

Oral Cancer Clinical Presentations – An Illustrative Review

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Abstract Oral cancer (OC) is a global health burden with a 5-year survival rate of 50%. It is traditionally defined as oral squamous cell carcinoma due to more than 90% of oral cancers histologically originating in the squamous cells. Early detection of OC improves morbidity accompanying its treatment therefore it is vital for clinicians to recognise the various clinical presentations of OC to facilitate prompt referral and early management. OC has a wide range of presentations with a spectrum ranging from a small asymptomatic lump, red or white, or mixed red and white patch to a large extensive ulcer or growth. In locally advanced cases, pain is usually present accompanied by referred pain to the ear, halitosis, trismus, dysphagia and odynophagia, intra-oral bleeding, weight loss and neck swelling. Due to the wide variation in clinical presentation, general dental practitioners and dental specialists may be unsure of suspicious lesions and the urgency of referrals required in such cases. This review aims to illustrate the clinical presentations of OC using representative clinical photographs from patients attending our Oral Medicine Clinic.

Keywords: oral cancer, oral squamous cell carcinoma, oral potentially malignant disorders, oral dysplasia, early detection

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1. Introduction

One of the most significant causes of mortality and morbidity worldwide is cancer [1]. Oral cancer (OC) represents 2% of the cancer burden worldwide with an annual number of new cases exceeding 377,000 and 177,000 mortalities [2]. It most commonly presents as oral squamous cell carcinoma (OSCC) in 90% of the cases [3]. The mucosal lining epithelium is the site at which OSCC originates [3]. OSCC is a tumour involving invasive epithelial cells with a ranging degree of squamous differentiation [4]. OC most commonly presents in males between the ages of 60-79 [5]. The incidence of OC has a diverse geographic variation, and a greater burden is observed in low- and middle-income countries such as Latin America, South-East Asia, and Western Europe [6]. This diverse incidence rate seems to be linked to the adaptation of different OC behavioural risk factors [7].

The modality of management of OC is primarily through surgical resection of the tumour site and may include radiotherapy or chemotherapy [2]. Cancer treatment usually leads to the development of oral symptoms including dysphagia, salivary gland dysfunction, and mucositis [7]. Salivary gland dysfunction may result in altered taste, difficulty swallowing and

infections of fungal origin [7]. Patients who undergo radiotherapy or chemotherapy may end up with mucositis which is inflammation of the tissues, resulting in sores and ulcers in 40% of the cases [7].

Table 1. Anatomical subsites derived from the International Classification of Diseases for Oncology [9]

Lip	Mucosa of upper lip Mucosa of lower lip Commissure of lip Overlapping lesion of lip
Tongue	Dorsal surface of tongue Border of tongue Ventral surface of tongue Anterior two thirds of tongue Lingual tonsil Overlapping lesion of tongue
Gum	Upper gum Lower gum
Floor of mouth	Anterior floor of mouth Lateral floor of mouth Overlapping lesion of floor of mouth
Palate	Hard palate Soft palate Uvula Overlapping lesion of palate
Other and Unspecified parts of the mouth	Cheek mucosa Vestibule of mouth Retromolar area
Salivary glands	Parotid gland Submandibular gland

The management of oral cancer through surgery and radiotherapy may not only result in disfigurement but may also interfere with daily activities such as talking, eating, and drinking [8]. Changes in appearance may follow even with successful reconstructive surgery and patients may end up with an increased risk of airway obstruction, hence may require a tracheostomy and a feeding tube [2]. Anatomical sites in which OC presents are listed in Table 1. These sites are important for speech, swallowing, and taste, therefore OC and its treatment may have considerable functional sequelae with subsequent impairment of quality of life. This review illustrates a plethora of clinical features of oral cancer presenting in different oral cavity subsites.

2. Clinical Presentations

OC may arise in any oral cavity subsite (Table 1). According to the affected subsite, clinical features may vary. OC may be detected at its early stages where lesions may appear as asymptomatic small ulcers or lumps. The size of initial OC lesions can range from a few millimeters to several centimeters as the lesions progress. Lesions may appear as erythroleukoplakias with central ulcerations indicating suspicion for carcinoma in situ or invasive squamous cell carcinoma at the time of detection (Figure 1). Late-stage disease however appears as large growths with rolled margins and surface ulcerations (Figure 2). The tongue is a common oral cavity subsite for the development of OC (Figure 3). Suspicious tongue lesions may present as a small growth-like lesion (Figure 4) to a larger ulcerative lesion extending to the ventral surface (Figure 5). Some tumours present within large non-homogenous leukoplakias (Figure 6-8). In advanced cases, tumours present as ulceroproliferative growths with areas of necrosis and extension to surrounding structures such as muscle, bone, and layers of the skin with neck metastasis (Figure 9). The floor of mouth represents the second most common site for the development of OC (Figure 10). Lesions are likely to arise from a pre-existing leukoplakia or erythroplakia (Figure 11). The palate may also be affected with OC when lesions present as non-healing indurated ulcers with a depressed alveolar mucosa (Figure 12). It is worth noting that appropriate retraction of oral tissues aids in the detection of suspicious lumps presenting in edentulous spaces such as the lower posterior alveolar ridge (Figure 13).

3. Risk factors

Risk factors for the development of OC include alcohol abuse, tobacco consumption and betel-quid chewing [10]. Individuals who are heavy smokers and binge drinkers are 38 times more likely to develop OC in comparison to abstainers [6]. This may be due to acetaldehyde, a metabolite of alcohol and a component of tobacco, which is classed as a carcinogen [6]. Acetaldehyde prevents the synthesis of DNA and its repair [2]. Heavy smokers are three times more likely to develop OC than their non-smoking counterparts [2]. Tobacco and alcohol together have a synergistic effect on the risk of developing OC [1].

Smokeless tobacco such as betel quid is sometimes combined with ground areca nut [2]. Areca nut alone without its combination with tobacco is associated with the development of OC as it causes cytotoxic damage of the mucosa through hypoxia and inflammation of the tissues [2]. These behavioural risk factors are thought to cause OC as they interfere with cellular processes and alter genetics [7]. Human Papilloma Virus (HPV) also seems to be linked to the development of OC [10]. A study from 27 countries examining head and neck squamous cell carcinoma revealed a greater risk in those with a low educational background and income regardless of behavioural risk factors such as alcohol consumption and smoking [11]. This shows the independent effect of one's socioeconomic status on their OC development risk [11].

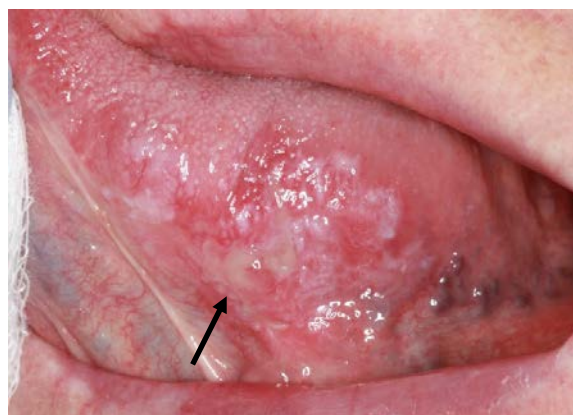


Figure 1. (Tongue) A large erythroleukoplakia with central ulceration (arrow) suspicious for OSCC



Figure 2. (Tongue) An extensive growth-like lesion highly suspicious for OSCC



Figure 3. (Tongue) A large growth-like lesion with surface ulceration suspicious for OSCC



Figure 4. (Tongue) Growth-like lesion with a red ulcerative surface suspicious for OSCC



Figure 8. (Tongue) Highly suspicious growth-like lesion (arrow) presenting superior to a non-homogenous leukoplakia



Figure 5. (Tongue) Large ulcerative lesion extending from the lateral to ventral surface of tongue

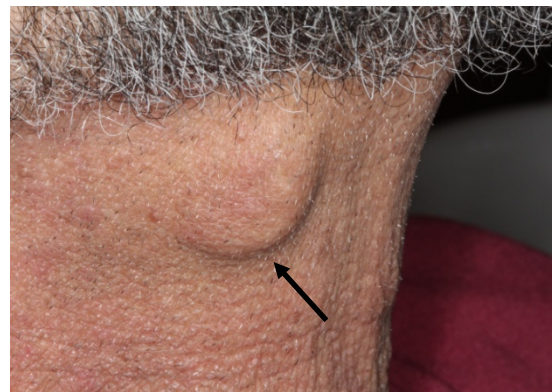


Figure 9. (Neck) Metastasis from primary oral cancer



Figure 6. (Tongue) Suspicious tumour in the left aspect (arrow) of the dorsum surface surrounded by an extensive verrucous leukoplakia



Figure 10. (Floor of mouth) Suspicious growth-like lesion



Figure 7. (Tongue) Large erythroleukoplakia suspicious for OSCC



Figure 11. (Floor of mouth) High-risk non-homogenous leukoplakia



Figure 12. (Palate) A large suspicious ulcer with indurated margins and depressed alveolar mucosa

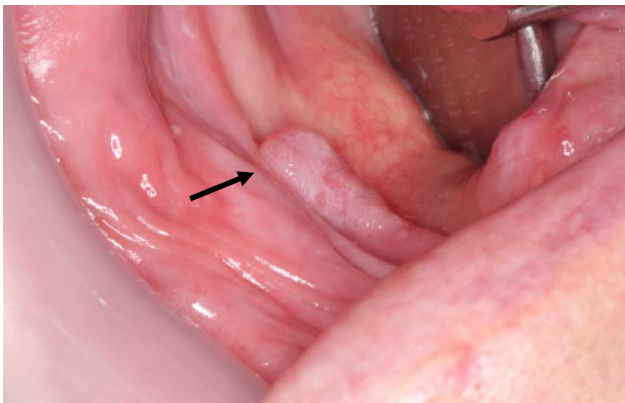


Figure 13. (Lower alveolar ridge) A soft tissue lump with irregular surface texture recently developed (arrow), suspicious for carcinoma in situ or OSCC

4. Advanced Stages

In advanced stages of OC, ulceration is one of the most common features presenting with an irregular floor and margins, elevation, and induration. With large lesions, the pain is severe and usually radiates to the ipsilateral ear [12]. Less common presentations include paraesthesia of the chin or delayed healing following a dental extraction or sometimes a lump with abnormal blood vessel supply, dysphagia, or weight loss. In these advanced cases, neck metastases and cervical lymph node enlargement can be seen (Figure 8). Large OC lesions (Stages T3-T4) with lymph node involvement (N2a-N2b) were most associated with mortality in a study on 216 patients over a period of 5 years [13]. Despite advances in medicine, OC has high rates of mortality with a global five-year survival rate of 50% [10]. Treatment leaves patients with high rates of morbidity [14]. In comparison to other cancers such as breast or colon, OC has worse survival rates due to failure of thorough screening, low index of suspicion, and poor dental attendance which all delay the diagnosis [14]. When the diagnosis is delayed, patients present late with more advanced disease which is more challenging to treat and hence a greater negative impact on their quality of life is observed. Cancer survival is heavily dependent on the stage of diagnosis [6]. More than half of patients (60%) with OC present in stages three and four, hence more

complex treatment is required [6]. Higher survival rates are seen in patients treated with early stages of OC, hence early disease detection and referral improve survival [5]. A higher incidence of OC is seen in patients with a low socio-economic background and those patients tend to have worse outcomes such as worse survival rates [10]. OC seems to be closely linked to economic and social deprivation, with the highest incidence of disease occurring in those most deprived [6]. Cancer survival trends revealed a gap in survival rates between the most deprived and affluent groups [5]. This may be due to several factors including barriers to access and inadequate awareness [1].

5. Clinical Significance

At the time of diagnosis, approximately half of OC patients present with metastases either regional or distant, leading to greater rates of mortality [15]. Late presentation is also associated with more complex treatment of an increased cost and increased morbidity [3]. In order to detect disease at early stages, a comprehensive oral examination should be routinely carried out by clinicians and if a potentially malignant lesion is present, referral to a specialist is required for a definitive diagnosis [14]. Malignant transformation is determined after histopathological grading of a specimen is completed to determine the presence and extent of oral epithelial dysplasia [15]. OSCC is usually preceded by oral potentially malignant disorders such as leukoplakia, erythroplakia and submucous fibrosis [16]. On some occasions, OSCC may develop from sound epithelium free of dysplastic changes [14]. However, a visible pre-clinical phase of dysplasia precedes most OSCC cases [17]. Screening could prevent malignant changes or ensure that disease is diagnosed at earlier stages [18]. It is the process of identifying individuals at increased risk of a disease from an apparently healthy population [18]. Screening is seen in multiple forms such as screening an entire population, or selectively where the focus is only on high-risk individuals, or opportunistically when individuals are screened after attending for other reasons [6]. OC screening is a straightforward, quick, cheap procedure that involves good lighting, gloves, and gauze in comparison to breast cancer screening which involves mammograms [3]. The incidence and mortality rates have been significantly improved after screening programmes have been introduced for common cancers such as breast and bowel cancer [6]. Screening programmes may allow for early disease detection and improved survival [3]. Clinicians are also encouraged to keep a detailed record of a lesion including the site, size, texture, borders, colour, and clinical photography is advised to monitor the lesion.

Guidelines on practices and treatment enhance outcomes as they set the standards for managing patients [1]. It is encouraged that local guidelines are developed for the referral of patients with potentially malignant lesions. In the United Kingdom, a 2 week wait pathways has been developed to ensure patients with a red/white patch, ulcer, or a new growth present in the mouth for more than three weeks are referred urgently to specialist services [14]. Having a clear referral system reduces error

and ensures that patients are seen in a timely manner. Developing national guidelines may bridge the gap between general practitioners and specialists, hence minimising abuse of the system with unnecessary referrals and maximising effectiveness.

It is important to emphasise the crucial role of disease prevention in which General Dental Practitioners (GDP) identify risk factors through history taking and address them appropriately as part of the holistic treatment plan. Cultural barriers should be overcome especially when taking a social history. GDPs are expected to give smoking cessation and alcohol advice or signpost patients to the appropriate services. Managing those risk factors will not only reduce the risk of OC, but of other diseases as well. HPV vaccinations have been introduced globally. Patients should be encouraged to take the vaccine at appropriate ages. Governments tend to place resources on cancer treatment with a low emphasis on prevention [1]. According to the World Health Organization, it is advised that measures are put in place for prevention of OC as part of local cancer control programmes [3]. Hence campaigns should be developed to shed light on risk factors, signs, and symptoms of OC. Policy makers could work on initiatives to address risk factors such as taxing tobacco.

Additionally, the awareness of General Medical Practitioners and medical disciplines including otolaryngologists, gastroenterologists, and dermatologists with regards to OC is important. Many patients with oral diseases present to otolaryngology departments since patients consider the oral cavity to be within the realm of the throat, while many gastroenterologists assume oral lesions develop due to gastrointestinal disease [19]. The ultimate aim is to enhance early detection thereby improving prognosis for patients presenting with OC.

6. Conclusion

Oral cancer is a preventable disease and early detection can reduce cancerous transformation hence potentially improve survival rates. General dental practitioners and medical disciplines have an important role in giving advice on risk factors implicated in OC and to recognise and promptly refer suspicious lesions. This review illustrates a plethora of clinical features of OC presenting in different oral cavity subsites. Knowledge of the various clinical features facilitates prompt referral to specialist services for diagnosis and management.

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