

# Oral medicine case book 74: Marijuana-induced Oral Leukoplakia

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## CASE REPORT

A 55-year-old male presented at the Oral Medicine Clinic of the University of the Western Cape, Oral Health Centre, Tygerberg Campus, for the evaluation of a persistent white patch on his right edentulous mandibular ridge. He had been referred from the Prosthodontics Clinic where he was seen for complete denture rehabilitation. The patient had no significant medical history and informed us that he had been smoking marijuana five times a day for more than twenty years and consumed alcohol occasionally. He had never worn a dental prosthesis and did not use tobacco in any form.

Extra-oral examination revealed bilateral submandibular lymphadenopathy and asymptomatic clicking of both temporomandibular joints during jaw opening. Intraoral examination showed completely edentulous upper and lower arches with a healing extraction socket in the posterior third quadrant. An asymptomatic, white homogenous plaque measuring 3x5mm, which could not be wiped off, was present on the crest of the right mandibular ridge (Figure 1).

Due to the small size of the lesion, an excisional biopsy was performed under local anaesthesia. Following the surgical procedure, the patient was prescribed 0.2% chlorhexidine digluconate oral rinse and 500mg Paracetamol four times daily.

Histological examination of the excised white plaque disclosed a fragment of squamous mucosa with acanthosis and hyperkeratosis (Figure 2). The sub-epithelial connective tissue was densely collagenized and showed a mild chronic inflammatory cell infiltrate. There was no evidence of dysplasia or malignancy in the histological sections examined. The Periodic Acid Schiff (PAS) stain was negative for fungal elements.

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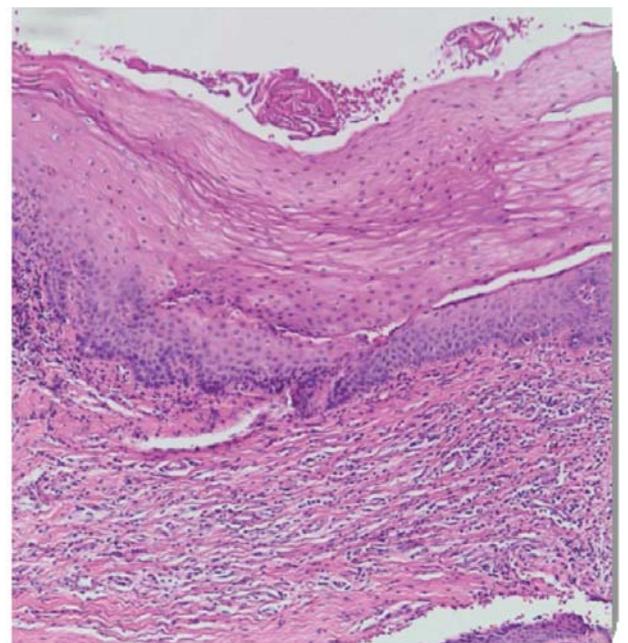
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## ACRONYMS

<b>LBC:</b>	liquid based cytology
<b>PMDs:</b>	potentially malignant disorders
<b>TB:</b>	Toluidine blue
<b>WHO:</b>	World Health Organization



**Figure 1:** A small homogenous white plaque on the right mandibular alveolar ridge.



**Figure 2:** The low power photomicrograph of the lesion seen in Figure 1 shows hyperparakeratosis of the surface epithelium (H & E, x 40). The fibrous connective tissue stroma exhibits mild chronic inflammation..

Evaluation of the biopsy site after two weeks showed complete resolution of the lesion. Based on the clinical and microscopic features, a diagnosis of non-dysplastic marijuana-induced oral leukoplakia was established. The patient was advised to stop smoking marijuana since there is a risk of possible malignant change. He was instructed to return to the clinic in six months for his periodic follow up visit.

## DISCUSSION

Oral white lesions reflect many different diseases and pathological changes. Leukoplakia was first defined by the World Health Organization (WHO) in 1978<sup>1</sup> as a white patch or plaque which cannot otherwise be characterized clinically or pathologically as any other disease. A revised definition was proposed in 2007 by the WHO Collaborating Centre for Oral Cancer and Pre-cancer Working Group, in which leukoplakia was defined as “a white plaque of questionable risk, having excluded other known diseases or disorders, that carry no increased risk for malignant transformation.”<sup>2</sup>

Worldwide, the estimated prevalence of oral leukoplakia is 1.7% to 2.7% for all age groups.<sup>3</sup> Between 16% and 62% of oral squamous carcinomas are reported to arise from an area of oral leukoplakia,<sup>4</sup> emphasizing the need for routine oral screening programs and regular monitoring of high risk individuals.

Globally, leukoplakias are reportedly diagnosed after the fourth decade of life and are six times more common among smokers than non-smokers.<sup>2</sup> A clinical diagnosis of oral leukoplakia is made when a predominantly white lesion cannot be clearly diagnosed as any other disease or disorder of the oral mucosa. A biopsy is mandatory, since the differential diagnosis of leukoplakia is broad and may include oral lichen planus, pseudomembranous candidiasis, chemical injury, frictional keratosis, oral lichen planus, oral epithelial dysplasia and squamous cell carcinoma.<sup>2</sup>

The most common aetiological factor for leukoplakia is tobacco smoking, cessation of which may lead to regression or total disappearance of oral leukoplakia.<sup>5</sup> A definite link between marijuana use and oral leukoplakia has not been established. Most studies of oral leukoplakia have focused on the role of tobacco as an aetiological factor, since tobacco smoking is a more socially acceptable behaviour. In addition, the legal use of marijuana is restricted to certain countries.

More recently, marijuana use has been legalized in many states in America and some European countries. An American study found that marijuana use among adults in the United States has doubled in the last decade.<sup>6</sup> In South Africa, the use of drugs such as marijuana, “tik” (metamphetamine) and cocaine is twice the global average and the highest in Africa.<sup>7</sup>

Marijuana is derived from the macerated flowers of *Cannabis sativa* and contains the toxic compound A9 tetrahydrocannabinol (THC), a cannabinoid, which constitutes 1-6% m/v of the total weight of the plant flowers.<sup>8</sup> In addition, more than 60 other cannabinoids have been identified in cannabis. When cannabis is smoked as marijuana, the resultant heat leads to aromatization of the cannabinoids and to carcinogenic substances such as polycyclic aromatic hydrocarbons, benzo[a]-pyrene,

phenols, phytosterols, acids and terpenes, which are detectable in marijuana smoke.<sup>9</sup> Marijuana thus carries the same carcinogens found in cigarette smoke and these carcinogens are known to cause DNA damage, which could potentially lead to malignant transformation.

In general, leukoplakias with dysplasia pose a higher risk for malignant transformation, compared with non-dysplastic leukoplakias.<sup>5,10</sup> Several molecular biomarkers have been proposed, but currently, no single biomarker can accurately predict the potential for malignant transformation.<sup>11</sup>

Currently, a range of non-invasive adjunctive diagnostic methodologies are available to screen oral potentially malignant disorders (PMDs), such as oral leukoplakias. These include vital staining techniques (using toluidine blue/tolonium chloride/ lugol's iodine),<sup>12</sup> light based detection systems<sup>13</sup> and exfoliative cytology.<sup>14</sup>

Toluidine blue (TB) is a basic thiazine metachromatic dye, which stains tissues rich in nucleic acids because of its high affinity for acidic tissue components. Both dysplastic and neoplastic cells contain more nucleic acids than normal cells. TB-stained tissue may appear dark or pale royal blue and has been used for many years as an aid for the screening and post-surgical management of PMDs and oral cancer.<sup>15,16</sup> It has been reported that TB staining could assist in early detection of oral cancer compared with conventional visual inspection alone.<sup>17</sup> A systematic review revealed that TB has a sensitivity of 84% and a specificity of 70% and can be a valuable diagnostic tool in screening of large group of patients.<sup>18</sup> A high percentage of false positive results have been associated with TB due to its ability to stain cells in benign hyperplastic and inflammatory lesions, which also contain large quantities of nucleic acids.<sup>19</sup>

A number of light-based detection systems such as Vizilite, Vizilite plus, Microlux DL, narrow mission tissue fluorescence and the Velscope, have been developed. The principle of these light-based detection systems is based on the fact that mucosal tissues undergoing inflammatory, abnormal metabolic or structural changes have different absorbance and reflectance profiles when exposed to various forms of light sources, enabling the differentiation of oral mucosal abnormalities.<sup>20</sup> ViziLite shows high sensitivity (77%) and low specificity (28%)<sup>20</sup> in detecting oral PMDs and oral cancer.<sup>21</sup> Some studies found that ViziLite could not differentiate between keratotic or inflammatory oral PMDs and oral cancer.<sup>22,23</sup> The Vizilite Plus combines the features of the Vizilite and TB and can further delineate ViziLite-positive lesions, thus improving its specificity as a diagnostic tool.<sup>24</sup>

Exfoliative cytology is a quick and simple procedure based on a relatively atraumatic semi-invasive technique, allowing for the collection of a rich concentrate of cells over a wider area than selective tissue biopsy and is ideal for use in large leukoplakic lesions. Recent cytologic techniques, such as liquid based cytology (LBC), have further improved the quality of oral cytologic smears.<sup>25</sup> With LBC; the residual liquid based material can be used for immunocytochemistry and molecular testing.

Currently, none of the adjunctive diagnostic tests could be recommended as a replacement for scalpel biopsy and histopathological assessment.<sup>18</sup> However, the use

of adjunctive tests (e.g. the use of Velscope to guide biopsies, and exfoliative cytology in large leukoplakic lesions), can further improve the overall accuracy of the histological assessment.

## CONCLUSION

The current case report describes a unique case of marijuana-induced oral leukoplakia. With the increased use of marijuana in South Africa, a rise in marijuana – induced oral leukoplakic lesions may be expected. Dentists and oral hygienists should be aware of the possibility of marijuana use when confronted with oral leukoplakic lesions and their potentially malignant nature. The use of adjunctive screening tests may further improve the overall accuracy of histological examination.

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