Oral Cavity Plasmablastic Lymphoma in Patient without Human Immunodeficiency Virus Infection: Case Report

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Linfoma Plasmablástico de Cavidade Oral em Paciente sem Infecção pelo Vírus da Imunodeficiência Humana: Relato de Caso

Linfoma Plasmablástico de Cavidad Oral en Paciente sin Infección por el Virus de la Inmunodeficiencia Humana: Informe de Caso

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ABSTRACT

Introduction: Plasmablastic lymphoma comprises a rare tumor, accounting for approximately 2% of non-Hodgkin lymphomas, with a higher prevalence in men, with a mean age at diagnosis of 50 years and aggressive evolution, its diagnosis is common in patients with human immunodeficiency virus (HIV) infection, as well as Epstein-Barr virus (EBV) infection. **Case report:** Given the scarcity of data in the literature and the need for a better understanding of its diagnosis, management, and prognosis, the case of a male patient without HIV infection but with positive serology for EBV, diagnosed with plasmablastic lymphoma of the oral cavity mucosa is reported. The patient was treated for a periapical abscess approximately 30 days before the initial consultation with little improvement, progressing to mucosal ulceration. Due to suspicion of mucosal carcinoma, a biopsy was performed, revealing plasmablastic lymphoma, and treatment was initiated with CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone). Approximately one month after starting the first cycle, the patient was admitted to the emergency room with a decline in general condition, mental confusion, fever, and septic shock due to febrile neutropenia refractory to supportive measures, ultimately resulting in death. **Conclusion:** A detailed description of plasmablastic lymphoma and its clinical course is important for providing information to the scientific community, given the limited data available on this aggressive disease.

Key words: Plasmablastic Lymphoma/diagnosis; Lymphoma, Non Hodgkin/diagnosis; Epstein-Barr Virus Infections; Mouth/injuries.

RESUMO

Introdução: O linfoma plasmablástico compreende um tumor raro que corresponde a cerca de 2% dos linfomas não Hodgkin, com maior prevalência em homens, com idade média de diagnóstico de 50 anos e de evolução agressiva, sendo comum seu diagnóstico em pacientes portadores do vírus da imunodeficiência humana (HIV), bem como com infecção por Epstein-Barr vírus (EBV). **Relato do caso:** Em vista da escassez de dados na literatura e da necessidade de maior entendimento sobre o seu diagnóstico, manejo e prognóstico desses pacientes, relata-se o caso de um paciente do sexo masculino, sem infecção pelo HIV, com sorologia positiva para EBV, diagnosticado com linfoma plasmablástico de mucosa da cavidade oral. O paciente em questão foi tratado de um abscesso periapical há cerca de 30 dias da primeira consulta com pouca melhora, evoluindo com ulceração da mucosa. Por suspeita de carcinoma de mucosa, foi realizada biópsia com diagnóstico de linfoma plasmablástico e iniciado tratamento com esquema quimioterápico CHOP (ciclofosfamida, doxorrubicina, vincristina e prednisona). Aproximadamente um mês após início do primeiro ciclo, o paciente foi admitido em sala de emergência com quadro de queda do estado geral, confusão mental, febre e choque séptico por neutropenia febril refratários às medidas de suporte, evoluindo a óbito. **Conclusão:** A descrição detalhada sobre o linfoma plasmablástico e seu curso clínico faz-se importante ao fornecer informações ao meio científico, considerando a escassez de dados sobre essa doença tão agressiva.

Palavras-chave: Linfoma Plasmablástico/diagnóstico; Linfoma não Hodgkin/diagnóstico; Infecções por Vírus Epstein-Barr; Boca/lesões.

RESUMEN

Introducción: El linfoma plasmablástico comprende un tumor raro que corresponde aproximadamente al 2% de los linfomas no Hodgkin, con una mayor prevalencia en hombres, con una edad media de diagnóstico de 50 años y una evolución agresiva. Es común su diagnóstico en pacientes con infección por el virus de inmunodeficiencia humana (VIH), así como con infección por el virus de Epstein-Barr (EBV). **Informe del caso:** Dada la escasez de datos en la literatura y la necesidad de comprender mejor su diagnóstico, manejo y pronóstico, se presenta el caso de un paciente masculino sin infección por el virus de inmunodeficiencia humana, pero con serología positiva para el virus de Epstein-Barr, diagnosticado con linfoma plasmablástico de la mucosa de la cavidad oral. El paciente había sido tratado por un absceso periapical aproximadamente 30 días antes de la primera consulta con poca mejoría, progresando a ulceración de la mucosa. Debido a la sospecha de carcinoma de mucosa, se realizó una biopsia que reveló linfoma plasmablástico, y se inició el tratamiento con el régimen de quimioterapia CHOP (ciclofosfamida, doxorrubicina, vincristina y prednisona). Aproximadamente un mes después de comenzar el primer ciclo, el paciente fue admitido en la sala de emergencias con un deterioro del estado general, confusión mental, fiebre y shock séptico debido a neutropenia febril refractaria a las medidas de apoyo, lo que finalmente resultó en su fallecimiento. **Conclusión:** Una descripción detallada del linfoma plasmablástico y su curso clínico es importante para agregar información a la comunidad científica, especialmente dada la limitada disponibilidad de datos sobre esta enfermedad agresiva.

Palabras clave: Linfoma Plasmablástico/diagnóstico; Linfoma no Hodgkin/diagnóstico; Infecciones por Virus de Epstein-Barr; Boca/lesiones.

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INTRODUCTION

Lymphomas are widely known hematological neoplasms that can be divided in Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). The diffuse large B-cell lymphoma corresponding to 25% to 40% of the cases is one of the most common among several subtypes of classifications of non-Hodgkin's lymphomas. It occurs predominantly in males (55%) with different categories, among them, the plasmablastic lymphoma (PBL)[1-4], a rare tumor accounting for nearly 2% of NHL.

It is a as high-grade large B-cell neoplasm with plasmocytic phenotype highly prevalent in males of mean age of 50 years at diagnosis and clinically aggressive evolution, quite common in human immunodeficiency virus (HIV) infected patients and likely associated with Epstein-Barr virus (EBV) infection.

Extranodal presentation is quite frequent[4], the most affected sites are the oral cavity and gastrointestinal tract. The clinical diagnosis can be challenging because the tumor cells may be indistinguishable from high-grade lymphomas and plasmocytic cells malignancy[4-6]. More intensive chemotherapy regimens are recommended but there is no standard of care globally established with dismal prognosis for most of the cases.

Due to scarce literature-based data, a clinical case of a non-immunocompromised male patient (HIV negative and EBV positive) diagnosed with oral cavity PBL is reported for best understanding of the diagnosis and clinical course, further to management and prognosis of these patients.

The Institutional Review Board (IRB) approved the study, report number 6724433 (CAAE (submission for ethical review): 32884214.5.0000.0065); the consent for future investigations was waived due to the outcome, in compliance with Directive 466/2012[7] of the National Health Council.

CASE REPORT

Man, 88 years of age, sporadic and second-hand smoker, history of controlled hypertension, in dental treatment due to periapical abscess of left lower canine during 30 days with little improvement, evolving with mucosa ulceration in addition to fast and progressive worsening. A biopsy of the lesion initially performed by the odontologist on October 26, 2021, revealed little differentiated malignant neoplasm, pending complementary immunohistochemistry and referred the patient to the head and neck service for the first consultation on November 8, 2021.

Oroscopy (Figure 1) revealed a 3.0 x 2.5 cm infiltrative vegetative lesion, whose epicenter was the left lower gingival edge affecting the incisors up to the first molar, compromising dental elements, presence of central tumor necrosis and anterior floor of the mouth. Bilateral levels I and II lymph node enlargement were found, with significant compromise of the performance status (KPS = 70; ECOG = 2).

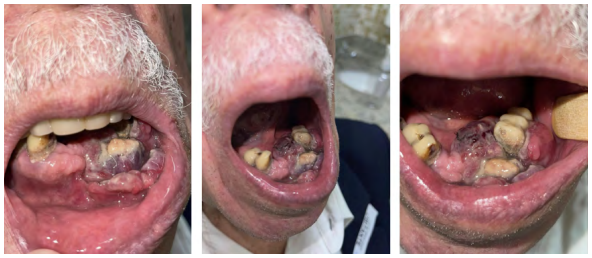

Figure 1. Oroscopy portraying approximately 3.0 x 2.5 cm infiltrative vegetative lesion of the lower gingiva edge with compromise of dental elements and central tumor.

Positron emission tomography (PET) scan for staging (Figure 2) performed on December 10, 2021 revealed a 5.2 x 3.5 cm infiltrative expansive lesion in the body of the left mandible (maximum standardized uptake value – SUV of 44.7), with erosion of the mandible extending to the mean line and left floor of the mouth with no additional significant findings.

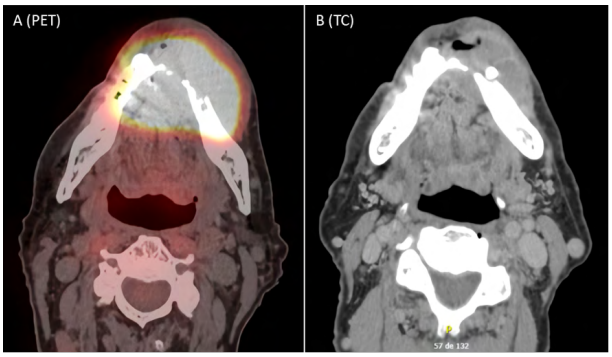

Figure 2. PET-scan portraying expansive and infiltrative lesion, heterogeneous enhancement in left alveolar edge mandible involving the mentonian symphysis and bilateral parasymphysis with maximum SUV of 44.77.

The results of a new biopsy and definitive anatomopathological study indicated a PBL on the mucosa after immunohistochemistry showing negative CD3, negative CD20 and positive CD138, in addition to positive EBV. The patient was referred for evaluation and management by hematology.

The patient initiated treatment with full dose CHOP regimen (cyclophosphamide, doxorubicin, vincristine and prednisone) (D1 on December 20, 2021) since he had

controlled comorbidities but although his advanced age, the disease was aggressive.

After the first cycle, he evolved with oral bleeding, severe leukopenia with asymptomatic neutropenia and thrombocytopenia which were dully managed. Nevertheless, was admitted to the emergency on January 2, 2022 due to decline of the general condition, confused, fever and septic shock by febrile neutropenia refractory to support measures, wide-spectrum antibiotic therapy and vasoactive drugs, fastly evolving to death.

DISCUSSION

Few cases in the literature are found due to the disease's rarity, but some factors can help to identify or raise suspicions. PBL is an immunoblastic variant and generally presents in HIV-positive, immunocompromised patients and EBV related[1-3]; as seen in this case, it is usually aggressive with bulky mass on the oral cavity and fast evolution in only 30 days.

As in the present case, extranodal presentation is quite common[4] mainly affecting the oral cavity, one of the most impacted locations due to its phenotype. The investigation of immunohistochemistry through biopsy as the presence of some markers (CD38, CD138, PRDM1, IRF4 and CD79a) and the absence of others (CD19, CD20 and PAX5) is essential to reach a diagnosis[4,5].

There was absence of CD20 usually expressed as mature B cells or other types of lymphomas as Burkitt's and presence of CD138 (marker of plasmocytic differentiation) associated with EBV, justified by the theory of inhibition of apoptosis through intracellular mechanisms which favor the appearance of this neoplasm.

This immunohistochemistry associated with affection of the oral mucosa and aggressive clinic led to diagnosis of the lymphoma, nevertheless, the presentations not always follow the same pattern as with this patient with compatible clinical presentation but without HIV-infection or immunocompromise history.

PET scan is essential to determine the initial staging of the disease since this imaging test may change the therapeutic in some cases, by upstaging or downstaging when compared with CT alone[6]. However, due to scarce evidence and studies comparing the sensitiveness and specificity of CT results alone with PET scan for the same patient through the gold standard (pathological analysis), most of the results of oncologic outcomes is determined by long-term follow-up to confirm the presence or absence of the disease[6].

The treatment of PBL is not well established but most of the literature-based recommendations indicate more intensive regimens, reason for which full dose CHOP regimen was applied to the present patient due to the disease's aggressiveness.

There are studies that also concluded on the effectiveness of the EPOCH regimen (etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin) for patients with HIV-associated lymphomas, although is applicability to PBL was not specified. A review article on the biology and treatment of PBL published by the American Society of Hematology[4] concluded that the most common regimen treatments today are EPOCH, CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, methotrexate alternating with iphosphamide, etoposide and cytarabine) and hyper-CVAD (hyperfractioned cyclophosphamide, vincristine, doxorubicin and dexamethasone) alternating with methotrexate and cytarabine due to their intensity and higher survival compared with other regimens.

Although the CHOP regimen is not the most recommended, two articles referenced in that review did not find difference between CHOP and EPOCH regimens. As it is an aggressive disease, difficult to diagnose and requiring aggressive treatment, a dismal prognosis is quite common[4,5,8-10]. Some articles and systematic reviews[4,5,10] indicate an overall survival of 15 months for HIV-positive PBL patients and between seven and nine months for PBL HIV-negative patients (11 months for immunocompetent HIV-negative). The patient of the present case survived little more than two months, even if HIV-negative and non-immunocompromised but due to the severe oncologic complication.

CONCLUSION

The detailed and reported description of PBL and its clinical course is important because it adds new information into the scientific mean where available data about this disease are scarce.

Given the high volume of differential diagnosis, unspecific symptoms, not well-defined therapeutic regimens and dismal prognosis, the thorough description of the cases, regimens utilized, well-described immunohistochemistry and explanation of the association with other viral diseases is important for best diagnosis accuracy, better treatment, extended survival specially for a very aggressive disease.

CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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