Case Report

Oral *Candidal* Leukoplakia Treated With CO_2 Laser

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Abstract

Oral leukoplakia (OL) is one of the most common physiologic as well as pathologic white lesions in oral cavity. Of the many variants of OL, chronic hyperplastic candidosis, also called candidal leukoplakia (CL), is associated with *Candida* yeast species, which generally is an opportunistic microbe of normal oral microbiota. Many published cases and researches suggest a positive role of *Candida albicans* as potential culprit in malignant transformation of leukoplakia to squamous cell carcinomas at molecular level as trigger at cell signaling pathway. This article describes a case report of CL in the light of current information with clinical and histological aspect in a young patient, which was successfully treated with CO_2 laser. This article also makes an attempt to provide and update the knowledge about potential malignant disorders such as leukoplakia and cofactors such as candidiasis superimposed to leukoplakia to health-care providers in order to help in early detection and treatment, thus decreasing mortality.

Keywords: *C. albicans, CO_2 laser, oral candidal leukoplakia, potential malignant disorders*

Introduction

Leukoplakia is a term that has been used for many decades with different definitions as to indicate a white plaque or patch occurring on the surface of a mucous membrane, not only in the oral cavity but also in the uvula, cervix, urinary bladder, and upper respiratory tract. This term has often been used to describe a non-scrappable white patch that cannot be diagnosed as any other disease, but many believe such a diagnosis should only be given strictly on the bases of histological criteria rather than on loose clinical connotation.[1] Oral leukoplakia (OL) is presently classified as potentially malignant lesions, earlier called precancerous lesions, which occur in the oral cavity either as asymptomatic homogeneous-type or nonhomogeneous-burning-sensation-type variant. The cause of leukoplakia though remains obscure, it is associated to the use of tobacco (smoke or smokeless) and other probable cofactors such as *Candida albicans*, human papillomavirus HPV-16 and HPV-18, and chronic trauma.[2]

Chronic hyperplastic candidosis (CHC) or candidal leukoplakia (CL) is a variant of oral candidosis that typically presents in the oral mucosa. The major etiological factor associated with CL is yeast species of the many variants of *C. albicans*, other than fungal etiology; systemic disease, vitamin deficiency, and immunosuppression may also contribute in disease progression. Krogh in 1990 suggested the casual role of yeast (*C. albicans*) as a potential culprit in malignant transformation and found in many of his studies that 68%–82% of *C. albicans* was associated or superimposed with leukoplakia and difference in biotype isolated with it, thus establishing the association as a triggering factor in malignant transformation.[3]

Case Report

A 39-year-old male patient reported to the outpatient department with a chief complaint of bilateral whitish red raised patch in inner side of cheek extending to corner of the lips from past 1 year. On eliciting history, patient had the deleterious habit of chewing pan with

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tobacco, lime, and smoked cigarette (10 cigarettes per day) for past 15 years. He developed burning sensation in the mouth and noticed a white growth in cheeks 1 year back. On intraoral examination, he had a very poor oral hygiene. A reddish white patch with irregular undefined margins without any tenderness was noticed in the buccal mucosa [Figure 1]. On palpation, bilateral 3 × 3-cm non-scrappable corrugated raised patch extending from corner of the lips to buccal mucosa could be felt. The surface of the lesion was rough and firmly adherent to the underlying connective tissue. Regional lymph nodes were not palpable. To arrive at a definitive diagnosis, an incisional biopsy was performed after routine blood and urine investigations.

In histopathological examination, the epithelium showed hyperparakeratinization with papillary projections and parakeratin plugging in the crypts between the papillary projections. It also showed broad and bulbous rete ridges and acanthosis with basal cell hyperplasia. Hyperparakeritinization with candidal hyphae can be seen in superficial layer of epithelium in ×20 magnification. The underlying connective tissue showed moderate inflammatory cell infiltration with no dysplastic changes [Figure 2]. Keeping the clinical and histopathological examination, a diagnosis of oral CL was arrived at.

The treatment was planned in two stages wherein in stage 1, the patient was treated for CL by repeated counseling, oral hygiene maintenance by scaling, motivation, and restraining from the habit, so as to make the patient realize the damage caused by the habit. Patient was systemically advised antifungal therapy with tablet ketoconazole 200 mg once daily orally along with topical use of fluconazole dispersible tablets diluted in 10-mL water as mouth wash thrice daily for a period of 14 days. Topical application of 2% clotrimazole oral ointment four times a day was also advised. After achieving satisfactory oral hygiene maintenance, he was taken up for stage 2 of the treatment by surgical removal of CL with CO_2 laser.

Surgical Procedure

The facial skin around the oral cavity was scrubbed with 7.5% povidone–iodine solution, and the intraoral surgical site bilaterally was painted with 5% povidone–iodine solution. Patient was locally anesthetized with 2% lignocaine with 1:80,000 adrenaline. After obtaining local anesthesia, CO_2 laser (wavelength of 10,600 nm) was used with continuous ultra-pulse mode at a frequency of 20 Hz and a duration of 450 µs at a power of 6.2 W in noncontact mode (spot size of 0.7 cm^2 for duration of 10 ms) in sweeping motion to completely remove the lesion along with 2-mm safety margin by evaporation [Figures 3 and 4]. Postsurgical instructions, antibiotics, and analgesics with rigorous oral hygiene were advised. Immediately after surgery, no sutures or any periodontal dressing was advised [Figure 5]. The patient is on regular follow-up from last 6 months and did not show any recurrence of CL postoperatively [Figure 6].

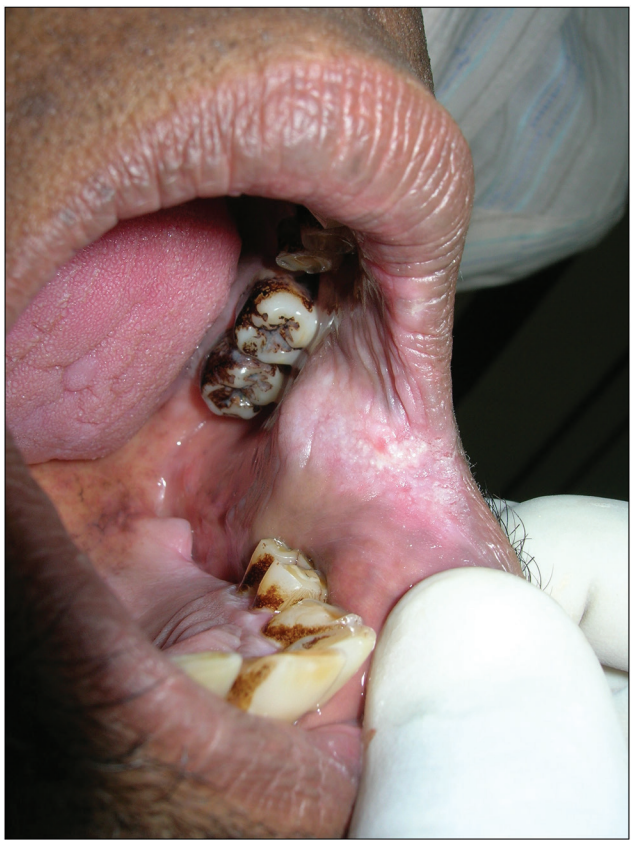

Figure 1: Preoperative

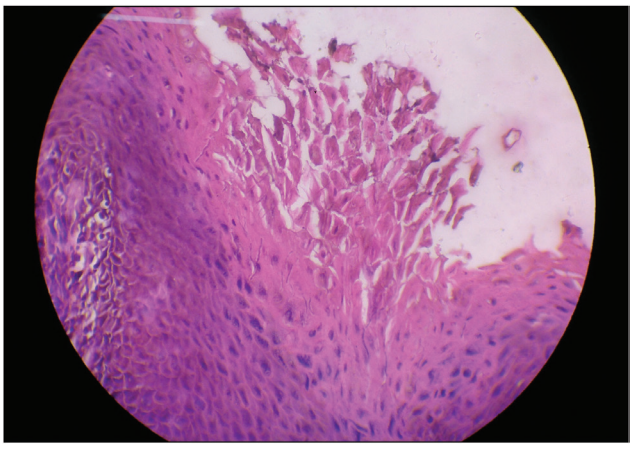

Figure 2: Histopathology at ×20 magnification

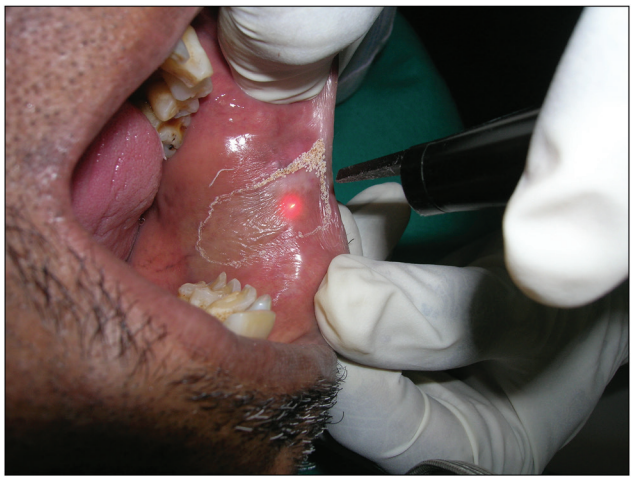

Figure 3: Extent marking by CO_2 laser

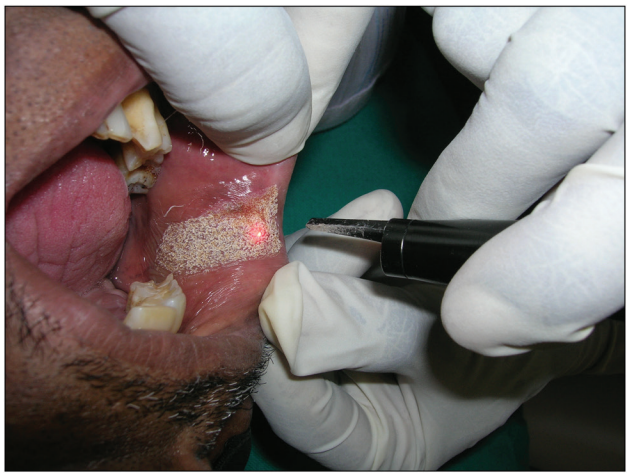

Figure 4: CO_2 laser ablation

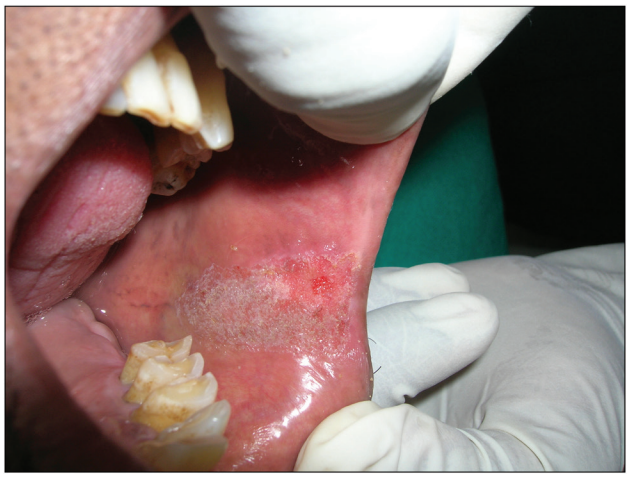

Figure 5: Immediate postoperative

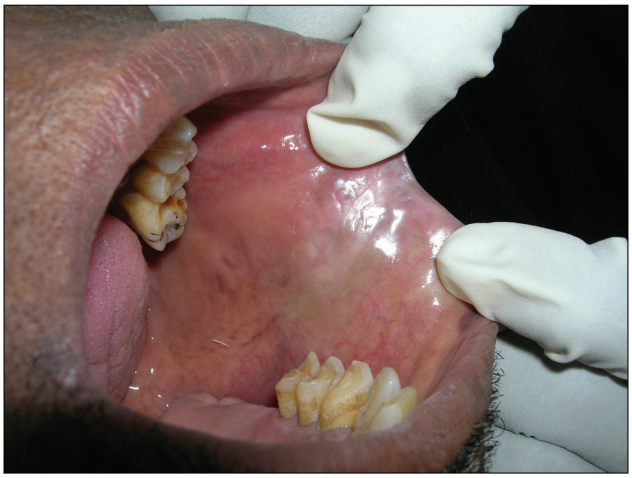

Figure 6: Postoperative 6 months

Discussion

Till date no attempt has been made to classify potential malignant disorders (PMDs), but broadly it can be grouped into high-risk category oral lesions such as erythroplakia, leukoplakia, oral submucous fibrosis, erosive lichen planus, actinic cheilitis, and reverse smokers palate. Low-risk group of PMD comprises oral infections acting as cofactors of risk potential such as hyperplastic candidiasis, viral etiology, syphilis, immunodeficiency, and inherited disorders, such as dyskeratosis, epidermolysis bullosa, and fanconi's anemia.[4]

Leukoplakia is purely a clinical terminology but has suffered from an excess of diagnostic terms and definitions till 2005, wherein World Health Organization defined it as "a white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk of cancer." Multiple studies over the years have shown a malignant transformation rate of 3.6%–17.5%, whereas few Indian studies have shown a transformation rate as low as 0.3%–0.5%.[5] Though according to many studies OL is associated with *Candida* infection, the term and a different identity to CL was coined by Lehner,[6] which is synonymously used with CHC. Later in 1991, Samaranayake[7] proposed a revised classification as follows:

> Group 1: primary or oral candidiasis—confined localized lesions of oral cavity only, and
> Group 2: secondary or oral lesions with extraoral manifestation sites in skin and conditions such as familial chronic mucocutaneous candidiasis and associated with endocrinopathy syndromes.

The genus *Candida* belongs to yeasts. It is also the most common cause of opportunistic mycoses worldwide. It is a frequent colonizer of human skin and mucous membranes. *Candida* is a member of normal flora of skin, mouth, vagina, and bowel. The genus *Candida* includes around 154 species. Among these, six are most

frequently isolated in human infections. Although *C. albicans* is the most abundant and significant species, *Candida tropicalis, Candida glabrata, Candida krusei*, and *Candida lusitaniae* are also isolated as causative agents of *Candida* infections. These widespread opportunistic microbes that usually are innocent normal commissural of oral cavity become invasive when systemic and local host defense system is compromised. They adhere to oral mucosa membrane by growing hyphae, thus extracting nutrition (chemotropism) and thigmotropism (secure hiding) leading to successfully evading host defense. They also show dimorphic behavior and multiply by process of budding and spore formation with blastospores and chlamydospores for survival and deeper penetration.[8]

Epidemiological studies in India by many authors reported 0.2%–4.9% cases of OL in rural Indian population. According to several reports, the candidal hyphae harboring OL constituted to about 7%–50% cases.[9] The ability of these organisms to adhere to mucosal and artificial surfaces in the mouth was extensively studied by Samaranayake and Ellepola[10] in 2000. The studies suggest the surface compounds on yeast cell walls and their interaction with oral epithelial cells such as van der Waals interactions, plydrophocity and electrostatic bonding aid in host invasion. Other than that at molecular level, studies suggest nitrosamine compounds produced by *Candida* species may activate specific proto-oncogenes leading to amplification and over expression of oncogene leading to malignancies.[10]

Though there are many surgical treatment options of oral premalignancies, many preferable choices are scalpel and laser cryoprobes as modalities of choice. Since 1970, lasers have been highly used in oral maxillofacial head and neck surgeries. Their effect on tissues determined by their wavelengths and tissue-specific absorption opens a vista of new dimension in choices of lasers in dentistry. CO_2 laser, one of the earliest gas lasers invented by Bells Labs by Kumar Prasad, is still most widely used for PMD due to its continuous high-power waves, availability at site, and maximal energy absorption in water-containing oral tissues.[11] In the present light, there are several recommended treatment protocols with no high evidence-based consensus in treatment options. Therefore, the treatment intervention should be specific patient based. Further, the need for oncologist for radiotherapy as an adjuvant should be considered on severity of PMD. There is also an uncompromising need for good communication with oral pathologist for all oral lesions as part of an holistic treatment approach.

Conclusion

It has been well established by researchers around the world that visibly all oral cancers are preceded by clinical changes in oral mucous membrane usually in form of red or white patches. PMDs often go undiagnosed due to lack of public awareness and due to lack of knowledge among medical professionals. Prevention and early detection of such potentially malignant conditions not only decline the incidence but also improve the survival chances. Diagnostic biopsy and histopathological examination should be considered for any mucosal lesion that persists for more than 14 days after obvious irritants have been removed. The aim/intention of reporting this case was to sensitize the general dentist of such occurrence, early detection, and surgical management with CO_2 laser, thus adding a new dimension in patient care.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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