

Oral hairy leukoplakia-like in an immunocompetent patient

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Abstract:

Oral hairy leukoplakia is seen in immunosuppressed persons caused particularly by human immunodeficiency virus or organ-transplanted subjects and in individuals presenting malignant neoplasias. Epstein-Barr virus (EBV) is associated with hairy leukoplakia and its presence must be proved to confirm the diagnosis. We report a case of oral hairy leukoplakia like-lesion in a immunocompetent young person where *in situ* hybridization was EBV negative.

Keywords: Leukoplakia; Oral leukoplakia; Hairy Leukoplakia; In situ hybridization.

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Dear Editor,

Recently, we examined a 37-year-old HIV-positive African American male patient with clinical and histopathological features of oral hairy leukoplakia (OHL), involving the lateral borders of the tongue. The microscopic appearance was typical, showing acanthosis and hyperparakeratosis, ballooning cells, corrugate surface and no chronic inflammatory infiltrate in the subjacent connective tissue (Figure 1- A and B).. The in-situ hybridization (ISH) for Epstein-Barr virus - encoded small nuclear RNA (EBER) was performed using peptide nucleic acid (PNA) probes conjugated with 5-carboxy-fluorescein (code Y5200), anti-fluorescein isothiocyanate-alkaline phosphatase (FITC/AP), and substrate bromochloroindolyl phosphate-nitro blue tetrazolium (BCIP/NBT) (code K5201) (EBER PNA probes; Dako, Denmark), which was positive (Figure 1- C). The EBER PNA probe is complementary to the nuclear RNA portion of EBER-1 and EBER-2. Plasmablastic lymphoma was used as positive control and included in this assay. Hybridization liquid replaced by phosphate-buffered saline (PBS) served as negative control.

Interestingly, at the same month, we evaluated a 29-year-old Caucasian male patient complaining of a bilateral discoloration on the tongue with two months of evolution". The medical history was noncontributory, and the intraoral examination revealed white lesions on the lateral borders of the tongue highly suggestive of OHL (Figure 2- A and B). The patient denied any risk behavior, systemic disease, and any harmful habit such biting the tongue, smoking, or alcohol consumption. Under local anesthesia, an incisional biopsy of the right lateral border of the tongue was performed and the histopathological analysis on H&E section showed an acanthotic and hyperparakeratinized epithelium with superficial projections of parakeratin, ballooning cells beneath the parakeratinized layer, nuclear alterations, and absence of inflammatory cellular infiltrated in the connective tissue (Figure 3- A and B). ISH staining for EBER was also carried out, however, it was negative (Figure 3- C). In agreement with the patient, a HIV-antibody test was requested, which was negative. Based on these findings the diagnosis of OHL-like was established. The patient returned two weeks later and complete spontaneous remission of the bilateral OHL-like lesions was observed.

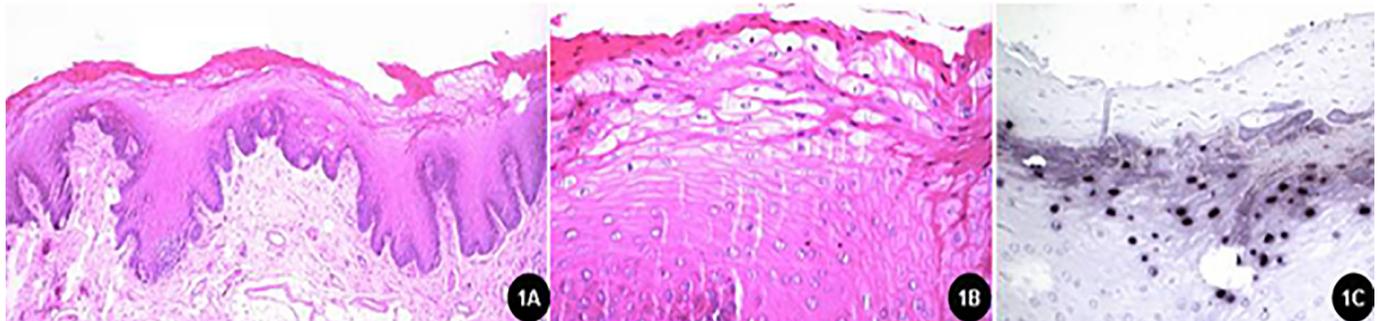


Figure 1. A - Typical OHL, showing acanthosis, hyperparakeratosis, an irregular surface and absence of inflammatory cellular infiltrate in the lamina propria. (H&E stain, x 50). B - In high power, notice the ballooning of the cell cytoplasm beneath the hyperparakeratotic stratum (H&E stain, x 200). C- ISH for EBER1/2 disclosed the presence of numerous positive nuclei. (ISH, x 200).



Figure 2. Superficial irregular, corrugated white plaques on the bilateral borders of the tongue (A and B).

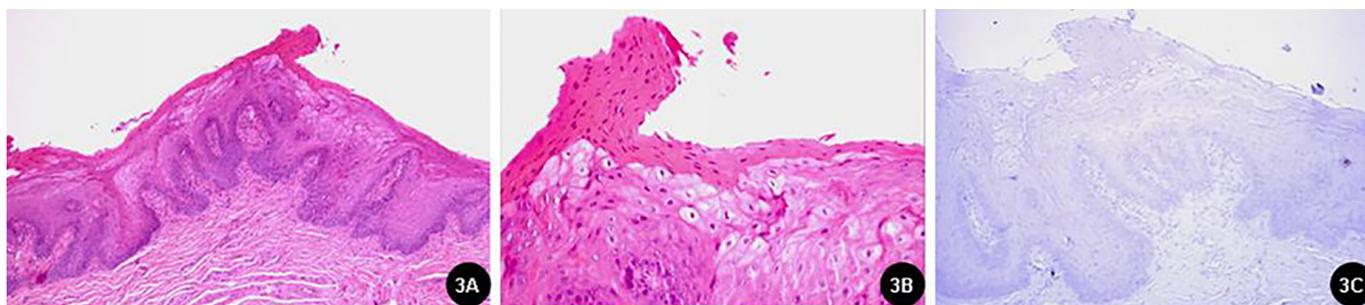


Figure 3. The histopathological features were similar to the figure 1 (H&E stain, A, x 50 and B, x 200), nevertheless the nuclei of the epithelial cells were negative for EBV1/2 (C- ISH, x 100).

EBV - the OHL's etiologic virus- is a ubiquitous virus that persistently infects approximately 95% of healthy adults. While primary infection is usually sub-clinical in nature, the virus is maintained indefinitely as a plasmid in the cytoplasm of resting B-cells. In EBV-infected cells the most abundantly expressed viral transcripts are the EBV1/2, which are generally resistant to degradation and participate in maintaining latency. In immunodeficient states, suppressor and cytotoxic functions are often defective and EBV can resume proliferation affecting lymphoid and epithelial cells. Several studies have show that OHL is a marker of immunosuppression (i.e. steroids treatment, transplant recipients) and not just a sign of HIV infection, as thought when OHL was first described in 1984¹⁻⁷.

A few papers reported that non-HIV and nonimmunosuppressed patients may develop OHL but all of them presented EBV positivity by ISH study⁸⁻¹¹. One interesting report described the onset and posterior remission of an OHL bilateral white patches of the tongue in an immunocompetent patient, suggesting an acute and transient infection by EBV. However, no HIV testing was done on the patient and this case could have been a case of chronic candidiasis presenting with concomitant EBV¹².

1989, McMillan et al.¹³ reported a case of an 18-year-old male HIV-negative patient who had typical features of OHL and suggested the use of the term "OHL-like lesions". Again, the ISH for EBV was not performed. Also in 1989, Green et al.¹⁴ described fifteen HIV-negative patients with oral lesions that clinically and histologically resembled OHL but were EBV negative by ISH (that they called "pseudo-hairy leukoplakia"). These authors reassured the importance of a correct clinical and histological diagnosis, as well as the confirmation of the EBV presence and the immunostate of the patient. Gold-standard laboratory exams should also be performed for the diagnosis of OHL, always associated

with molecular tools to EBV detection, Opening a new perspective to use less invasive diagnostic methods for this condition^{15,16}.

The current case showed similar clinical and histopathological features with the cases described by Green et al.¹⁴ and according with these findings we think that there is a group of lesions mimicking OHL and they would have to be named pseudo-OHL or OHL-like lesion, since they are EBV negative. In summary, the findings of the current case and those described in the English-language literature suggest that OHL is not specific for HIV infection, but may be associated with immunosuppression also due to other causes. OHL-like are rare lesions, affecting commonly the tongue of apparent immunocompetent patients, nevertheless their definitive diagnosis requires the demonstration of EBV negativity.

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