Multidisciplinary approach to the management of oral cancer

Why do we need to know about oral cancer, radiotherapy and chemotherapy ??

With an aging population you will get more patients that have been subjected to extensive treatments and different modalities

Treatment modalities of oral cancer :

* Surgery
* Radiotherapy
* Chemotherapy
* Targeted therapy
* Combination of 2 or more

What is radiotherapy ?

Is the medical use of ionizing radiation as part of cancer treatment to control malignant cells

How does radiotherapy work ?

By 2 ways :-

* Indirect radiotherapy(The most commonly used) : we use x-ray but with much more higher power or by using gamma radiation (photons)

What does those photons do ?

When you put photons at a very high speed they do ionization of water forming free radicals (OH-/H+) which is toxic and when we do ionization of water at specific site it will damage cells at specific site also

Why does it work in destroying cancer cells ?

Because cancer cell are undifferentiated so they reproduce more, and they have a diminished ability to repair sub-lethal damage compared to healthy cells making them more susceptible to damage by ionization so triggering apoptosis to cancer cells as the damage accumulate in their DNA .

* Direct radiotherapy: through heavier particles as protons or big atoms not light atoms, when these particles hits the DNA it will cause breakage to the DNA

What are the disadvantages of indirect radiotherapy ?

* Scattering, which will cause damage to adjacent normal structures, while direct radiotherapy using protons which are heavier than photons will cause less scattering and damage to adjacent normal structures
* They do not really differentiate between bad cells from healthy cells, but healthy cells multiply slower than cancer cells , so they are affected less , that’s why they say radiotherapy at young age will develop other cancer later on because sublethal damage happened to normal tissues.

What is the importance of water in the ionization process ?

Angiogenesis takes place in the 1st stages of cancer, tumor cells starts as single cell and start to increase in number with time forming a ball then the blood supply will not reach the inner part of the ball causing hypoxia that’s why one of the drawbacks of indirect radiotherapy(conventional radiotherapy) it needs water to ionize it, so if tissues are hypoxic then it's not going to work.

And one of the advantages of the heavy protons (charged particles) that they are not affected by the presence of water, they don't need the ionization process to cause damage.

Radiotherapy can be used as soul treatment for cancer.

EX:- T1 tumor in the mouth, evidence shows that if you provide surgery as primary treatment or radiotherapy as soul treatment you will get the same prognosis (5 years survival)

However what is the problem in providing radiotherapy ?

Radiotherapy can be given once and the tissues will become different for life, in other words, if the patient suffered from recurrence surgery will become much more complicated because tissues that have been exposed to radiotherapy they are different and they don't heal easily while if we did surgery instead of radiotherapy we still can do further surgeries or we go for radiotherapy.

Principles of treating oral cancer :

* Radical therapy: aims to cure without surgery
* Palliative therapy: aiming to relieve symptoms when the patient is too old or when the patient is in T4 stage
* Multimodal treatment: which is combination of surgery and radiotherapy and usually radiotherapy commences 2-4 weeks after surgery

**Radiotherapy techniques**:

* Teletherapy: a cone from outside the body is used to give the radiation, and it is the used technique in oral cancer treatment.
* Brachytherapy: a radioactive rods that is inserted in the tumor that releases radiation slowly and continuously. This technique is mainly used in breast/lung cancer treatment not used with oral cancer usually but tongue is the only structure that we can use brachytherapy with it.

**Modes of radiation delivery:**

* Conventional: there is one single beam targeting the tumor from different sides after locating it on a CT. you should mask areas around the tumor to prevent toxicity and high scatter. This mode is considered quick and reliable to be used to treat oral cancer.
* Three dimensional conformal radiotherapy: through this mode the beam will perfectly fit the 3D profile of the tumor to minimize the damage to adjacent structures but it's really very expensive.

**The Dose of radiation:**

 We measure the intensity of radiation by Gray. The dose is determined by the radiotherapist depending on the type of tumor and stage of cancer being treated, but for curative purposes the typical dose ranges from 60-80 grays. The problem with giving high dose of radiation is that you can’t give the same dose to the same area later on if any recurrence occurs.

**Fractionation Schedule**:

 This applies only to photon radiotherapy when you fractionate the total dose for many reasons:

* It allows normal cells to recover, while if you give it in full dose the healthy cells will die
* It allows tumor cells that were in a relatively radio-resistant phase to cycle into a sensitive phase before the next fraction.
* Tumor cells that were chronically or acutely hypoxic may reoxygenate between fractions,more blood which will lead to more water circulating in the cells causing more ionization improving the tumor cell kill.

For the tumor to live it needs blood that carry oxygen. When tumor gets larger, blood won’t reach the inner cells leading to necrosis. Necrotic or hypoxic cells will be radio-resistant. So by fractionation, you allow the tumor to shrink and the radiation to reach the inner cells.

We deliver the conventional fractionation in 30 fractions over 30 days (5 days a week for 6 week)

**Unconventional Fractionation**:

* Hyperfractionation: more than one fraction per day. Total daily and weekly doses are kept equivalent and the total treatment time is kept constant. By this method cancer cells will not have the chance to become active again this way is more effective.
* Accelerated hyperfraction (CHART): 3 more fractions/day daily for 12 days. Shorter treatment time preventing the tumor stem cell repopulation. You are eradicating the entire tumor. But it is very expensive and difficult on the pt.

**Chemotherapy:**

 By using chemicals that act by interfering with rapidly growing tumor cells. They are used for treating many types of malignancies as an adjunct to radiotherapy and surgery. The chemicals are not totally selective but affect normal cells to some extent. They tried to give it intra-arterial to make it more selective but still it has many side effects. Chemotherapy might be given Before doing surgeries to shrink the tumor and ease its excision.

But it can't be used as soul treatment and the most commonly used chemoradiotherapy regime is 100mg/m2 cisplatin every 3 weeks and 60 Gy delivered in 30 fractions of 2 Gy for 6 weeks

Chemotherapy side effects :-

* Mucositis
* Neutropenia
* Anemia

Targeted Therapy

 Immunotherapy is very promising

The most used drug in treating oral cancers is Cetuximab(an IgG1 monoclonal antibody), which is given IV. It might be used along with surgery and radiotherapy.

Oral cancer is a nasty cancer as it keeps changing its profile, so it's not a single clone it’s several clones with different antigens that’s why it's difficult to use targeted therapy.

The final decision in treating oral cancer depends on number of factors including site, tumor type, extent of spread and biopsy results.

Example:-

* In situ carcinoma and stage 1 tumor we go for surgery alone +/- neck dissection
* Stage 1,2,3 the treatment is usually multimodal.

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