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RESEARCH ARTICLE

# THE SLAUGHTERING FIELD- A CASE STUDY.

**Chaudhary MS ,Tare KS , Gawande MN ,Patil SK ,Hande AH ,Gadbail AR , Agrawal AB**

**Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Medical Sciences (DU), Sawangi (M), Wardha, State- Maharashtra, Country- India**

**Corresponding Author: DR. Tare KS**

**ABSTRACT:**

Slaughter in the year 1953 first proposed the theory of field cancerization. Concomitant occurrence of two (pre) malignant lesions at two distinct anatomical locations can be seen in patients with oral squamous cell carcinoma. These processes are not just only independently occurring isolated phenomena but results as a consequence of epigenetic changes and accumulation of genetic alterations caused by the carcinogens. Current case study presents three cases of field cancerization with special emphasis on its concept.
**Key words**- Field cancerization, Second primary tumor

## INTRODUCTION

Oral squamous cell carcinoma is the sixth most common malignancy and is rising at an alarming rate with 270,000 new cases annually worldwide. [1,2]. Head and neck squamous cell carcinomas accounts for about 50% amongst all malignant tumours in the developing countries of Southeast Asian continent. [2]

The concept of field cancerization lies in the development of multiple tumours at different site as a consequence of genetic aberration induced by various tobacco carcinogens. [3,4]

The concept of field cancerization is also called as field defect, field carcinogenesis, field effect or condemned-mucosal syndrome. [5]

It can be defined as “the presence of one or more areas consisting of epithelial cells that have genetic alteration. A field lesion has a monoclonal origin and does not show invasive growth and metastatic behaviour, the hallmark criteria of cancer.” [1]

The prognosis is adversely affected by the development of second primary tumours (SPT) in HNSCC.

With this background, we designed a study at our institute and 4 years of archival data from 2011-2014 was retrieved and assessed with special emphasis on to the degree of dedifferentiation between primary index tumour and SPT.

## MATERIALS AND METHODS-

The institutional ethical committee gave approval for the study.

This retrospective study was carried out in the department of Oral Pathology and Microbiology, Sharad Pawar Dental College, DMIMS(DU) and the data was obtained from the departmental

archives .The study group comprised of histopathologically diagnosed cases of oral squamous cell carcinoma in the time span of 4 years (2011-2014).

All the cases were evaluated by considering the demographics, habit history, clinical features at the time of diagnosis, site of involvement of the index tumour, histopathological grade of differentiation of the index tumor, disease free period, second incidence site and histopathological grade of SPT. The following inclusion and exclusion criterias were considered;

*Inclusion criterion* –

1. Incidence of second primary tumour, with or within 6 months after the confirmation of index tumor, at a distant site.
2. Second primary tumour atleast 2cm away from the index tumour were included.
3. Second primary tumour arising in the same location of the index tumor after a disease free period of not less than 5 years were also been included in the study.

*Exclusion criterion*-

1. Tumours recurring in the same region with less than 2cm distance from the index tumour were excluded.
2. Tumours recurring in the same region with disease free period not more than 3 years were excluded.

Details of the cases are as under.

**Table 1**

| Sr no | Age/ Sex | Habit history | First incidence and site | Year of first incidence | Histopathological diagnosis of index tumour | Disease free interval | Second primary tumour incidence year with site | Year of second incidence | Histopatho-logical diagnosis of Second primary tumour. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 47/M | Tobacco chewing since 20 years; 5-6 times /day | Malignancy in Right buccal mucosa | 2007 | Verrucous carcinoma | 5 years | Right buccal mucosa | 2011 | WDSCC |
| 2 | 55/F | Tobacco chewing since 32 years ; 4-5 times/ day | Malignancy in Right buccal mucosa with OSMF | 2006 | MDSCC | 6 years | Right buccal mucosa | 2012 | MDSCC |
| 3 | 60/F | Tobacco chewing habit since 15 years ; 3-5 times/day | Malignancy in Right buccal mucosa | 2008 | WDSCC | 3 years | Left buccal mucosa | 2011 | WDSCC |
| 4 | 51/F | Tobacco chewing since 20 years 3-5 times/day | Malignancy of tongue | 2010 | WDSCC | 2 years | Right side retromolar region | 2012 | MDSCC |

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|---|---|---|---|---|---|---|---|---|---|---|
| 5 | 45/M | Tobacco chewing since 20 years, 5-6 times /day | Malignancy involving left GB sulcus. | 2011 | WDSCC | 1 year | Right side GB sulcus | 2012 | MDSCC | |
| 6 | 75/F | -Tobacco chewing with lime since 50 years; 3-4 times/day - Pan chewing since 45-50 years 6-7 times/day | Malignancy right buccal mucosa & Carcinoma left buccal mucosa alongwith retromolar region. | 2014 | WDSCC of right buccal mucosa & Verrucous carcinoma of left buccal mucosa | Simultaneous occurrence | ---------- | ---------- | ---------- | MPT |
| 7 | 46/M | Tobacco chewing since 15-20 years , 3-5 times/day | Carcinoma right lateral borer of tongue | 2011 | Verrucous carcinoma | 2 years | Carcinoma of right side palate & Carcinoma right retromolar region | 2013 | - MDSCC on right side palate. -Verrucous carcinoma of right retromolar region. | MPT |
| 8 | 65/M | Tobacco chewing since 35-40 years, 8-10 times/day | Carcinoma right buccal mucosa & Malignancy left lateral border of tongue | 2014 | WDSCC of right buccal mucosa & Verrucous carcinoma of left lateral border of tongue. | ---- | ---- | ----- | ----- | MPT |
| 9 | 42/M | Tobacco chewing since 20 years, 5-6 times/day | Malignancy left alveolar mucosa in | 2012 | WDSCC | 1 year | Malignancy of right lateral border of tongue | 1.5 years | MDSCC | |
| 10 | 52/M | Tobacco with lime chewing since 30-35 years, 5-6 times/day | Malignancy of right GB sulcus & Malignancy of left maxillary vestibule. | 2014 | WDSCC of right GB sulcus & WDSCC of left maxillary vestibule | ---------- | ---------- | ------- | ---------- | MPT |

WDSCC- Well differentiated squamous cell carcinoma, MDSCC- Moderately differentiated squamous cell carcinoma, MPT- Multiple primary tumour, GB- gingivobuccal

**RESULT-**

Out of 1000 histologically diagnosed cases of oral squamous cell carcinoma in the time span of 4 years from (2011-2014), with due consideration of inclusion and exclusion criterias, 10 cases were selected. In this study, slight male predilection was observed but was found to be insignificant. The mean age at the time of diagnosis was found to be 53.8years. The contributing habit of tobacco chewing with average of 26.5 years was also found. Out of 10 cases, 4 cases were of simultaneous multiple primary tumours (40%) whereas the other 4 showed anatomically distinct sites from primary index tumour and thus were considered under the category of second primary tumours (SPT).2 cases showed the same anatomical site of origin of SPT from primary index tumour ,however after the time lapse of minimum 5 years as per our inclusion criterion.

4 cases (40%) out of 10 showed decreased in grade of differentiation in SPT as compared to the primary index tumour ; 4 cases showed multiple primary tumours with varying degree of tumour differentiation and in only 2 cases, no deterioration in grade of malignancy was seen as compared to primary index tumour.

**DISCUSSION**

The phenomenon of field cancerization is explained by the fact that oral cancer is not just an isolated cellular event but is a cumulative anaplastic tendency of many cells at once, which as a consequence, results into multifocal development of cancer at various sites with an entire field in response to carcinogens, tobacco being the most common. [6]

The maiden work in the *field of cancerization* is attributed to Slaughter in the year 1953 who first questioned about the clinical significance of development of second primary irrespective of being synchronous or metachronous, tumours in the vicinity of primary index tumour and local recurrences.[7]

Boudewijn et al have proposed a definition of field lesion based on molecular findings as 'the presence of one or more areas consisting of epithelial cells that have genetic alterations." [8]

Field cancerization or the "field effect" was previously assumed and is still continued to be used in the context of the existence of (pre-) neoplastic processes at multiple sites, often with the unproven assumption that these have developed independently. [8]

Warren and Gates in the year 1932 first conceived the criterias to designate a tumor as second primary. They were as under-

1. Histologic confirmation of malignancy in both the index and secondary tumors.
2. There should be at least 2 cm of normal mucosa between the tumors.
3. If the tumors are in the same location, then they should be separated in time by at least 5 years. [9]

Cunliffe et al divided the SPT's into two groups namely *synchronous* and *metachronous.*

*Synchronous SPTs*- develop simultaneously **with or within** 6 months after the index tumor.

*Metachronous SPTs*- they are **considered as regional spread or metastatic lesions** which develop >6 months after the initial tumor.[10]

Clinically, Local recurrence can be defined as cancer that develops from same place of the primary tumor or occurring at a distance <2 cm from the initial tumor within 3 years after the primary tumor. [11]
The phenomenon of FC can also be demonstrated in cancers involving skin, oropharynx, larynx, lungs, esophagus, breast, colon, bladder, cervix and vulva besides HNSCC.[12]

The probability of developing second primaries in patients with head and neck squamous cell carcinoma is about 20%.[13]
The average incidence rate of second primary tumour ranges upto 35%. [14]
In our study, we attempted to measure the prevalence of field cancerization which was found to be 1% in this area.
In all the cases, habit of tobacco chewing for average of about 26.5 years was common. IARC has categorized tobacco as group I carcinogen and is responsible for conversion of proto-oncogenes into oncogenes which in turn triggers oncogenic events which ultimately results in the formation of field from a patch.
'Patch' can be defined as group of cells that share a common genotype, contiguous at the moment of consideration. [15]
The SPT's can be differentiated into 2 types based upon its etiology, one group originating from the same field in which the first primary tumor developed and the second group which has an independent origin. [16]
This explains the similarities & differences in the grade of tumour differentiation in the study.

According to Manjunath *et al* 'true' SPT is defined as an independently evolved carcinoma. [5]
Occurrence of multiple primary tumors can be explained on the basis of the following theories-
a. Monoclonal theory in which a single cell is transformed, and through mucosal spread, gives rise to multiple genetically related tumors.
b. Polyclonal theory in which multiple transforming events give rise to genetically unrelated multiple tumors. [17]
In the present study, 4 cases (4/10) showed occurrence of MPT with difference in the grade of differentiation at the time of diagnosis, which can be explained by polyclonal theory of field cancerization.
Also, 2 cases (2/10) showed same degree of differentiation of SPT in comparison to primary index tumour which can be aptly described by monoclonal theory of field cancerization.

**CONCLUSION-**

The process of field cancerization is a well documented fact and can satisfactorily explain the concurrent and recurrent carcinomas in the oral cavity. Owing to high probability of occurrence of field cancerization, proper chemopreventive management and regular follow up is advised so as to reduce the death toll .There is a wide scope for furthur research to detect the early presence of field cancerization with easier diagnostic aids which will be an awaiting boon for patients suffering from cancer all over.

## REFERENCES

1. Arunachalam Meyyappan, Ramya Malini, Raghavendra Karthik, Priyadarshini Natarajan, K. Raj Kumar Field effect in oral cancer: An update ;SRM Journal of Research in Dental Sciences Vol. 6 Issue 1 January-March 2015
2. Adonis M, Gil L. The need to strength collaborative teams in lung cancer research. Electron J Biotechnol 2003;6:1‐1
3. Aparna M.,Prashanth Shenai,Laxmikanth Chatra, Veena K. M.,Prasanna Kumar Rao, Rachana V. Prabhu, Shahin K. A, Archives of Medicine and Health Sciences Jul-Dec 2013 Vol 1 Issue 2
4. Oijen MG, Slootweg PJ. Oral field cancerization: Carcinogen induced independent events or micrometastatic deposits? Cancer Epidemiol Biomarkers Prev 2000;9:249-56.
5. S. M. Manjunath, Robin Sabharwal, Manish Kumar, Aditi Sinha, Shivangi Gupta, Shipra Sepolia Oral Field Cancerization: An Update Universal Research Journal of Dentistry · January-April 2014 · Vol 4 · Issue 1
6. Angadi PV, Savitha JK, Rao SS, Sivaranjini Y. Oral field cancerization: current evidence and future perspectives. Oral Maxillofac Surg 2012;16:171-180.
7. Slaughter DP. Multicentric origin of intraoral carcinoma.Surgery 1946;20:133–135.
8. Boudewijn JM, Braakhuis T, Tabor MT, Kumar JA, Leemans R, Barkenhoff RH et al. A genetic explanation of slaughter's concept of field cancerization: evidence and clinical implications. Cancer Res 2003;63:1727–1730.
9. Warren S, Gates O. Multiple primary malignant tumors. A survey of the literature and a statistical study. Am J Cancer 1932;16:1358-414.
10. Cunliffe WJ, Hasleton PS, Tweedle DE, Schofield PF. Incidence of synchronous and metachronous colorectal carcinoma. Br J Surg 1984;71:941-3.
11. Braakhuis BJ, Tabor MP, Leemans CR, van der Waal I, Snow GB, Brakenhoff RH. Second primary tumors and field cancerization in oral and oropharyngeal cancer: Molecular techniques provide new insights and definitions. Head Neck 2002; 24:198-206.
12. Meijer GA, Baak JP. Quantification of proliferative activity in colorectal adenomas by mitotic counts: Relationship to degree of dysplasia and histological type. Clin Pathol 1995;48:620‐5.
13. Dakubo G, Jakupciak J, Birch-Machin M and Parr. Clinical implications and utility of field cancerization. Cancer Cell International 2007; Mar 15; 7:2.
14. Ankle MR, Kale AD, Charantimath S, Charantimath S. Comparison of staining of mitotic figures by haematoxylin and eosin‐and crystal violet stains, in oral epithelial dysplasia and squamous cell carcinoma. Indian J Dent Res 2007;18:101‐5.
15. Srikant N, Mahajan S, Karen B, Thomas G. Morphometric analysis of nuclear feature and volume‐corrected mitotic index in the prognosis of oral squamous cell carcinoma. Oral Sci Int 2009:85‐94.
16. Ploton D, Thiry M, Menager M, Lepoint A, Adnet JJ, Goessens G. Behaviour of nucleolus during mitosis. A comparative ultrastructural study of various cancerous cell lines using the Ag‐NOR staining procedure. Chromosoma 1987;95:95‐107
17. Kiernan JA. On chemical reactions and staining mechanisms. Special Stains and H and E. 2nd ed. North America, Carpinteria, California: Dako; 2010 p. 172‐4.