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Squamous Cell Carcinoma with Apparently No Risk Habits in Elderly Male – An Area of Research

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Summary: *Non smoking and non drinking patients with oral squamous cell carcinoma has been identified as a unique and growing subgroup in the literature. In this article we describe a case of squamous cell carcinoma of right maxillary alveolus in an elderly male with no associated traditional risk factors like tobacco and alcohol. Patient had no family history of oral cancer and no environmental exposure of confounding factors like second hand smoke. Tumour was managed by surgical and adjuvant radiotherapy and is under follow up. Further investigations and genetic analysis are required to delineate the etiology of these carcinomas as treatment algorithm may be different for such patients. Thus identification of risk factors in such cases still remains an active area of clinical research.*

Background: *Squamous cell carcinoma is a predominant oral cancer with recognized etiological agents being tobacco chewing, alcohol and smoking. This cancer can be inherited and environmental exposure to second hand smoke could be a major confounding factor.*

Non-smoking nondrinking patients with oral squamous cell carcinoma were more likely to be female with higher median age at presentation.[1,2,3,4]

The purpose of this report is to describe an elderly male patient with carcinoma of maxillary alveolus apparently with no etiological factors and there is no family history of cancer. The etiology of this non smoking nondrinking elderly patient is as yet unknown and management algorithm may be different for this age group. Despite the advances of therapeutic approaches, no significant improvement in morbidity and mortality of oral squamous cell carcinoma have been found during the last 30 years. Analysis of tumour biology of such groups may help us in identifying an unknown etiology which can guide treatment decision.

Key Words:*squamous cell carcinoma, non drinkingnon smoking, etiological factors*

I. Case Presentation:

The patient is a 62 years old male who noticed ulcer in right upper side of the mouth 2 months back. He showed to local dentist and was given medication for the same and the ulcer subsided. Then he noticed ulcer again in the same area one month back which was progressively increased to its present size approximately 3x2 cm with on and off pain with respect to lesion along with bleeding while brushing. The patient had no complaint of fever and weight loss. Patient's hygiene was fair. Patient was allergic to diclofenac. Medical history was non significant. Negative social history for contributing factors like tobacco, alcohol or chemical exposure and there were no smokers in the house. Clinical or family history was non-significant for genetic or immunologic disease with cancer predisposition.

Clinical examination revealed no gross asymmetry of face and lymph nodes palpable with respect to level 1b and level 2 both were mobile and firm in consistence and approximately 1x2cm in size. (Fig.1).

Fig. 1: Extra oral profile

Intraoral examination revealed a tender ulcerative lesion of approx 3x2cm in size involving alveolus extending from right maxillary canine to right maxillary third molar. Lesion was oedematous, firm in consistency with irregular surface. The lesion was tender on palpation and there was bleeding on touch.(Fig. 2). Mobility was present in relation to 13,14,16,18.

Fig. 2: Intra oral examination

II. Investigations:

Histopathological examination: Report of incisional biopsy revealed moderately differentiated squamous cell carcinoma of right maxillary alveolus (fig.3)

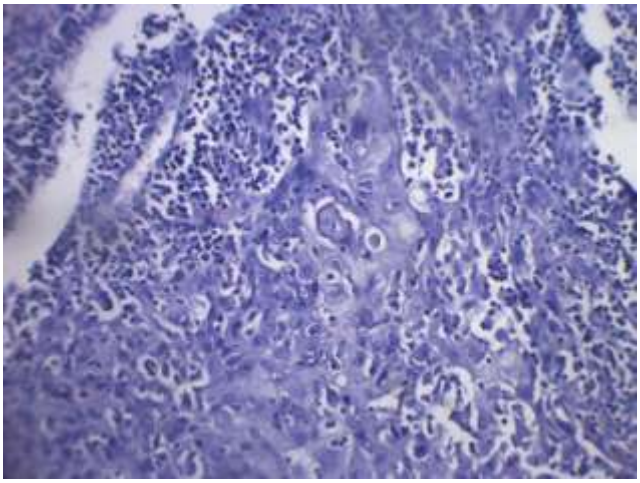

Fig. 3: Histological Examination

Ct scan showed hetrogenously enhancing soft tissue mass in the right maxillary alveolus infilterating into the ipsilateral maxillary sinus with multiple lymph nodes in level 2 and submandibular lymph nodes, largest measuring 14mm in the right level 2.(fig.4)

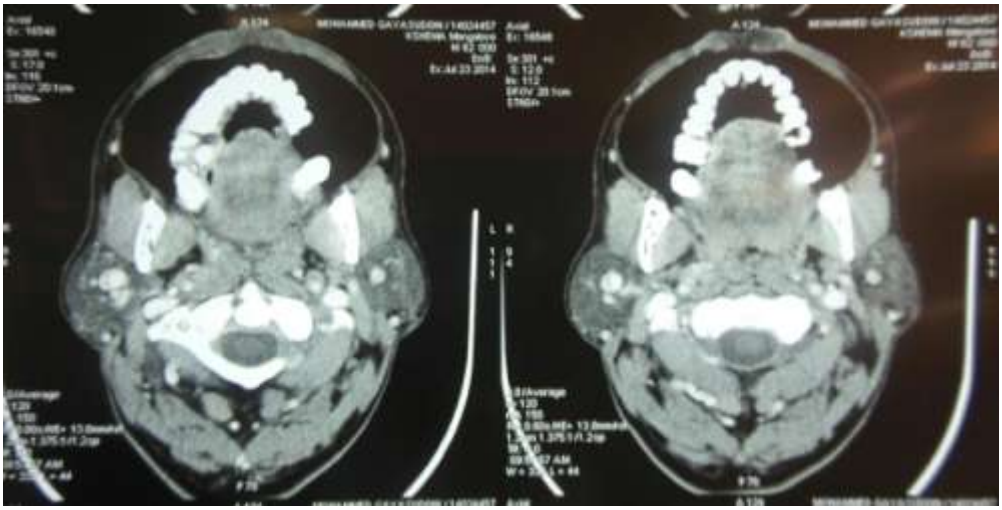

Fig. 4: C.T Scan

III. Treatment & Outcome And Follow-Up

Inferior partial maxillectomy(fig.5) with supraomohyoid neck dissection(fig.6) and primary closure was done with obturator . Patient is undergoing radiotherapy with a dose of 60 Grays in 30 fractions for 6 weeks.

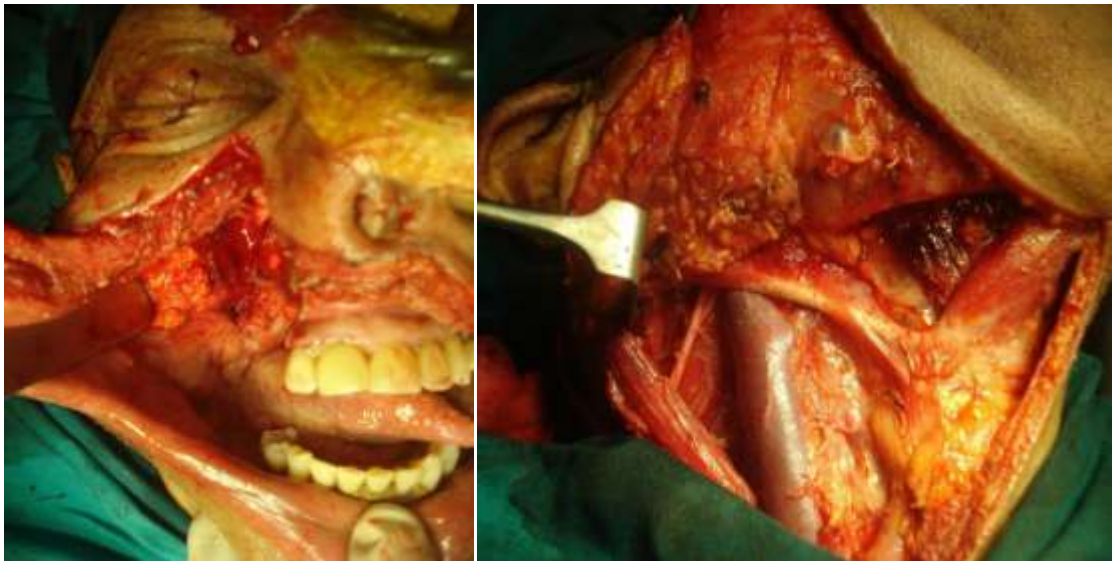

Fig. 5 &6 : intraoperative procedure-maxillectomy

Histopathological examination of surgical specimen was negative for the presence of residual tumour.(Fig 7) Specimen from Maxillary antral lining was free of tumour. Lymph node specimen showed features of reactive hyperplasia with no metastasis.(fig8) Patient postoperative healing was uneventful with resolution of lesion. Patient is under close follow up.(fig.9)

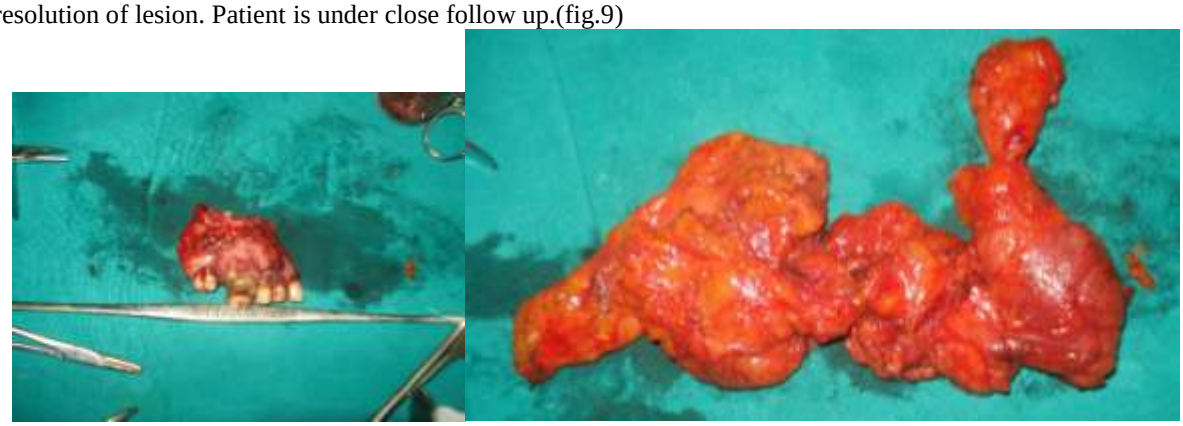

Fig. 7: specimen , Fig. 8: Lymph node specimen

Fig 9: postoperative

IV. Discussion:

Oral cancers constitute 80-90 % of head and neck cancers with around 2,70000 new cases occurring annually.[4,5,6] Squamous cell carcinoma accounts for 80-90 % of oral cancers(5,6).oral squamous cell carcinoma is defined as A malignant condition of the tissues lining the oral cavity that can arise at any location within the anatomical confines of the oral cavity,which is capable of local, regional and distant spread.[7]

Distribution of oral cancer by subsites: tongue(43%), maxillary gum(6%), mandibular gum(7%), floor of the mouth(14%), buccal mucosa (8%), hard palate (4%), retromolartrigone(7%), oral cavity NOS(11%).[8,9] Oral cancer traditionally being regarded as a disease of male smokers and drinkers.in our case patient has never smoked or chewed tobacco and never consumed alcohol. He had no family history of oral cancer and no other smoker in household. Such patients, without typical risk factors for developing squamous cell carcinoma of the oral cavity may have a worse prognosis compared with patients with usual risk factors like tobacco and alcohol.[10,11,12]

The nonsmoking and nondrinking population accounts for 13-35% of the oral squamous cell carcinoma population and were more likely to be female.[13,14] The various etiological factors for squamous cell carcinoma includes tobacco , alcohol being the major and other factors can be betel quid chewing, HPV and familial inheritance.

Koo k et al describe the bimodal age distribution of non smoking and nondrinking patients with oral squamous cell carcinoma, Most common site being maxillary alveolus and tongue whereas in smoking and drinking the most common site being mandibular alveolus and retromolar trigone.[13]

According to Koch wm et al, the nonsmokers with head and neck tumour contain a lower frequency of genetic alteration ,suggesting that underlying changes in these cancers remains undiscovered.[14]

Epidermal growth factor receptors (EGFRs) are amplified and overexpressed in many different human cancers, a phenomenon generally associated with poor prognosis. Non-smoking status is a positive predictor of tumour epidermal growth factor receptor (EGFR) expression in oral squamous cell carcinoma, which is a marker for the response to cetuximab,[15]. This is also the case in lung cancers where non-smokers are more likely to respond to erlotinib and gefitinib.[16] altered treatment protocols might provide improved outcomes in nonsmoking and nondrinking patients.

Farshadpour et al, non-smoking and non-drinking patients present differentially expressed genes which possibly indicate the presence of a different cellular response to carcinogenic events in such patients. A set of 49 differentially expressed genes were detected. Among others, seven genes related to interferon-γ were upregulated(*LAP3*, *MUC16*, *HLA-E*, *HLA-F*, *HPS6*, *ECHF1*, *ECFG1)* and two genes linked to NFKB pathway(*NFKBIA*, *HSPA1A)* were downregulated. Further studies are required to validate this gene set and provide different therapeutic implications to improve prognosis for these patients.[2]

Not much work is done in never smokers and never drinkers with oral cancer group thus we suggest that such group should be evaluated and further investigations are required to identify the unknown etiology and this may guide us the treatment plan of oral cancer as overall prognosis of oral cancer is not very good.

V. Learning Points/Take Home Messages:

Oral lesion should be suspected for squamous cell carcinoma even if patient has no family history of cancer and has never smoked or chewed tobacco or consumed alcohol.

Non smoking and non drinking squamous cell carcinoma patients have worse prognosis as compared to those who smokes or drink alcohol. So these should be diagnosed as early as possible.

The molecular biology of oral cancers and mainly the emerging trends of molecular epidemiology is an area necessitating further investigations.

Non smokers with oral cancers have lower frequency of genetic changes, so underlying changes remains undiscovered in such group. Analysis of these patterns may improve understanding and management of this disease.

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