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ORAL FIELD CANCERIZATION: THE PERPLEXING ENIGMA

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Abstract – Oral field cancerization is a term used to describe the process of multiple areas of the oral cavity being affected by cancerous or precancerous changes as a result of exposure to carcinogens, rather than a single lesion. It is believed that certain risk factors, such as smoking, excessive alcohol consumption, and chronic infections, can lead to genetic changes in the cells of the oral cavity that make them more susceptible to developing cancer.

Key words: Oral Cancer, field cancerization, Carcinogens.

INTRODUCTION

An important physiologic function of epithelia is their protective role that inevitably exposes them to environmental substances, including carcinogens that can create a vast area of genetically altered cancer fields and can undergo abnormal proliferation.[1]
Several carcinogens such as tobacco, alcohol, Human Papillomavirus (HPV) have been associated with an increased risk of oral cavity cancer. According to International Agency for Research on Cancer (IARC), in 2020 worldwide burden of oral cancer is 377713 new cases and 177757 deaths with an average 5-year survival rate is 40%. [2]

CASE REPORT

A 60-year-old female patient reported to our Institute with a chief complaint of swelling on right side of face since 1 month. She also complained of mild pain since 3-4 days. Swelling was initially small. History and general physical examination revealed no relevant findings and she was not under any treatment. No tobacco-chewing habit was evident. On extra-oral examination, diffuse swelling was seen on right side of face extending superoinferiorly from middle of the face to 1 cm above the lower border of mandible & anteroposteriorly from angle of mouth to 3 cm in front of tragus of ear (Fig 1). Swelling was stony hard & tender on palpation. Right submandibular lymphadenopathy was present. Intraoral examination revealed multifocal large irregular, non-scrapable lesions with clear borders located on right buccal mucosa, mandibular alveolar ridge, floor of the mouth, lateral border and ventral surface of the tongue, palate, lip (Fig 1 to 5). Most of the lesions were plaque type whitish in colour with verrucous surface. Some lesions were greyish white in colour. These lesions were leathery and rough on palpation but non tender. There was reddish white lesion on alveolar ridge of 45,46 region (Fig 6). Mandibular arch was edentulous. The intraoral examination revealed in jugal mucosa and labial commissure.
Teeth were present in the maxillary arch (11-18, 21-23, 27) with generalized Grade 1 mobility, generalized gingival recession, generalized attrition. Based on the history and clinical examination, a provisional clinical diagnosis of oral proliferative verrucous leukoplakia was made.

figure 1: diffuse swelling on lower right side of face

figure 2: whitish patch on lower lip from left angle of mouth crossing the midline

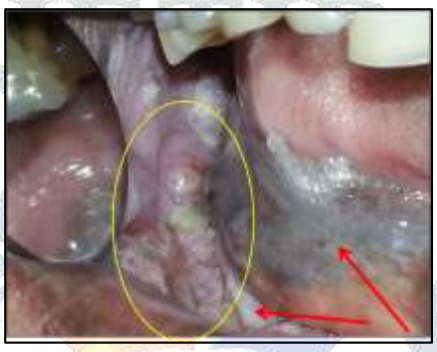

fig 3: verruciform white plaque on right buccal mucosa, retromolar region and alveolar ridge (yellow oval outline); greyish white patch extending from floor of the mouth to ventral surface

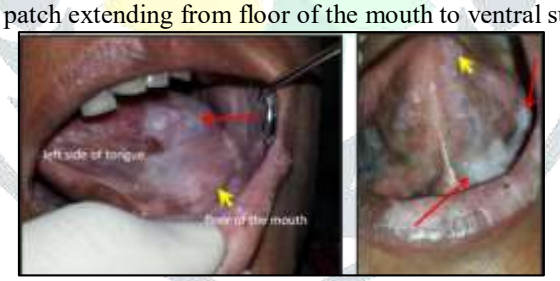

figure 4: whitish lesions on left side of the tongue and floor of the mouth

figure 5: whitish patch on posterior part of the palate near right maxillary tuberosity and on left palatal gingiva from 23 to 27 of the tongue (red arrows)

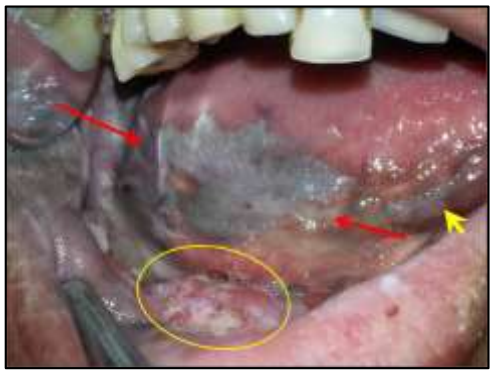

fig 6: reddish white lesion on right alveolar ridge (yellow oval outline); greyish white plaque from floor of the mouth to ventral surface of the tongue (red arrows); extending near the tip of the tongue (yellow arrow)

INVESTIGATIONS

Routine haematological investigation, CT of mandible & neck was performed. Incisional biopsy was performed from two different sites under local anaesthesia.

Haematological investigation values were found within normal limits. CT neck with mandible revealed lesion involving alveolar process of mandible right side suggestive of Ca alveolus with few mildly enlarged lymph nodes in level IA, IB and level II right side.

HISTOPATHOLOGY

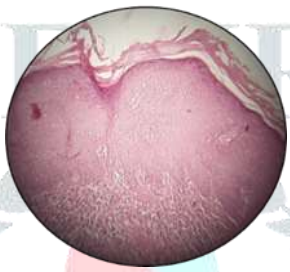

fig 7: photomicrograph of the lesion showing corrugated hyperorthokeratosis and corrugated epithelium, acanthosis; numerous inflammatory cells infiltration also noticed in the connective tissue (×10)

fig 8: photomicrograph of the lesion showing parakeratin plugging (red arrow) (×40)

figure 9: photomicrograph of the lesion showing finger-like papillary projection lined by hyperorthokeratinized stratified squamous epithelium with fibrovascular connective tissue core (×40)

fig 10: photomicrograph of the lesion showing epithelial hyperplasia with dysplastic features and bulbous rete ridges individual cell keratinization, keratin pearl formation seen in a superficial layer of epithelium (×10)

The given H and E-stained section showed epithelium and connective tissue. The epithelium was stratified squamous & ulcerative in some areas. Corrugated hyperorthokeratosis and corrugated epithelium was present in some places (Fig 7). Parakeratin plugging was also evident (Fig 8). In few areas, papillary projection of epithelium with thin core of connective tissue was seen (Fig 9). The epithelial cells showed dysplastic features. Break in Basement membrane was evident. The dysplastic cells were invading the underlying connective tissue in the form of sheets. Keratin pearls & epithelial pearls were seen (Fig 10). Collagen fibres were dense to loose fibrillar in nature interspersed with fibroblasts. Abundant chronic inflammatory infiltrate were seen in the connective tissue. Plenty of blood vessels & extravasated RBCs were present.

The overall picture is suggestive of Oral Field Cancerization with Well Differentiated Squamous Cell Carcinoma in the alveolar region of 45,46 region.

DISCUSSION

The concept of field cancerization:

Slaughter et al. in 1953 proposed the concept of field cancerization to explain the development of multiple primary tumors and locally recurrent cancer while studying the presence of histologically abnormal tissue surrounding oral squamous cell carcinoma. Since then, the concept of field cancerization has been recognized in various organ systems, including the head and neck (oral cavity, oropharynx, and larynx), lung, vulva, esophagus, cervix, breast, skin, colon, and bladder.[3]

Field cancerization theory presumes that, after repeated carcinogenic exposures, the entire epithelium has an increased risk for developing (pre)malignant lesions because of multiple genetic abnormalities. This theory well explains the strong potential with malignant transformation and regional recurrence in cancer, and helps to better understand the pathogenesis, and thus provides a new idea for prevention and treatment of this disease.[4]

Field cancerization can occur without apparent morphological changes. Field cancerization refers to the presence of genetically altered or histologically abnormal cells in a wider field of tissue surrounding a tumor or potentially malignant disorder. These altered cells may not exhibit visible or detectable morphological changes under standard histopathological examination. The genetic and molecular alterations associated with field cancerization precede the development of visible morphological changes. This implies that relying solely on histopathology may miss the presence of genetically altered cells and underestimate the risk of cancer development. Therefore, additional molecular markers or techniques are needed to better identify and assess field cancerization.

The concept of field cancerization provides an explanation for the development of second primary tumors (SPTs) in the oral cavity following the occurrence of a primary malignant tumor. The "classical" mechanism, as observed by Slaughter, suggests that individuals with adverse habits (such as tobacco or alcohol use) experience long-term exposure to carcinogens, leading to the involvement of large areas of the aerodigestive tissue. Within this preconditioned epithelium, multifocal carcinomas can arise independently through separate mutations, resulting in genetically unrelated tumors.

However, the introduction of the "clonal theory" brought about a shift in this understanding. The clonal theory challenges the notion of independent and genetically unrelated tumors in the classical mechanism. According to the clonal theory, a single cell within the oral mucosa, upon exposure to carcinogens, undergoes transformation and gives rise to a large extended premalignant field through clonal expansion. Gradually, the transformed cells replace the normal mucosal cells. Within this field of genetically diverse subclones, additional genetic alterations can accumulate, leading to the development of two separate tumors. It suggests that there is clonal relatedness between the primary tumor and the subsequent SPTs, as they share at least one common genetic alteration that occurred prior to clonal expansion.

The evolving understanding of field cancerization highlights the complex nature of tumor development and the importance of genetic alterations in the process.[5]

CONCLUSION

In oral field cancerization, the genetic and epigenetic changes can affect various genes involved in cell cycle control, DNA repair, and tumor suppression. These changes can result in the development of precancerous conditions, such as leukoplakia and erythroplakia, as well as multiple primary tumors.

The management of oral field cancerization involves regular surveillance and monitoring of the oral cavity to detect and treat any premalignant or malignant lesions that may arise. This may include the use of techniques like brush biopsies, exfoliative cytology, and tissue biopsies to evaluate suspicious areas.

Additionally, lifestyle modifications, such as smoking cessation and reducing alcohol consumption, are crucial in reducing the risk of further genetic damage and progression to cancer.

REFERENCES

1.Dakubo, G.D., Jakupciak, J.P., Birch-Machin, M.A. et al. Clinical implications and utility of field cancerization. Cancer Cell Int 7, 2 (2007).
2.Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer.
3.Boudewijn J. M. Braakhuis, Maarten P. Tabor, J. Alain Kummer, C. René Leemans, Ruud H. Brakenhoff; A Genetic Explanation of Slaughter's Concept of Field Cancerization: Evidence and Clinical Implications1. Cancer Res 15 April 2003; 63 (8): 1727–1730.
4.Wei ZH, Gong W, Zhou M, Chen QM. [The concept of field cancerization and its clinical application]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2016 Sep;51(9):562-5.
5.Raviraj Jayam. Oral Field Cancerization: A Review January 2010 Journal of Indian Academy of Oral Medicine and Radiology 22(4):201-5