Oral medicine

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Oral cancer

Carcinogenesis: abnormal behavior of cells resulting in changes of their morphology and function

Premalignant lesions

Leukoplakia A white plaque that does not rub off and cannot be clinically identified as another entity. Most cases of leukoplakia are a hyperkeratotic response to an irritant and are asymptomatic, about 20% of leukoplakic lesions show evidence of dysplasia or carcinoma (mostly floor of mouth and ventral tongue)

Erythroplakia A red lesion that cannot be classified as another entity. Far less common than leukoplakia, such lesions have a flat, macular, velvety appearance and may be speckled (highest rate of transformation) with white spots representing foci of keratosis.

Lichen planus It is frequently difficult to differentiate lichen planus from epithelial dysplasia; one study found that 24% of oral lichen planus cases had criteria for epithelial dysplasia.

submucous fibrosis is a chronic, complex, premalignant lesion of the oral cavity, characterized by epithelial inflammatory reaction and progressive fibrosis of the submucosal tissues, as the disease progresses, the jaws become rigid to the point that the person is unable to open the mouth

Screening and Early Detection

Screening for oral cancer should include a thorough history and physical examination. The clinician should visually inspect and palpate the head, neck, oral, and pharyngeal regions. This procedure involves digital palpation of neck node regions, bimanual palpation of the floor of mouth and tongue, and inspection with palpation and

observation of the oral and pharyngeal mucosa with an adequate light source; mouth mirrors are essential to the examination. Forceful protraction of the tongue with gauze is necessary to visualize fully the posterior lateral tongue and tongue base, in addition, lymph nodes in the head and neck area-particularly along the jugular chain-must be palpated

Diagnosis

Any oral lesion that does not regress spontaneously or respond to the usual therapeutic measures should be considered potentially malignant until histologically shown to be benign. A period of 2-3 weeks is considered an appropriate period of time to evaluate the response of a lesion to therapy before obtaining a definitive 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 second malignancies.

Cytology Under certain conditions, exfoliative cytology (cell scrapings or brush cytology) serves as an adjunct to clinical diagnosis, as it enables more extensive screening and provides microscopic material if there is a delay in or contraindication to biopsy. However, cytologic smears are used infrequently, and patients are not treated on the basis of cytologic findings alone. Smears are most helpful in differentiating inflammatory conditions, especially candidiasis, from dysplastic or neoplastic surface lesions. Cytology may also be helpful when ulcerations following radiation are suspicious and biopsy is delayed.

Fine needle aspiration (FNA) biopsy of subsurface masses is also an accepted diagnostic test, one that has increased in popularity over the past few years. This technique is extremely useful in evaluating clinically suspicious changes involving salivary glands and lymph nodes. It expedites diagnosis and staging and avoids incisional or excisional biopsies that may interfere or complicate definitive treatment. When used by a skilled clinician, fine needle aspiration can often be the best way to establish a definitive diagnosis of unexplained masses of the neck or salivary glands. It is also valuable in following up cancer patients with suspicious enlargements.

Toluidine blue (vital staining) also is a useful adjunct to clinical examination and biopsy. The mechanism is based on selective binding of the dye to dysplastic or malignant cells in the oral epithelium. It may be that toluidine blue selectively stains for acidic tissue components and thus binds more readily to DNA, so neoplastic cells will get deeper stain than normal because its DNA is larger and more active.

Immunohistochemical Techniques

The use of immunohistochemical techniques to establish a definitive diagnosis has expanded during the past decade and continues to be refined. These diagnostic tests help to establish a definitive diagnosis when, by routine histopathology techniques, a lesion appears morphologically benign or its classification is in doubt. Research on the biochemical, genetic, and cellular levels should yield information that will identify high-risk groups for many types of cancer including oral cancer.

Clinical Photodetection

Photodynamic therapy, also known as PDT, and photodetection of cancer may be useful in the oral cavity. Two important variables that must be considered are the uptake of the dye and the dye contrast by normal and neoplastic tissue after injection.

Imaging the Oral Cavity

A diagnostic imaging evaluation consisting of either computer tomography (CT) scanning or magnetic resonance imaging (MRI) is also used to assess the extent of local and regional tumor spread, the depth of invasion, and the extent of lymphadenopathy. CT is superior in detecting early bone invasion and lymph node metastasis, but MRI is preferred for assessing the extent of soft tissue involvement and for providing a three-dimensional display of the tumor. MRI is also the preferred technique for imaging carcinoma of the nasopharynx or lesions involving paranasal sinuses or the skull base.

Diagnostic imaging often detects subsurface masses and intraosseous lesions. Although imaging of pathologic lesions does not produce a definite diagnosis, it frequently helps to define the extent of the tumor. For example, patients who have an unexplained neck node and a negative head, neck, and oral examination may undergo CT scanning followed by a biopsy of the nasopharynx or base of tongue that reveals a suspicious area or tissue change.

Both CT and MRI have limitations as well as advantages, a fact that frequently makes them complementary rather than competitive studies. The advantages of CT include its rapid acquisition time (2-3 seconds per section), patient tolerance, relatively low cost, and superior osseous detail compared with MRI. However, the soft-tissue contrast resolution of CT is relatively poor, which makes it difficult to distinguish between tumor and normal muscle. CT also may require the administration of intravenous contrast material to differentiate vessels from lymph nodes, thereby increasing the risk of an allergic reaction. In addition, CT is frequently degraded by scattered artifacts because of metallic dental appliances.

Staging of the Disease

The stage of the disease depends on several factors, including the size of the primary lesion, local extension, lymph node involvement, and evidence of distant metastasis. Tumor size, the organ or tissue affected, and the extent of spread are considered to be

the best indicators of the patient's prognosis. This system has 3 basic clinical features: the size (in centimeters) of the primary tumor; the presence, number, size, and spread (unilateral or bilateral) to the local lymph nodes; and the presence or absence of distant metastasis.

Tumor-Node-Metastasis (TNM) Staging System for Oral Carcinoma

Primary Tumor (T)

TX Primary tumor cannot be assessed

T0 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)

T4 (oral cavity) Tumor invades adjacent structures (e.g.,

through cortical bone, into deep

[extrinsic] muscle of

tongue, maxillary sinus, skin)

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greater dimension

N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; in bilateral or contralateral lymph nodes, none more than 6 cm in

greatest dimension

N2a Metastasis in 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 lymph nodes, none more than 6 cm in greatest dimension

N3 Metastasis in a lymph node more than 6 cm in greater dimension

Distant Metastasis (M)

MX Presence of distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

The individual clinical parameters in the TNM classification system are grouped to determine the appropriate disease stage, stages are ranked numerically from 0 (which has the best prognosis) to IV (the worst prognosis). In general, oral staging classifications do not use histopathologic findings except to determine the definitive diagnosis.

TNM Clinical Stage Grouping

STAGE 0	*Tis*	*N0*	*M0*
STAGE I	*T1*	*N0*	*M0*
STAGE II	*T2*	*N0*	*M0*
STAGE III	*T1*	*N1*	*M0*
	T2	*N1*	*M0*
	T3	*N0,N1*	*M0*
STAGE IV	*T4*	*N0,N1*	*M0*
	Any T	*N2,N3*	*M0*
	Any T	*Any N*	*M1*

Tumors of Epithelial tissue origin

- **Binign tumors of epithelial tissue**

Papilloma: It seems to be associated with papilloma virus (HPV 6 & 11), the one causative in common skin warts (verruca vulgaris). All HPV lesions are infective, but oral papilloma do not seem to be contagious. Clinical features: It is an exophytic, painless growth made up of numerous, small finger-like projections, which result in a lesion with a roughened or verrucous. Intraorally it is found most commonly on the tongue, lips, buccal mucosa, gingiva & palate**.**

- ***Malignant tumors of epithelial tissue***

Basal cell carcinoma: Most frequently develops on the exposed surfaces of the skin, face and scalp in middle aged or elderly fair-skinned persons**.** It is slow growing and rarely metastasizes but can cause significant local destruction

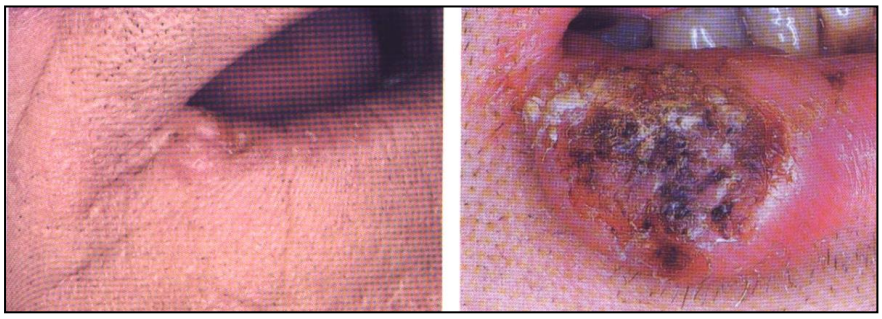
Etiology UV light (chronic sun ray exposure), radiation like X-rays, Chemicals like arsenic Immunosuppression

Clinical features : Most frequently in the fourth decade of life, Male :female =2:1. Most frequently seen on the middle third of face .Does not arise from the oral mucosa so is not seen intraorally except for invasion from an adjacent skin surface.

Squamous cell carcinoma: (SCC)

SCC of the lip: Chiefly occurs in the elderly men , in the lower lip. One of the most common cause is pipe smoking.

Clinical features :Usually begins on the vermilion border of the lip to one side of the midline. Often starts as a small area of thickening, induration, and ulceration or irregularity of the surface. Generally slow to metastasize.



SCC of the tongue:

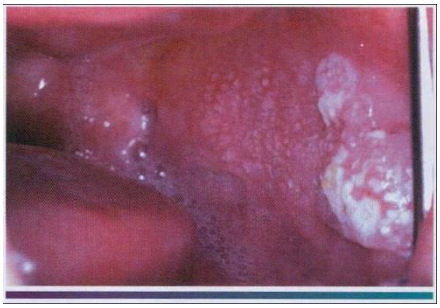
Clinical features : It presents as a painless mass or ulcer, which might become painful if secondarily infected. May begin as a superficially indurated ulcer with slightly raised borders and may develop into a fungating exophytic mass or infiltrate the deep layers of the tongue, producing fixation and induration. Develops on the lateral border or ventral surface of the tongue. Lesions on the posterior portion are usually of a higher grade of malignancy, metastasize earlier and offer a poorer prognosis, especially because of their inaccessibility for treatment.

SCC of the floor of the mouth

Smoking, especially pipe or cigar is the most important in its etiology.

Clinical features :An indurated ulcer of varying size, situated on one side of the midline. More frequently in the anterior portion of the floor. Because of its location, early extension into the lingual mucosa of the mandible, into the mandible proper, into tongue, and even into the submandibular and sublingual glands has been recorded. Sometimes it may produce limitation of motion of the tongue or slurring of speech. Contra lateral metastasis is common as the primary lesion occurs most commonly near the midline, where lymphatic cross-drainage occurs.

SCC of buccal mucosa It happens in people with chewing tobacco habit for years.



Clinical features : Usually develops along or inferior to a line opposite the plane of occlusion. Lesion is often a painful ulcerative one where induration and infiltration of deeper tissues is common. Some lesions may even be exophytic. Metastasis is very frequent.

Treatment : Combined use of surgery & radiation.

SCC of gingiva: Its similarity to common dental infections has frequently led to delay in diagnosis or even to misdiagnosis.

Clinical features :

More commonly found in the mandibular gingiva. Initially presents as an area of ulceration. Arises more commonly in edentulous areas. Fixed gingiva is more commonly involved than the free gingiva. Erosion of the underlying bone is frequent. Metastasis is more common from the mandibular gingiva.

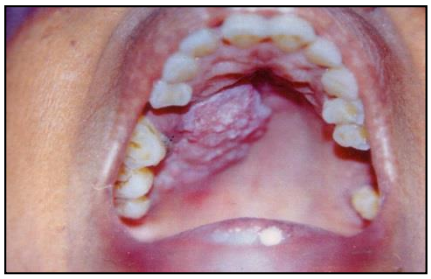
SCC of the palate: Not a common lesion of the oral cavity.

Clinical features :

Poorly defined, ulcerated, painful lesion on one side of the midline. It frequently crosses the midline and may extend laterally to include the lingual gingiva or posteriorly to involve the tonsilar pillar or even the uvula. It may invade the bone or occasionally the nasal cavity, while infiltrating lesions of the soft palate may extend into the nasopharynx.

Metastasis occurs quite commonly.

Treatment: Both surgery and radiation are used. Prognosis is not very good.



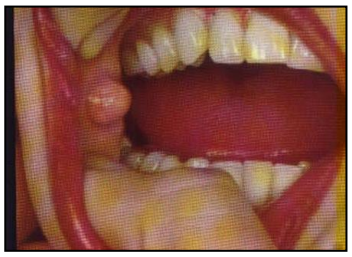
Verroucus carcinoma: A warty variant of SCC, It is a predominantly exophytic overgrowth of well differentiated keratinizing epithelium having minimal atypia, and with locally destructive pushing margins at its interface with c.t.

Clinical features : Usually in elderly, on an average between 60-70 years. Most commonly on buccal mucosa and gingiva. Appears papillary, with a pebbly surface, which is sometimes covered by a white leukoplakic film. Lesions on the gingiva may grow into the soft tissue and invade and destroy the underlying bone. Regional lymph nodes are enlarged and tender, simulating metastatic tumor. Pain and difficulty in mastication are the common complaints. This disease has a high occurrence rate in tobacco chewers, smokers or snuffers, or in patients having ill fitting dentures. Growth is usually slow and metastasis occurs late, if at all. It may become more aggressive if irradiated.

Benign tumors of the connective tissue

Oral fibroma: Most common benign soft tissue neoplasm of the oral cavity.

Clinical features :



May occur at any oral site, most commonly on the buccal mucosa along the plane of occlusion. Appears as an elevated nodule of normal color with a smooth surface, and a sessile or pedunculated base. A well defined, slow growing lesion, most common in the third, fourth, and fifth decades. Females are affected twice more commonly than the males.

Lipoma: Rare intraoral tumor though it is common in other areas, esp. subcutaneous tissues of the neck. Benign slow growing neoplasm composed of mature fat cells.

Clinical features : Usually found in adults. Intraorally they occur in the tongue, floor of mouth , buccal mucosa and gingiva. Morphologically intraoral lipomas can be classified as DIFFUSE FORM affecting the deeper tissues, and a SUPERFICIAL & ENCAPSULATED FORM. Superficial form appears as a single or lobulated, sessile or pedunculated, painless lesion. it presents as a yellowish surface discoloration and well encapsulated. it is freely movable beneath the mucosa

Tumor like lesions of connective tissue

Peripheral giant cell granuloma: It is relatively common tumor like growth of the oral cavity. It probably does not present a true neoplasm but rather is a reactive lesion caused by local irritation or trauma. The role of trauma has been emphasized by some investigators who believe it to be considerable importance in the etiology of these lesions. The trauma is caused chiefly by tooth extraction, denture irritation or chronic infection.

Clinical features: It can develop at any age but show peak prevalence in the 5th and 6th decades of life. Approximately 60% cases occur in females. Mandible is affected more commonly than maxilla. But it may develop anteriorly or posteriorly. It occurs exclusively on the gingiva or edentulous alveolar ridge, presenting as red or reddish blue nodular mass. Most lesions are smaller than 2 cm in diameter. The lesion can be sessile or pedunculated and may or may not be ulcerated.

Radiographic appearance: Although peripheral giant cell granuloma develops within the soft tissue, “cupping” resorption of underlying bone sometimes is seen.

Treatment: local surgical excision down to the underlying bone with removal of source of irritation.

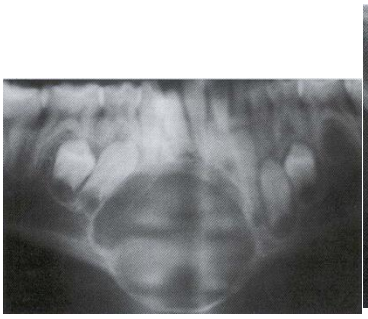
Giant cell granuloma

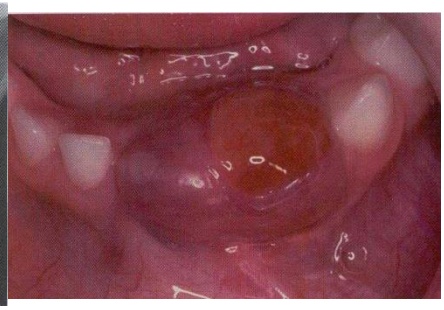
Clinical & radiographical features: majority of giant cell granulomas are noted in females , and approximately 70% arise in the mandible. Lesions are more common in the anterior portions of the jaws, and mandibular lesions frequently cross the midline, asymptomatic and first come to attention during a routine radiographic examination or as a result of painless expansion of the affected bone. A minority of cases, *however, may* be associated with pain, paresthesia, or perforation of the cortical bone plate, occasionally resulting in ulceration of the mucosal surface by the underlying lesion.

Based on the clinical and radiographic features, several groups of investigators have suggested that central giant cell lesions of the jaws may be divided into two categories

1- Nonaggressive lesions make up most cases, exhibit few or no symptoms, demonstrate slow growth, and do not show cortical perforation or root resorption of teeth involved in the lesion.
2- Aggressive lesions are characterized by pain , rapid growth. cortical perforation. and root resorption. They show a marked tendency to recur after treatment

Radiographically, central giant cell lesions appear as radiolucent defects, which may be unilocular or multilocular. The defect is usually well delineated, but the margins are generally noncorticated





Malignant tumors of connective tissue

Kaposi's sarcoma

A multicentric proliferation of vascular and spindle cell components.

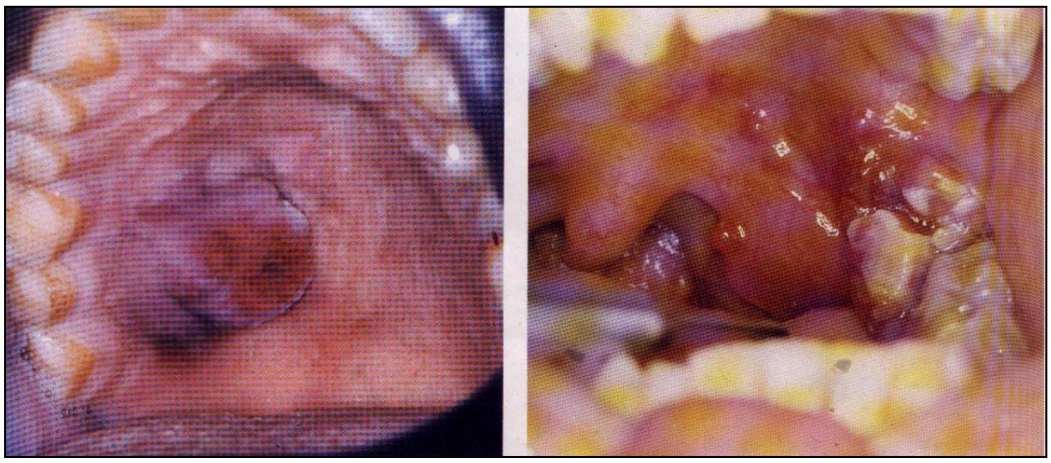
Now considered as a viral associated tumor, it is not clear whether it is a true neoplasm or a simple hyperplasia. It is currently incriminated with HIV/AIDS, though HIV does not seem to be the direct cause.

Etiology

Is unknown. It has been suggested that the combined effect of various infectious agent, host factors and environmental factors encourage Kaposi's sarcoma's proliferation. The evidence also suggests that the disease is promoted by the effects of immonosuppression and immune activation, possible combined with a sexually transmissible infectious agent. Also herpes virus like DNA sequences, HHV 8 or KSHV has been isolated from lesions and in Kaposi's sarcoma-derived cell cultures.

AIDS related kaposi's sarcoma

Approximately 40% of homosexual AIDS patients will develop Kaposi's sarcoma, often as an early sign of the disease. Patients are usually young adults or early middle aged males. Oral lesions can occur on any mucosal surface but have a strong predilection for palatal and gingival mucosa. Early lesions are flat and slightly blue, red or purple plaques, and may be completely asymptomatic. With time lesions become more deeply discolored, surface papules and soft nodules develop, may become exophytic and ulcerated, and may bleed. Cervical lymph nodes and salivary gland enlargement may also be seen. Patient may have oral candidiasis and AIDS related gingivitis as well. These lesions may interfere with eating and speaking, cause tooth loss or compromise the airways.



Disease Progression

Oral malignant tumor spread primarily by local extension and somewhat less often by the lymphatics. The extent of tumor invasion depends upon the anatomic site, the tumor's biologic aggressiveness, and host response factors.

The lymphatic system is the most important and frequent route of metastasis. Usually the ipsilateral cervical lymph nodes are the primary site for metastatic deposits, but occasionally contralateral or bilateral metastatic deposits are detected. The risk for lymphatic spread is greater for posterior lesions of the oral cavity, possibly because of delayed diagnosis or increased lymphatic drainage at those sites, or both.