Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/2655
DOI URL: http://dx.doi.org/10.21474/IJAR01/2655
ISSN NO. 2320-5407

*RESEARCH ARTICLE*

# SQUAMOUS CELL CARCINOMA - A SERIES OF 4 CASE REPORTS.

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*Manuscript Info*

***Manuscript History***

Received: 30 October 2016
Final Accepted: 29 November 2016
Published: December 2016

***Key words:-***
Squamous cell carcinoma,
Epidemiology, cancer, oral cavity.

*Abstract*

Oral squamous cell carcinoma is a crucial oncological problem in the areas of the world where tobacco habits in the form of chewing and/or smoking with or without alcohol intake are common. In India, cancer of the oral cavity is one of the five leading sites of cancer in either gender. More than 90% of the oral cancers occur in patients over the age of 45, with a male predilection. Squamous cell carcinoma (SCC) is the most common neoplasm of the oral cavity. In this paper, we report a series of four cases clinical presentation of oral squamous cell carcinoma in buccal mucosa and lateral border of tongue. Squamous cell carcinoma is defined as a malignant epithelial neoplasm exhibiting squamous differentiation as characterized by the formation of keratin and/or the presence of intercellular bridges according to Pindborg et al



## Introduction:-

The squamous cell carcinoma is the most common malignant neoplasm of the oral cavity. Although, it may occur at any intraoral site, certain sites are more frequently involved than others. Because of the differences in clinical appearance, the nature of the lesion and the prognosis, it is well to describe the tumors individually. Oral SCC more frequently affects men than women (M:F = 1.5:1) most probably because more men indulge in high-risk habits. The incidence of squamous cell carcinomas of the oral cavity differs widely in various parts of the world and ranges from approximately 2-10 per 100,000 population per year. The use of tobacco in its various forms, including smokeless tobacco, is regarded as the main cause of oral cancer, particularly when associated with the use alcohol. High exposure to ultraviolet light increases the chance of developing cancer of lower lip. Diets with low levels of vitamins A and C or inadequate consumption of vegetables and fruits may contribute to the risk of oral cancer. Patients who are immune supressed, eg: renal and homograft recipients and HIV infected patients, have a higher incidence of subsequent cancer development, particularly of lower lip. A number of rare conditions predispose to the development of oral cancer; such as Xerodermapigmentosum, Fanconis anemia and Blooms syndrome. HPV positive oropharyngeal tumors appear to represent a distinct clinical and histopathological entity with improved prognosis.[1]

Almost all oral cancers, except those in the earliest stages have two characteristic features in the form of ulceration and an indurated margin. However, in different sites there are certain variations.[1]

Histopathologically, all carcinomas exhibit following features of epithelial dysplasia, keratinization, local invasion by break in the basement membrane and invasion and proliferation into the underlying connective tissue, metastasis by blood or lymphatic channels seen as invasion of tumor cells into the capillaries and lymphatic ducts permeation and peri neural invasion some of the tumor cells may have atypical invasion pattern along the nerve sheath.[2]

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DIAGNOSIS, various diagnostic tests can be employed to detect potentially malignant and malignant lesions. In routine practice, vital staining, brush biopsy, exfoliative cytology, tissue biopsy and various imaging modalities like plain radiography, CT, MRI, Ultrasonography etc. can be used effectively. Here we present a series of 4 case reports with review of literature.[3]

## Case Report:-

**Case 1:-**

A 47 yr old male patient reported to the department of OMR with a chief complaint of burning sensation in his right buccal mucosa for the past 5 months. Patient had habit of smoking for the past 20 years and no history of consumption of alcohol. History revealed patient had trauma before 4 months following which ulceration started and was growing gradually in size which is associated with pain that was partially subsided on medication. Patient gives history of burning sensation on taking spicy foods and restricted mouth opening for past one month

On intra oral examination(Figure 1) of right buccal mucosa, a single irregular, ulcerated region present on the right buccal mucosa measuring approximately 2x3 cm in relation to 45, 46, 47; 1cm away from the corner of the mouth and up to pterygo mandibular raphae region and superior inferiorly upper vestibule to lower vestibule in relation to 15,16,17 and 45,46,47. The surface of the ulcer appears erythematous with small elevated projection and irregular margin. On palpation ulcer was rough, non tender and firm in consistency. No bleeding on provocation was evident, margins are elevated and fixed. The mucosa immediately adjacent to the ulcer appears slightly erythematous. Single right sub mandibular lymph node is palpable measuring approx 1x1.5 cm which is fixed, hard in consistency and tender on palpation. Based on the clinical features provisional diagnosis is given as the malignant ulcer in right buccal mucosa. Patient was subjected for incisional biopsy and histopathology reveals (Figure 2)well differentiated squamous cell carcinoma in the right buccal mucosa.

**Case 2:-**

A 50 yr old male patient reported to the department of Oral medicine and radiology with a chief complaint of pain and swelling in his right cheek for the past 6 months. Patient had habit of smoking for the past 25 years and no history consuming alcohol. History revealed that the patient initially developed pain in the right buccal mucosa before 6 months. Pain was pricking type and intermittent in nature, aggravates on taking food and subsided on medication. Patient medical history was non-contributory. Patient noticed a growth on the cheek for the past 2 months. It was initially small in size and gradually increased to attain the present size. Patient gives H/O burning sensation on taking spicy food and restricted mouth opening for past 6 months. On intra oral examination (Figure 3) of the right buccal mucosa, a single irregular ulcer present on the posterior aspect of right buccal mucosa measuring approximately 1x2cm, extending superiorly 1cm below the upper buccal vestibule, inferiorly till the occlusal level of 47, also involves the pterygo mandibular raphae region. The surface of the ulcer appears irregular with small elevated whitish projections which is due to teeth indentation. On palpation all inspectory findings regarding site, size, shape and extent were confirmed. The growth was rough on palpation, tender on palpation, no bleeding on provocation evident, and base was indurated. The mucosa surrounded by the ulcer appears erythematous. Mouth opening was restricted [inter incisal distance 14mm]. A single right submandibular lymphnodemeasuring approx. 1x1 cm is palpable which is fixed and hard in consistency and tender on palpation.Based on clinical features provisional diagnosis is given as chronic non healing ulcer in right buccal mucosa suggestive of malignancy. Patient was subjected to incisional biopsy and histopathology reveals (Figure 4)well differentiated squamous cell carcinoma of right buccal mucosa.

**Case 3:-**

A 63 yr old male patient reported to the department of Oral medicine and radiology with a chief complaint of ulcer in the tongue for the past 1 month. History revealed sharp teeth in relation to right back teeth region for the past 1 month which was irritating the ulcer on the lateral border of tongue. The growth did not subside in size even after the smoothening of the teeth before one month. Patient had a habit of chewing gutka for the past 30 years. Patient medical history was non contributory. On intra oral examination (Figure 5) presence of a nodular, well defined growth approximately of 3x2cm in size is seen on the right lateral surface of the tongue extending to the ventral surface. The growth is round in shape and well defined, surface is ulcerated. On palpation the growth was firm with indurated borders fixed, and severely tender on palpation. Based on clinical features and etiology a provisional diagnosis of malignant tumour was given. Patient subjected to incisional biopsy and histopathology reveals well differentiated squamous cell carcinoma.

**Case 4:-**

A 65 yr old female patient reported to the department of Oral Medicine and Radiology with a chief complaint of sharp tooth in the left lower back tooth region for the past two months. History revealed traumatization of the left lateral border of the tongue by the sharp teeth and development of an ulcer on the tongue associated with burning sensation and pain in the same region. No history of deleterious habits. Patient was a known hypertensive for the past 5 years and is under regular medication for the same. On intra oral examination (Figure 6) presence of an ulcerative growth of ovoid shape of size approx. 2X2 cm in diameter is seen on the left lateral border of tongue in relation to 37. Severe attrition with sharp margins of entire crown is seen in 37. The edges of the ulcer are raised and slightly everted. Floor of the ulcer appears to be erythematous. The margins are well defined and everted. On palpation the ulcer is firm, tender and margins are indurated. Surrounding area appears normal. Based on clinical features and etiology a provisional diagnosis of chronic non-healing traumatic ulcer in relation to left lateral border of the tongue is given. Patient was subjected to incisional biopsy and histopathology reveals poorly differentiated squamous cell carcinoma.

## Discussion:-

Oral cancer is abroad term that includes various malignant diagnoses that present in the oral tissues.[4,5] The older literature often combines oral cancer and oropharyngeal cancer making the evaluation of epidemiology, pathogenesis and outcomes difficult to access as it is now recognized that oral and oropharyngeal carcinoma must be evaluated individually.[4,5]The oral cavity includes the lips, the labial and buccal mucosa, the anterior two thirds of the tongue, the retromolar pad, the floor of the mouth, the gingiva and the hard palate.[4,5]

**Epidemiology:-**

The incidence of squamous cell carcinomas of the oral cavity differs widely in various parts of the world and ranges from approximately 2-10 per 100,000 population per year.[1]Such differences can to some extent be explained on the basis of environmental differences or lifestyle and habits among certain populations, such as betel quid chewing, snuff dipping or the habit of reverse smoking.[1]The incidence of oral carcinoma in blacks is somewhat lower than in whites, which is mainly due to the low incidence of lower lip cancer in blacks.[1]In most parts of the world the male to female ratio is approximately 2:1 for oral carcinoma, except for carcinoma of the vermilion border of the lower lip. In the latter site there is a strong male predilection. Oral squamous cell carcinomas are mainly found after the fourth decade.[1]

**Oral cancer classification:-[6]**

Oral cancer nomenclature represents basically the histopathological characteristics of the lesion. A classification system was established by the world health organization (WHO)

**WHO classification of oral cancer[6]**

**Epithelial cancer:-**

- Squamous cell carcinoma
- Lymphoepithelial carcinoma

**Salivary gland cancer**

- Salivary gland carcinomas
- Salivary gland adenomas

**Soft tissue cancer:-**

- Kaposi sarcoma

**Hematolymphoid cancer:-**

- Burkitt lymphoma
- Mantle cell lymphoma
- Langerhans cells hystiocytosis

**Secondary tumors/metastatic tumours:-**

**Etiology and risk factors:-**

The incidence of oral cancer is age related, which may reflect time for the accumulation of genetic changes and duration of exposure to initiators and promoters. These include chemical and physical irritants, viruses and hormonal effects. In addition, decreased immunologic surveillance over time may be another explanation to the age relation, such as seen in individuals following solid organ and hematopoietic stem cell transplantations, individuals treated with chemotherapy and HIV infected individuals.[5]

**Tobacco and alcohol:-**

Tobacco products and alcohol are acknowledged risk factors for oral cancer. Tobacco contains potent carcinogens, including nitrosamines, polycyclic aromatic hydrocarbons, nitrosodiethanolamine, nitrosoproline and polonium. Tobacco smoke contains carbonmonoxide, thiocyanate, hydrogen cyanide, nicotine and metabolites of their constituents.Nicotine is a powerful and addicting drug. Epidemiologic studies have reported that up to 80% of oral cancer patients were smokers. In addition to the risk of recurrent and second primary oral cancers is related to continuing smoking after cancer treatment. The effect of smoking on cancer risk diminishes 5 to 10 yrs after quitting. Other forms of tobacco use have been associated with oral cancers. Benign hyperkeratosis and epithelial dysplasia have been documented after short term use of smokeless tobacco products and it is likely that chronic use is associated with an increasing incidence of malignant lesions. The potential risk of oral cancer with cannabis is unclear as data are inconsistent.All forms of alcohol, including hard liquor, wine and beer have been implicated in the etiology of oral cancer. In some studies, beer and wine are associated with greater risk than hard liquor. Several studies identified subpopulations in which alcohol is not arisk factor for oral cancer such as non smoking, non betel chewing subjects.[7]

**Betel (areca) nut:-**

People with a betel quid chewing habit, with or without added tobacco are at a higher risk to develop oral cancer. In parts of Asia where the use of betel nut mixed with lime to form a quid is widespread, the incidence of oral cancer is high and more commonly involves the buccal mucosa. Furthermore, substitutes for betel quid, such as gutka and pan are potential carcinogenic as well.[8]

**Human papilloma virus (HPVs):-**

HPVs are DNA viruses that infect various epithelial surfaces. There are more than 120 types of Human Papilloma Viruses. HPV-16 and HPV-18 are considered high risk subtypes due to their association with malignant tumors. Malignant transformation occurs through the expression of two HPV viral oncogenes, $E_6$ and $E_7$.

**Nutritional factors:-**

Consumption of fruits and vegetables is associated with a reduced risk for oral cancer. This may be due to the antioxidant vitamins C and E and flavinoids. Elevated but inconsistent oral cancer risks have been observed for diets high in eggs and butter and for certain types of meats. Vitamin A may play a role in oral cancer. This hypothesis was supported by the fact that vitamin A may cause regression of premalignant leukoplakia.[1]

**Other risk factors:-**

There is no evidence that denture use denture irritation, irregular teeth or restorations and cheek biting habits are related to oral cancer risk. However, the role of local trauma in the development of oral cancer remain controversial. It is possible that chronic trauma, in the presence of other risk factors promote the transformation of epithelial cells, has been demonstrated in animal studies. One of our case had no habits but only sharp tooth could be the etiology, such cases should require proper documentation in the literature.[10]

High alcohol content in mouthwashes has been implicated in oral cancer in the past. More recent studies suggest no significant trend in risk with increasing daily use and on association between use of mouthwash containing alcohol and oral cancer risk has been found.[10]

In lip cancer, sun exposure, fair skin, pipe smoking and alcohol are identified risk factors.[10]

Patients undergoing allogenic hematologic stem cell transplantation are at an increased risk of developing secondary neoplasms, particularly leukemias and lymphomas which may manifest in the oral tissues.[10]

**Presenting signs and symptoms[7]:-**

- Discomfort is the most presenting symptom
- Patient is aware of the growth in the oral cavity or neck
- Dysphagia, otalgia, limited movement, oral bleeding, neck masses and weight loss may occur with advanced disease
- Loss of sensory function especially where it is unilateral may indicate neural involvement and requires that cancer can be ruled out.
- Tissue changes may include red ,white or mixed lesions, change in surface texture producing a smooth granular ,rough or the presence of mass or ulcerated lesion
- The lesion may be flat or elevated and minimally palpable or indurated
- High risk sites are lowerlip, anterior floor of the mouth, lateral border of the tongue.
- It can present as veruccous carcinoma which can be described as grainy, papillary, verucciform, fungating or cauliflower like.

**Carcinomas can be categorized based on presence of lesion, and its size, nodal involvement and metastasis.**
**TNM Clinical Classification[11,12]**

- **T—Primary tumor** TX Primary tumor cannot be assessed
- TO No evidence of primary tumor Tis Carcinoma *in situ*
- T1 Tumor 2 cm or less in greatest dimension
- T2 Tumor more than 2 cm but not more than 4 cm in greatest
- dimension
- T3 Tumor more than 4 cm in greatest dimension
- T4 Lip: Tumor invades adjacent structures, e.g. through cortical bone, tongue, skin of neck, Oral cavity: Tumor invades adjacent structures, e.g. through cortical bone, into deep (extrinsic) muscle of tongue, maxillary sinus, skin.

**N—Regional lymph nodes** NX Regional lymph nodes cannot be assessed

- NO No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
- N2 Metastasis in a single ipsilateral lymph node, more than 3cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N2a: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
- N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
- N2c: Metastasis in bilateral or contralateral lymphnodes, none more than 6 cm in greatest dimension
- N3 Metastasis in a lymph node, more than 6 cm in greatest dimension
- **M—Distant metastasis** MX Presence of distant metastasis cannot be assessed
- **MO** No distant metastasis
- **M1** Distant metastasis.

| STAGE GROUPING | | | |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T1, T2, T3 | N1<br>N1<br>N0 N1 | M0<br>M0<br>M0 |
| Stage IV | T4, Any T, Any T | N0, N1<br>N2, N3<br>Any N | M0<br>M0<br>M1 |

**Histopathological Grading of Oral Squamous Cell Carcinoma**[11,12]

a) Classic microscopic histopathologic alterations observed with squamous cell carcinoma include:
b) Enlarged nuclei as well as cell size
c) Large and prominent nucleoli
d) Increased nuclear/cytoplasmic ratio
e) Hyperchromatic (dark staining) nuclei
f) Dyskeratosis (premature keratinization of cells)
g) Increased and/or aberrant mitotic activity.

In general, tumors that more closely resemble their native tissues are considered to be well differentiated and tend to have a better long-term prognosis. In contrast, tumors with abundant amounts of cellular and nuclear alterations with little or no resemblance to squamous epithelium or those that lack keratin production may be classified as poorly differentiated tumors. These lesions, also termed as anaplastic or high grade, have an increased propensity for regional metastasis and correlated a poor prognosis. Additional features that favor a more aggressive nature include perineural spread, lymphatic invasion, and tumor extension beyond the lymph node capsule. Hematogenous spread is an uncommon mode of spread for carcinomas.

**Criteria for the Diagnosis of Oral Epithelial Dysplasia:-**

- The diagnosis and grading of oral epithelial dysplasia is based on a combination of architectural and cytological changes

**Mild dysplasia (*Grade-1*):-**

Demonstrates proliferation or hyperplasia of cells of the basal and parabasal layers which does not extend beyond the lower third of the epithelium. Cytological atypia is generally slight with only mild pleomorphism of cells or nuclei. Mitoses are not prominent, and when present are usually basally located and normal.

**Moderate dysplasia (*Grade-2*):-**

Demonstrates a proliferation of atypical cells extending into the middle one third of the epithelium. The cytological changes are more severe than in mild dysplasia and changes such as hyperchromatism, and prominent cell and nuclear pleomorphism may be seen. Increased and abnormal mitoses may be seen, but these are usually located at the basal layers of the epithelium. Architectural changes may be seen in the lower half of the epithelium where there may be loss of basal polarity and hyperplasia leading to bulbous retepegs. However, stratification and maturation are relatively normal, often with hyperkeratosis of the surface epithelium.

**Severe dysplasia (*Grade-3*):-**

There is abnormal proliferation from the basal layer into the upper third of the epithelium. Cytological and architectural changes can be very prominent. All the changes seen in mild and moderate dysplasia are present but in addition there is prominent or even multiple nucleoli present. Prominent and supra basal mitoses are usually evident and abnormal tripolar or star shaped forms may be seen. Apoptotic bodies (cell death) may also be prominent. Architectural changes are severe, often with complete lack of stratification and with deep abnormal keratinization and even formation of keratin pearls. Abnormal forms of retepegs are usual and bulbous retepegs are particularly significant in the diagnosis. Occasional lesions may show prominent acantholysis. Although the epithelium may be thickened, severe dysplasia is sometimes accompanied by marked epithelial atrophy (thinning). This is especially prominent in lesions from the floor of the mouth, ventral tongue or soft palate and may be a feature of lesions which have presented clinically as erythroplakia (red patch). In these cases there may be minimal evidence of stratification or keratinization and atypical cells may be extended to the surface.

## Diagnosis:-

**Biopsy:-**

A definitive diagnosis requires a biopsy of the tissue. Biopsies may be obtained using surgical scalpels or biopsy punches and typically can be performed under local anesthesia. Incisional biopsy is the removal of a representative sample of the lesion; excisional biopsy is the complete removal of the lesion, with a border of normal tissue. The clinician can obtain multiple biopsy specimens of suspicious lesions to define the extent of the primary disease and to evaluate the patient for the presence of possible synchronous second malignancies. Punch biopsy may be used for either incisional biopsy or excision of a small lesion at an accessible site. The lateral tongue and buccal mucosa are

appropriate sites for punch biopsy, as it must be feasible for the device to approach the mucosal surface perpendicularly. The punch is placed on the lesional tissue, and a downward, twisting motion is applied[13]

**Vital tissue staining using toludine blue:-**
Vital staining with toludine may be used as an adjunctive aid in assessing potentially malignant oral mucosal lesions. Toludine blue is a meta chromatic dye, which has an affinity to bind with DNA. Toludine blue can be applied directly to suspicious lesions or used as an oral rinse. Positive retention of toludine blue may indicate the need for biopsy or assist in identifying the site of biopsy. False positive dye retention may occur in inflammatory and ulcerative lesions, but false negative retention is uncommon

**Computer assisted cytology of oral brush biopsy specimens:-**
The oral brush biopsy with computer-assisted analysis is simple to perform, non-invasive, and has the potential to overcome many of the obstacles that have hindered early detection of early stage cancers and dysplasia. In published studies in which oral lesions were subjected to both brush biopsy and scalpel biopsy concomitantly, the brush biopsy was found to have a sensitivity and a specificity of greater than 90% in identifying dysplasia and carcinoma

**Management:-**
There are three recognized treatment modalities for managing head and neck cancers: surgery; radiotherapy and chemotherapy stage I and stage II cancers can be managed either by surgery or radiotherapy. However, stage III and stage IV cancers are managed using a combination of radiation therapy and surgery.

**Surgical management:-**
Surgical management aims at complete removal of the primary as well as the metastatic nodes. It is never used as a palliative mode of treatment. Criteria for choosing surgical management are; tumors which are non-sensitive to radiation, tumors involving bone, recurrent tumors in sites that have been previously irradiated, to reduce bulk of tumor prior to radiation therapy, where side effects of surgery are expected to be less significant than those associated with radiation and when nodes are to be removed.[14]

**Radiation therapy:-**
Radiation therapy plays an important role in the management of head and neck cancer. The radiation disrupts the electron orbital structure of tissue atoms, which subsequently damages individual cells and tissues. Cells are more vulnerable to injury when they are in the process of dividing and multiplying. The radiation may damage the DNA directly or indirectly by inducing the formation of free radicals. In addition to anti tumor effects, ionizing irradiation causes damage in normal tissues located in the field of radiation. This becomes particularly evident in the head and neck region, a complex are composed of several dissimilar structures that respond differently to radiation; mucosal linings, skin covering, subcutaneous connective tissue, salivary gland tissue, teeth and bone/cartilage. Acute changes produced by radiotherapy are observed in the oral mucosa (erythema, pseudo membrane-covered ulceration), salivary glands (hypo salivation, changed saliva composition), taste buds (decreased acuity) and skin (erythema, desquamation) [15]

**Chemotherapy:-**
Chemotherapy is provided as an induction therapy before local therapies. It is also an adjunctive modality for other cancers. The objective of induction chemotherapy is to promote initial tumor reduction and to provide early treatment of micro metastases. The goal of chemotherapy is to eradicate the rapidly growing cells of the tumor and modify their growth. Chemotherapeutic agents affect the rapidly dividing cells of the target tumor and the lining epithelium, the oral ecology and the vascular, inflammatory and healing responses of the oral cavity. These alterations may result in mucositis and ulceration of the mucosa. Chemotherapeutic agents also target the hemopoietic cells of the bone marrow, resulting in anemia, thrombocytopenia and leucopenia.[15]

**Drugs used in oral cancer chemotherapy:-**
Various drugs are seen in cancer chemotherapy of the head and neck such as **cetuximab**(epidermal growth factor receptor inhibitor), **docetaxel, cisplastin, 5-flurouracil, leucovorin, methotrexate and bleomycin**.

**Methotrexate** is an anti metabolic and an inhibitor of folic acid metabolism. The rationales for intra arterial route are that, prolonged contact of the tumor cell population with the anti metabolite will result in sequential death of

cells as the cells enter the most fragile metabolic phase of cellular division. Systemic methotrexate is given in intermittent weekly or semiweekly IV injection of 40-60 mg/$m^2$ of body surface area.
Methotrexate is known to cause bone marrow suppression, mucositis, anorexia, nausea, emesis, renal toxity and hepatic dysfunction.

**Bleomycin** acts by interfering with the DNA function of the cell. The ideal dose of bleomycin is 0.25-0.50 unit/kg given weekly or twice weekly.

Care should be taken not to exceed a dose of 400 units and this dose can cause pulmonary toxicity and death. Some patients may complain of skin rashes and erythema. The greatest advantage with bleomycin is its lack of causing myelo suppression.

**Cisplastin** is a relatively new drug which acts by altering DNA structure. It is given IV (80-120 mg/$m^2$, IV for 3-4 weeks).

It is important to maintain adequate hydration before the drug is administered.

**Fluorouracil** is usually administered along with cisplastin. It acts by interfering with the cellular metabolism. The standard dosage is 1,000 mg/$m^2$/day.
Stomatitis is a common side effect. Bone marrow suppression is seen when weekly or daily bolus injections are administered.

Oral Squamous Cell Carcinoma cases requires attention of clinician along with an analysis of etiologic factors associated with the disease so that early detection could help in identifying the disease at early stage, to ensure good prognosis.

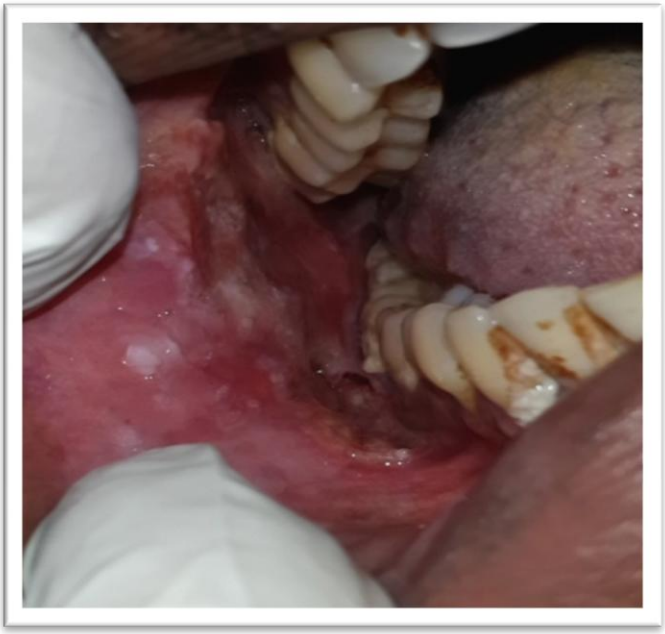

**Figure 1:-** Ulcerated Region evident on the Right Buccal Mucosa

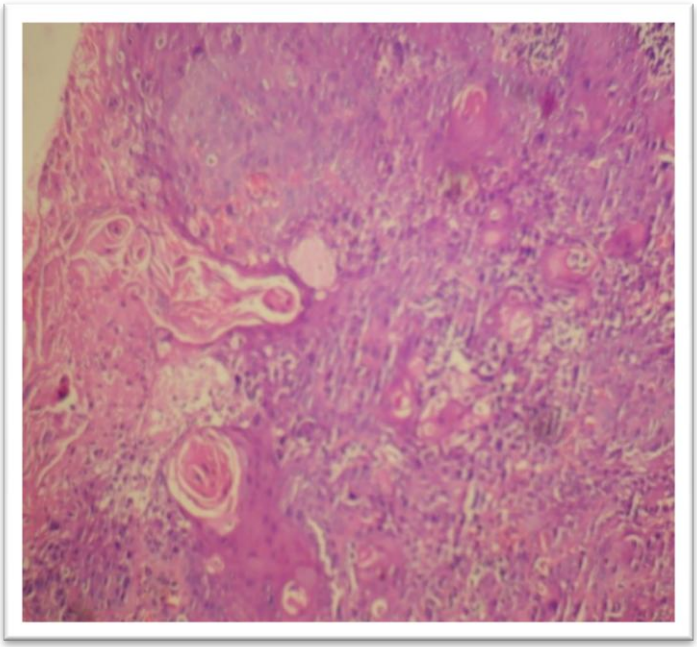

**Figure 2:-** The Given H&E Stained Section Shows Sheets of Epithelial Cells Infiltrated in Connective Tissue Stroma and Epithelial Pearl Formation is also Evident.

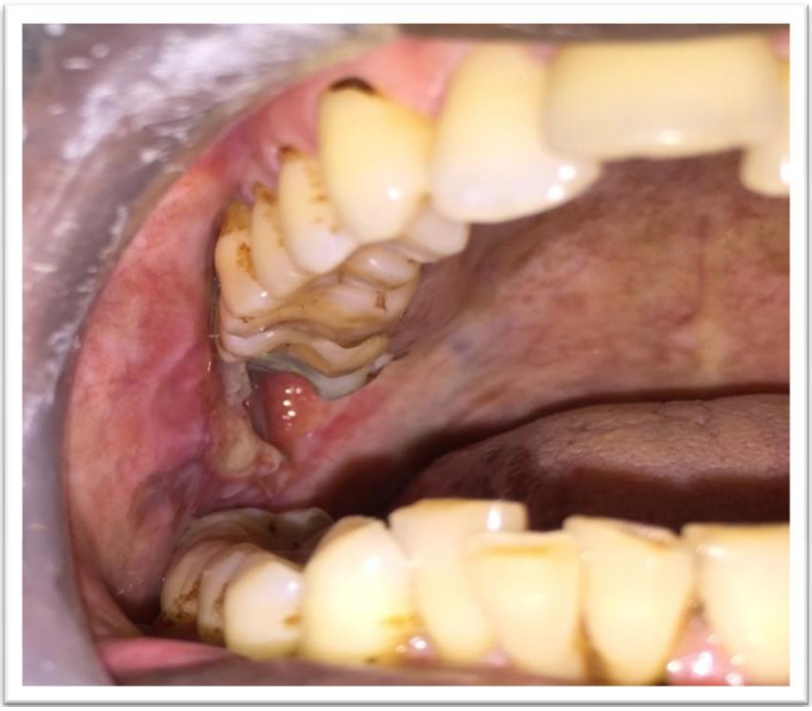

**Figure 3:-** Ulcer Evident on the Posterior Aspect of Right Buccal Mucosa

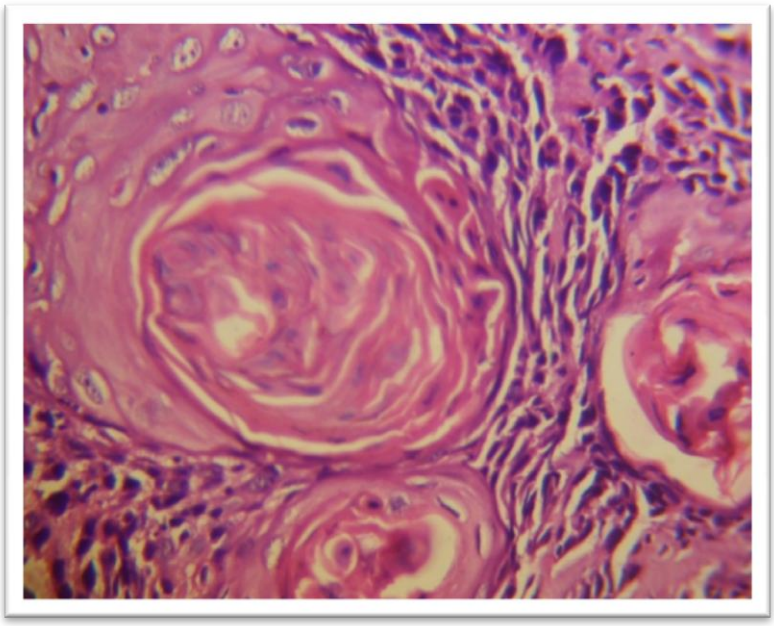

**Figure 4:-** Keratin pearl formation is evident

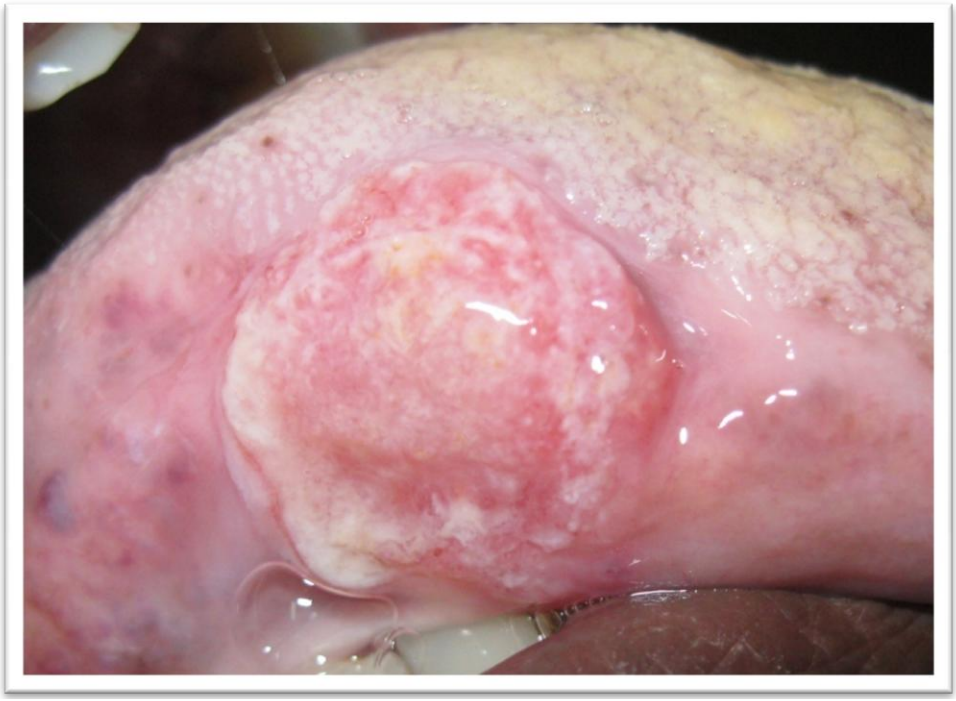

**Figure 5:-** Nodular Well Defined Growth Evident on Right Lateral Border of Tongue

**Figure 6:-** Ulcer on the Left Lateral Border of Tongue

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