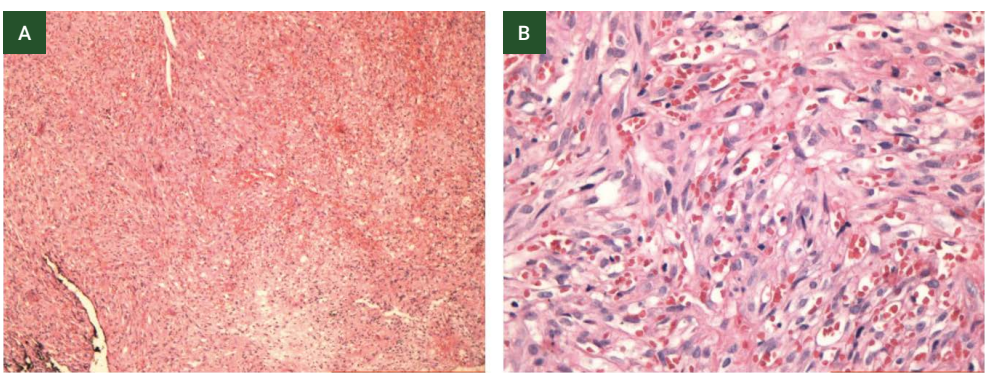

Figure 2. Low (A-100x) and high (B-400x) power microscopic view of Oral Kaposi's Sarcoma, showing a hypercellular tumoral mass with atypical vascular channels and extravasated red blood cells (Hematoxylin & Eosin).

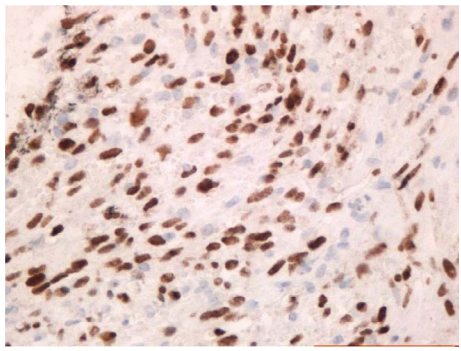

Figure 3. High power view (400x) of Oral Kaposi's Sarcoma showing a positive immunohistochemistry stain for HHV-8.

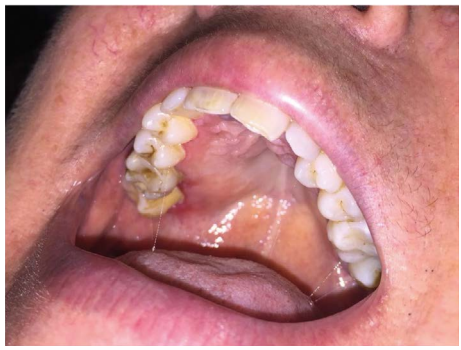

Figure 4. Patient remains disease free after conservative surgery in the 17 months follow-up.

Discussion

While OKS is a common finding in patients with HIV infection and is infrequently described in the immunocompromised population, this manuscript aimed to report a rare case of classic OKS in a non-HIV and non-immunocompromised patient. KSHV has been frequently identified all types of KS lesions, suggesting a causative role and, according to Duus et al.[6] (2004), KSHV is harbored in the oral cavity of healthy individuals and it is capable of infection in oral epithelial cells, even in absence of severe immunosuppression and the infection may persist at a low level for the lifetime of the host, being controlled by the immune system.

The diagnosis of OKS may be challenging in non-HIV individuals or for patients undergoing through immunosuppressive therapy due to its rarity and clinical similarities with common oral lesions such as pyogenic granuloma and haemangioma and this may lead to misdiagnosis. Histopathologic evaluation is necessary to achieve a definitive diagnosis and hematoxylin/eosin (H&E) is the standard staining method for it. Microscopically, in the early stages of the tumor growth, the diagnostic spindle cell proliferation is not always evident and later it may resemble benign vascular lesion such as pyogenic granulomas. Atypical vascular channels, extravasated red blood cells, hemosiderin, and inflammatory cells are characteristic of advanced KS,

however, typical KS lesions do not exhibit marked cellular pleomorphism, necrosis or many mitotic figures, though, mildly atypical endothelial cells and monomorphic spindle cells may be observed[8,9,11,15]. Therefore, it is also possible that a biopsy can be initially misdiagnosed and for that reason KS should be diagnosed with histology and immunohistochemistry due to a large range of similarities within diseases[2,8,16].

The differential diagnosis of KS includes benign and malignant tumors and for early lesions can be included lesions such as benign vascular proliferation like as hemangioma, acroangiodermatitis, benign lymphangioendothelioma, bacillaryangiomatosis and pyogenic granuloma. More advanced and cellular lesions must be differentiated from angiosarcoma, lymphoma, haemangioendothelioma, aneurysmal fibrous histiocytoma, spindle cell hemangioma, dermatofibrosarcoma protuberans, vascular or pilar leiomyomas and even undifferentiated scamous cells carcinoma[2,8,10,11].

The immunohistochemistry panel suggested for this particular case included the detection of KSHV/HHV8 which, when present in a lesion, it may strongly indicate the diagnostic for KS and because all KSHV-infected cells express LANA-1, both LANA-1 and KSHV/HHV8 immunohistochemistry are useful for diagnosis of KS. Those markers also act as differential diagnosis since angiosarcoma and benign vascular tumors are negative for those antigens[2,8,10]. By performing immunohistochemical staining for endothelial cell markers such as CD31 and CD34 which are endothelial markers expressed in vascular tumors, KS can be differentiated from nonvascular neoplasms[10,16,17]. The sample also showed immuno-positivity for ERG (erythroblast transformation-specific family or ETS) which is a highly specific marker for benign and malignant endothelial/vascular tumors and KS, while carcinomas and epithelial tumors usually were ERG negative[16,18] The negative stain for S-100, cytokeratins (40, 48, 50 and 50.6 kDa) and Desmin antibodies exclude respectively other tumors of neural, epithelial and muscle origins[17]. On the basis of the above immohistochemistry observations, the H&E and clinical features it was possible to conclude the OKS final diagnosis.

In conclusion, this manuscript described a rare case of classic primary OKS presenting on a female patient who was HIV-negative and wasn't immunosuppressed alerting clinicians and pathologists to be aware of the clinical and histopathologic features of KS so as not to misdiagnosis it, leading to a profound impact on patient therapeutic and prognostic. KS must also therefore be diagnosed including clinical, histopathology and immunohistochemistry due to a large range of similarities within diseases including, mainly, antibodies against KSHV/HHV8 and LANA-1.

Competing Interests

The authors of this manuscript declare no conflict of interest.

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Ethical Approval

This case report manuscript is in compliance with Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

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