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Case Report

EARLY DIAGNOSIS AND INTERVENTION OF ORAL POTENTIALLY MALIGNANT DISORDERS: THE ROLE OF AN ORAL MEDICINE SPECIALIST – A CASE REPORT

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ABSTRACT
Oral potentially malignant disorders precede the onset of oral cancer. Leukoplakia, erythroplakia and oral submucous fibrosis are common potentially malignant lesions which if left untreated can transform into malignancy. Oral squamous cell carcinoma is the most common cancer of the oral cavity attributing to about 90% of the cases of oral cancer. The main etiologic factors are habits like smoking, smokeless tobacco, consumption of alcohol and malnutrition. We present a case of well differentiated squamous cell carcinoma involving the right buccal mucosa in a middle-aged adult male which was diagnosed early and intervention was done by means of complete excision of the lesion. This presentation reinforces the need for a detailed intraoral examination by an oral medicine specialist for early diagnosis and intervention of potentially malignant oral lesions.

Keywords: *Oral Potentially Malignant Disorders, Smokeless Tobacco, Oral Squamous Cell Carcinoma, Oral Medicine Specialist*

INTRODUCTION
The term 'oral potentially malignant disorders' conveys that not all lesions and conditions described under this term may transform to cancer, rather that there is a family of morphological alterations among which some may have an increased potential for malignant transformation (Warnakulasuriya *et al.,* 2007). Most of these lesions are asymptomatic and are diagnosed during a routine oral mucosal examination. The clinical appearance of oral potentially malignant lesions can vary as a non-scrapable white plaque, nodular or polypoid outgrowths or a mixed red and white lesion. The reason to treat potentially malignant lesions is to prevent malignant transformation. Most potentially malignant lesions in their early stages can be resolved by elimination of the causative agents including tobacco use.
Oral cancer accounts for 2%–4% of all the cancer cases worldwide and oral squamous cell carcinoma (OSCC) represents the most frequent (more than 90%) of all oral neoplasms (Choi and Myers, 2008).
Smokeless tobacco in the form of Gutkha, Khaini, Mishri, Mawa etc. are known risk factors for the development of oral potentially malignant disorders. It is estimated that around 100 million people use smokeless tobacco in India and Pakistan alone (Imam *et al.,* 2008). Therefore, the burden of oral potentially malignant lesions and cancer is more in the south Asian countries (Khan *et al.,* 2014).
The main reasons for morbidity associated with oral potentially malignant lesions and oral cancer are ignorance of the patient or the physician, misdiagnosis of the potentially malignant disorders, lack of accessibility to healthcare facilities, social priorities, delayed definitive treatment and delay in seeking care leading to diagnosis at an advanced stage.
In this case report we are discussing the case of a middle-aged adult male with a painless exophytic lesion on the right buccal mucosa which was diagnosed early as a well differentiated squamous cell carcinoma. He had the habit of tobacco chewing for a period of 15 years.

CASE
A 45-year-old male patient presented himself at Department of Oral Medicine and Radiology at Tamil Nadu Government Dental College and Hospital in August 2019 with a chief complaint of a painless

growth in the right inner side of cheek for the past 3 months. The patient gave a history of alteration in the surface of the right inner side of the cheek initially which led to an elevated growth which increased in size gradually to its present size. He mentioned mild burning sensation in the same area on having spicy food. The patient had a habit of tobacco chewing in the form of ghutka 3 to 4 times a day for the past 15 years. There was no significant past medical or dental history.

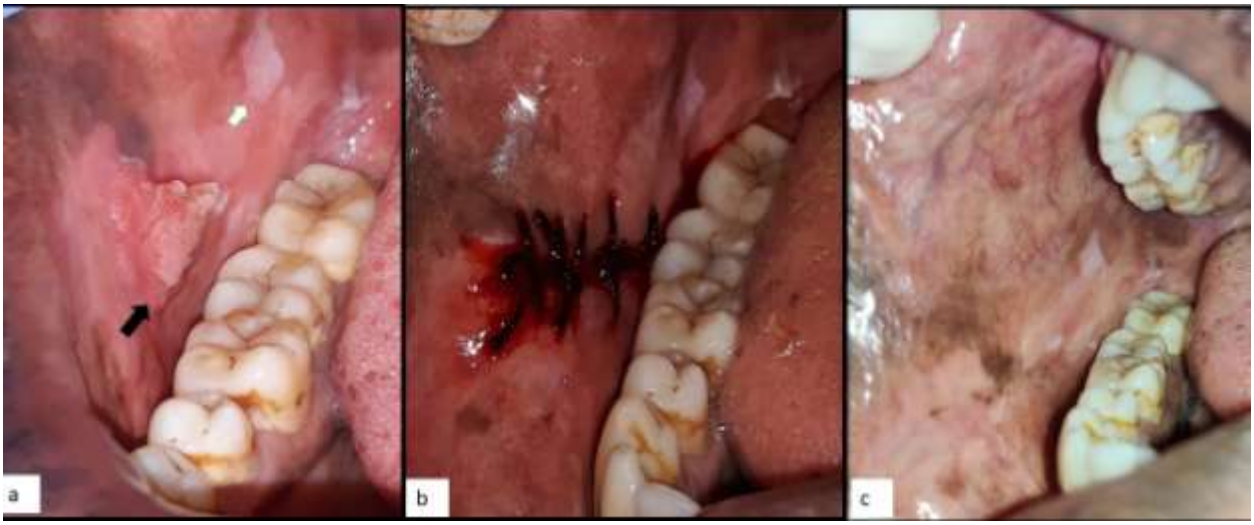

Figure 1: (a) Preoperative image showing the exophytic lesion (black arrow) and leukoplakic patch (white arrow) on the right buccal mucosa
(b) Immediate post-operative image
(c) Clinical image of six months follow up

On examination the patient showed a symmetric face and normal skin with no extra oral changes. There were no palpable lymph nodes. On intra oral examination on a dental chair with a mouth mirror and probe, the patient was found to have a fair oral hygiene with mild calculus and moderate extrinsic stains. There was an elevated red and white lesion measuring about 1 cm x 1.5 cm on the right buccal mucosa. The lesion was predominantly red in color with a few white areas and had an irregular surface. The lesion extended anteriorly 1 cm away from the commissure of the lip up to 5 cm short of retromolar trigone region posteriorly, superiorly 4 cm below the upper buccal vestibule, and inferiorly 3 cm short of lower buccal vestibule. The lesion appeared elevated with mild central ulceration (Figure 1a). On palpation the lesion was soft to firm in consistency and non-tender with no induration. The surrounding mucosa showed areas of small non-scrapable white patches near the line of occlusion measuring about 0.5cm x 0.5cm. There was no limitation of the mouth opening and a normal dentition was seen.

Based on the history of tobacco use and the clinical appearance of the lesion we arrived at a clinical diagnosis of a malignancy arising from existing leukoplakia on the right buccal mucosa. A differential diagnosis of verrucous carcinoma of right buccal mucosa was considered. The clinical TNM staging of T1 N0 M0 was given.

Exfoliative cytology was carried out and cytologic smear revealed the presence of a few dysplastic cells.

An excisional biopsy of the lesion was planned. Patient motivation and tobacco cessation counselling was done leading to discontinuation of the tobacco chewing habit. The results of the routine blood investigations (complete blood count, blood sugar, clotting time bleeding time) and urine investigations were within the normal limits. Before the biopsy, oral prophylaxis and elimination of the sharp buccal cusps of tooth 46, 47 and 48 was done to remove any traumatic factor. Patient was explained about the surgical procedure and consent was taken for the same.

Local anesthesia was given by infiltration of 2% lignocaine solution with adrenaline around the lesion. An incision was made around the lesion on the buccal mucosa and complete surgical removal of the lesion was done with sufficient margin (about 2-3 mm) of surrounding healthy tissue and without mutilation of tissues. After the removal of the lesion, hemostasis was achieved and the surgical site was primarily closed with 5 sutures of 3-0 silk suture material (Figure 1 b). The patient was prescribed Paracetamol 500 mg, Amoxicillin 500 mg and Metronidazole 400mg thrice daily for 3 days. He was also prescribed systemic antioxidants twice daily.

The excised specimen was sent for histopathologic examination. The histopathologic section showed severely dysplastic surface epithelium invading into the highly inflamed fibrous connective tissue in the form of islands of malignant epithelial cells with keratin differentiation. This led to a histopathologic diagnosis of a well differentiated squamous cell carcinoma (Figure 2).

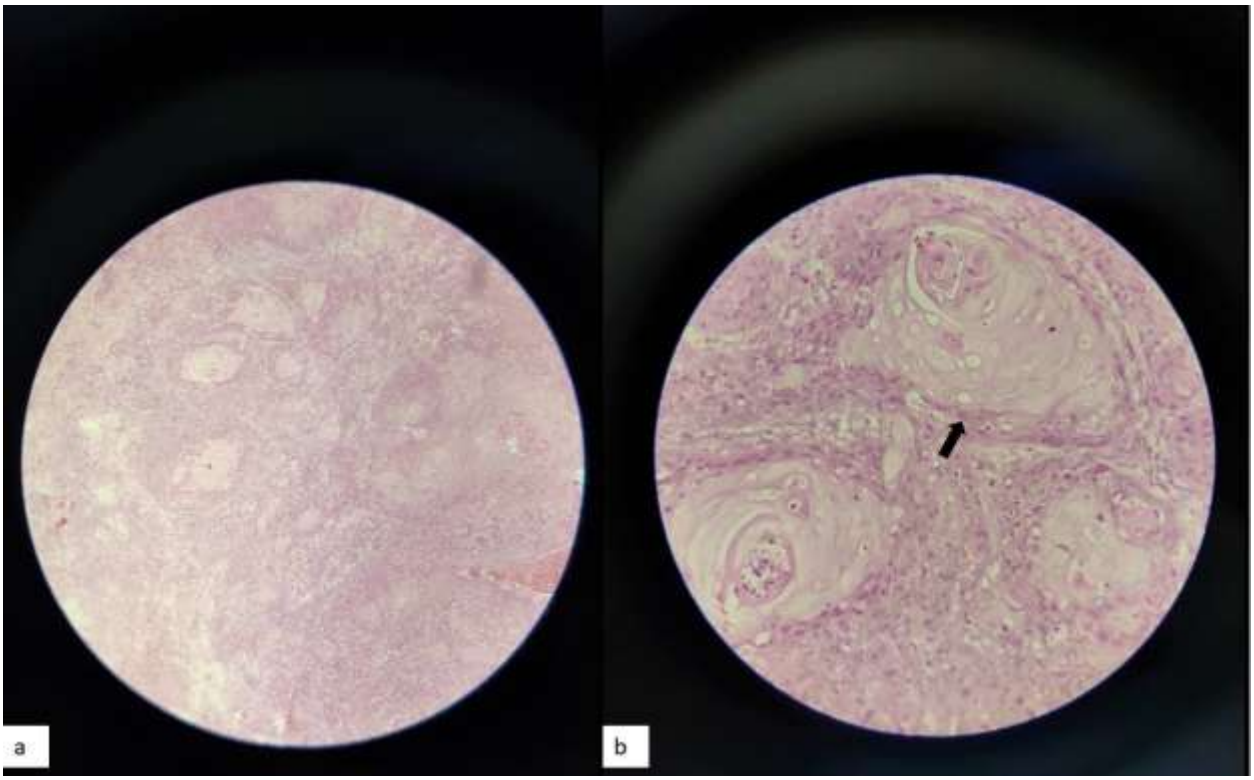

Figure 2: Histopathologic photomicrograph (H&E staining)
(a) Under 10 X magnification
(b) Under 40 X magnification (arrow indicating a keratin pearl)

A final diagnosis of a well differentiated squamous cell carcinoma was confirmed based on the history, clinical examination, and histopathological report.

Suture removal was done on the 7th postoperative day. The biopsy site showed good healing.

The lesion was adequately excised and no positive lymph nodes were noted, so no further treatment was recommended. The patient was advised to report regularly for follow up. Patient was asked to continue systemic antioxidants.

The patient was reviewed after 6 months and the site showed good healing (Figure 1c). The surrounding white lesions too had reduced in size. This case is an example of an early diagnosis and intervention in the management of a well differentiated squamous cell carcinoma of buccal mucosa. The patient is under regular follow up.

DISCUSSION

The commonly encountered oral potentially malignant disorders are leukoplakia, erythroplakia, oral submucous fibrosis, lichen planus and actinic cheilitis. These lesions if left untreated can transform into oral squamous cell carcinoma (OSCC) which is the most common malignant epithelial neoplasm affecting the oral cavity. The various rates of malignant transformation include 14%–51% for erythroplakia, 60%–100% for proliferative verrucous leukoplakia and 7%–26% for oral submucous fibrosis (Khan *et al.,* 2019).

Tobacco consumption in the form of smoking and smokeless form of tobacco and alcohol consumption have been long associated as principal etiological factors in the development of oral premalignant disorders. Smokeless tobacco contains around 28 known carcinogens including the nonvolatile alkaloid-derived tobacco-specific N-nitrosamine and N-nitrosamino acids as the major group while volatile tobacco-specific nitrosamines, volatile aldehydes, and some poly nuclear agents (Khan *et al.,* 2014). A variety of other risk factors like chronic irritation, poor oral hygiene, viral infection like HPV, betel quid chewing, arecanut chewing, candidiasis, occupational exposure to carcinogens, malnutrition, physical inactivity and genetic factors have been postulated as other etiologic agents (Radoi *et al.,* 2013). The role of tobacco cessation counselling is very significant as most potentially malignant disorders in their early stages can be resolved by elimination of the causative agent which in majority of the cases is tobacco use.

In the initial stages of the disease i.e. in the potentially malignant lesion stage the patient may be completely asymptomatic with the symptoms like pain or burning sensation developing at later stages. Lesions may be flat, raised, exophytic or ulcerated without any initial symptoms (Corso *et al.,* 2016). With time patients may complain of difficulties chewing, limited tongue movement or an abnormal sensation secondary to swelling. As malignant transformation occurs, more symptoms like bleeding, paresthesia, mobile teeth and induration and fixation of soft tissues occur. If any suspicious lesion with the above-mentioned features are encountered, it should be biopsied and followed up meticulously by the clinician.

The strongest predictor for malignant transformation of precancerous lesions like leukoplakia is the dysplastic changes as are seen within the epithelium. Studies have been reported that all leukoplakia lesions should be treated irrespective of the presence of any dysplastic changes. Nonsurgical modalities like consumption of carotenoids (β-carotene, lycopene); Vitamins A, C, and K; and fenretinide, bleomycin, and photodynamic therapy have shown significant regression of the lesion (Pavan *et al.,* 2018). In the present case, administration of systemic antioxidants containing Alpha Lipoic Acid, Beta-Carotene, copper, Lycopene, selenium, Vitamin E and Zinc Sulphate has caused regression of the lesion.

Visual and tactile examination is the conventional diagnostic technique for the initial diagnosis and biopsy remains the gold standard for the diagnosis of oral precancers and cancer. Newer diagnostic aids for detection of epithelial changes are Microlux DL (AdDent, Danbury, CT) and ViziLite Plus (Zila Pharmaceuticals, Phoenix, AZ) based on tissue reflectance. VELscope (LED Dental Inc, Vancouver, Canada) is a device used in assessing lesion margins in patients with oral malignancies based on the principle of tissue fluorescence. Vital tissue staining using toluidine blue and OralCDx Brush Biopsy (CDx Laboratories, Suffren, NY) techniques and exfoliative cytology are also useful diagnostic aids (Patton *et al.,* 2008). Molecular biological markers have been suggested to be of value in the diagnosis and prognostic evaluation of potentially malignant disorders.

Awadallah et al. have proposed a treatment and follow up algorithm for oral potentially malignant lesions based on the oral epithelial dysplasia (OED) (Figure 3) (Awadallah *et al.,* 2018).

Once the malignant transformation to OSCC has taken place, the treatment depends on the TNM staging which is based on the anatomic extent of the primary tumor and tumor spread (tumor size T, lymph node involvement N, and metastasis to distant sites M) (Patel *et al.,* 2005). Bloom and Spiro reported the most significant prognostic factor for survival in case of OSCC of buccal mucosa was the presence or absence of nodal metastasis (five-year survival 38 vs. 74 per cent; $p<0.005$) (Bloom and Spiro, 1980). Diaz et al.

also reported the presence of nodal metastasis reducing five-year survival from 70 to 49 per cent (p=0.01) (Diaz *et al.*, 2003).

Adequacy of excision and achieving oncological resection margins is a fundamental factor in head and neck SCC. Since in this case report the OSCC is in Stage 1 i.e. the cancer is less than 2 centimeters in size (T1) without metastasis, the treatment options are surgery and/or radiation therapy with surgery being the preferential treatment , and its goal is to remove the entire malignant tissue reaching a negative surgical margin which was achieved in this case.

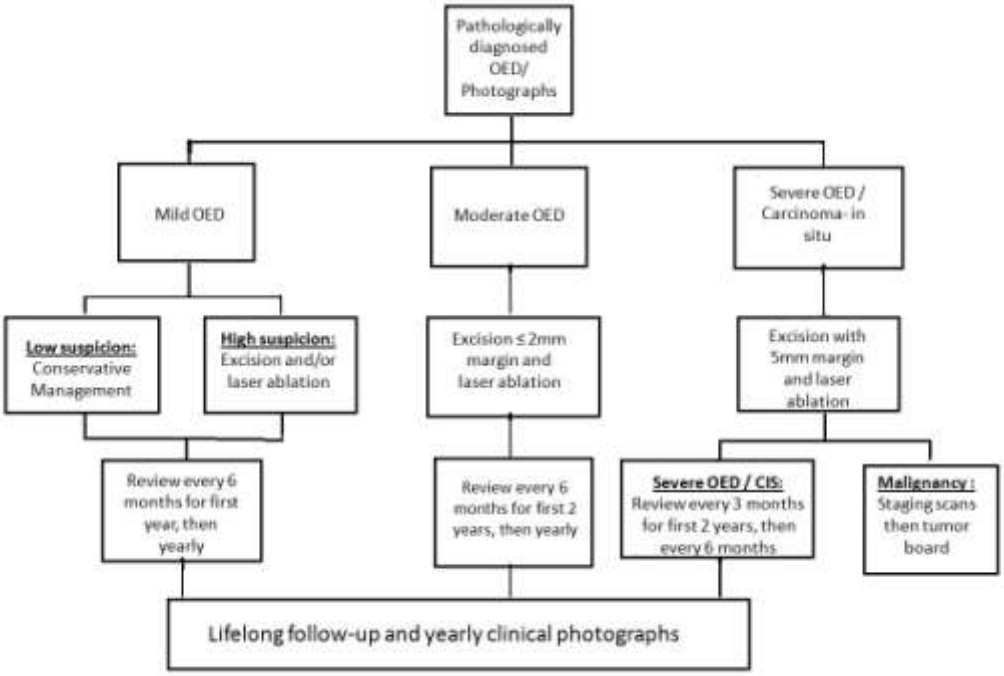

Figure 3: Treatment and follow up algorithm for oral potentially malignant lesions based on oral epithelial dysplasia (OED) (Awadallah *et al.*, 2018).

CONCLUSION

The early diagnosis and appropriate intervention of oral potentially malignant disorders is extremely essential as it may reduce the rate of progression of these conditions to invasive cancer. The early recognition of oral potentially malignant disorders by an oral medicine specialist is of utmost importance. By prompt diagnosis and treatment strategies the quality of life of these patients can be improved and survival rate can be prolonged further. Furthermore, tobacco cessation counselling should also be a priority and regular follow up is the key to the success of management of oral potentially malignant lesions. Awareness should be spread amongst the general public about the risk factors in order to aid in primary prevention through the elimination of tobacco consumption.

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