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Case Study

CONCEPT OF FIELD CANCERIZATION & SECOND PRIMARY TUMORS IN ORAL CAVITY: A CASE SERIES OF THREE CASES

Priyanka Agarwal*, Alka Hande, Minal Chaudhary ***, Puneet Agarwal****, Swati Patil *****

*** MDS oral pathology, jodhpur Rajasthan;**
Corresponding author- drpriyankaagarwal@gmail.com
**** Associate Professor MDS oral pathology, Sharad Pawar Dental College,Wardha Maharashtra**
***** Professor MDS oral pathology, Sharad Pawar Dental College,Wardha Maharashtra**
******Fellow Georgrtown university Washington DC**

Corresponding Author: Dr. Priyanka Agarwal

ABSTRACT

The concept of "field cancerization" was first introduced by Slaught et al. [D. P, Slaughter et al., Cancer (Phila.), 6: 963–968, 1953] in 1953 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 3 clinical cases.

Key words: field cancerization, second primary tumor

INTRODUCTION

The idea of field cancerization was conceived by Slaughter almost a decade prior to introducing the term in 1953. In an earlier publication he stated that; "cancer does not arise as an isolated cellular phenomenon, but rather as an anaplastic tendency involving many cells at once" [2]. The term "lateral cancerization" was subsequently used to indicate that the lateral spread of tumors was due to progressive transformation of cells adjacent to a tumor, rather than the spread

and destruction of the adjacent epithelium by pre-existing cancer cells [1]. In a more extensive histopathologic review of 783 oral cancer patients, Slaughter and colleagues then used the term field cancerization to describe the existence of generalized carcinogen induced early genetic changes in the epithelium from which multiple independent lesions occur, leading to the development of multifocal tumors [6]. In some cases, multiple contiguous tumor foci coalesce that partly explain the lateral spread of squamous cell cancers. It was also observed

that normal looking cells in close proximity to malignant cells were histologically abnormal and therefore were part of the transformed cells in a particular tumor field, and consequently were responsible for the occurrence of local tumor recurrences.[2]

CASE 1:

A 53 year old male patient reported to the OPD of Sharad Pawar Dental College with the chief complain of intraoral painful ulcer in upper right region of jaw since 1 month. The associated pain was gradual in onset, intermittent in nature , dull aching, radiating and localized in upper right back region.

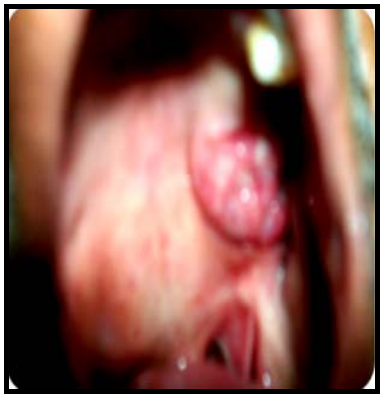
The ulcer was initially of size 1x1 cm then gradually increased to present size i.e. 2x1 cm Patient also gives associated complaint of burning sensation in same region. There was no discharge associated.

Patient has habit of tobacco chewing since 20 yr for 5-6 times a day. According to him he left the habit 6 years back.

He gives history of previous hospitalization for carcinoma of lower right gingivobuccul sulcus, which then was treated by wide local excision of the lesion with hemimandibulectomy with radical neck dissection and forehead flap and SSG under GA on 25/8/2004.

Face was asymmetrical due to hemimandibulectomy .Single right submandibular lymph node was palpabale,which was about 0.5x 1cm, ovoid in shape , firm in consistency, nontender, fixed to underlying structures. Single right jugulo digastric lymph node was also palpable, which was about approx. 0.5x0.5 cm, soft in consistency and, mobile.TMJ Movement were restricted absent on right side

Intraoral Examination revealed a single, roughly circular growth about 2x2.5cmin size approx. & which shows surface ulceration present in right maxillary tuberosity region.



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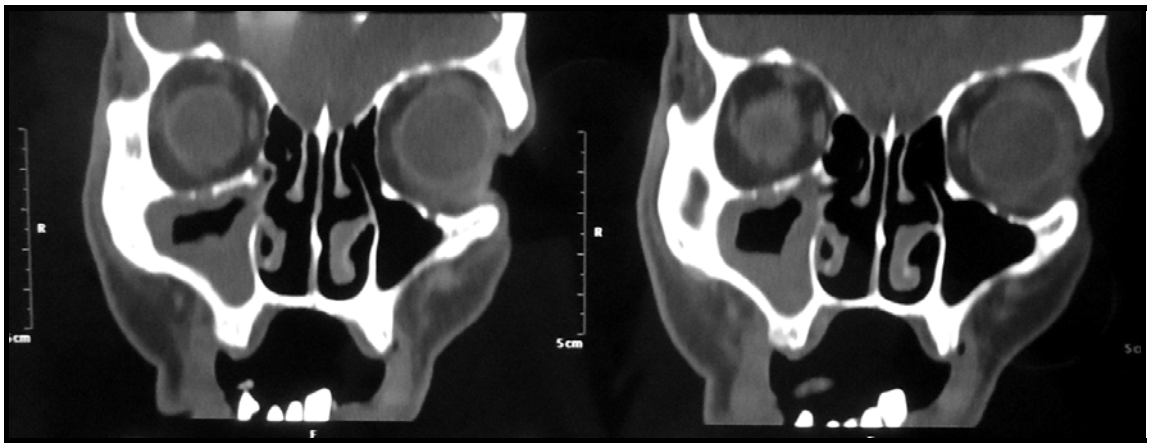
Anterioposteriorly it extends from alveolar ridge i.r.t. 17 going posteriorly to 0.5 cm beyond maxillary tuberosity. Mesiodistally from right buccul vestibule involving palatal mucosa on right side.

On palpation it was tender, base was indurated & soft in consistency.



Coronal CT view shows single, large, lesion on upper right alveolus which is extending superiorly till maxillary sinus involving the inferior and posterio- lateral wall of maxillary sinus.

Biopsy was done & histopathological report suggestive of Well differentiated Squamous cell carcinoma.

Case 2:

A 58 year old male patient reported to the OPD of Sharad Pawar Dental College with the chief complain of intraoral painful ulcer in lower right region of jaw since 1 month. The associated pain was gradual in onset, intermittent in nature , dull aching, and localized to lower right back region.

The ulcer was initially of size 1x1 cm then gradually increased to present size i.e. 2x1 cm. There was no discharge associated.

Patient has habit of tobacco chewing since 30 yr for 5-6 times a day. He gives history of previous hospitalization for carcinoma of lower left gingivobuccul sulcus, which then was treated by wide local excision of the lesion with hemimandibulectomy with radical neck dissection under GA on 25/4/2005.

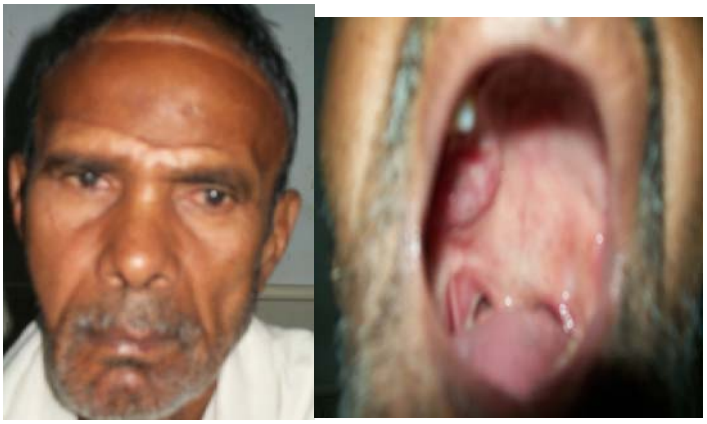
Face was asymmetrical due to segmental resection. Single right submandibular lymph node was palpabale,which was about 2.5x 1cm, ovoid in shape , firm in consistency, nontender, fixed to underlying structures.

Intraoral Examination revealed a single, roughly circular growth about 2x1.5cmin size approx. & which shows surface ulceration present in right mandibular molar region. It extends from 44 to 47 mesiodistally. On palpation it was tender with indurated base. Radiographic survey of the skeleton

and ultrasonography of the abdomen were done to rule out distant metastasis.

Biopsy was done & histopathological report suggestive of Well differentiated Squamous cell carcinoma.

Case 3:



A 63 year old male patient reported to the OPD of Sharad Pawar Dental College with the chief complain of intraoral painful ulcer in upper right region of jaw since 1 month. The associated pain was gradual in onset, intermittent in nature , dull aching.

The ulcer was initially of size 1x1 cm then gradually increased to present size i.e. 2x2 cm Patient has habit of tobacco chewing since 40 yr for 2-4 times a day. According to him he left the habit 6 years back.

However he gives history of previous hospitalization for carcinoma of lower right gingivobuccul sulcus, which then was treated by wide local excision of the lesion with hemimandibulectomy with radical neck dissection and forehead flap and SSG under GA on 05/5/2003.

Face was asymmetrical due to hemimandibulectomy .Single right submandibular lymph node was palpabale,which was about 0.5x 1cm, ovoid in shape , firm in consistency, nontender, fixed to underlying structures.TMJ Movement were restricted absent on right side

Intraoral Examination revealed a single, roughly circular growth about 2x2 cmin size approx. & which shows surface ulceration present in right maxillary tuberosity region.

Anterioposteriorly it extends from alveolar ridge i.r.t. 17 going posteriorly to 0.5 cm beyond maxillary tuberosity. Mesiodistally from right buccul vestibule involving palatal mucosa on right side.

On palpation it was tender and base was indurated. Radiographic survey of the skeleton

and ultrasonography of the abdomen were done to rule out distant metastasis.

Biopsy was done & histopathological report suggestive of Moderately differentiated differentiated Squamous cell carcinoma.

Wide excision of the lesion and modified radical neck dissection with reconstruction using pectoralis major myocutaneous flap were realized, in all the three case. The patients at present are at regular follow up.

DISCUSSION:

Cancer does not arise as an isolated cellular phenomenon, but rather as an anaplastic tendency involving many cells at once" [6]

The pattern of distribution_of the primary lesions is important because it suggests a regional carcinogenic activity of some kind ,in which multiple cell groups undergo a process of irreversible change toward cancer. This is the basis of the concept of field cancerization (ie area of epithelium has been preconditioned by an as yet unknown carcinogenic agent). If such an exposure is continued for a long time, produces an irreversible change in cell and cell groups in the given area.

According to extended slaughter concept, the genetically altered tissue, malignancy could also involve the contralateral side of a frank malignancy or a new site subsequent to the primary tumor. So our three cases are examples of second primary tumors. (A second primary cancer (SPC) is a new primary cancer developing in a person with a history of cancer in a new site or tissue and subsequent to the initial cancer). Further the formation can be explained by carcinogenesis model_in which the development of a field with genetically altered cells plays a central role. In the initial phase, a stem cell acquires genetic alterations and forms a “patch,” a clonal unit of altered daughter cells. The conversion of a patch into an expanding field is the next logical and critical step in epithelial carcinogenesis. Additional genetic alterations are required for this step, and by virtue of its growth advantage, a proliferating field gradually displaces the normal mucosa. In the mucosa of the head and neck, as well as the esophagus, such fields have been detected with dimensions of >7 cm in diameter, whereas they are usually not detected by routine diagnostic techniques. Ultimately, clonal divergence leads to the development of one or more tumors within a contiguous field of preneoplastic cells.[3] An important clinical implication is that fields often remain after surgery of the primary tumor and may lead to new cancers, designated presently by clinicians as “a second primary tumor” or “local recurrence,” depending on the exact site and time interval [4,5].

Warren and Gates defined SPTs in 1932 as new lesions that can arise either from the same

genetically altered “field” as the first tumor or independently from a different clone.[9-12]

Two possible hypotheses have been proposed that account for the process of field change: the first considers the development of a malignant cell as a rare event which generates a monoclonal population spreading throughout the mucosa and giving rise to multiple lesions [13,14]; the second maintains that exposure to carcinogens leads to both the independent transformation of multiple epithelial cells at different sites and the development of distinct lesions from several altered clones [8,9,11].

Comparison of the spectrum of genetic changes in dysplastic and malignant lesions has revealed a complicated molecular basis for the process of field cancerization. Two hypotheses have been proposed to explain why some patients develop multiple lesions as summarized by Bedi *et al.*. One concept is based on the premise that development of a malignant cell is a rare event and that multiple lesions arise due to widespread migration of an altered cell throughout the

upper aerodigestive tract mucosa. The alternative view is that prolonged exposure of the upper aerodigestive tract epithelium to carcinogens leads to the independent transformation of multiple epithelial cells at diverse sites. These altered cells may give rise to individual lesions or cells may collide such that lesions are due to coalescence of cells from several altered clones.

In patients with oral squamous cell carcinoma, the incidence rate of second primary tumor is 14%.[7]Many authors have stressed that the incidence of multiple neoplasms will increase. Careful screening procedures, carried out to detect multifocal tumors at an early stage, should improve survival in these patients.

Conclusion:

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.

N o Conflict of interest

No disclosures

REFERENCES:

1. Slaughter DP: Multicentric origin of intraoral carcinoma. Surgery 1946, 20:133-146.
2. Slaughter DP, Southwick HW, Smejkal W: Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer 1953, 6:963-968.
3. Braakhuis BJ, Tabor M, Kummer JA, Leemans CR, and Brakenhoff R. A genetic explanation of Slaughter's concept of field cancerization: Evidence and clinical implications. Cancer Research 2003; 63: 1727-30.
4. Braakhuis, B. J. M., Tabor, M. P., Leemans, C. R., Van Der Waal, I., Snow, G. B., and Brakenhoff, R. H. Second primary tumors and field cancerization in oral and
5. oropharyngeal cancer: Molecular techniques provide new insights and definitions. Head Neck, 24: 198–206, 2002.
6. Tabor, M. P., Brakenhoff, R. H., van Houten, V. M. M., Kummer, J. A., Snel, M. H. J., Snijders, P. J. F., Snow, G. B., Leemans, C. R., and Braakhuis, B. J. M. Persistence of genetically altered fields in head and neck cancer patients: Biological and clinical implications. Clin. Cancer Res., 7: 1523–1532, 2001.
7. Slaughter DP: The multiplicity of origin of malignant tumors: collective review. Internat Abstr Surg 1944, 79:89-98.
8. F. Cianfriglia, D.A. Di Gregorio, A. Manieri. Multiple primary tumors in patients with oral squamous cell carcinoma. Oral Oncology; 1999; 35; 157-163.
9. Prevo LJ, Sanchez CA, Galipeau PC, Reid BJ. p53-mutant clones and field effects in Barrett's esophagus. Cancer Res 1999;59:4784–4787.
10. Tabor MP, Brakenhoff RH, Ruijter-Schippers HJ, et al. Multiple head and neck tumors frequently originate from a single preneoplastic lesion. Am J Pathol 2002;161: 1051–1060.

11. Simon R, Eltze E, Schafer KL, et al. Cytogenetic analysis of multifocal bladder cancer supports a monoclonal origin and intraepithelial spread of tumor cells. Cancer Res 2001;61:355–362.
12. Braakhuis BJ, Tabor MP, Leemans CR, et al. Second primary tumors and field cancerization in oral and oropharyngeal cancer: molecular techniques provide new insights and definitions. Head Neck 2002;24:198–206.
13. Califano J., Leong P. L., Koch W. M., Eisenberger C. F., Sidransky D., Westra W. H. Second esophageal tumors in patients with head and neck squamous cell carcinoma: an assessment of clonal relationships. Clin. Cancer Res., 5*:* 1862-1867,1999.
14. Bedi G. C., Westra W. H., Gabrielson E., Koch W., Sidransky D. Multiple head and neck tumors: evidence for a common clonal origin. Cancer Res., 56*:* 2484-2487, 1996.