Reconstruction in previously irradiated patients

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ABSTRACT

Radiation therapy, which forms the mainstay of the treatment in many head and neck cancers, is viewed by many surgeons with skepticism. But many are not fully conversant with radiobiology and the effect of the radiation in tissues. This article aims at bringing the reader acquainted with the beneficial and harmful effects of radiation on the tissues. The alterations in tissue healing with radiation and the problems associated with surgery in a previously irradiated patient is discussed in detail. The role of free tissue transfer, in this setting is also dealt with.

KEY WORDS

Head and neck cancer; radiation therapy, reconstructive surgery, salvage surgery

RADIATION BIOLOGY

In 1901 when Becquerel left a vial containing 200 mg of radium in his breast pocket for 6h, he was surprised to find that after initial erythema the lesion progressed to frank ulceration and refused to heal for a quite long period. This led to the recognition of the harmful effects of ionizing radiation. When radiation comes in contact with biological tissues, energy is absorbed from it, leading to excitation of electrons or ionization of the atoms or molecules comprising these tissues. Radiation of sufficiently high energy to completely eject one or more electrons from an atom or a molecule is said to be ionizing. Ionizing radiations may be electromagnetic or particulate. X-rays and gamma rays are types of electromagnetic radiation while particulate radiations consist of electrons, protons, neutrons, alpha particles and pi-mesons. Exposure of living tissues to such radiations may result in death of a cell. If that cell happens to be cancerous, it is considered therapeutic and if otherwise it is detrimental to the normal tissues.

Therapeutic radiation may be delivered to the target tissues in two forms. Sealed radioactive sources may be kept directly in contact with the tissues via interstitial or intracavitary route. This method is called Brachytherapy and it delivers a high dose to the target tissues with rapid falloff into the surrounding tissues. The use of external beam radiation using gamma rays (produced by remotely placed radioactive sources e.g., cobalt, caesium) or X-rays (produced with linear accelerators orthovoltage machines) or particulate beams of electrons or protons is termed Teletherapy.

This beam of radiation while travelling in tissues goes on depositing its energy in the tissues in a predictable way. From the surface the amount of energy getting deposited goes on increasing. This is termed the region of dose build-up. The maximum dose is deposited at a certain distance from the surface (called \( D_{\text{max}} \)) after which the beam is attenuated by the tissues. Higher the beam energy longer is the dose build-up region. Linear accelerators produce high-energy megavoltage beams capable of deep tissue penetration and are replacing the orthovoltage machines. Therefore they are skin-sparing. There may be times when maximum dose has to be given at a depth lesser than the \( D_{\text{max}} \) then a material is placed directly on the skin to act as a tissue. This tissue compensating material is called a Bolus.

Radiation may act directly upon a critical target within...
the cell (usually the DNA, possibly cellular membranes or microtubules) and cause the resultant damage or may act indirectly through free radicals. The lifetime of free radicals measured in milliseconds, is increased by the presence of oxygen. Therefore cells irradiated in the presence of oxygen are two to three times more sensitive to the same dose than in an anoxic environment. Presence of oxygen is thought to make the DNA damage irreparable. Some of the tumour cells in the body may be surviving in a relatively hypoxic environment making them less radiosensitive. In general cells are most sensitive in the G2-M stage of cell cycle, while they are most resistant in the S phase. To catch the tumour cells in the act of division it is necessary to fractionate the total dose of radiation over a few days. Fractionation also allows the normal tissues to repair themselves.

**RADIATION EFFECTS**

When considering the effects of the radiation on the tissues four parameters need to be considered - total dose, dose fraction size, total volume treated and elapsed time. At this point it will be appropriate to define the unit of dose i.e. The Gray: A unit of absorbed radiation equal to the dose of one joule of energy absorbed per kilogram of matter or 100 rad. The unit is named after the British physician L. Harold Gray (1905-1965), an authority on the use of radiation in the treatment of cancer. The abbreviation for a gray is Gy. Complications increase when the dose exceeds 60Gy and rapidly rise when the dose is above 70Gy. For a given dose of radiation normal tissue tolerance reduces when larger volumes are irradiated. Prolonging the overall treatment time allows tissues to repair themselves reducing acute reactions. When few and larger doses are given, late and chronic reactions tend to be severe.

When radiotherapy is administered to the head and neck, erythema, conforming exactly to the shape of the irradiated field appears as early as one to 24h due to increased capillary permeability. The main erythematous reaction occurs due to the inflammatory response to epidermal cell damage approximately a week later and then requires another week to reach its peak. With each fractionation there is an overlap of erythematous reaction from each dose. At moderate dose levels many epidermal cells die and when repopulation occurs from the surviving population from basement layers it presents as dry desquamation. At higher doses, (required to cure most skin cancers) all the basal cells within the treatment field may be killed, exposing the dermis as moist desquamation. Repopulation after moist desquamation occurs from within the hair follicles within the irradiated area. If acute radiation damage is severe enough dermo-epidermal separation occurs and is seen as a bulla.

Radiation stimulates melanocytes to produce more pigment. As with any other injury, radiation causes dermal deposition of pigment. This results in darkening of skin. Higher doses may destroy melanocytes resulting in depigmentation.

In the acute phase radiation reduces the ability of dermal fibroblasts to proliferate. Also inflammation of the dermis occurs with swollen collagen bundles. Very high doses may result in necrosis and ulcer formation. Late changes in the dermis appear as collagen bundle swelling and hyalinization. New collagen is formed throughout the irradiated field, evident as fibrosis. Several months later this fibrous tissue is deposited in the subcutaneous and submucosal layer reducing their elasticity.

Acutely, radiation produces degeneration of basement membranes leading to increased vascular permeability. This leads to loss of plasma followed by thrombosis, occlusion and ultimately secondary fibrosis. Vessels show endothelial cell proliferation, oedema of the vascular walls and thrombosis as acute changes. After four to six months of radiotherapy capillaries progressively dilate appearing as telangiectasia in the skin as well as mucosa. Large vessels may be completely occluded leading to ulceration.

Hair dysplasia, alopecia and impaired metabolism of growing hair follicles results with small doses. Permanent hair loss with replacement of follicles by scar may result in skin with chronic radiation dermatitis. Sebaceous glands are also absent in such skin. Eccrine glands are the most radio-resistant and are usually present. Mucosal, salivary glands and taste buds have a high sensitivity to radiation and damage to them is evident as mucositis, dry mouth and loss of taste by three to four weeks.

When followed for 10 years life-threatening complications will occur in half the patients. Osteoradionecrosis of the mandible affected 40% of the patients.
ALTERATION OF NORMAL HEALING PROCESS BY RADIATION

If full course of radiation is given then endothelial blood vessels, mesenchymal cells and epithelial cells have severely impaired proliferative capacity. Depletion of fibroblasts leads to reduction in wound strength. Many epithelial cells die and the epithelium is thinned or completely destroyed. Obliteration of capillaries and larger vessels along with radiation fibrosis results in ischemia of the tissues. Irradiated endothelial cells are unable to respond to tissue ischemia by production of new vessels leading to hypoxic state. This interferes with collagen synthesis and polymorphonuclear cell function.

SURGERY OF THE IRRADIATED PATIENT

The irradiated patient will present with indurated or atrophic skin, alopecia, hyperpigmentation, friable mucosa, xerostomia and trismus. The patient should be put on a high-protein diet with vitamin, mineral and other nutritional supplements as deemed necessary. Use of tube feedings and parenteral nutrition should be seriously considered if oral intake is not satisfactory.[11,12]

Surgery in the irradiated area may have to be undertaken in an emergency to treat complications of radiotherapy, to excise and reconstruct recurrences or electively to improve oral function. These problems can be very severe in patients who have received total dose of more than 60Gy making them less favoured candidates for elective surgery.[13]

After preoperative radiotherapy, vascularization of the radiated area reduces continuously as a function of the total dose and time. It is strongly advocated to wait one week per each 10Gy of total radiation dose to allow acute inflammation (of the skin and mucosa) to subside.[1] A window period is said to exist between six to eight weeks when optimum conditions for surgery may exist following radiotherapy though no clinical trials support it.[15,19-21] Sharp dissection with knife under loupe magnification is advocated as irradiated vessels are more prone to spasm when compared to the nonirradiated vessels of the same calibre.[22] Clipping of the side branches is preferred over electro coagulation for fear of inducing thrombosis and its progression into the main branch.

A preventive approach to avoid complications is the best option available. Preoperative antibiotics should be given whenever oral cavity is entered.[14,15] Skin incision should cross the carotid vessels only once.[16] Use of electrocautery near the neck vessels and sub adventitial dissection should be avoided at all costs. Neck skin flaps need to be elevated without excessive use of electrocautery. Avoid tight closure as it may lead to necrosis or wound dehiscence in the already ischemic environment.[17]

Fibrosis of the muscles of mastication occurs when they are included in the field leading to trismus. This may mean difficulty during intubation. There will be fibrosis in the radiated field with thrombosis and obliteration of vessels and reduced capacity to fight infection due to hypoxic environment. Fibrosis in the radiated field increases difficulty in dissection. Patients with prior radiation exposure have a slightly higher risk for developing complications at the recipient site most of which are related to wound healing problems. Formation of a seroma, infection, abscess, wound dehiscence, hardware exposure and orocutaneous or pharyngocutaneous fistula may increase the hospital stay but eventually may not need an intervention.

FREE TISSUE TRANSFER FOLLOWING RADIOTHERAPY

Free flaps are often the only acceptable choice in head and neck reconstructions after irradiation.[18] They have become the accepted method of reconstruction as a result of increased success rates with superior aesthetic and functional results.

Following radiotherapy there is perivascular fibrosis that makes vascular dissection difficult.[15,19-21] Sharp dissection with knife under loupe magnification is advocated as irradiated vessels are more prone to spasm when compared to the nonirradiated vessels of the same calibre.[22] Clipping of the side branches is preferred over electro coagulation for fear of inducing thrombosis and its progression into the main branch.

Under a microscope irradiated arteries display a significantly greater wall thickness and higher incidence of intimal dehiscence compared with nonirradiated vessels. Calcification and atheromatous plaque formation is more frequent in irradiated vessels.[23] Micro thrombi adherent to the intima are visible and are not cleaned by flushing with heparinised saline. Veins do not show any appreciable changes.[24] Largest available vessels in the neck should be
Post RT reconstruction

selected as they will have fastest flow and are less prone to spasm. This means utilizing the external carotid artery and internal jugular vein and performing end to side anastomosis in most of the cases. There is an advantage in passing the suture from inside out in irradiated vessels to prevent intimal separation.

Due to radiation there is increase in the amount of heparinase released which dissolves the heparin from endothelial matrix. There is definite impairment in endothelial cell repair due to damage to the cellular DNA. Radiated vessels are known to have slower flow rates and are prone to spasm. Both these facts strongly favour use of anticoagulation though there is no published data to support its benefits. But in the event of a re-exploration full anticoagulation should be seriously considered as the salvage rate in such cases is extremely poor.

Microvascular transfer in previously irradiated patients is technically demanding due to difficulty in the vessel dissection and changes in the vasculature. However, proper planning and meticulous technique can ensure, that in such patients, there need not be more failures than...
REFERENCES


SUGGESTED READING


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