Field Cancerization Of Oral Cavity - A Case Report And An Update
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Citation

Abstract
Field cancerization was first described in 1953 as histologically altered epithelium surrounding tumor samples taken from the upper aerodigestive tract. Since then, the term has been used to describe multiple patches of premalignant disease, a higher than expected prevalence of multiple local second primary tumors and the presence of synchronous distant tumors within the upper aerodigestive tract. We discuss field cancerization with a case report of a 70-year-old male patient.

INTRODUCTION
Head and Neck Squamous Cell Carcinoma (HNSCC) is a major cause of worldwide cancer death.(1) Although surgery and radiotherapy are highly effective treatments for early-stage disease with cure rates ranging from 70 to 85% for stages I and II HNSCC, advanced disease (stage III, IV) remains difficult to control, with estimated 5-year survival rates of 30-40%.(2) Field cancerization of the mucous membranes of the aerodigestive tract frequently develops in response to tobacco and alcohol usage. It is characterized by a variety of premalignant and frankly malignant epithelial changes that may lead to the development of multiple primary cancers of the aerodigestive tract. The purpose of this case report is to present a case of Field cancerization occurring independently in both the right and left buccal mucosa.

CASE REPORT
A 65 year old male patient reported to our institution with a complaint of an ulcer on the right corner of the mouth since two months. It was gradual in onset and grew slowly to the present state. It was not associated with any discomfort on chewing and on having spicy food. Patient gave a history of weight loss. This was his first dental visit, his medical history was unremarkable. The family history was also non-contributory. He was found to be a chronic smoker, smoking one or two beedis per day since the past ten years and a chronic alcoholic, consuming one to two bottles of arrack occasionally. He also had the habit of chewing beeda (a combination of tobacco, betel nut, betel leaves and slaked lime) seven to eight times a day for the past thirty years. The patient was moderately built and nourished and the vital signs were within the normal limits.

Extra-oral examination revealed an ulceroproliferative lesion on the right corner of the mouth measuring 1cm in diameter.

Figure 1
Fig.1 Ulceroproliferative lesion on the right corner of the mouth
The lesion appeared crusted. The surrounding skin seemed normal. The lesion extended anteriorly from the commissure and extended to involve the oral mucosa (Fig. 2). Posteriorly, it extended 1 cm behind the commissure. Superiorly, the extend was along a line running laterally from the commissure and inferiorly up to a line along the vermilion border of lower lip. On palpation, it was found to be firm in consistency and moderately tender. Induration and fixity to underlying connective tissue were also noted. No significant lymphadenopathy was evident. However, patient’s mouth opening was severely restricted.

Intra-oral examination revealed red and white areas on the retrocommisural region interspersed with erosive areas (Fig. 3). A small area of the lesion was covered with a pseudomembrane. Intra-oral dimension was around 1.5 cm in diameter and extended along the level of occlusal plane. Induration was noticed and the pseudomembrane was scrapable.

Examination of left buccal mucosa also revealed red and white areas extending from the retrocommisural region to mid buccal mucosa approximately covering an area less than 1 cm along the level of occlusal plane (Fig. 4). The lesion was rough and non-tender on palpation. There was no evidence of induration or fibrosis. The whitish component was scrapable. The dorsum of the tongue appeared atrophic and depapillated extending from the tip to posterior third. It was stiff and sticky on palpation. (Fig. 5)
Based on the history and the clinical presentation, a provisional diagnosis of carcinoma of right commisure region and speckled leukoplakia of left buccal mucosa were arrived at. Hematological investigation showed a normal blood picture. Incisional biopsy of the right buccal mucosa and excisional biopsy of the smaller lesion on the left side was carried out at subsequent visit. Histopathological examination of the lesion of right buccal mucosa revealed highly dysplastic stratified squamous epithelium with dysplastic epithelial cells invading the connective tissue and abundant keratin pearls favoring the diagnosis of a well differentiated squamous cell carcinoma (Fig. 6). Specimen of the left buccal mucosa revealed moderate dysplastic changes. The epithelium revealed hyperchromatism, altered nuclear cytoplasmic ratio and loss of stratification with intact basement membrane (Fig.7). The features were suggestive of Carcinoma-in-situ.

Based on the clinical and histopathology findings, a final diagnosis of field cancerization was made. A diagnostic work up including orthopantomograph, chest radiograph and abdominal ultrasound were carried out to rule out any evidence of local invasion or distant metastasis. Habit counseling and antioxidant supplementation was advised. Surgical excision of the lesion on the right buccal mucosa was carried out with a margin of healthy skin and mucosa (Fig.8), a nasolabial flap was raised to cover the defect (Fig.9). Satisfactory healing was observed when reviewed after 2 weeks (Fig.10, 11) Patient was recalled regularly for follow up and to ensure restrain from habits.
DISCUSSION

The term field cancerization was first coined by Slaughter et al. in 1953. The investigators examined pathology slides from 783 patients with head and neck cancer in an effort to understand the gross changes found in epithelia surrounding these tumors and explain their clinical behavior. It was discovered that all of the epithelium beyond the boundaries of tumor possessed histologic changes, and 88/783 (11%) of patients were found to have more than one independent area of malignancy. The conclusion drawn was that the mucosa of the head and neck had undergone a change, perhaps due to carcinogen exposure, and was therefore more susceptible to the development of many foci of malignant
transformation. At the time of this study, there was no molecular basis for the observation. They emphasized that oral SCC developed in a multifocal fashion within a field of tissue bathed by carcinogens. Organ systems in which field cancerization has been described since then are: head and neck (oral cavity, Oropharynx and larynx), lung, vulva, esophagus, cervix, breast, skin, colon and bladder.(4)

By performing extensive histological examinations, a concept was proposed describing issues covered by the term field cancerization (5): (a) oral cancer develops in multifocal areas of precancerous change; (b) abnormal tissue surrounds the tumor; (c) oral cancer often consists of multiple independent lesions that sometimes coalesce; and (d) the persistence of abnormal tissue after surgery may explain SPTs (Second Primary Tumors) and local recurrences. The theory claims that, after repeated carcinogenic exposures, the mucosa accumulates genetic alterations resulting in the induction of multiple, independent, malignant lesions. In the present case, the patient’s oral mucosa was exposed to different forms of tobacco products for a long period (smoke form since 10 years and smokeless form since 30 years) resulting in the development of independent malignant lesions in different sites of the oral cavity.

The criteria used to diagnose multiple primary carcinomas, as originally described by Warren and Gates and modified by Hong et al., were as follows: (6)

(1) Each neoplasm must be anatomically separate and distinct (if the intervening mucosa demonstrates dysplasia, it is considered a multicentric primary).

(2) The possibility that the second primary represents a metastasis or a local relapse must be excluded. A second primary had to be separated from the first by at least 2 cm of normal epithelium or had to occur at least 3 years after the first diagnosis.

Synchronous carcinomas were defined as second neoplasms at the same time or within 6 month period of primary lesion. After this period they were considered metachronous neoplasm.(7) The prognosis of HNSCC patients is adversely influenced by the development of second primary tumors. The incidence rate of second primary tumors is 10–35%, depending on both the location of the first primary tumor and the age of the patient.

Many recent studies have addressed the molecular basis of the process of cancer development and genetic progression models have been proposed for various tumor types.(8) It is now well established that an accumulation of genetic alterations forms the basis for the progression from a normal cell to a cancer cell, referred to as the process of multistep carcinogenesis.

The phenomenon of field cancerization has often been bought up to explain the occurrence of SPTs.(9) A number of recent studies have looked into this in more detail and have addressed the genetic relation between multiple neoplastic and preneoplastic lesions within one organ system. For a rather high proportion of cases in oral cavity, bladder and oesophagus, it was shown conclusively that there was a common clonal origin, even if the lesions were >7cm apart. The decision that the lesions are genetically related is based on the similarity of genetic changes.

Three theories have been proposed to explain the common clonal origin of multiple primary tumors: first, single cells or small clusters of cells migrate through the submucosa or secondly, are shed in the lumen of an organ at one place and regrow at another. However, recent findings in the head and neck, oesophagus and bladder are in strong support of a third theory: a large contiguous genetically altered field exists in the epithelium in which multiple clonally related neoplastic lesions develop. The results indicate that a large proportion of multiple primary tumors in the same or adjacent anatomical area have developed within a single preneoplastic field.

CONCLUSION

The presence of a tissue ‘field’ with genetically altered cells is a risk factor for cancer. The large number of preneoplastic cells in the proliferating fields is likely to increase cancer risk dramatically. Conditions like Oral sub mucous fibrosis that involve considerably larger mucosal areas predispose to development of field cancers or multiple primaries. The theory of field cancerization suggests that there is an increased likelihood of concurrent or future disease in patients with head and neck lesions. Therefore, it is incumbent upon the care providers to be more diligent about screening and directed biopsies in these patients. It should be taken into account in treatment planning of a patient with cancer so that all treatment options, including the use of radiation therapy, be kept open as long as possible in the event that the patient may develop multiple primary tumors.

References

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