Oral Cryptococcosis

Wilson Delgado*
Department of Oral Pathology and Medicine, Universidad Peruana Cayetano Heredia, Peru

Abstract
Oral mucosal lesions of cryptococcosis are extremely rare and have been mainly reported in AIDS patients who suffered of disseminated infection. The oral manifestations very rarely represents a primary infection. The few oral cases reported in the literature has been the result of hematogenous spread of the infection localized in the lungs of AIDS patients and in persons with predisposing factors such as lymphoma, chronic leukemia, prolonged use of corticosteroids, and organ transplant. The oral lesions have been described as ulcer in tongue, palate, non healing ulceration after tooth extraction, hyperplastic tissue or mimicking bening or malignant tumors localized in different zones of the oral cavity. Sample biopsies and the use of appropriate laboratory techniques are fundamental for the correct diagnosis of any of these lesions found in immune suppressed persons or in AIDS patients, particularly if not receiving HAART.

ABBREVIATIONS
CNS: Central Nervous System; AIDS: Acquired Immune Deficiency Syndrome; CD4: T helper cell; HIV: Human Immunodeficiency Virus; HAART: Highly Active Antiretroviral Therapy

ORAL CRYPTOCOCCOSIS

Cryptococcosis is a chronic mycotic infection caused by Cryptococcus neoformans that affects immune compromised as well as immune competent patients [1]. The fungus is found in the roosting sites of birds, especially pigeons. There are more than 100 species of the fungus. The two cryptococcus species able to cause infection are C. neoformans and C. gattii. The primary site of criptococcal infection is the lung. It occurs through aspiration of airborne spores that lodge in this organ, which produces pulmonary cryptococcosis, and by hematogenous dissemination develops lesions in other parts of the body mainly in the CNS, and occasionally in the skin and oral mucosa. Other organs involved are prostate, medullary cavity of bone and rarely liver.

The infection affects mainly immunocompromised patients. Cryptococcosis incidence is closely related to the number of AIDS cases. Disseminated cryptococcosis is most commonly seen in patients with very low CD4 counts and high viral loads. It is estimated that more than 80% of cryptococcosis cases worldwide are associated with HIV infection. The incidence of cryptococcosis in AIDS patients in the era before HAART ranged from 6 to 12%. Recent studies estimate that cryptococcal infection is the AIDS-defining illness in 3% of HIV patients. The decrease in frequency of cryptococcosis in AIDS patients is attributed to highly active antiretroviral therapy (HAART).

In immunocompromised non-AIDS patients, fungal dissemination is seen in those that have received organs transplantation and are under immunomodulatory drug therapy or suffer of diseases in which altered cell mediated immunity is present for other causes [2]. Therefore in addition to advanced AIDS, other predisposing factors for cryptococcosis are lymphoma, chronic leukemia, prolonged use of corticosteroids, solid organ transplant recipients, patients with autoimmune diseases and, in general those persons on immunosuppressive drugs.

The more common complication of hematogenous dissemination of cryptococcosis is meningoencephalitis, followed by skin lesions in approximately 10%-20% [3].

Different species of fungus produce lesions in the oral mucosa of AIDS patients which can be primary infections or, more frequently, a result of pulmonary infection with subsequent dissemination. In immune compromised patient, oral canidiasis, histoplasmosis, paracoccidioidomycosis and cryptococcosis are probably the main mycotic infections affecting the oral cavity [4,5].

Oral mucosal lesions are extremely rare and have been mainly reported in AIDS patients who suffered of disseminated cryptococcosis. Cryptococcosis of the oral mucosa very rarely represents a primary infection. The few oral cases reported in the literature are the result of hematogenous spread of the infection localized in the lungs of AIDS patients. However, oral cryptococcosis can be the first manifestation of a disseminated infection.

Apparently, the first case of oral cryptococcosis was reported in 1987 as an indurated ulcer with elevated margins measurement 1cm of diameter located in the lateral border of the tongue. In addition, the patient had multiple Kaposi sarcoma plaques in the palate and skin. Similar ulcers located in the anterior and the posterior parts of the hard palate together with facial lesions were described in a patient with disseminated cryptococcosis [6].
A non-healing ulceration after tooth extraction [7], was proved to be produced by crytococcus in a patient without previous diagnosis of AIDS was reported in a homosexual patient, complementary studies concluded in the diagnosis of AIDS. Oral crytococcosis non associated to systemic disseminated infection in a patient diagnosed of AIDS was reported as an indurated ulcer located in the palate [8].

Although, the few cases of oral crytococcosis lesions has been described as ulcers, in 2008 a case of oral cryptococcosis was reported as a multifocal tumor-like lesions located in the gingival tissues in a 36-year-old male patient with AIDS [9]. The gingival lesions were the initial manifestation of disseminated cryptococcosis from which central nervous system involvement was later established. The only general symptom manifested by the patient at the time of diagnosis of oral cryptococcosis was a headache. He had not received HAART.

Clinically the lesions appeared as tumor-like masses, with erythematous color, granular texture and micro-ulcerations covered by serous secretions and some bleeding. They were located in the gingivae of the anterior part of the maxilla, mandible, and left tuberosity.

Both buccal and lingual/palatal gingiva was involved. The lesion of the tuberosity involved part of the hard and soft palate (Figure 1,2). Neither of the lesions produced any symptoms. The patient manifested that he had noticed the gingival enlargements for approximately 3 months.

Biopsies of the upper and lower gingiva demonstrates a massive proliferation of cryptococi present as extra-and intracellular yeast cell with some budding forms together with reactive macrophages, minor lymphocytic infiltrate and few neutrophils. The epithelium showed marked hyperplasia of rete ridges surrounded the micro organisms. PAS and mucicarmine stains depicted clearly the cryptococci (Figure 3-5).

Oral Cryptococcosis can also present as malignant epithelial tumor. In 2006 was reported a 38-year-old HIV positive man with a deeply infiltrating and destructive tumor resembling a stage IV squamous cell carcinoma involving the retromolar region and the adjacent anatomical spaces. No histological evidence of malignancy was found instead the patient was diagnosed as having cryptococcosis [10].

Recently, a case of oral cryptococcosis manifested as a mass on the alveolar ridge of the left lower jaw was reported in a 68-year-old man diagnosed with chronic lymphocytic leukemia. The patient had received rituximab for 18 months. The gum mass...
CONCLUSION

Oral cryptococcosis can manifest in diverse forms, being the most common as indurated ulcers located in different parts of the oral mucosa, the other forms are as hyperplastic benign lesion or mimicking malignant tumors. Most of the lesions have been found in AIDS patients associated with hematogenous dissemination of the fungal infection, however, ulcers and masses have also been described in patients with other immune deficiencies.

Any lesion of the oral cavity found in an AIDS patient, particularly if not receiving HAART, should lead to the suspicion of fungus infection, particularly cryptococcosis, since it constitutes one of the major opportunistic infections associated with immune suppression.

It is necessary to emphasize that adequate sample biopsies and the use of appropriate laboratory techniques are fundamental for the correct diagnosis of any hyperplastic tissue, tumor-like lesion, or persistent ulcerations detected in the oral mucosa of normal or immunosuppressed patients.

REFERENCES