

## Oral leukoplakia: risk of malignant transformation and the importance of surgical excision

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### Abstract

Leukoplakia is the most frequent potentially malignant lesion of the oral mucosa. Its diagnostic and therapeutic present a challenge for dentist. Two clinical cases of oral leukoplakia were reported. The first was a patient using chewed tobacco consulted for a verrucous oral lesion that was surgically completely removed. Histopathological examination of the specimen revealed verrucous carcinoma. The second was a smoker man presenting an oral leukoplakia with fungal infection. After antimycotic treatment and periodic follow up, the clinical signs of candidiasis regressed but the mucosal white patch persisted. A large part of the lesion was removed. Histopathological examination indicated a well-differentiated squamous cell carcinoma.

**Keywords:** Leukoplakia, Oral mucosa, Biopsy, Dysplasia, Carcinoma.

### Introduction

White lesions of the oral mucosa, single or multiple, are often associated with abnormal keratinization whose causes are numerous. Those caused by tobacco for which no etiology can be raised are grouped under the term oral leukoplakia.

According to the World Health Organization (WHO) in 1978, oral leukoplakia is defined as a white lesion that cannot be clinically or pathologically be characterized as any other disease<sup>1,2,3</sup>. In 2012, “Van der Waal” proposed a new definition, which includes the histological confirmation: “A predominantly white lesion or plaque of questionable behavior having excluded, clinically and histopathologically, any other definable white disease or disorder”. This one has not been assessed yet by WHO but it has good chances for acceptance.<sup>4</sup>

Clinically, they may be in varying aspects and cannot be detached by simply scratching. It is important to make the diagnosis because of some precancerous character. The clinical examination must be associated with histological monitoring with biopsies in doubt.

### Cases Reports

The aim of this article was to report clinical cases of two patients who were referred for oral leukoplakia to the department of Medicine and Oral Surgery of the Dentistry Clinic of Monastir, Tunisia.

The first patient, an 87-year-old man, hypertensive, former consumer of chewed tobacco since the age of 12. The intraoral examination revealed the presence of a verrucous, exophytic, asymptomatic white lesion measuring 1.5cm in diameter, located in a hyperkeratotic base in retro commissural of the mouth, which progressed over three years (Fig. 1). Because the higher suspicious of appearance and small size of the lesion, we

opted for its complete removal by surgery (Fig. 2). After one month, the lesion was completely regressed (Fig. 3). The histopathological result indicated the presence of averrucouscarcinoma (Fig. 4) the patient was periodically controlled in order to prevent any risk of recurrence.



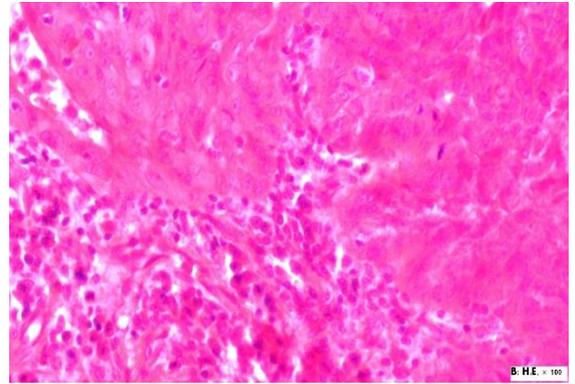
**Fig. 1: Proliferative verrucous lesion localised on right buccal mucosa**



**Fig. 2: Surgical excision of the lesion**



**Fig. 3: Healed surgical site after one month of surgery**

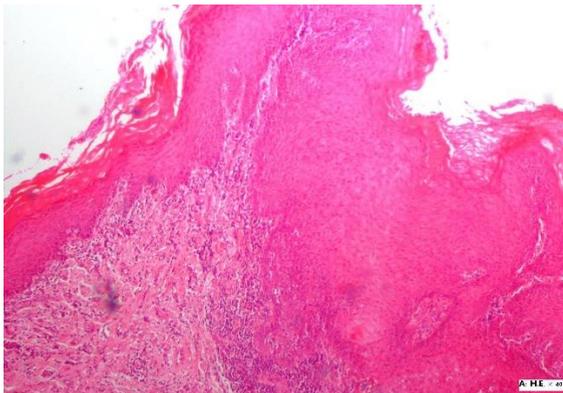


**Fig. 4: A case of malignant cell proliferation invading chorion, mitosis, inflammatory cells. A: H.E, × 40; B: H.E, × 100**

The second case, a 58-year-old man, edentulous and smoker in excellent health with no serious systemic disease. The extraoral examination revealed an angular cheilitis (Fig. 5). The physical exam of buccal mucosa revealed firm, non-tender, homogeneous and asymptomatic white lesion measuring 1.5 x 2.5 cm, which appeared ten years ago with the port of total prosthesis (Fig. 6). The clinical diagnosis was oral leukoplakia with a chronic candidiasis. An incisional biopsy was performed (Fig.7) and the histopathological result confirmed the presence of epithelial hyperplasia associated with spores and hyphae (Fig. 8).The patient has received antimycotic treatment and was periodically followed up. We noted that the clinical signs of candidiasis decreased whereas white patch has not regressed. For this reason, we decided to perform a larger removal of the lesion by surgery (Fig. 9). The histopathological report affirmed that it was a well differentiated squamous cell carcinoma (Fig. 10).After that, the patient was transferred to an oncology service.



**Fig. 5: Right labial commissure showing angular cheilitis**



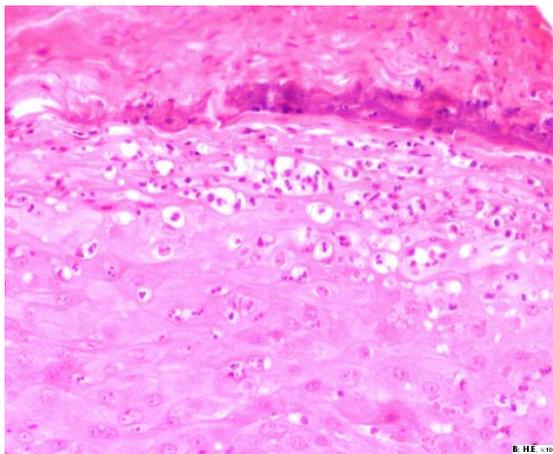
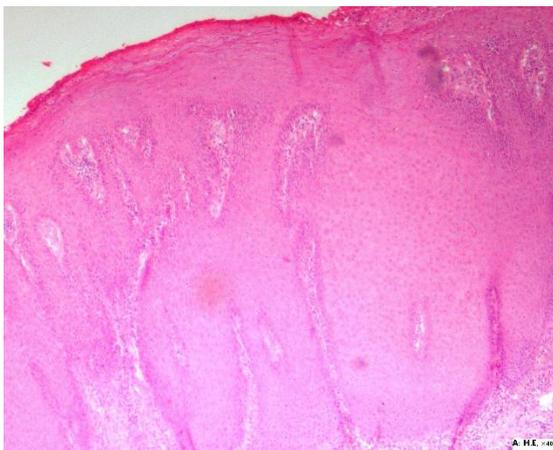
**Fig. 6: Indirect view of a white inhomogeneous lesion on right buccal mucosa**



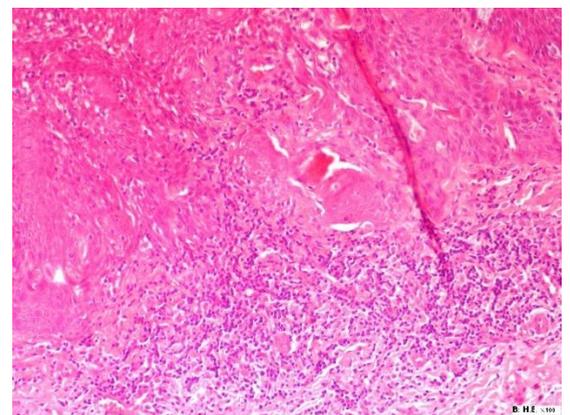
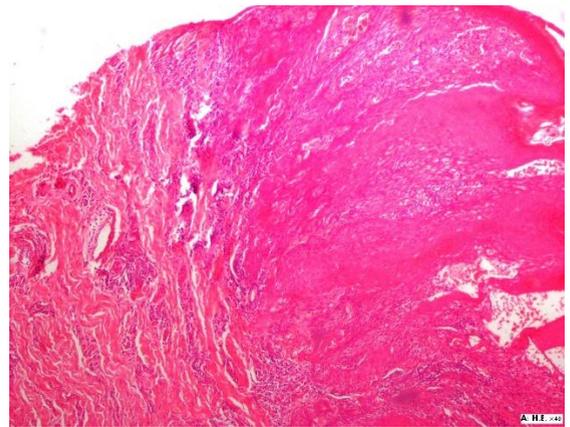
**Fig. 7: First biopsy of the lesion**



**Fig. 9: Second biopsy after regression of candidiasis clinic signs**



**Fig. 8: Microscopic aspects of candidiasis: Parakeratotic, hyperplasia. A: H.E, x40, B: H.E, x100**



**Fig. 10: A case of malignant cell proliferation invading chorion, hyperplasia. A: H.E, x40, B: H.E, x100**

**Discussion**

Oral leukoplakia is the most frequent potentially malignant disorder of oral mucosa<sup>4,5,6,7,8,9,10</sup>. Its etiology is considered multifactorial, and smoking is considered to be the frequently involved factor<sup>4,11</sup>. Alcohol consumption, human papilloma virus (HPV) infections, candida, traumas, vitamin deficiency and ultraviolet radiation are other factors that could be associated with this disease. Leukoplakia may affect any mucosa location.<sup>11,12,13,14</sup>

Leukoplakia is a clinic-pathological diagnosis that can only be made after histological examination of the tissue<sup>1</sup>. It may exist under different forms such as benign hyperkeratosis, mild dysplasia, moderate dysplasia, severe dysplasia or microscopically invasive carcinomas.<sup>12</sup>

Although, the risk of transformation of leukoplakia to oral cancer remains difficult to assess, some clinical factors have been identified as indicators of higher risk. These factors include older age, gender, tobacco and alcohol consumption, during of evolution, anatomical location and size of the lesion.<sup>1,15</sup> All these factors may contribute to the progression of oral leukoplakia into cancer.<sup>16</sup>

According to Mishra M<sup>3</sup> et al., (2005), the percentage of oral leukoplakia is higher in men (53,76%) than in women (46,24%). The maximum percentage of patients (55,47%) were seen in the 21-30 years age group followed by the 4<sup>th</sup>, 5<sup>th</sup> and 2<sup>nd</sup> decades. In the younger age group, males tended to outnumber the females, but above the age of 40 years, females were more in number.<sup>3</sup>

Smoking and alcohol intake play important roles in the development of oral leukoplakia may be generally accepted, but the roles of these in the malignant transformation of oral leukoplakia remains controversial and still unclear.<sup>15</sup>

According to Liu W<sup>3</sup> et al., (2012), high malignant incidences for patients with high-grade dysplasia occurred during the first 2–3 years of follow-up<sup>3</sup>. High-risk areas for malignant transformation have been identified as floor of the mouth, lateral borders of the tongue and the soft palate/retromolar areas.<sup>1</sup> A size of the lesion upper than 200 mm<sup>2</sup> is considered as risk factor for malignant transformation.<sup>16</sup>

Homogeneous oral leukoplakia lesions are flat, thin and uniformly white colored; they have a low risk of malignant transformation. However, non-homogeneous mixed white and red lesions with irregularly flat, nodular or verrucous areas are more exposed to malignant transformation. Some molecular markers have shown promise in predicting the progression of premalignant oral lesions to squamous cell carcinoma.<sup>16,17</sup>

On initial discovery of a white lesion, the clinician should aim to find an explanation for its presence. If any possible cause is evident, such as local irritation by a broken restoration, it should be removed and the patient will be contacted in two to four weeks. Some leukoplakias are related to tobacco habits and candida infection<sup>14,18,19</sup> as our second case report. Therefore, it should be treated by cessation of smoking<sup>4,16</sup> and by anti-mycotic treatment. If no change in the clinical appearance of the lesion is visible after the waiting period or if no explanation for its presence could be found in the first place, a diagnosis of provisional leukoplakia is made and a biopsy is mandatory. The role of histological analysis of the leukoplakia is two-fold: to exclude other pathologies that might be responsible for

the white lesion as well as evaluating the presence and degree of epithelial dysplasia within the lesion.<sup>1</sup>

Biopsy of such lesions and the degree of dysplasia are important before starting any treatment<sup>7</sup>. Despite being the gold standard method to predict malignant potential, there is little agreement between pathologists regarding the ability of epithelial dysplasia grading and no dysplastic lesions to transform<sup>16</sup>. Thus, the leukoplakias without epithelial dysplasia present a different epithelium, in a worrying morbid state, with biochemical alterations but without morphological alterations. This factor is already sufficient to reinforce the real clinical meaning of leukoplakia, which should not be interpreted as a simple hyperkeratotic alteration of the oral mucosa, but might be seen as a potentially dangerous lesion.<sup>20</sup>

Patients with high-risk of developing oral leukoplakia are suggested to undergo multiple biopsies and histologic examination in order to detect early malignant events for more aggressive management<sup>15</sup>. Indeed, the prognosis and overall survival of a patient with oral cancer is dependent on the early detection of any lesion that might identify a patient with higher risk than normal or with early infiltration before metastatic disease associated with an increased risk of malignant change.<sup>1,4</sup>

Various therapeutic strategies can be used for leukoplakia such as surgery, cryosurgery, CO<sub>2</sub> laser, electrocoagulation, photodynamic therapy, or the use of medication therapy with lycopene<sup>2,4,21,22</sup>. However, complete removal of the lesion alone does not guarantee cure<sup>2</sup>. Previous studies have demonstrated the possibility of leukoplakia recurrence even when it has been excised, and in some cases, recurrence as carcinoma. For this reason, the patient with leukoplakia must be periodically followed up in order to prevent the appearance and progression of more aggressive behavior of leukoplakia<sup>2</sup>.

To conclude, it must be assumed that generally leukoplakia should be removed totally, if possible. Patients should be regularly monitored for any relevant mucosal change and instructed to avoid the major risk factors of oral epithelial dysplasia, especially tobacco usage and alcohol consumption<sup>4,7,16,18,23</sup>. However, previous studies of surgical treatment of premalignant lesions have demonstrated that the risk of recurrence is not completely eliminated.<sup>24</sup>

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