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ORIGINAL ARTICLE

Anaplastic Large Cell Lymphoma CD30+ ALK- in the Oral Cavity as a Primary Manifestation in HIV+ Patient: Case Report

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Abstract:

Anaplastic large cell lymphoma (ALCL) is a rare subtype of T-cell lymphoma that may involve mucocutaneous sites, in primary form, or secondary to systemic disease. It is a systemic malignancy characterized by an extranodal phenotype that rarely occurs in the oral cavity as the first manifestation of acquired immunodeficiency syndrome. In the primary forms, ALCL stands out for its favorable prognosis, being important to differentiate them clinically from the secondary ones, which have a rapid and aggressive evolution. For its diagnosis, it requires a rigorous physical and clinical examination and a duly oriented anatomopathological and immunohistochemical evaluation. In the present work, a clinical case of ALCL secondary to HIV is presented, detailing clinical characteristics, anatomopathological description, immunohistochemical profile and evolution against treatment.

Keywords: Lymphoma; HIV; Mouth, Neoplasms

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INTRODUCTION

Human immunodeficiency virus (HIV) infection predisposes individuals to the development of malignant neoplasms. These include Kaposi's sarcoma, high-grade non-Hodgkin's lymphoma (NHL) and immune phenotype (B-cell or unknown), primary central nervous system lymphoma, and invasive cervical carcinoma[1].

NHL appear in 3% of HIV-seropositive patients[2]. Anaplastic large cell lymphoma (ALCL) is a systemic malignancy characterized by an extranodal type that rarely occurs in the oral cavity as the first manifestation of acquired immunodeficiency syndrome (AIDS)[1].

ALCL is a rare subtype of T-cell lymphoma that may involve mucocutaneous sites, either primary or secondary, as part of systemic disease. ALCL is generally composed of large atypical cells with abundant cytoplasm, pleomorphism and kidney-shaped nuclei[3-4]. In most of the ALCL reports, the tumor cells are CD30^{+} and in most cases they express the protein associated with cytotoxic granules (perforin). In addition, a significant percentage of ALCL hosts the translocation t (2; 5) (p23; q35), based on the expression of the resulting gene product: anaplastic lymphoma kinase (ALK) which allows classifying the ALCL into two categories: ALK () and ALK (-) [4]. Tumors showing a positive reaction to ALK have greater cell proliferation and have a relatively better prognosis.

On the other hand, cases of ALK (-) ALCL show inaccurate behavior with a relatively unfavorable prognosis[4].

Primary ALCL may involve different locations of the mucous membranes of the head and neck, constituting a spectrum that includes both neoplasms and reactive conditions (i.e. traumatic ulcerative granuloma with stromal eosinophilia). However, there is no standard classification for the lymphoproliferative processes of CD30 positive T-cells of the mucosa. The head and neck region show susceptibility to a broad spectrum of lymphoproliferative disorders, and ALCL has been described as a rare entity[7-11]. Similar to primary cutaneous ALCL (C-ALCL), ALCL limited to sites of the head and neck mucosa is characterized by large atypical neoplastic cells with diverse morphology, CD30 and ALK- (Anaplastic Protein Kinase of Anaplastic Lymphoma). Some studies described that ALCL limited to sites of oral mucosa can show an indolent behavior as an outstanding feature[7,8,12]. This has led some authors to suggest that ALCL that arise mainly in the mucosa of the head and neck (M-ALCL) can be "equivalent" to C-ALCL and that CD30+ T-cell lymphoproliferative skin disorders can extend to sites of the mucosa of the head and neck[11,13,14]. However, systemic ALCL, other types of aggressive lymphoma, and some reactive lesions with a CD30+ phenotype may also affect sites of the oral mucosa, and it is essential to distinguish M-ALCL from other similar disorders, since its biological behavior, clinical course, and therapeutic options may differ[12-14].

When a primary, cutaneous extranodal or mucosal lymphoma is suspected, the most important thing is to rule out a CD30+ lymphoma lesion with secondary skin or mucosal involvement, being a comprehensive physical examination of the patient of great relevance[12].

For its diagnosis, a properly oriented anatomopathological and immunohistochemical evaluation must be carried out. These anaplastic large cell lymphomas CD30+ are malignant tumors with aggressive histomorphological features [11,15,16].

Immunohistochemistry shows that approximately 75% of tumor cells are CD30+. Most cells are positively marked for CD3, CD4, and ACL. The CD8 marker may be slightly positive in some cases. In addition, cells are negatively marked for CD 15, EMA and ALK[15].

Given the heterogeneity of their presentation and the low incidence of this type of lymphoma, the availability of comparative treatment trials is limited. In most health centers, the first line of treatment is a polychemotherapy regimen that includes anthracyclines, with CHOP (cyclophosphamide, vincristine, doxorubicin and prednisone) or schemes related to it being the most used. Although an adequate initial response to treatment is frequently observed, the relapse rate is high, leading to poor prognosis of this entity[10,12,17-19]. The overall 5-year survival of patients with ALCL CD30+ ALK-, reported in different bibliographies varies from 30% to 49%.[12,17-19].

CLINICAL CASE

Male patient, 32 years old, Argentinean nationality. Referred to the Department of Oral Medicine of the School of Dentistry, Faculty of Health Sciences at Universidad Católica de Córdoba for facial asymmetry due to an increase in progressive volume and trismus that makes feeding difficult, with 2-month history.

Relevant data in his medical history include chronic sun exposure and agrochemical exposure because he was a rural worker. The patient was a smoker,

with 5 cigarettes per day for two years. In addition, the patient was a drinker of 5 liters of beer, plus some measure of distilled beverages, per week from 18 to 30 years. In the last two years he reduced the consumption of alcohol to 1 liter of beer per week. His mother died of breast cancer.

Clinically, a lobulated tumoral lesion of violaceous coloration could be seen, measuring 5.8cm (2.28in) in anteroposterior direction, and 3cm (1.18in) in transverse direction; with an ulcerated surface extending from teeth 33 to 37, and covering the lower left gum, lingual ridge, vestibular sulcus up to the abutment area. The lesion was soft on palpation and painless (Figures 1 and 2).

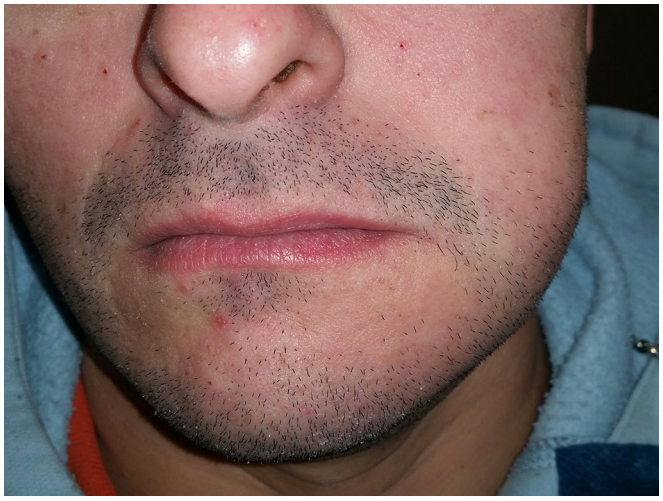

Figure 1. Facial Asymmetry.

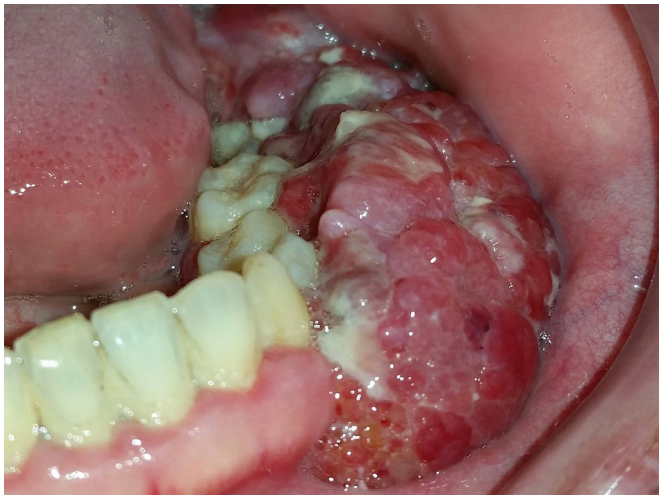

Figure 2. Intraoral Examination.

Additional diagnostic studies such as routine testing, orthopantomography (Figure 3), and HIV serology are requested due to suspicion of a lymphoproliferative lesion. Other possible diagnoses considered were squamous cell carcinoma and metastatic tumors.

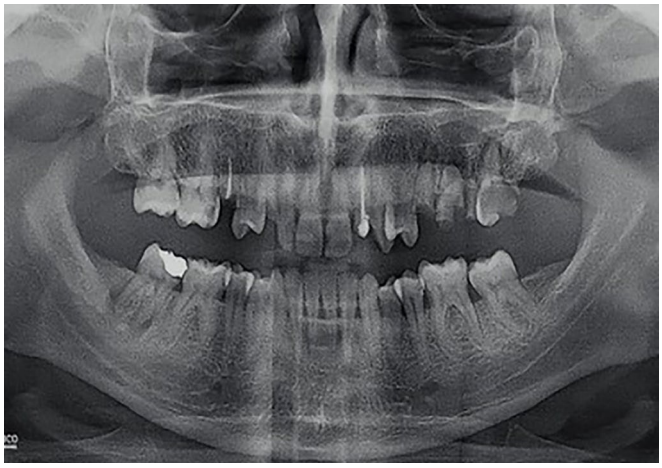

Figure 3. Orthopantomography.

DIAGNOSIS:

After clinical evaluation and complementary diagnostic examinations, an incisional biopsy was performed on the most representative site of the lesion, the anterior pole of the lesion. Obtaining a portion of tissue from the lower gum area, around teeth 34, 35 and 36, which was fixed in 10% formalin and analyzed at the Department of Anatomic Pathology of Clínica Universitaria Reina Fabiola. Tissue sections of the material sent presented infiltration by neoplastic cells population in the corium, confirming a diffuse growth pattern, with monomorphic and discohesive aspect, intermediate to large size cells with hyperchromatic macronuclei and basophilic cytoplasms (Figure 4). Mitosis is observed accompanied by a moderate lymphocyte infiltrate compatible with malignant neoplasia with lymphoproliferative process (Figure 5). The decision taken was to perform the corresponding immunohistochemistry using the Streptavidine-Biotin-Peroxidase method with monoclonal antibody demonstrating CD20+, CD3+, CD30+, Melan A-, EBV-, ALK-, HHV8-, KI67/MIB1+ in 90% of the nuclei of the tumor cells to confirm and categorize the diagnosis, resulting in Anaplastic Lymphoma of Large Cells CD30+ ALK- (Figure 6). After the diagnosis and HIV-positive serology were confirmed, the patient was referred to Hospital Rawson in Córdoba, Argentina to receive appropriate treatment from HIV infection specialists, and to Hospital Oncologic for the treatment of the lymphoproliferative disorder (ALCL). It consisted of 4 cycles of chemotherapy, CHOP scheme (cyclophosphamide, vincristine, doxorubicin and prednisone) for 45 days and then consolidation with external radiation therapy and linear accelerator with a field-in-field technique for 30 days being the daily dose 2Gy and the total dose received 40Gy. Regarding antiretroviral treatment, the drug of choice was ATRIPLA (Efavirenz, Emtricitabine, Tenofovir), 1 tablet per day.

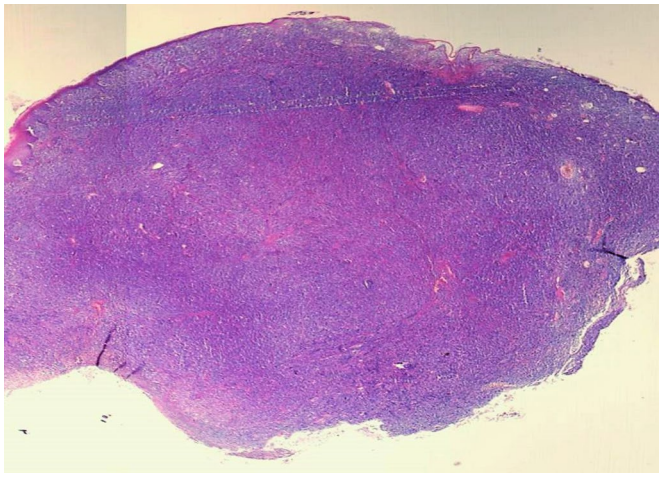

Figure 4. Hematoxylin-Eosin staining where diffuse lymphomatous infiltration is seen with intermediate to mainly large size cells. (2x).

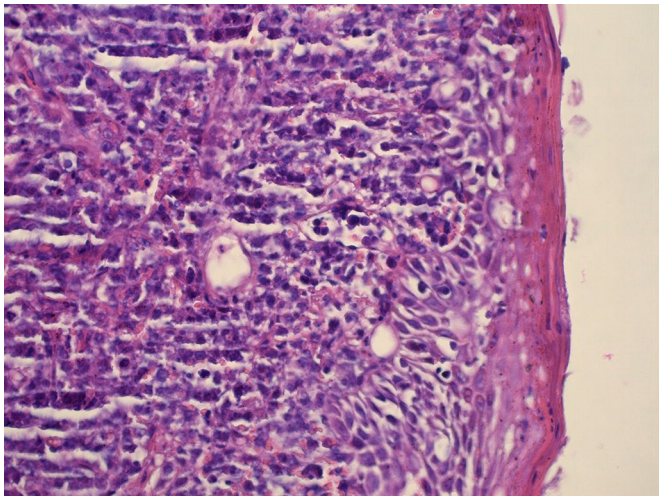

Figure 5. Hematoxyline-Eosin staining with 40x showing in detail lymphomatous cells with voluminous macronuclei that make up the lesion and numerous mitotic figures.

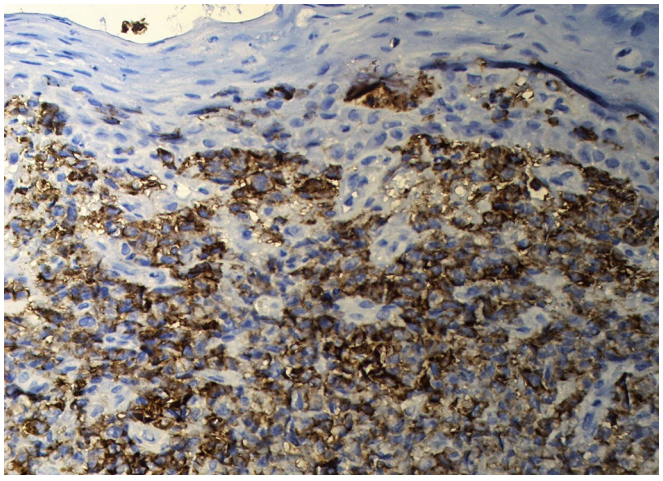

Figure 6. Immunoreaction with anti-CD30 antibody strong in lymphoma cells, which in areas are also infiltrating the epithelium. (40x).

The patient is currently undergoing exhaustive oncological controls and follow-up with a complete clinical and radiographic response (Figure 7).

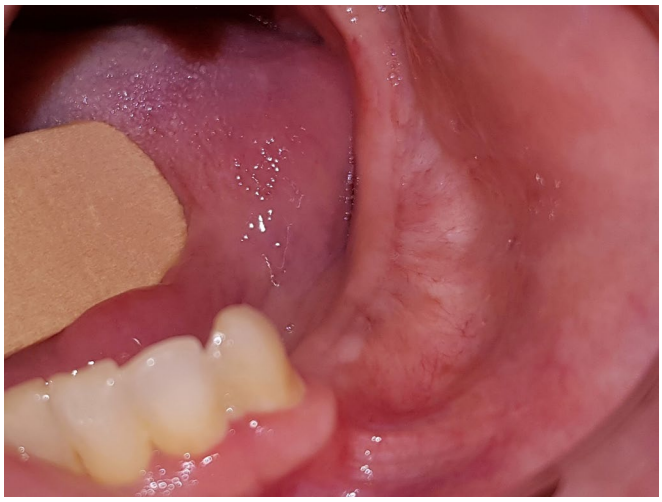

Figure 7. Current follow-up.

DISCUSSION

Certain sites in the head and neck show susceptibility to a broad spectrum of lymphoproliferative disorders, and ALCL has been described as a rare entity[7-10,16]. Similar to primary cutaneous ALCL(C-ALCL), ALCL limited to the mucosal sites of head and neck is characterized by large atypical neoplastic cells with diverse morphology, CD30 expression, and ALK negativity[9,12]. In addition, some studies have described that ALCL limited to mucosal sites may show indolent behavior[8,10,12], a prominent feature of C-ALCL. However, systemic ALCL, other types of aggressive lymphoma and some reactive lesions with a CD30 phenotype may also affect the mucosa and it is vital to distinguish M-ALCL from other similar disorders, and how its biological behavior, clinical course and therapeutic options may differ[13]. It is therefore important to perform an accurate clinical examination, histological and immunohistochemical analysis of oral lesions to establish a correct diagnosis.

It is also important to highlight the overall survival since the case we are presenting reflects the generally unfavorable prognosis of anaplastic large cell CD30+ ALK- lymphoma (30-49% overall survival over 5 years) compared to anaplastic large cell cutaneous lymphoma (90% overall survival over 5 years) or anaplastic large cell lymphoma ALK positive (70% overall survival over 5 years)[20].

The relevance of this clinical case, besides its rarity and infrequent primary manifestation in the

oral mucosa of this type of anaplastic lymphoma to large cells CD30 ALK-, was to have also diagnosed the patient HIV infection associated with this pathology due to the immunosuppression that he himself suffered which makes it even more interesting. It is important to highlight the importance of the multidisciplinary work of the health care providers as it is essential to make an early diagnosis, considering that it is a rapidly evolving neoplasm, aggressive in its behavior. A timely diagnosis represents a higher survival rate since this is, in general parameters, unfavorable.

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