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Raghavandra KINI

Vathsala NAIK

Smit SINGLA

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FIELD CANCERIZATION OF ORAL CAVITY: A CASE REPORT AND ITS CLINICAL IMPLICATIONS

Raghavendra Kini* Vathsala Naik** Smit Singla***

Abstract

In 1953, Slaughter et al. proposed the concept of field cancerization when studying the presence of histologically abnormal tissue surrounding oral squamous cell carcinoma. It was observed that all of the epithelium beyond the boundaries of tumor is submitted to histological changes and were found to have more than one independent area of malignancy. In conclusion, the mucosa undergoes a change, perhaps due to carcinogen exposure and is therefore more susceptible to the development of many foci of malignant transformation. These observations help to explain the high incidence of recurrence, despite excision of tumor or other therapies. So, diagnosis and treatment of oral cancer should not only be focused on the lesion, but also on the field from which it developed. In this article, we emphasize on the concept of field cancerization, its clinical implications by presenting a clinical case.

Keywords: field cancerization - squamous cell carcinoma – leukoplakia - dysplasia.

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CANCÉRISATION DE CHAMP DE LA CAVITÉ BUCCALE. À PROPOS D'UN CAS CLINIQUE ET SES IMPLICATIONS CLINIQUES

Résumé

En 1953, Slaughter et coll. ont proposé le concept de champ de cancérisation en étudiant la présence, à l'échelle histologique, de cellules anormales entourant le carcinome épidermoïde. Il a été observé que tout l'épithélium au-delà des frontières de la tumeur présentait des changements histologiques, en plus d'une zone indépendante libre de malignité. En conclusion, l'épithélium subit un changement, peut être en raison de l'exposition à des substances cancérogènes et devient donc plus propice au développement de plusieurs foyers de transformation maligne. Ces observations aident à expliquer la haute incidence de récurrence, malgré l'excision tumorale associée ou non à d'autres thérapies. Le diagnostic et le traitement du cancer oral devraient être établis, non seulement au niveau de la lésion, mais aussi au niveau du champ à partir duquel il s'est développé. A travers cet article, nous soulignerons l'importance du concept de champ de cancérisation et ses implications cliniques, par la présentation d'un cas.

Mots clés: champ de cancérisation - carcinome épidermoïde - leucoplasie - dysplasie.

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* MDS, Oral Medicine,
Professor- Postgraduate Guide,
A.J. Institute of Dental Sciences, Rajiv Gandhi
University of Health Sciences, India.
raghkini@yahoo.co.in

** MDS,
Professor,
Head Department of Oral Medicine,
A.J. Institute of Dental Sciences, Rajiv Gandhi
University of Health Sciences, India.

*** BDS,
Post-graduate student, Oral Medicine
A.J. Institute of Dental Sciences, Rajiv Gandhi
University of Health Sciences, India.

Introduction

Oral cavity is one of the prevalent sites for the development of pre-malignant diseases. It is well known that these pre-malignant pathologies may progress to dysplastic lesions then to invasive carcinomas. Field cancerization is a well known and well documented process of malignant transformation. The term "field cancerization" was proposed by Slaughter et al. [1] in 1953, when studying oral cancer. The term field cancerization has been, since then, utilized to explain the followings: (a) oral cancer developing

in multifocal areas of a precancerous change; (b) abnormal tissues surrounding the tumor; (c) oral cancer often consisting of multiple independent lesions that may coalesce; (d) the persistence of abnormal tissue even after surgery may explain secondary primary tumor and recurrences [2].

Case report

A 78 year old female patient presented to the Department of Oral Medicine and Radiology of A.J. Institute of Dental Sciences, Mangalore, with a complaint of growth in the lower

right molar region since 2 months. The growth was insidious in onset and gradually increased in size. Since the first week, the growth was associated with localized, severe and throbbing pain. Intake of hot and spicy food caused severe burning sensation. Past dental and medical histories were non-contributory, even though reporting some weight loss. The patient had the habit of chewing beeda (a combination of betel leaves, betel nut, tobacco and slaked lime) 4-5 times a day for the past 12 years.

On extraoral examination, there was no gross facial asymmetry. A soli-

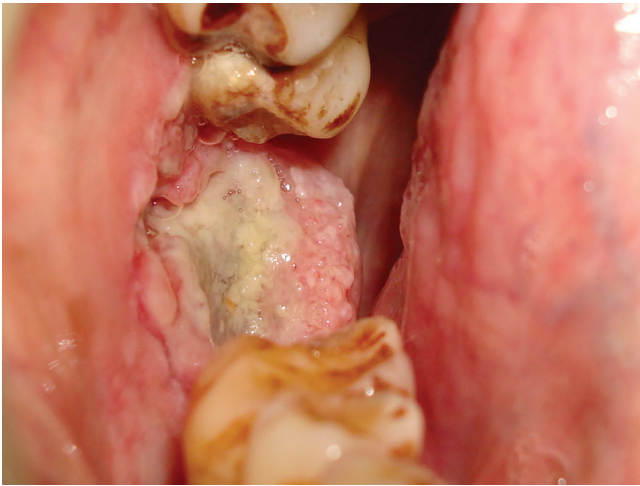


Fig.1: Ulceroproliferative lesion in right retromolar area.



Fig.2: Speckled leukoplakic lesion on left buccal mucosa.

tary submandibular lymph node was palpable on the right side, measuring 1.5 cm in size, tender, firm in consistency and freely movable.

Intraorally, an ulceroproliferative lesion was evident on right retromolar area, measuring about 3.5x2.5 cm in size. It was irregular in shape with rolled out edges. The centre of the lesion was composed of whitish-yellow slough (Fig.1). The lesion was tender on palpation with indurated base. The first molar was mobile (grade II), second and third molars were missing.

On left buccal mucosa, an elevated white patch was present at the level of maxillary second and third molars, measuring about 1.5 cm in size. The surface was white, with multiple red pin sized papules. The lesion wasn't tender on palpation (Fig.2).

The surrounding mucosa was blanched and opaque. Buccal mucosa of either side had lost its normal elasticity and was leathery in consistency. Multiple fibrous bands were palpable on both right and left buccal mucosa. The tongue was smooth and shiny and its movements were restricted (Fig.3).

A provisional diagnosis of carcinoma of right retromolar area ($T_1N_1M_0$), speckled leukoplakia on the left buccal mucosa and oral submucous fibrosis were made. Before undertaking biopsy, routine blood investigations were car-

ried out; the parameters were well within normal limits.

Radiographic survey of the skeleton and ultrasonography of the abdomen were done to rule out distant metastasis. Incisional biopsy of the lesion on right retromolar area and excisional biopsy of the lesion on the left buccal mucosa were undertaken. Biopsy specimen revealed discontinuity in the basement membrane with dysplastic epithelial cells invading connective tissue and islands with keratin pearls. Individual tumor epithelial cells showed various degrees of pleomorphism, suggesting moderately differentiated squamous cell carcinoma, whereas the biopsy specimen from the left buccal mucosa revealed mild to moderate epithelial dysplasia.

Orthopantomograph, C.T. (Fig.4) didn't show any bone erosion. Ultrasound of the neck revealed involvement of upper jugular lymph nodes measuring 15 mm on the right side and 10 mm on the left side.

Wide excision of the lesion and modified radical neck dissection with reconstruction using pectoralis major myocutaneous flap were realised (Fig.5). Patient is currently undergoing treatment for oral submucous fibrosis and is under regular follow-up to detect any local relapse or formation of any secondary primary tumors.



Fig.3: Shiny and smooth tongue.

Discussion

In field cancerization, an area of epithelium has been preconditioned by long term exposure to carcinogens. In this preconditioned epithelium, multifocal carcinomas can develop as a result of independent mutations and this would not be genetically related.

Thus, the carcinoma occurs from multifocal areas of precancerous change and not from one cell that suddenly becomes malignant. It is well accepted that the progression from normal to cancer cell is a multistep process in carcinogenesis [3, 4]. It would also explain, in part, the high recurrence rate in oral carcinoma after surgery or radiation therapy. In case of surgery, the margins seldom extended beyond the limits of abnormal epi-

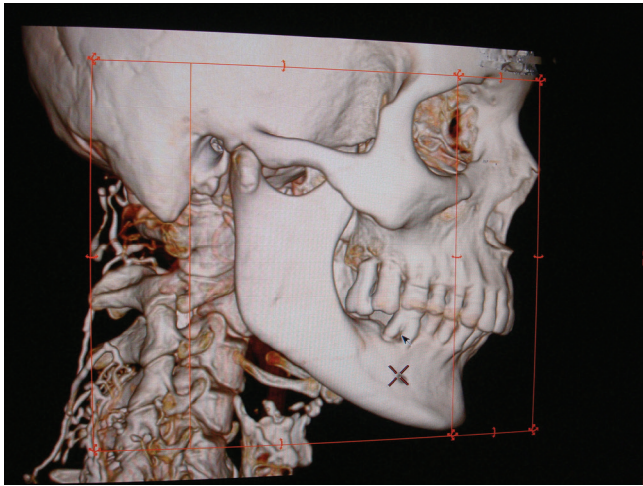


Fig.4: No bony involvement on the C.T.



Fig.5: Post-operative 10 days after surgery.

thelium, whereas radiation therapy is less effective on the benign epithelium and leukoplakia than on cancer cells. However, Rennemo et al. [5] observed lower incidence of secondary primary tumors in irradiated patients, suggesting preventive effect of radiation on malignant translocation of subclinical premalignant foci.

The recurrence may be due to changes toward cancer of a benign, preconditioned epithelium, which have been opposed in a suture line, after excision of a tumor, or has healed over the site of a tumor destroyed by radiation. Many recent studies have shown the presence of altered fields of mucosa remaining beyond the limits of resection, both on histopathological and on molecular basis [6].

The criteria used to diagnose multiple primary carcinomas, as originally described by Warren and Gates [7] and modified by Hong et al. [8] were as follows:

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

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

A number of parameters can determine whether a field develops into a new tumor. A very important factor might be the follow-up period, since a premalignant field may need a longer time to progress into a new tumor than a tumor that develops from remaining tumor cells. Meo et al. [9] and Rosin et al. [10] have reported that oral premalignant lesions might need up to 67 or 96 months, respectively, to progress into invasive carcinoma.

Clinical implications

The presence of a 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.

The probability of developing a second primary tumor in a patient who once had head and neck squamous cell cancer is around 20% [11].

Cancer begins with multiple cumulative epigenetic and genetic alterations, leading to sequential cellular transformations. The early genetic events might lead to clonal expansion of pre-malignant daughter cells in a particular tumor field. Subsequent genomic changes in some of these cells drive them toward the malignant phenotype. Histologically, these transformed cells are diagnosed as cancer owing to alterations in their morphology. Thus, a population of daughter

cells with early genetic changes (without histological changes) remains in the organ, demonstrating the concept of field cancerization [12]. For early detection of a cancer, one can rely on tumor markers. But what is important, in the context of field cancerization, is identification of molecular signatures in the genetically transformed but histologically normal cells (peri-tumoral cancer field). So, identification of such tumor specific biomarkers will have excellent utility in monitoring the tumor progression and if possible, in preventing transformation of pre-malignant lesions into invasive cancer.

Conclusion

The presence of a field with genetically altered cells is a risk factor for cancer. A good research in this field has a strong potential to reveal new diagnostic markers for early detection, modalities to prevent progression, and lastly ways to combat development of second primary tumor (or second field tumors).

Finally, not only early detection and management of oral cancer are important, but equally important are early identification and management of a field, so as to have profound implications on cancer prevention and outcome of the treatment.

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