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Oral Hairy Leukoplakia -A Comprehensive Review

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ABSTRACT

Background: Oral Hairy Leukoplakia (OHL) was described three years after the first patient with acquired immunodeficiency syndrome(AIDS) were reported in 1981. It is a clinical manifestation of Epstein-Barr virus (EBV) infection almost exclusively found in patients with untreated advanced HIV disease and typically occurs on the lateral border of the tongue of HIV–infected individuals and other groups of immunocompromised individuals.

It appears as a soft, corrugated, painless plaques or white patches on lateral borders of tongue and can extend to involve the dorsum of tongue and buccal mucosa. The surface may be so thick as to produce hair-like projections. It is asymptomatic and rarely seen in children. Most often it coexists with oral candidiasis and may be masked by it. It is an indication of advanced immunodeficiency, a more rapid progression to AIDS and a poor prognosis.

It can be diagnosed by demonstration of EBV antigens in epithelial cell nuclei by in-situ hybridisation. Incisional biopsy is also useful in its diagnosis, as it shows characteristic EBV nuclear inclusions in upper-layer keratinocytes. Oral Hairy Leukoplakia rarely requires treatment, it may resolve spontaneously. This review article is to highlight the History, Etiopathogenesis, Demographics, Clinical features, Diagnostic aids, and Differential Diagnosis of Oral Hairy Leukoplakia

Keywords: *Oral Hairy Leukoplakia, Immunodeficiency, Tongue, White.*

Introduction

Oral Hairy Leukoplakia was described three years after the first patients with acquired immunodeficiency syndrome (AIDS) were reported in 1981.[1] It is a clinical manifestation of Epstein-Barr virus (EBV) infection almost exclusively found in patients with untreated advanced HIV disease and typically occurs on the lateral border of the tongue of HIV–infected individuals and other groups of immunocompromised individuals. The prevalence of Oral Hairy Leukoplakia in recent studies of HIV-infected adults varies from 0.42 to 38% in both developed and developing countries. The increased prevalence of Oral Hairy Leukoplakia might be related to higher exposure to EBV, a lower CD4+ count, and a higher HIV viral load.[2]

It may herald HIV disease in the vast majority of cases, and also may be present after AIDS is established. It is the second most prevalent oral lesion in the world. Oral Hairy Leukoplakia is highly characteristic of HIV infection, especially in male homosexuals. It appears as a soft, corrugated, painless plaques or white patches on lateral borders of tongue and can extend to involve the dorsum of the tongue and buccal mucosa. The surface may be so thick as to produce hair-like projections. It is asymptomatic and rarely seen in children. Most often it coexists with oral candidiasis and may be masked by it. It is an indication of advanced immunodeficiency, a more rapid progression to AIDS and a poor prognosis.[3]

The probability of developing AIDS in patients with Oral Hairy Leukoplakia is 48 percent by 16 months and 83 percent by 31 months. Oral Hairy Leukoplakia has now been documented in all recognized risk categories for HIV infection, including partners of HIV-positive individuals, intravenous drug abusers, transfusion recipients, haemophiliacs, and HIV- seropositive children. Variation of the prevalence rate depends on many factors including clinical expertise, patient selection and diagnostic criteria. Earlier reports suggested a co-infection of EBV and candida, however, this has now been shown not to be the case. The clinical behaviour of Oral Hairy Leukoplakia includes spontaneous remission and progression that may represent indicators of the patient's immune status.[4]

Presumptive criteria for Oral Hairy Leukoplakia: Bilateral whitish/grey lesions on the lateral margins of the tongue which are not removable and may exhibit vertical corrugations. Lesions may extend onto the ventral and dorsal surfaces of the tongue, where they are usually flat and rarely occur on the buccal mucosa.[2]

Definitive criteria for Oral Hairy Leukoplakia: Demonstration of EBV in the lesions. In the absence of facilities to demonstrate the presence of EBV, a lack of response to anti-fungal treatment or the demonstration of an immune-deficient status will add weight to the presumptive diagnosis.[2]

It can be diagnosed by demonstration of EBV antigens in epithelial cell nuclei by in-situ hybridisation. An Incisional biopsy is also useful in its diagnosis, which shows characteristic EBV nuclear inclusions in upper-layer keratinocytes. Oral Hairy Leukoplakia rarely requires treatment, it may resolve spontaneously.[3]

The present review focuses on the History, Etiopathogenesis, Demographics, Clinical features, Diagnostic aids, and Differential Diagnosis of Oral Hairy Leukoplakia with a comprehensive literature review.

History

Greenspan et al, 1984 investigated Oral Hairy Leukoplakia in 1981and published the initial report of its existence among homosexual men in San Francisco in 1984.[5]
Greenspan et al, 1986, Rindum et al, 1987, Ficarra et al, 1988 recognised Oral Hairy Leukoplakia in all risk categories for HIV infection.[6]

In **1993, Classification and Diagnostic Criteria for Oral Lesions in HIV infection** listed Oral Hairy Leukoplakia in the classification of oral lesions as a Group 1 lesion strongly associated with HIV infection.[6]

Triantos et al, 1997 stated that the relationship between EBV infection and the development of OHL remains un-defined, the results of recent studies provide insight into the intriguing virus-host relationship that underlies Oral Hairy Leukoplakia.[7]

Nicolatou et al, 1999 concluded that Oral Hairy Leukoplakia is not pathognomic for HIV infection since it has been described in patients who are iatrogenically immunosuppressed as seen in patients with bone

marrow transplantation, solid organ transplantation, patients receiving cytotoxic chemotherapy for acute leukaemias.[6]

Silva A et al, 2004 suggest that identification of the EBV by immunohistochemistry or in situ hybridization is required to confirm a diagnosis of Oral Hairy Leukoplakia, as accurate diagnosis of Oral Hairy Leukoplakia may be of prognostic value.[8]

Reginald and Sivapathasundharam, 2010 stated that Exfoliative Cytology is a good option for the diagnosis of Oral Hairy Leukoplakia, for being a simple, reliable, safe, non-invasive and non-traumatic method.[9]

Brasileiro CB et al, 2014 stated that in some patients Oral Hairy Leukoplakia may present with symptoms including mild pain and alteration of taste.[10]

Etiopathogenesis

Although candidal hyphae are found abundantly in Oral Hairy Leukoplakia lesions. and Candida can be isolated from 43% to 80% of the lesions. Although an etiologic link between candidal infection and Oral Hairy Leukoplakia is unlikely, there is some evidence for the potentiating role of candidal infection. An etiologic association with HPV corrugated white patches on the lateral borders of the tongue was initially suggested. However, this association has not been confirmed by detailed studies using electron microscopy, immunostaining, and DNA hybridization.[7]

Greenspan et al, 1984 stated that in HIV positive persons Oral Hairy Leukoplakia heralds more rapid progressions of AIDS.[5]

Snijders et al, 1990 proposed EBV as the etiologic agent of OHL.[8]

Glick et al, 1994; Lifson et al, 1994 concluded that the incidence of Oral Hairy Leukoplakia is reported to be 20% in CDC II individuals, increasing as CD4 count falls and patient's clinical condition deteriorates.[5]

Sirois, 1998 concluded that Oral Hairy Leukoplakia has subsequently been reported in other immune deficiency states as well as in immunocompetent individuals. For example among organ or bone marrow recipients and those receiving long-term steroid therapy.[5]

Iain et al, 2000 stated that the Epstein Barr virus (EBV) is the likely cause of Oral Hairy Leukoplakia, and which should probably now be renamed according to its Aetiology as "EBV Leukoplakia".[5]

Walling D M, 2000 concluded that the productive Epstein Barr virus (EBV) replication appears to be necessary but not sufficient for the pathogenesis of hairy leukoplakia. The co-factors that contribute to the pathogenesis of the lesion have not yet been identified. Hairy Leukoplakia and the biology of EBV infection in this disease have some unique features that likely contribute to the pathogenesis of this lesion. He postulated the following pathogenesis.

1. Hairy Leukoplakia frequently contains multiple, co-infecting, EBV strains. In hairy leukoplakia, the productively replicating EBV undergoes genetic recombination and sequence mutation, generating a complex population of multiple EBV strains, sub-strains, and recombinant variants. The pathogenicity of EBV may be enhanced by this genetic heterogeneity.
2. Many EBV genes that typically are associated with latent EBV infection are surprisingly expressed during productive EBV replication in hairy leukoplakia. Some of these genes are known to have profound effects on cellular proliferation, differentiation, and apoptosis, and these EBV gene products

may induce the cellular changes that ultimately give rise to the histopathologic features of hairy leukoplakia. Interestingly, many of the "latent" genes expressed in hairy leukoplakia also sustain high rates of genetic mutation in hairy leukoplakia, potentially altering their pathogenicity or their immunogenicity.

3. There is a marked decrease or an absence of Langerhan's cells in hairy leukoplakia biopsy tissues. Langerhan's cells are the antigen-presenting immune cells that are required for an immune system response to the viral infection. This deficiency of Langerhan's cells may permit EBV to persistently replicate and escape immune recognition.[11]

Bravo, et al, 2006 stated that Oral hairy leukoplakia is caused by Epstein-Barr virus and 50% of individuals with HIV present with this condition and it is a very good indicator of immunosuppression. The lesion usually presents itself when the CD4 cell counts fall below 0.3*109/L.[12]

Krishna R et al concluded that the pathogenesis of Oral Hairy Leukoplakia is due to the replication of Epstein-Barr virus and increased virulence in conjunction with a decrease in local and systemic host immunity.[12]

PiperiEet al,2010 concluded that the pathogenesis of oral hairy leukoplakia is complex and includes an interplay of persistent Epstein–Barr virus replication and virulence, systemic immunosuppression and suppression of the local host immunity.[13]

Brasileiro CB et al, 2014 concluded that the pathogenesis of Oral Hairy Leukoplakia is related to the infection of oral squamous epithelial cells with the Epstein-Barr virus (EBV). The absence of or high reduction of Langerhans cells in Oral Hairy Leukoplakia has been demonstrated. Langerhans cells are the antigen-presenting immune cells that are required for an immune system response to a viral infection. This deficiency of Langerhans cells may permit EBV to replicate.[10]

Demographics

Greenspan et al, 1984; Glick et al, 1994; Lifson et al, 1994 stated that it is slightly less common in women than in men, and it is also rare in children.[5]

Becker J et al, 1991 concluded that the basal epithelial cell layer of the lateral border and the dorsum of the tongue is probably a potential reservoir for EBV in HIV-seropositive and non-immunocompromised HIV-seronegative individuals. In heavily immunosuppressed patients latently EBV infected epithelial cells may be co-activated during terminal differentiation of the epithelium.[14]

McCullough M.J et al, 1997 concluded that Oral Hairy Leukoplakia develops most frequently on the lateral surface of the tongue, but it may extend to the dorsal or ventral surfaces and in some instances, it has been observed on the cheek mucosa, soft palate, pharynx, and oesophagus.[4]

Triantos et al, 1997 stated that typically Oral Hairy Leukoplakia manifests as unilateral or bilateral, adherent white or gray patches on the lingual lateral margins and to a lesser extent, the dorsum or ventrum of the tongue.[7]

Krishna R et al, concluded that Oral Hairy Leukoplakia presents themselves as white, corrugated lesions on the lateral surface of the tongue and are not painful.[12]

Walling D M, 2000 concluded that in adults, hairy leukoplakia is more common in men and in cigarette smokers. He also stated that Hairy leukoplakia may also involve dorsal and ventral tongue surfaces, the

buccal mucosa, or the gingiva. On the ventral tongue, buccal mucosa, or gingiva, the lesion may be flat and smooth, lacking the characteristic "hairy" appearance.[11]

Moffat et al, 2005 proposed that the size distribution on the lateral aspect of the tongue include the fact that the tongue is susceptible to trauma allowing access of EBV in saliva to viral receptors in the prickle cell layers i.e auto-inoculation.[6]

Ukpebor M, 2007 stated that Hairy leukoplakia is highly characteristic of HIV infection especially in male homosexuals.[3]

Brasileiro CB et al, 2014 concluded that Oral Hairy Leukoplakia appears clinically as an asymptomatic white lesion on the lateral border of the tongue, unilaterally or bilaterally, with imprecise boundaries, a flat, corrugated or hairy surface, that is not removed by scraping.[10]

Clinical Features

Reichart PA et al, 1989 concluded that the Oral hairy leukoplakia is clinically characterized as a white lesion of the lateral border of the tongue, occasionally also occurring in the buccal mucosa with slightly raised, poorly demarcated and corrugated "hairy" surface. Lesions cannot be rubbed off and are reported to be usually symptomless. Hairy leukoplakia has so far not been observed in other mucosal areas than the oral.[1]

Triantos et al, 1997 stated that the Oral Hairy Leukoplakia manifests as unilateral or bilateral, adherent white or gray patches on the lingual lateral margins and, to a lesser extent, the dorsum or ventrum of the tongue. The surface of the patches is usually irregular, forming prominent folds or projections (sometimes so marked as to resemble "hairs") but more commonly giving rise to a corrugated or shaggy appearance, hence its name. Occasionally the lesion can be flat, particularly at the ventral surface of the tongue. Less developed lesions can be detected as barely discernible white areas on the posterolateral lingual borders. Although Oral Hairy Leukoplakia is usually asymptomatic, it may induce soreness or a burning sensation.[7]

Walling D M, 2000 stated that the Oral Hairy Leukoplakia lesions may be either continuous or discontinuous along both tongue borders, and they are often not bilaterally symmetric. Lesions are adherent, and only the most superficial layers can be removed by scraping. There is no associated erythema or edema of the surrounding tissue. Lesions may frequently appear and disappear spontaneously. Hairy leukoplakia is often asymptomatic and many patients are unaware of its presence. Some patients with hairy leukoplakia do experience symptoms including mild pain, dysesthesia, alteration of taste, and the psychological impact of its unsightly cosmetic appearance.[11]

Silva A et al, 2004 stated that in Oral Hairy Leukoplakia clinical presentation is that of an asymptomatic white, non-removable patch of variable size with a smooth, corrugated or "hairy" surface.[8]

Cho H H et al, 2010 concluded that in Oral Hairy Leukoplakia the distinctive feature is produced by the proliferation of the mucosal epithelium, which is caused by the reactivation of a previous Epstein-Barr virus (EBV) infection.[15]

Brasileiro CB, 2014 stated that Oral Hairy Leukoplakia appears clinically as an asymptomatic white lesion on the lateral border of the tongue, unilaterally or bilaterally, with imprecise boundaries, a flat,

corrugated or hairy surface, that is not removed by scraping. He also added that some patients may present with symptoms including mild pain and alteration of taste.[10]

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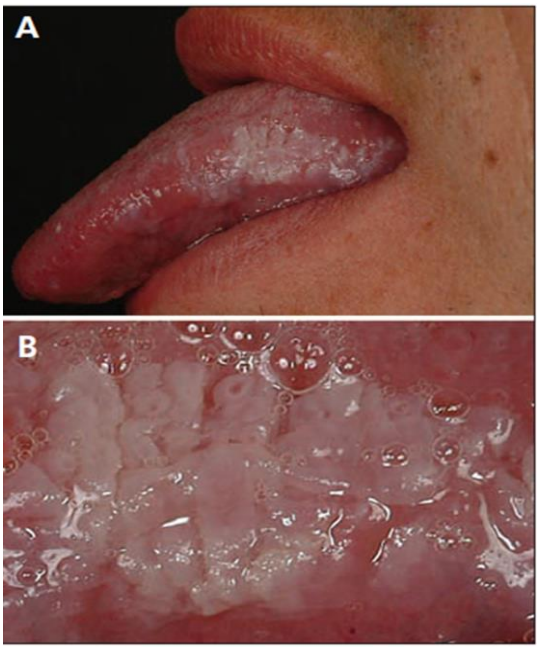

Figure : (A) Painless white adherent plaques on the dorsal tongue surfaces of a male patient. (B) Close-up view of a lesion: the surface of the patch has a corrugated appearance forming prominent folds.

Diagnostic Aids

The diagnosis of Oral Hairy Leukoplakia is not always easy based only on clinical or morphologic criteria. Unfortunately, several white lesions, especially when occurring on the lateral border of the tongue, resemble Oral Hairy Leukoplakia. Because of the serious prognostic implications of Oral Hairy Leukoplakia, the clinician must be certain of this diagnosis before alarming the patient.[16]

A most important issue in the diagnosis of Oral Hairy Leukoplakia is the question of whether the diagnosis is based on information on HIV seropositivity or negativity. As soon as a clinician is informed about the HIV status of a patient he is inclined to assess a lesion on the border of the tongue as Oral Hairy Leukoplakia. In addition to this bias the problem of oral candidiasis involving the lateral border of the tongue must be considered. Only alter anti-mycotic therapy should a diagnosis of Oral Hairy Leukoplakia be made. The fact that Oral Hairy Leukoplakia also occurs in non-HIV individuals makes the diagnosis of Oral Hairy Leukoplakia even more complicated.[1]

The diagnosis of Oral Hairy Leukoplakia is therefore based on patient's history, clinical features, cytopathology, histopathology, immunohistochemistry, in situ hybridization, polymerase chain reaction (PCR), and electron microscope.[8]

A. Exfoliative Cytology

Exfoliative Cytology in Oral Hairy Leukoplakia diagnosis was an innovative study done by **Lumerman et al in 1990**. These findings were confirmed later by other investigators.[9]

Fraga-Fernandez and Vicandi-Plaza (1992), Migliorati et al (1993), Epstein et al (1995) and Dias et al (2000) reported that conventional cytopathology can be used as a method for the diagnosis of Oral Hairy Leukoplakia based on nuclear changes, mainly nuclear beading.[8]

An ultrastructural examination of exfoliative cells was studied by Frank and Greenspan and they were found to contain EBV in koilocyte cells.[9]

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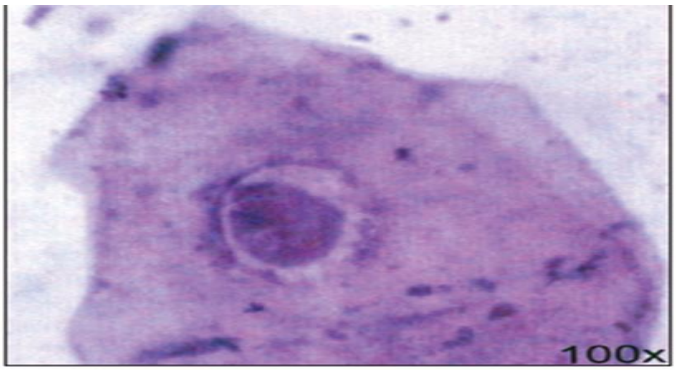
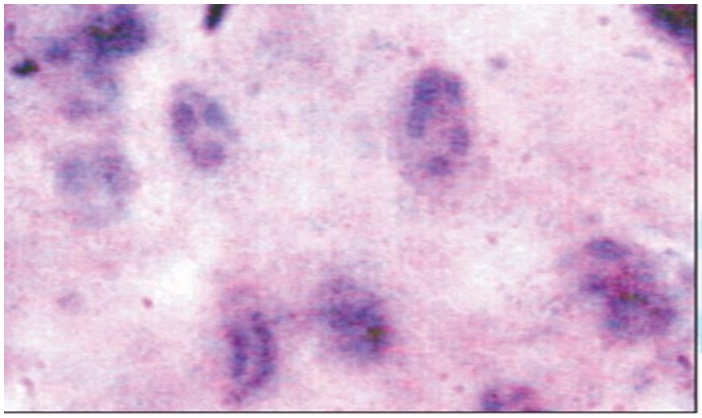
The characteristic features of Oral Hairy Leukoplakia were identified and recorded accordingly-

- **Cowdry A inclusion bodies-** An eosinophilic and central intranuclear inclusion body surrounded by a clear space.
- **Ground glass nuclei-** An eosinophilic or basophilic inclusion body homogenizing the whole surface and exhibiting peripheral margination of chromatin.
- **Nuclear beading-** A prominent peripheral margination and clumping of the nuclear chromatin.[9]



Photomicrograph showing PAP-stained, Cowdry type A inclusion bodies along with perinuclear halo 100X magnification.



Photomicrograph showing PAP-stained, Ground glass appearance of the nucleus and a peripheral nuclear beading 100X magnification.

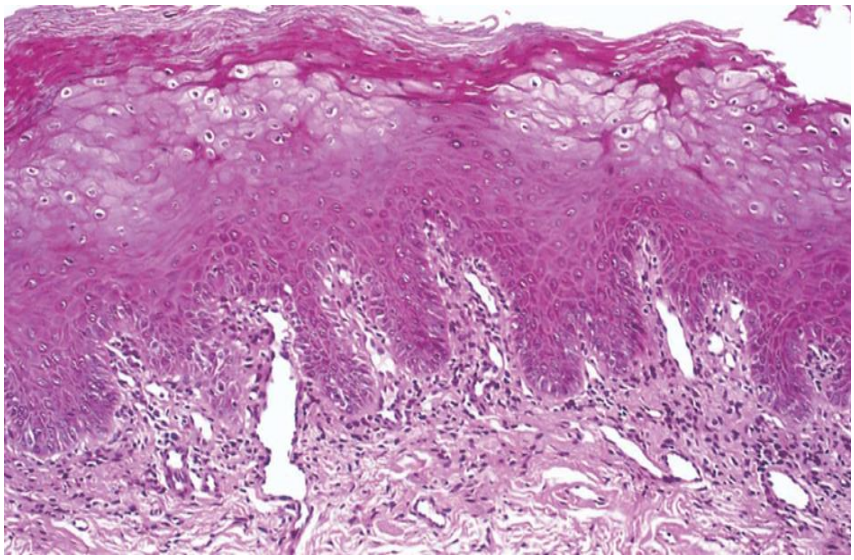
B. Histopathology

Greenspan et al, 1984 in his original description of Oral Hairy Leukoplakia stated that the histopathology of Oral Hairy Leukoplakia was similar to that of the flat wart of the skin and proposed the following criteria; 1; keratin projections 2; some degree of parakeratosis and acanthosis. 3; characteristic ballooning of cells in the prickle cell layer (pyknotic nuclei and perinuclear halos); these changes were compared to koilocytosis

as described in dermal warts and uterine condylomata,4: little or no inflammation, 5;mild epithelial atypia in some cases.[1]

Fraga-Fernadez et al, 1990 described for the first time the histopathologic criteria for Oral Hairy Leukoplakia diagnosis.[8]

Triantos et al, 1997 stated that epithelial hyperplasia with hyperparakeratosis and acanthosis are consistent features of Oral Hairy Leukoplakia. The thickened surface layer may separate from the underlying cells, giving rise to projections that produce the characteristic folds or "hairs". Varying numbers of swollen, ballooned cells with pyknotic nuclei and perinuclear halos are usually present in the prickle cell layer and occasionally in the suprabasal cell layer. These koilocytes superficially resemble those of human papilloma virus (HPV) infection. However, although the nuclei of HPV-infected ballooned cells are enlarged and hyperchromatic and the perinucleolar cytoplasmic halo is clear, the nuclei of ballooned cells of Oral Hairy Leukoplakia are small and pale, and the cytoplasm adopts a glassy appearance. In patients with Oral Hairy Leukoplakia the vacuolated keratinocytes demonstrates the characteristic migration of the nuclear chromatin against the nuclear membrane ("nuclear beading"). This histopathologic feature is highly suggestive of Oral Hairy Leukoplakia and has been believed to result from rampant EBV replication in the nucleus, which displaces chromatin to the nuclear margin.[7]



Photomicrograph of a Surgical biopsy specimen with characteristic histologic features of Oral Hairy Leukoplakia :hyperparakeratosis,acanthosis, and balloon cells in the middle epithelial layer (hematoxylin-eosin stain; original magnification, X40).

Walling D M, 2000 stated that although the characteristic histologic features of hairy leukoplakia are highly suggestive of the diagnosis, none are unique to the lesion. Thus, a definitive diagnosis of hairy leukoplakia requires both an appropriate histologic, cytologic appearance and the demonstration of EBV DNA, RNA, or protein within the epithelial cells of the lesion. ***The histopathology of hairy leukoplakia is characterized by 5 major histologic features.*** *[11]*

1. There is a hyperkeratosis of the upper epithelial layer that represents an altered pattern of keratin expression in the squamous epithelial cells. This hyperkeratosis is largely responsible for the characteristic

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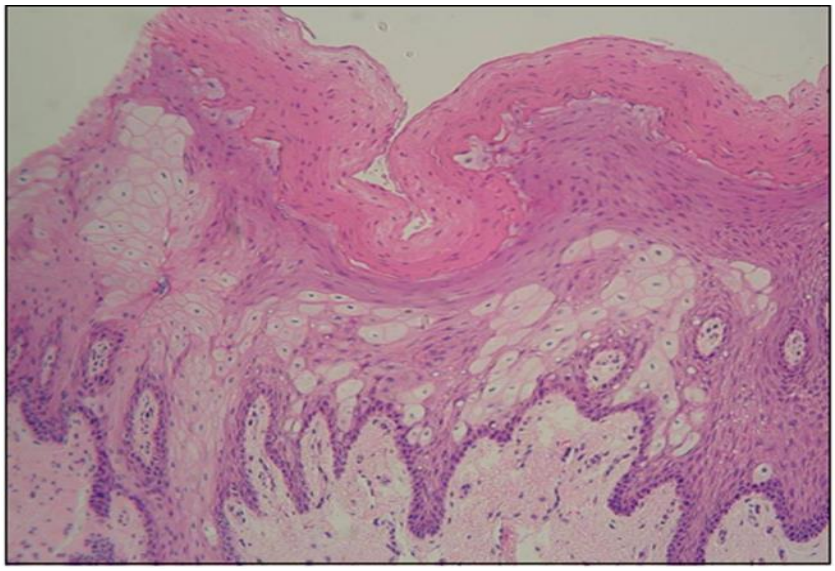
shaggy or "hairy" gross appearance of the lesion. Superficial infections of the hyperkeratinized epithelium with bacteria or Candida may also be seen.

2. There is a parakeratosis of the superficial epithelial layer. This abnormal persistence of cell nuclei in the superficial epithelial layers may represent incomplete squamous differentiation.

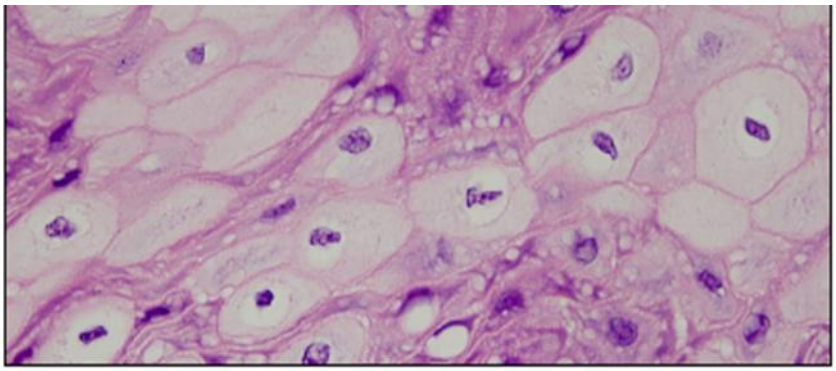
3. There is an acanthosis of the stratum spinosum in the epithelial midlayer. This abnormal expansion of cells occurs with foci or layers of ballooning "koilocyte"like cells.The cell nuclei have a homogenous ground glass appearance and may contain Cowdry type A intra-nuclear inclusions.

4. There is minimal or absent inflammation in the epithelial and sub-epithelial tissues.

5. The basal epithelial layer is histologically normal. [11]



Photomicrograph showing Hyperkeratosis, parakeratosis, acanthosis, ballooningdegeneration in the stratum spinosum and vacuolated cells with small, round, deeply basophilic nuclei surrounded by a narrow clear halo are shown (H&E, ×100).



Photomicrograph showing Cytoplasmic halo surrounding the nucleus and peripheral margination of chromatin in the nucleus are shown (H&E,×1,000).

C. Immunohistochemistry

Reichart PA et al, 1989 stated that DNA hybridization studies with Epstein-Barr virus (EBV) probes in Southern blots demonstrated Epstein-Barr virus DNA in epithelial cells of Oral Hairy Leukoplakia.Other immunohistochemical studies using in situ hybridization to detect Epstein-Barr virus DNA confirmed the presence of this virus in Oral Hairy Leukoplakia.However, Epstein-Barr virus DNA was also found in an HIV-1-seronegative patient. Using semithincryosections in conjunction with the APAAP staining technique, EBV capsid as well as nuclear antigen of EBV was demonstrated in cases of Oral Hairy Leukoplakia, while the presence of HPV was stated using immune-histochemical methods and electron-microscopy in the first reports on Oral Hairy Leukoplakia it was not revealed in subsequent studies,HIV structural proteins were detected using immunohistochemistry.[1]

Becker J et al, 1991 stated that immune labelling for antibodies against the ORFs BcLF1 (VCA), BRLF1, BMLF1, and BHRF1 was limited to Oral Hairy Leukoplakia biopsies. The antiserum against c-fos did not show any immunoreaction as was also noted in HIV-seronegative patients. [14]

BcLF1(p50)- The VCA was observed only in the nuclei of epithelial cells and in the extracellular space in the upper stratum spinosum.

BZLF1- Oral Hairy Leukoplakia biopsies showed an intense fluorescence for BZLF1 throughout almost the entire basal epithelial layer.The adjacent stratum spinosum was completely negative. In the upper stratum spinosum and in the ballooned keratinocytes a nuclear fluorescence was noted, and double immunofluorescence experiments revealed in this area a nuclear co-distribution of BZLF1 and BcLF1.

BRLF1- Oral Hairy Leukoplakia biopsies showed a nuclear fluorescence for BRLF1 in the upper stratum spinosum and in the overlying ballooned keratinocytes.

BMLF1- BMLF1 fluorescence was observed only in the upper stratum spinosum of Oral Hairy Leukoplakia biopsies and showed a nuclear co-distribution with BcLF1 fluorescence.

BHRF1- showed as a nuclear fluorescence in the upper stratum spinosum and in the overlying ballooned keratinocytes of OHL biopsies as was observed for BcLF1.

Silva A et al, 2004 concluded that immune-histochemical analysis for EBV-related antigens include LMP-1 and ZEBRA .Both antibodies shows positivity in the superficial layers of the epithelium.[8]

D. Electron Microscopy

Electron microscopic studies have revealed the presence of herpes type virus with clusters of nucleocapsids located in nuclei and enveloped complete particles occurring in the cytoplasm and extracellular spaces. In addition, tubule reticular structures as well as membrane differentiations were revealed in Oral Hairy Leukoplakia. Crystalline inclusions in epithelial cells of Oral Hairy Leukoplakia have recently been described.[1]

Differential Diagnosis

Walling D M, 2000 concluded that the gross appearance of the hairy leukoplakia lesion may be variable, resulting in possible misdiagnosis. Other oral lesions with a similar appearance to hairy leukoplakia include the following:

- ***Candidiasis or thrush*** typically occurs as a flat lesion, removable by scraping and revealing an erythematous base. However, hyperplastic candidiasis lesions are adherent and do not wipe off,making this disease especially difficult to distinguish from hairy leukoplakia. Resolution of the

lesion with antifungal therapy suggests candidiasis over hairy leukoplakia. However, hairy leukoplakia lesions are commonly also infected with Candida, further confusing the clinical diagnosis.

- ***Frictional keratosis*** typically occurs on the lateral borders of the tongue as a consequence of tongue biting by the molar teeth or some other abrasive irritant. This lesion should quickly resolve after removal of the provoking stimulus.
- ***Tobacco induced leukoplakia*** occurs in smokers and individuals who chew tobacco. These lesions are typically not shaggy like hairy leukoplakia, and they may occur anywhere in the oral cavity. They are often premalignant and should be evaluated by biopsy and histologic examination.
- ***Lichen planus or lichenoid eruptions*** occur as autoimmune or allergic reactions to an unknown stimulus. In HIVinfected patients, lichen planus often occurs on the buccal mucosa, typically with a reticulated pattern. Oral lichen planus may also be associated with cutaneous lesions.[11]

Silva A et al, 2004stated that the differential diagnosis for Oral Hairy Leukoplakia includes hyperplastic candidiasis, lichen planus, white sponge nevus, frictional hyperkeratosis, geographic tongue, keratotic reaction associated with electrochemical interaction, squamous cell carcinoma, or any other white non-removable lesion in the mouth.[8]

Cho H H et al, 2010 concluded that Oral Hairy Leukoplakia should be differentiated from white sponge nevus, frictional keratosis, lichen planus and idiopathic leukoplakia. [15]

Brasileiro CB et al, 2014 concluded that the differential diagnoses include oral candidiasis, lichen planus, tobaccoassociated leukoplakia, human papillomavirus– induced oral intraepithelial neoplasia, and oral squamous cell carcinoma. [10]

References

1. Reichart PA, Langford A, Gelderblom HR, Pohle HD, Becker J, Wolf H Et Al. Oral Hairy Leukoplakia: Observations In 95 Cases And Review Of The Literature. J Oral Pathol Med 1989; 18; 410-415.
2. Prabhu et al. Oral Manifestations Of HIV. J Trop Dis.2013; 1(3): 111.
3. M Ukpebor, O.B Braimoh. HIV/AIDS; Oral Complications And Challenges, The Nigerian Experience. Benin Journal Of Postgraduate Medicine.2007 Dec; 9(1).
4. Mccullough MJ, Firth NA, Reade PC. Human Immunodeficiency Viru Infection: A Review of The Mode Of Infection, Pathogenesis, Disease Course, And The General And Clinical Manifestations. Australian Dental Journal 1997;42:(1):30-7.
5. Agbelusi G.A, Eweka OM, Umeizudike KA, Okoh M. Oral Manifestations of HIV. Http://Dx.Doi.Org/10.5772/52941.
6. Moffat M, Jauhar S, Jones ME, MacDonald DC, Felix DH .Oral Hairy Leukoplakia. In An HIV-Negative Immunocompetent Patient. Oral Biosciences And Medicine.2005;2(4): 249-251.
7. Triantos D, Porter SR, Scully C, Teo CG. Oral Hairy Leukoplakia:Clinicopathologic Features, Pathogenesis, Diagnosis, And Clinical Significance. Clinical Infectious Diseases· 1997 Dec ; 25:1392–6.
8. Silva A, Nikitakis NG, Meeks V, Gracia CCB, Saraiva FMGC, Ferreira1 SMS et al. Oral Hairy Leukoplakia As A Sign Of HIV Infection. Braz J Oral Sci. 2004;3(11):628-632.
9. Reginald A, Sivapathasundharam B. Oral Hairy Leukoplakia-An ExfoliativeCytology Study. Contemporary Clinical Dentistry.2010; 1(1):10-13.

10. Brasileiro CB, Abreu MHNG, Mesquita RA. Critical Review Of Topical Management Of Oral Hairy Leukoplakia. World J Clin Cases 2014; 2(7): 253-256.

11. Walling D M. Oral Hairy Leukoplakia: An Epstein Barr Virus Associated Disease of Patients With HIV. The Center For AIDS Information & Advocacy. 2000 Dec:1-6.

12. Krishna R, Zemse S, Derossi S. Individuals With HIV/AIDS: Clinical Manifestations In The Oral Cavity In The Post-HAART Era. Global View Of HIV Infection. Georgia Health Sciences University, College of Dental Medicine. United States Of America.

13. Piperi E, Omlie J, Koutlas IG, Et Al. Oral Hairy LeukoplakiaIn HIV-Negative Patients: Report of 10 Cases. Int J Surg Pathol. 2010 ;18: 177-83.

14. Becker J, Leser U, Marschall M, Langford A, Jilg W, Gelderblom H et al. Expression of Proteins Encoded By Epstein-Barr Virus Trans-Activator Genes Depends On The Differentiation Of Epithelial Cells In Oral Hairy Leukoplakia. Proc NatiAcadSciUSA . 1991 ; 88 : 8332-8336.

15. Cho HH, Kim SH, Seo SH, Jung DS, Ko HC, Kim MB Et Al. Oral HairyLeukoplakia Which Occurred As A Presenting Sign Of Acute Myeloid Leukemia InA Child. Ann Dermatol.2010;22(1):73-76.

16. Ficarra G, Gaglioti D, Pietro MD, Storthz KA. Oral Hairy Leukoplakia: Clinical Aspects, Histologic Morphology And Differential Diagnosis. Head & Neck. 1991:514-521.

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