Classic Kaposi's sarcoma presenting in the oral cavity of two HIV-negative Quechua patients

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ABSTRACT

Traditionally, classic KS lesions have a general distribution, often involving the skin of the feet and legs, and to a lesser extent, that of the hands, arms, and trunk. Oral involvement is a rare manifestation. Initial oral involvement is an even rarer occurrence. We report two unusual cases of classic KS presenting in the oral cavity of two patients from indigenous origin; the first patient with primary oral KS lesion on the hard palate, with no other signs of the condition in any other region of the body; the second patient with generalized dermal KS lesions with lymph node and lower lip involvement. In conclusion, clinicians and pathologists should be aware of the typical clinical, gross, and histologic features of KS. Moreover, we would like to emphasize that oral KS may affect patients without AIDS or exposure to immunosuppression. The awareness of oral classic KS as a diagnostic possibility is important in the work-up of vascular lesions in the oral cavity of non-immunosuppressed individuals.

Key words: *Classic Kaposi sarcoma, oral cavity, palate, HHV-8, Quechua, Peru.*

INTRODUCTION

Kaposi's sarcoma (KS) is a well-known vascular tumor first described by Moriz Kaposi in 1872 (1). The four variants of KS (classic, endemic, epidemic, and post-transplant) differ not only in course and prognosis, but also in terms of the sites frequently involved; endemic KS can often be seen in the lymph nodes and internal organs; and post-transplant and epidemic KS patients show mucosal and internal organ lesions often preceding dermal lesions. Traditionally, classic KS lesions have a general distribution, often involving the skin of the feet and legs, and to a lesser extent, that of the hands, arms, and trunk. Oral involvement is a rare manifestation. Initial oral involvement, whether associated with posterior generalization of lesions or existing as the sole presentation of the condition, is an even rarer occurrence. Since the first documented case of primary oral classic KS by Feit (2) in 1928, few similar cases with primary involvement have been reported (3 - 9). Some cases have been mentioned on different case series, of those, few of them described a physical examination to confirm the absence of dermal lesions.

The aim of this article is to report two unusual cases of classic KS presenting in the oral cavity of patients from indigenous origin (Quechuas); the first patient with primary oral KS lesions on the hard palate, with no other signs of the condition in any other region of the body; the second patient with generalized dermal KS lesions with lymph node and lower lip involvement.

CASE REPORT

The first patient was a 71 year-old indigenous (Quechua) female with a 5 month history characterized by the progressive appearance of red papules on her hard palate. On physical examination multiple red, painless papules were evidenced on her hard palate. No other similar lesions in any other region of the body were detected. A biopsy of the papules was performed. The findings were those of a proliferation of bizarre shaped vessels, with strands of spindle cells and extravasated red blood cells, diagnostic of KS (Figure 1). There was no past medical history of sexually transmitted diseases. The patient was HIV-negative and there was no associated immunosuppression. Routine blood tests, renal and liver function tests were within normal limits. The patient was started on chemotherapy, being disease free for 5 years.

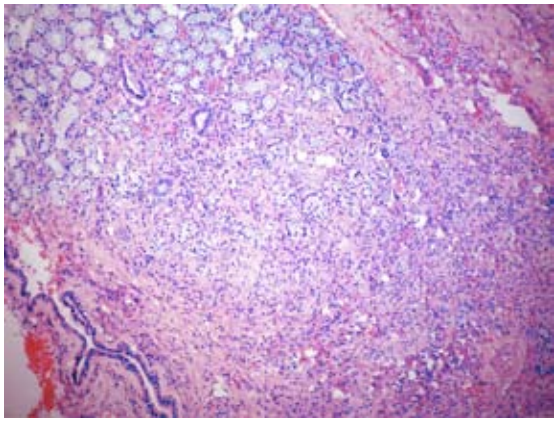

Fig. 1. In tissue from the palate, there is a proliferation of bizarre shaped vessels, with strands of spindle cells among extravasated erythrocytes, next to normal salivary acini. (H&E 100x)

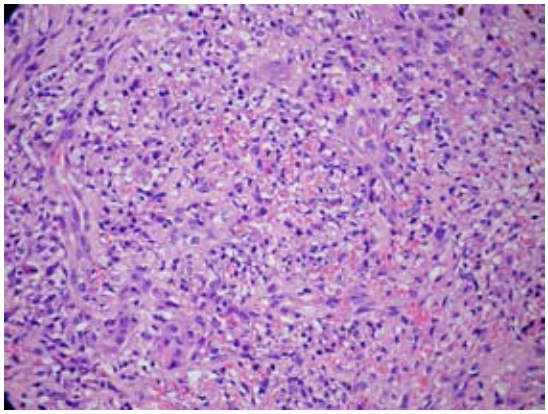

Fig. 2. The lip biopsy showed the classical histology of KS, that is, a proliferation of spindle cells among bizarre shaped blood vessels and extravasated red blood cells. (H&E 400x)

The second patient was a 46 year-old indigenous (Quechua) male with a 3 month history of progressive enlargement of a tumor on his groin. On physical examination a 3x3 cm painless tumor was evidenced. A biopsy of the tumor was performed, being confirmatory of KS. There was no past medical history of sexually transmitted diseases. The patient was HIV-negative and there was no associated immunosuppression. Routine blood tests, renal and liver function tests were within normal limits. The patient did not receive any other treatment besides surgical excision of the tumor. After one year of being disease free, the patient presented to consult with an ulcer on the sole of the foot. On physical examination an ulcerated nodule was evidenced in the middle of the sole of the foot, a nodule on the third toe, multiple small nodules on the anterior distal right leg, a reddish macule on the lower lip, and a nodule on the scalp. A biopsy of the lesions on the lip, leg and scalp were performed, being confirmatory of KS (Figure 2). ELISA for HIV was repeated being negative, but pulmonary tuberculosis was diagnosed. Treatment for tuberculosis and radiotherapy for generalized KS was started without a good response; the patient died within a few months.

DISCUSSION

KS-associated herpesvirus or human herpesvirus-8 (HHV-8) was detected in a KS lesion in 1994, by Chang et al (10). Since then, HHV-8 DNA has been detected in all four variants of KS. The AIDS epidemic led to a tremendous increase in the incidence of KS becoming one of the most common malignancies associated with HIV infection and one of the first diseases to define AIDS in the 80's. It is estimated that of all patients with AIDS who develop KS, up to 71% develop oral lesions concurrently with skin and visceral lesions. In an additional 22% of patients, the disease initially presents in the mouth and in some instances remains restricted to the oral cavity. In this clinical setting oral KS sometimes is associated with a poor prognosis (11, 12). On the other side, primary oral involvement in immunocompetent patients (classic KS) is an infrequent manifestation and is often clinically misdiagnosed (3, 11, 13 - 15). Oral classic KS could present initially as well-demarcated, painless, brownish red to violaceous macule or papule. It could appear as a single or multiple lesions with dimensions varying from a few millimeters to centimeters, increasing slowly in size, forming nodules or tumors with or without ulceration. Classic KS could invade bone and create tooth mobility. The most frequent locations are the hard palate and gingiva, whereas appearance on the buccal mucosa and tongue are rarer. Morbidity may be associated with pain, bleeding, and functional interferences caused by the tumor.

The few oral classic KS cases reported in the literature have been presented in retrospective and case series. For example, Cottoni et al (16) reported 279 patients with classic KS between 1977 – 2001; only 2 men presented primary oral involvement, 12 men and 1 woman presented with both oral and dermal involvement, 6 men and 1 woman presen-

ted with oral, conjunctiva and dermal involvement, 4 men presented with oral, genital and dermal involvement, and 1 man presented with oral, genital, conjunctiva and dermal involvement. Stratigos et al (17) reported 66 patients with classic KS during a 5 year period finding only 1 oral case. Hbid et al (18) reported 19 patients with classic KS during a 1 year period finding only 1 case with a lesion on the palate and multiple dermal involvement. Dal Maso et al (19) reported 874 patients with classic KS between 1985 - 1998 from 15 cancer registries finding 9 cases (1.4%) with lesions localized on lip, oral cavity and pharynx. Dilnur et al (20) reported 17 patients with classic KS between 1983 – 1998; none with oral involvement. Garcia et al (21) reviewed the clinical record of 79 patients with classic KS between 1935 – 1985 finding only 3 oral cases. As we can see, almost all of these reports lack from a complete description to confirm the absence of dermal lesions, the clinical appearance of the oral lesions, and the clinical behavior and outcome. Our first patient demonstrates that the absence of HIV or immunosuppression confers a good prognosis without recurrence on patients with localized oral classic KS, as mentioned by other studies (22). Whereas, our second patient had a generalized presentation of KS associated with pulmonary tuberculosis; our conclusion is that immunosuppression due to tuberculosis could have been involved in KS progression and outcome. These two patients represent the first classic KS cases with oral involvement reported in the Quechua population. This indigenous population has been reported to present classic KS since 1968 where the first case was published. Nowadays, more than 200 cases have been reported in Mestizo's and Quechuas (23 – 26). For this reason, it is important to consider Peru as an endemic country for HHV-8.

Definitive diagnosis of KS is made through a biopsy. The clinical differential diagnoses of KS include bacillary angiomatosis, pyogenic granuloma, oral nevus, lymphoma, oral hemangiomas or other benign vascular proliferations. However, these entities are easily ruled out on histologic examination. Kaposiform hemangioendothelioma and angiosarcoma are the most troublesome entities in the histologic differential diagnosis of KS. Microscopically, in the early stages of the tumor growth, the diagnostic spindle cell proliferation is not always evident. Therefore, it is also possible that a biopsy can be initially misdiagnosed as a benign vascular lesion. Several different treatment modalities have been used for classic KS. For localized lesions, treatment with surgical excision, or electro-cauterization and curettage are generally effective. An alternative method of treatment is intralesional chemotherapy (27). In more advanced cases with disseminated cutaneous or visceral involvement, radiation and single agent or combination systemic chemotherapy has achieved relatively good control of the lesions and effective short-term palliation. The most active cytotoxic agents include vinblastine, vincristine, bleomycin, etoposide, doxorubicin, daunorubicin and paclitaxel. After the introduction of highly active antiretroviral therapy (HAART) the pattern of KS lesions in HIV patients has changed and may continue to shift as a result of the availability and adherence to HAART. New cases of KS usually occur in patients with advanced immunosuppression, and these cases reflect delayed diagnosis and treatment of HIV infection (28).

In conclusion, clinicians and pathologists should be aware of the typical clinical, gross, and histologic features of KS. Moreover, we would like to emphasize that oral KS may affect patients without AIDS or exposure to immunosuppression. The awareness of oral classic KS as a diagnostic possibility is important in the work-up of vascular lesions in the oral cavity of non-immunosuppressed individuals.

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