

Radiotherapy & chemotherapy in head and neck cancer

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Radiotherapy in head and neck cancer

Radiotherapy forms an important modality to treat head and neck malignancies.

- It may be used:
 - A. Alone, to cure early cancers and thus preserve the function of the organ e.g, glottic cancer.
 - B. As an adjuvant to surgery or chemotherapy, to increase the survival rate in more advanced lesions.
 - C. As a palliative measure, in advanced lesions , to control local symptoms of pain, bleeding or obstruction to air and food channels, when total control of disease cannot be anticipated.
- Also been used in the treatment of certain benign vascular lesions where risks of surgery are great- angiofibroma or glomus tumour.

Types of radiation:

- **1. Photon beams-** these are the most common forms of radiation, both x-ray and gamma rays fall in this category.
- **2. Electron beams-** second most common forms of radiation.
- **3. Particle radiation-** neutrons, protons or pions (still under investigation)

Modes of radiotherapy:

1. External beam therapy or teletherapy:

- It uses photon or electron beams which are projected to the target area through the skin.

2. Brachytherapy:

- it uses radioactive materials which are placed in close contact with the tumour tissue.
- The radioactive materials is applied in the form of:
 - i. a mould.
 - ii. Interstitial implant-radioactive materials in the form of needles, wires, ribbons or seeds are inserted into the tumour tissue.
 - iii. Intracavitary implant-radioactive material is placed in a hollow cavity next to the tumour, eg, nasopharynx, maxillary antrum. For a specific period of minutes, hours or days.

Modes of radiotherapy:

3. Intensity modulated radiation therapy (IMRT)

- It is a recent development in delivery of radiotherapy and has been possible by
 - a). better delineation of target tissue by CT or MRI
 - b). computer-controlled delivery of radiation.

Sources of radiotherapy

- Various sources used for radiation are:
 1. **kilovoltage machines**: They produce x-ray of 50-400 kV.
 2. **Cobalt 60 machines**:
 - ❖ Most commonly used source for head and neck cancer.
 - ❖ It uses radioactive cobalt source which produces gamma rays of 1.17 and 1.33 MeV.
 - ❖ The source has its natural decay time and needs replacement after every 5 years.

3. **linear acceleration, betatron or microtron:** They are megavoltage machines which work on electricity and produce radiation of 4-25 MV.
4. **Radioactive materials:** Earlier, radium 226 was used in the form of needles but now its use has been replaced by safer radionuclides, e.g. Cesium 137 (in the form of pellets), Iridium 192 (in the form of wire), Gold 198 and Iodine 125 (in the form of seeds or grain).

Types of radiotherapy

1. Curative radiotherapy.

- Small cancerous lesions can be cured by radiotherapy alone.
- Surgery also gives equally good results in these cases but radiation has the advantage of preserving the function.
- the total dose of curative radiation in head neck cancer ranges from 6500 to 7500 rads.

Types of radiotherapy

2. Palliative radiotherapy.

- When cancer is too advanced, has distant metastases or the condition of the patient is too poor to undergo surgery due to poor nutrition or other factors such as heart, lungs, liver or kidney disease only palliative treatment is possible.

3. Combination therapy.

- Radiotherapy can be combined with both surgery and chemotherapy.

Types of radiotherapy

A. Radiotherapy and surgery.

- Radiotherapy can be given before or after surgery to achieve better control of disease.
- Each modality aims to overcome the deficiency of the other.
- Preoperative radiation:
- Advantages
 - A) it reduces the tumour bulk .
 - B) oxygenation of tissues has not been tampered with and therefore the response to treatment is better.
 - C) lymphatics are blocked by radiation and thus dissemination of tumour cells during is less.
 - D) eliminates microscopic spread beyond palpable tumour mass or occult metastasis to lymph nodes.

- **Disadvantage**
- Preoperative radiation reduces the vitality of tissues thereby delaying healing process.
- Also increase chances of flap necrosis, fistula formation, carotid blow-outs in post operative period.
- **Postoperative radiation**
- **Advantages.**
 - a). more effective as bulk of tumour mass had been removed by surgery.
 - b). extent of tumour has been defined and radiation can be given to suspected areas of residual disease or areas of positive margins.

Post operative radiation

- c). Surgical resection is technically easier and postoperative healing better.
- d). There are few complication of flap necrosis and infection, if surgery is done in non-radiated tissues.

Generally post operative radiotherapy should be given to all cases of cancer when:

- Margins or growth are reported too close or positive.
- When bone or cartilage is involved.
- Lymph nodes show extracapsular invasion.
- Neck nodes are multiple or the size of a node is greater than 3 cm.

Disadvantages

- After surgery, blood supply to the tissues interfered with and the hypoxic cells will not respond well to radiation.

B. Radiotherapy and chemotherapy

- Chemotherapy can be used either before, during or after radiotherapy.
- When used before radiotherapy, it reduces the bulk of tumour, while its vascularity is maintained or has been enhanced by decrease in size of the tumour.
- When used concomitantly with radiotherapy, chemotherapy acts as a radiosensitizer to improve the effect of radiation on the tumour cells.
- Concomitant chemotherapy and radiotherapy has been used in head and neck cancers.
- Chemotherapy can be used after radiation, but is less likely to penetrate the affected tissue due to poor blood supply.

Planning of radiotherapy

- Following points are considered when a patient is to receive radiotherapy:
 1. Types of radiotherapy
 2. Site of tumor and its lymphatic field
 3. Extent of tumor
 4. Histology of tumor
 5. Dose of radiation and fractionation

Planning of radiotherapy (cont).

1. **Types of radiotherapy**- whether it is curative, palliative or combination type of therapy.
2. **Site of tumour and its lymphatic field**- the primary tumour and its draining lymph nodes have to be included in the radiation field.
3. **Extent of tumour**- smaller the tumour bulk, better is there sponse to radiation. Field of radiation is planned according to the extent of tumour

Planning of radiotherapy (cont).

4. Histology of tumour:

- Tumours of lymphoid tissues are very sensitive and respond quickly.
- Adenocarcinomas are less sensitive.
- Sarcomas and bone tumours also have low sensitivity

5. Dose of radiation and fractionation:

- Generally, the curative dose is 6500 – 7500 c Gy.
- Conventionally, it is delivered in fractions of 200 c Gy per day for 5 days in a week (Monday to Friday) and thus it takes 6 1/2 to 7 1/2 weeks to complete the treatment.

Complications of radiotherapy

- Complications of radiotherapy depend on the site of radiation, total dose delivered and the daily fraction of radiation used.
- High total dose and large daily fractions cause more complications
- Complications following radiation can be divided into early or late.

Complications of radiotherapy (cont).

Early complications:

- Radiation sickness (loss of appetite and nausea)
- Mucocitis
- Dryness of mucous membranes.
- Skin reaction (erythema, dry or wet desquamation)
- Laryngeal oedema
- Candida infections
- Haematopoietic suppression
- Acute transverse myelitis.

Planning of radiotherapy (cont).

Late complications:

- Permanent xerostomia.
- Skin changes (atrophy of skin, subcutaneous fibrosis)
- Decaying of teeth
- Osteoradionecrosis
- Trismus (fibrosis of TM joint and muscles)
- Radiation retinopathy and cataract
- Endocranial deficit (thyroid, pituitary)
- Radiation induced malignancy (thyroid cancer, osteosarcoma of orbit)

Care of patient during radiotherapy

1. Nutrition:

- Particularly important in cancers of oral cavity and pharynx.
- Diet, rich in protein, vitamins and iron should be given.
- Nasogastric tube may be used where necessary.
- Blood transfusions may be required, if haemoglobin level is low.

2. Care of teeth:

- Any patient who is a candidate for irradiation particularly in the area of mandible should have dental evaluation and get all questionable teeth extracted before radiation.
- Wound must heal before radiation is started.
- Xerostomia adds to caries of teeth.
- Osteoradionecrosis of the mandible may follow extraction of teeth in an irradiated mandible.

3. Care of skin:

- Skin reactions are common with orthovoltage or electron beam therapy to skin but the modern megavoltage therapy has a skin sparing effect.
- During radiotherapy , patient is advised in the care of irradiated skin.
- He should:
- Keep the area dry and avoid washing with soap and water.
- Avoid exposure to sunlight.
- Avoid wet shaving.
- Not use adhesive plaster for dressing ,it peels off the skin at the time of removal
- Cover the area with soft cloth, like silk, which should provide free areation of the skin and
- Not use abrasive dressing or clothing.

4. Care of oral cavity:

- Mucositis and xerostomia are common complications. They also interfere with feeding.
- Patient should avoid alcohol, tobacco or highly spiced food to lessen further trauma.
- Irritating mouth washes which contain alcohol should not be used.
- Milk of magnesia can be applied to the area of mucositis to give protective coating.
- Pain and discomfort of mucositis can be relived by use of lignocaine 10% to enable the patient to eat.
- Acute radiation mucositis usually persists 8-12 weeks after radiation.

5. Care against infection:

- Patients receiving radiotherapy are generally debilitated and easily develop candida infection of the oral cavity and pharynx.
- It can be treated by topical application of nystatin or clotrimazole.
- Mycelia may be lie protected beneath organism debris and may require antifungal systemic therapy.

Chemotherapy in head neck cancer

- Chemotherapy may be used alone or in combination with other modalities of treatment.
- Most of the head and neck malignancies are squamous cell cancer and the drugs found effective are methotrexate, cisplatin, bleomycin and 5-fluorouracil.
- Adriamycin has been used for certain non squamous carcinomas (adenoid cystic carcinoma) and dacarbazine for melanomas.
- Lymphomas of the head and neck , both Hodgkin and non Hodgkin types, are also treated by chemotherapy because of their multifocal origin and wide spread involvement.

Types of chemotherapy

1. Palliative chemotherapy.

Cytotoxic drugs, singly or in combination are used to treat advanced, recurrent or metastatic disease with an aim to relieve the symptoms and to prolong life in some of them.

2. Adjuvant chemotherapy.

2. Adjuvant chemotherapy.

Here chemotherapy is used before, during or after treatment with other modalities.

- ❑ When used before surgery or radiation, it is called induction or anterior chemotherapy.

It helps to reduce tumor burden and micrometastases that can occur at the time of surgery or in the period before radiation.

- ❑ When used simultaneously with radiotherapy, it acts as a radio sensitizer to cells which are otherwise radio resistant.
- ❑ When used after surgery or radiation, it is called posterior chemotherapy and is aimed to cure micrometastases.

Single agent VS multidrug combination therapy:

- Methotrexate, cisplatin, bleomycin and 5-fluorouracil have been used as single agents in various dosage forms.
- They have also been used in combination with other drugs with the objects to improve overall response rate and duration of response.
- Combination of two or more drugs improves the response rate and definitely improves the quality of patients life .

Commonly used anticancer drugs and their side effects:

1. Methotrexate:

- Used in – squamous cell cancer, acute leukaemia, lymphomas.
- Conventional dose- 40mg/m² iv weekly
- Side effects- bone marrow suppression, mucositis of oral and GI mucosa. Renal and hepatic toxicity.

2. 5- fluorouracil (5-Fu)

- Used for- squamous cell cancers. Non-squamous tumours of breast and G I tract.
- Dose- 10-15 mg/kg iv daily.
- Side effects- myelosuppression (Neutropenia thrombocytopenia), mucositis (nausea, vomiting, stomatitis and diarrhoea), skin (alopecia, hyperpigmentation, maculopapular rash, hand-foot syndrome)

3. Cisplatin:

- Used for- squamous cell cancer.
- Dose – 80- 120 mg/m² iv infusion every 3 weeks.
- Side effects- G I T (nausea, vomiting) ,renal toxicity, haematologic (anaemia, neutropenia, thrombocytopenia), neurologic (peripheral neuropathy), ototoxicity

4. Bleomycin:

- Used for- squamous cell cancer, lymphoma.
- Doses- 10-20 mg/m² once or twice weekly, im or iv.
- Side effects- pneumonitis (dry cough and rales) and pulmonary fibrosis, fever and chills in first 24 hour, alopecia, erythema, hyperpigmentation, stomatitis.

5. Cyclophosphamide:

6. Vincristine:

7. Actinomycin-D

8. Adriamycin

PRETREATMENT WORK-UP OF THE PATIENT

- Patient who is a candidate for cancer chemotherapy should be worked up in the following manner:
 1. History and clinical examination-(Exclude kidney, heart and lung disease)
 2. Haematological tests:
Haemoglobin, total and differential count, platelet count
 3. Urine examination.
 4. Biochemistry:
Blood urea nitrogen, creatinine, liver function tests

5. Radiology:

- X-ray chest
- CT scan or MRI &
- Ultrasound of liver/spleen where indicated

6. Pulmonary function tests (for Bleomycin)

7. E C G (for Adriamycin)

8. Audiogram (Cisplatin causes high frequency hearing loss)

9. Nutritional status.

Toxicity of anticancer drugs

- Most of the drugs act on rapidly dividing cells and therefore include normal cells as those of hair follicles, gastrointestinal mucosa and bone marrow causing alopecia, stomatitis, nausea, vomiting, diarrhoea, anaemia, leukopenia and thrombocytopenia.
- Some drugs have selective action on
 - ✓ kidney (methotrexate , cisplatin),
 - ✓ nerves (vincristine and cisplatin),
 - ✓ heart (adriamycin) and
 - ✓ bladder (cyclophosphamide)