Oral Medicine

Benign, Premalignant & Malignant Lesions of The Oral Cavity
II

Lecture 22

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Oral Cancer

Over 90% of malignant neoplasms of mouth are squamous cell carcinoma arising from mucosal epithelium.
Most reminder are adenocarcinoma of minor salivary glands, and only a few are undifferentiated or metastases.
Oral cancer is an aged-related disease and 98% of patients are over the age of 40 years and it is more common in males than females.

Aetiology

The etiology of malignancy is complex & multifactorial.
Oral cancer is age related disease, 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.

Tobacco products and alcohol are the risk factors for oral cancer. 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 developing primary cancers, the risk of recurrent and second primary oral cancers is related to continuing smoking after cancer treatment.

Alcohol have been implicated in the etiology of oral cancer.

The combined effects of tobacco and alcohol result in a synergistic effect on the development of oral cancer which may include dehydrating effects of alcohol on the mucosa, increasing mucosal permeability, and the effects of potential carcinogens in alcohol or tobacco as well as influence central nervous system activity.

In addition, betel nut, human papilloma virus and nutritional factors are predisposing or precipitating factors.

Nutritional factors such as consumption of fruits and vegetables which is associated with a reduced risk for oral cancer.
This may be due to the antioxidant vitamins C and E and flavonoids. Vitamin A may play a protective role in oral cancer.

The WHO has listed several oral conditions as having the potential to transform into oral cancer, including leukoplakia, erythroplakia, actinic cheilitis, and submucous fibrosis.

Carcinoma in situ

Is cancer of the oral epithelium which is confined to the epithelial layer.
It presents most commonly as a persistent red plaque (erythroplakia) or a mixed white and red plaque. It may also appear as a white plaque.
Complete removal is the treatment. When completely removed, the prognosis is excellent, although the patient is at increased risk of developing new lesions at other locations on the oral mucosa.

Squamous cell carcinoma

Is the most common malignant neoplasm of the oral cavity. Tobacco and alcohol use and human papilloma virus infection have been identified as risk factors, but squamous cell carcinoma can occur in patients with no known risk factors.

Squamous cell carcinoma can occur anywhere on the oral mucosa, but is most common on the ventral and lateral surfaces of the tongue, floor of the mouth, soft palate, tonsillar pillar area, and retromolar trigone areas.

Early squamous cell carcinoma lesions appear as surface lesions rather than soft tissue enlargements.

They are almost invariably non-painful, and thus patients do not know they have a lesion.

Early lesions may be white rough epithelial thickening lesions, red persistent non-painful lesions, or a combination of the two.

It is important to recognize squamous cell carcinoma in its early stages when cure is possible without disfiguring surgery.

The main treatment for oral squamous cell carcinoma is complete surgical excision. Lymph node dissection is performed when lymph nodes are involved.

As carcinoma enlarge it may develop into raised nodule or become ulcerated.
Induration results from inflammation and fibrosis and infiltration of the tissues.

By the time the carcinoma has formed an indurated ulcer with the typical rolled border, it will has present for some time, diagnosis at this late stage is associated with very poor prognosis.

Ulceration may be associated with soreness or stinging pain when sharply flavored food is eaten.

Pain is of no value in the diagnosis, but it typically severe in late stages.
Bleeding either spontaneously or to mild trauma is also a late feature.

Oral cancer sites

The lower lip is the most common frequent site of oral cancer overall, while the tongue is the most frequent affected site within the mouth .

In the oral cavity the majority of cancers are concentrated in lower part of the mouth particularly the lateral borders of tongue, the adjacent floor of the mouth and lingual aspect of the alveolar margin forming U shaped area extending back toward the oropharynx, this area account of 20% of the interior of the oral cavity but 70% of oral cancer concentrated there.

This distribution may be due to the likelihood that carcinogens could pool and concentrated in the lower mouth before swallowing and for the same reason the hard palate and dorsum of the tongue are very rarely affected.

Carcinoma of the lip

The lip is the common site for oral cancer but infrequently seen in dental practice, because it being visible and easily recognized at a very early stage and so has a better prognosis than intra-oral cancer.
The usual site is the vermillion border of the lower lip to one side of the midline, men of middle aged or over are predominantly affected.

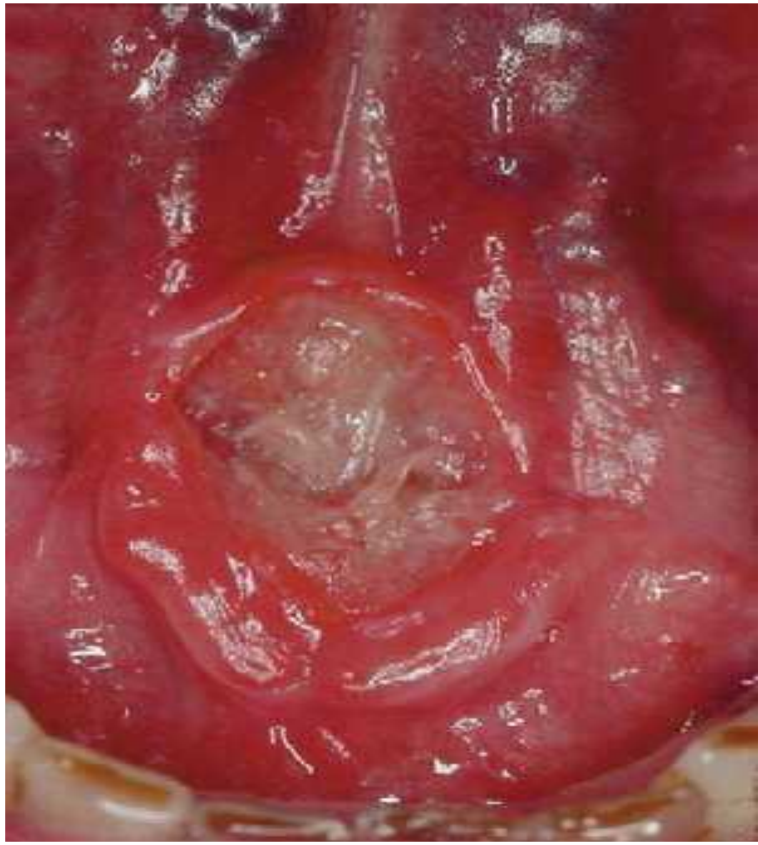
Clinically : It is common early presentation as an area of thickening, induration, crusting or shallow ulceration of the lower lip, less than centimeter in diameter.
Advanced, neglected tumor are unlikely to seen now.
Spread to lymph node tend to be slow, the submental lymph nodes are usually the first to be affected.

Carcinoma of the tongue and floor of mouth

The anterior part of the tongue particularly the lateral border and the adjacent ventral tongue and floor of mouth are frequently involved.

Early presentation with an ulcer 2 cm or more in diameter.

In more advanced diseases the usual picture of a typical malignant ulcer several centimeters in diameter, hard in consistency with rolled or irregular raised edges and a rough infected floor which bleed readily.
As growth proceeds, the carcinoma become fixed to the surrounding tissues and infiltrate the tongue.
Which become progressively stiffer and more painful, eating, swallowing and talking become difficult.



By this time the pain usually the main symptom and may radiate widely.
The lymph node become involved, affected lymph node enlarged and hard, the surface become irregular and fixed to deeper tissues and skin.

Carcinoma of the alveolar ridge, cheek and palate

These show the same features as carcinoma else where.

Carcinoma of the buccal mucosa is particularly associated with betel quid chewing.

Carcinoma of the alveolar ridge and palate are more erode bone at an earlier stage making treatment more complex.

Spread of carcinoma

Carcinoma invades adjacent tissue by direct extension.
Bone initially forms a barrier but is eventually destroyed, usually by superficial erosion, so that it can invade along the medullary cavity.
Metastatic spread of oral carcinoma is primarily via lymphatics to the regional lymph nodes.

The specific sites of metastasis is depend on the drainage of the tumor sit, but because most carcinomas arise posteriorly in the lower mouth , the submandibular and juglodigastric nodes are most frequently involved.
Lymphatic drainage from the tip of the tongue is to the submental nodes and then to the juglo-omohyoid group, low down in the neck.
Dorsum and lateral sides of the tongue, drainage to the submandibular nodes and then to the juglodiagastric group.

Metastatic carcinoma is initially limited to the affected lymph node but in time, spreads through the capsule into the tissues of the neck .

Excision is then difficult and the chances of survival are diminished.
This extra-capsular spread is evident clinically as fixation of the node.

Management

It is complex and depends on the age and medical condition of the usually elderly patient as well as it's exact site, degree of spread (stage) and histological type.

Preoperative assessment

The first stages in management are to identify the type, spread and stage of the carcinoma and to evaluate morbidity.
Spread is assessed by clinical examination and imaging, while biopsy of the carcinoma provides information on the degree of differentiation and pattern of spread.

Imaging

Routine radiograph, computed tomography CT, nuclear scintiscanning, magnetic resonance imaging MRI and ultrasonography can provide evidence of bone involvement and can indicate the extent of some soft tissue lesions.

Positron emission tomography PET using the radiolabeled glucose analog18-fluorodeoxyglucose (FDG) offers a functional imaging approach for the entire body to detect of cancer and the evaluation of cancer treatment, through measures metabolic activity of the cells of body tissues.

Histopathologic examination is required for diagnosis such as: fine needle aspiration, brush biopsy, incisional and excisional biopsy.

Dysplasia or atypia describe a range of cellular abnormalities that include changes in cell size and morphology, increased mitotic figures, hyperchromatism and alteration in normal cellular orientation and maturation.

When the abnormality involves the full thickness of the epithelium with intact basement membrane, the diagnosis carcinoma in situ. when basement membrane is violated the diagnosis squamous cell carcinoma.

Well-differentiated carcinoma may retain some anatomic features of epithelial cells and may retain the ability to produce keratin, whereas poorly differentiated carcinoma loss the anatomic pattern and function of epithelium.

TNM staging for oral carcinoma

The stage of disease is critical to survival, therefore staging system is used to plan the treatment. So every oral carcinoma patient should be staged according to TNM staging system.
Each carcinoma is given score for size (T), lymph node metastasis (N) and distant blood-borne metastasis (M).

T1 < 2cm greatest dimension
T2 2-4 cm greatest dimension
T3 > 4 cm greatest dimension
T4 Extending to adjacent structures e.g bone, sinus, skin
N0 No regional lymph node metastasis
N1 One ipsilateral node < 3cm diameter
N2 Ipsilateral or contralateral nodes 3-6 cm diameter
N3 Lymph node metastasis > 6 cm diameter
M0 No distant metastases
M1 Distant metastasis e.g liver, lung

Stage 1	T1	N0	M0
Stage 2	T2	N0	M0
Stage 3	T1,T2	N1	M0
	T3	N0	M0
Stage 4	Any T4		
	Any N2 or N3		
	Any M1		

Treatment

Most intra-oral carcinomas are treated by surgery combined with radiotherapy.

Surgery alone is indicated in:

1. All accessible and small carcinomas of the tongue that may be easily excised.
2. Tumors involving bone because of the risk of later radionecrosis.
3. Tumors lack sensitivity to radiation such as pleomorphic adenoma.
4. Recurrent tumor in areas that have previously received radiotherapy.
5. Verrucous carcinoma.

When surgery is used it's usually performed first, unless there has been a poor response or recurrence. The aim is to excise the carcinoma with a wide a margin as possible, ideally1cm or more.

Failure of surgery may due to :

1. Incomplete excision of the tumor.
2. Unrecognized lymphatic, hematogenous, neural or perinural spread.

Surgery is contraindicated :

1. When adequate surgical margins are required but may not attainable due to size and location of the tumor.
2. When surgery result in sacrifice of structure which have important esthetic and functional consideration.

Irradiation provides more acceptable cosmetic and functional result than major surgery but involves considerable discomfort during a long course of treatment and has unwanted effects in the long term.

Radiotherapy usually involves exposure to beams of x-rays or gamma-rays from x-ray generators or radioactive isotopes such as cobalt .

Ionizing radiation damages normal as well as neoplastic tissue, damage to the surrounding tissues is limited by fractionating the dose over many visits and by applying external beams from many angles, but avoiding radiosensitive tissues such as the eye and bone.

Unwanted effects of radiotherapy to the oral region

During treatment
-- Severe xerostomia
-- Mucositis and ulceration
-- Acute candidosis
-- Skin erythema

Long term
-- Xerostomia
-- Mucosal and skin atrophy
-- Risk of osteomyelitis (osteoradionecrosis)
-- Scaring and fibrosis of tissues
-- Cataract if eye irradiated (e.g antral carcinoma)
-- Risk of late radiation-induced malignancy.

Chemotherapy is less used, it alone gives a good initial control but relapse will always occur without surgery or radiotherapy.
For best effect is carried out concomitantly with radiotherapy and gives approximately 10% improvement in survival at best.

The principle agents that used alone or in combination in head and neck cancer are:
Methotrexate, Bleomycin, Taxoles & derivatives, Cisplatin and 5-fluorouracil.

All regimes have significant adverse effects particularly mucositis and immunosuppression and these are compounded by radiotherapy.
Only the fittest patients are able to tolerate concomitant chemotherapy.

Neoadjuvant chemotherapy is given before surgery or radiotherapy and adjuvant chemotherapy after, both reducing adverse effects but being less effective.

Chemotherapy agents act by radiosensitisation as well as their direct effects on cancer cells

Treatment failure

Approximately half the patients suffer from treatment failure and recurrence either at primary site, in lymph node or in distant sites such as lung, liver or bone.

Primary site recurrence usually signifies a poor prognosis.

Recurrence in lymph nodes usually appear within 2 years after treatment.

Recurrent carcinoma is often less well differentiated and more aggressive.

It invades more widely and unpredictably in the tissues, particularly if previously irradiated and is difficult to localize. Re-excision is often impossible.

Survival from oral cancer

In comparison with malignant neoplasms at other body sites, oral carcinoma has poor prognosis and the quality of life in the terminal stages is also poor.

Duration of survival after treatment depends on many factors.

The factors that adversely affecting survival from oral carcinoma include:
1. Delay in treatment
2. Advanced age
3. Male gender
4. Poor general health, usually smoking related diseases
5. Tumor size
6. Posterior location
7. Lack of histological differentiation
8. Lymph node spread