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Case Report

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Oral Hairy Leukoplakia: A Rare Involvement in a Patient with Polycythemia Vera

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ABSTRACT

Although there have been some reports of oral hairy leukoplakia (OHL) in patients with hematologic neoplasms, to the best of our knowledge, this study is the first to report this lesion affecting a patient with polycythemia vera. A 54-year-old male patient diagnosed with polycythemia vera presented with non-removable white patches with a rough surface on the bilateral border of the tongue. According to clinical, histopathological and in situ hybridization features, OHL was established. Two months after diagnosis, the patient developed splenomegaly and initiated ruxolitinib. Bone marrow biopsy showed post-polycythemia vera myelofibrosis. The patient underwent allogeneic haploidentical hematopoietic stem-cell transplant, achieving complete remission of the oral lesion. OHL is an important marker of immunosuppression. In the present case, OHL was diagnosed during the progression of polycythemia vera to myelofibrosis and its early diagnosis may have contributed to a better clinical outcome.

Keywords: Oral hairy leukoplakia; Polycythemia vera; Post-polycythemia vera myelofibrosis; Immunosuppression

INTRODUCTION

Oral hairy leukoplakia (OHL) is a mucosal lesion characterized by white, rough-textured patches that primarily affect both lateral borders of the tongue. It arises from permissive infection of epithelial cells by the Epstein-Barr virus (EBV) and is commonly associated with human immunodeficiency virus (HIV) infection[1,2]. It can also be linked to other immunosuppressive conditions, such as organ transplant recipients, malignant hematologic neoplasms, or autoimmune disease patients treated with high-dose corticosteroids[2,3].

Polycythemia vera is a malignant myeloproliferative neoplasm derived from myeloid stem cells. It is characterized by erythrocytosis and may be associated with leukocytosis and thrombocytosis. Patients with this condition have an increased risk of arterial and venous thrombosis, as well as progression to leukemia and myelofibrosis[4,5]. While there have been reports of OHL in patients with hematologic neoplasms[1,6,7], to the best of our knowledge, this study reports the first case of OHL affecting a patient with polycythemia vera.

Case presentation

A 54-year-old male patient was admitted to the Stomatology Department of A.C. Camargo Cancer Center presenting asymptomatic whitish lesions on both lateral border of the tongue, with a duration of 5 months. During the anamnesis, he reported a diagnosis of polycythemia vera 8 months ago and the treatment consisted of therapeutic phlebotomy and Hydroxyurea 1000 mg per day. Laboratory tests revealed leukocytosis (1.73 x 10^4/mm^3), neutrophilia (1.38 x 10^4/mm^3), IgG positivity for EBV, and negative serological tests for HIV and syphilis.

On clinical examination, multiple well-defined non-removable white plaques with rough surfaces were observed on the bilateral border of the tongue (Figure 1A-B). The diagnostic hypotheses included OHL and oral leukoplakia. An incisional biopsy was performed on the right border of the tongue. Histopathological analysis showed filiform parakeratosis, acanthosis, ballooning of keratinocytes, and some cells with perinuclear vacuoles (Figure 2A-D). Chromogenic in situ hybridization using ZytoFast Plus CISH Implementation Kit – HRP-DAB (ZytoVision, Bremerhaven, Germany) for EBV viral infection was positive (Figure 3A-B). According to these features, OHL diagnosis was performed. The patient had no cosmetic complaints or symptoms. For this reason, the lesion was not surgically removed. The patient was referred for further medical evaluation to investigate immunosuppression.

Two months later, the patient developed splenomegaly and initiated treatment with ruxolitinib. In addition, he also had episodes of fever, sweating, and lower limb edema. At this time, laboratory tests demonstrated leukocytosis (2.12 x $10^4/mm^3$), neutrophilia (1.43 x $10^4/mm^3$), thrombocytopenia (1.13 x 10^5/mm3) and increased levels of lactate dehydrogenase (1,491 U/L). Biopsy of the bone marrow was conclusive of post-polycythemia vera myelofibrosis. The patient underwent allogeneic haploidentical hematopoietic stem-cell transplant (HSCT), and complete remission of the oral lesion was achieved. One month after HSCT, he presented with acute graft-versus-host disease of the lower gastrointestinal tract, treated with budesonide 3 mg and methylprednisolone 90 mg. After years, the patient is asymptomatic with no recurrence of OHL (Figure 4) and no signs of hematological malignancy.

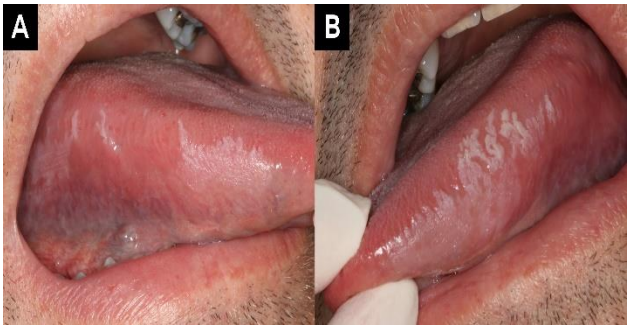

Figure 1. Well-defined, non-removable white plaques with rough surfaces located on the right (A) and left (B) border of the tongue

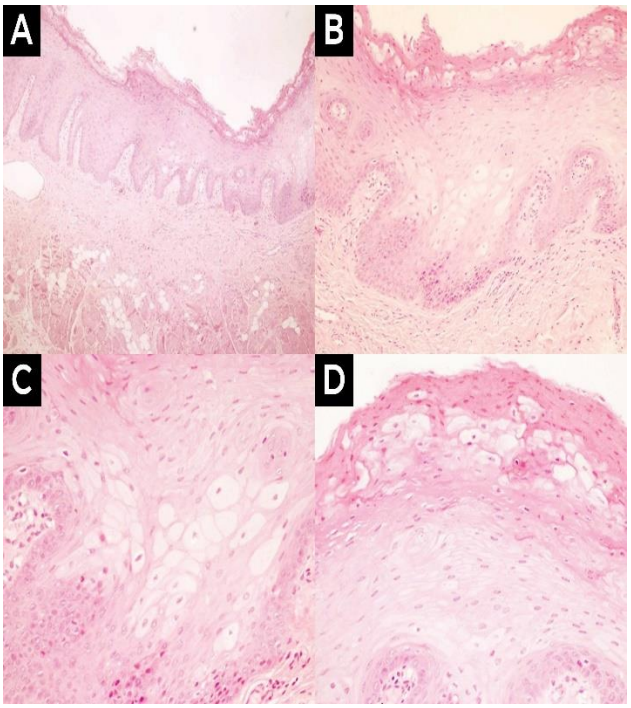

Figure 2. (A-B) Histopathological analysis showed a thickened corrugated/filiform parakeratin layer. (C-D) Some cells presented intracellular edema (ballooning cells) (A- HE 40x, B- HE 100X, C-HE 200x., D- HE 200x)

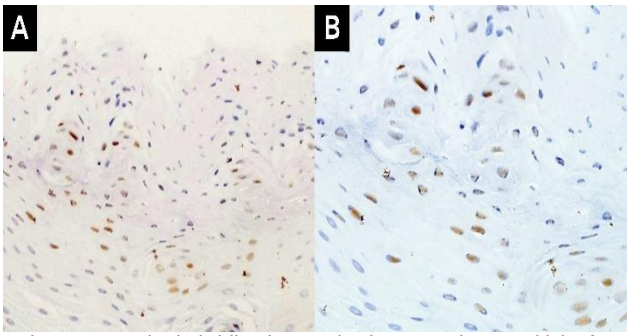

Figure 3. In situ hybridization study shows nuclear positivity for Epstein-Barr virus (A- CISH 200X, B CISH 400x)

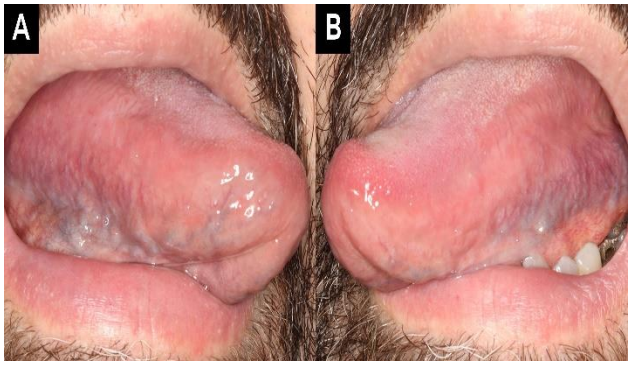

Figure 4 – Clinical postoperative appearance at 3 years, with no lesions on the right (A) and left (B) border of the tongue

DISCUSSION

EBV replicates in both B lymphocytes and oral epithelial cells, converting them into reservoirs of latent EBV[8]. However, the virus cannot replicate in the tongue epithelial cells in the absence of immunosuppression, underscoring the importance of early diagnosis of oral lesions and a screening of the patient's systemic immune status[3]. After the established diagnosis, a detailed medical history review is necessary, with a special focus on medications, particularly corticosteroid inhalers[9].

Approximately two-thirds of OHL cases manifest bilaterally, and most of them related to HIV[6]. In the present case, the alterations were subtle and might have been overlooked by dentists. Due to the known immunosuppression generated by polycythemia vera, oral hairy leukoplakia was our main diagnostic hypothesis. Differential diagnoses include oral leukoplakia, squamous cell carcinoma, traumatic hyperkeratosis, hyperplastic candidiasis, lichen planus, and other white lesions[10]. In our case, due to the clinical appearance of well-defined white plaques, we indicated a biopsy to exclude the possibility of oral leukoplakia.

OHL diagnosis is achieved through lesion biopsy along with in situ hybridization[11]. Histopathological features include hyperkeratosis, ballooning degeneration of keratinocytes, acanthosis, and underlying inflammatory infiltrate[8]. These features can be nonspecific and vary with sample size and quality. Therefore, in situ hybridization is considered the gold standard for diagnosing OHL[6,10], which was performed in our case. As a benign condition of low severity with a tendency to disappear naturally after the resolution of the immunosuppression condition, not all OHL cases require specific treatment. Therapy is offered to mitigate mild symptoms reported by some patients or for cosmetic reasons[10,11]. The patient in our report did not require specific treatment for the lesion, and was referred for evaluation by a hematologist.

Hydroxyurea is an antimetabolite agent that acts as an inhibitor of the enzyme ribonucleotide reductase and is used to arrest cells in the S phase of the cycle, inducing replication stress. It is a well-known and widely used drug that has proven effective in the treatment of myeloproliferative disorders and some hematological diseases[12]. Although it is generally well tolerated, it can sometimes induce immunosuppression, generating mucocutaneous adverse effects. These are extremely uncommon, but there have been reports of the appearance of oral ulcers, tongue depapillation and hyperpigmentation of the mucous membranes[13,14]. Although there are no reports, the immunosuppression caused by the medication may have contributed to the appearance of OHL in our patient.

The progression of a myeloproliferative neoplasm such as polycythemia vera may be preceded by clinical signs that may include thrombosis or thromboembolism development, significant bleeding, severe infections unresponsive to antibiotics, or an increase in symptom burden, such as painful splenomegaly, weight loss, night sweats, fever, and pruritus. Additionally, changes in hematological parameters, such as leukocytosis, presence of granulocytic precursor cells and blasts, or reduced red blood cells may be observed[15]. OHL is not considered a prognostic factor for diseases other than acquired immunodeficiency syndrome. However, previous OHL cases associated with more advanced stages or poor prognosis of hematologic neoplasms have been reported[1,6,7]. In addition to OHL, our patient also had splenomegaly, fever, sweating, lower limb edema, leukocytosis, and thrombocytopenia.

To the best of our knowledgement, this is the first case which showed the association between OHL and polycythemia vera and the patient had myelofibrosis two months later.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships, which could have appeared to influence the work reported in this article.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent to participate

Informed consent was obtained from the patient.

Consent to publish

The participant has consented to the submission of the case report to the journal.

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