

Therapeutic options in complication of Larynx cancers after high energy radiotherapy

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Introduction

Tissue transformations under radiotherapy have been estimated by experimental procedures. All this methods have permitted the identifications of pathologic phenomenal (mechanism) induced by radiation, eventually leading to the staging of dozes and fractioning of the tissue volume that has to bee irradiated.

Radiotherapy side effects can be acute or late accruing eider during radiation or after different periods following the above mentioned method.

Acute radiation side effects can have immediate onset during the treatment or after sever weeks at the end of it. Late side effects are sever and more persistent and have onset after a long period fallowing radiotherapy.

There are slight differences between the action of radiations on normal either tumor tissues but if this slight differences can be therapeutically exploited thus gives the corner stone of the about mentioned treatment.

We know today that radiation energy can induce irreversible lesions on cells and tissues having as main effect the destruction of those structures whit high division rate, this eventually leading to important cell depletion of the respective organ ^{1,2}.

Living tissues can be divided in two categories whit respect to the regenerative power of their cells populations.

A.

“H” compartment tissues having numerous stem cells such as the epidermis bowel mucosa, bone marrow and etc.

The most part of these stem cells are in the G0 division phase but can rich very quick the other phases of mitosis onset under certain stimulus connected to the depletion of mature cells.

Stems cells usually having high division rate can often escape from the normal feedback induced by mature cells, this changing proportion between division and maturation, genetically establish by apoptosis ^{3,4}.

At the opposite site is situated the compartment of mature cells differentiated functional which lost the division capacity. (These cells usually die old in the normal process of senescence)

Between these two compartments mentioned before is situated the middle compartment of those cells incompletely differentiated coming from the stem cells division.

B.

The so called “F” (uncompartment) tissues with stem cells. The major difference between these two types is the fact that in compartment structures cells manifest irreversible post mitotic qualities; Cells belonging to “F” tissues can keep otherwise all latent lesions induced by radiations which express only during mitosis⁵.

Tissue architecture has a paramount importance for the way in which cell lesions induced by radiotherapy can occur; the rate in which these lesions appeared is always correlated with the radiation dose.

Late side effects of radiotherapy represent the major factor influencing the therapeutic response, which contrasts with the acute side effects uncomfortable but transient.

This explains why late side effects always limit the so called “tumor killing dose” (which can seldom be applied).

The G2 fraction dose 4 times/week exceeding the total dose of 70-80 Grey gives the best therapeutic response, in which late complication and relapses have the lowest rate.

Work hypothesis:

Cell and tissue late dysfunctions induced by radiation using high energy doses have as consequence the onset of functional vicious circle in which tissue hypoxia represents the main factor.

A slight improvement of local microcirculation ensures a good nutrition and oxygenation leading to an ongoing regeneration;

Systemic treatment for at least 2 years following radiotherapy and surgical treatment with vascular flaps is the main two ways of therapeutic options.

These therapeutic options always require a strong coordination between E.N.T. specialist and radiotherapist.

Purposes:

This paper tries to emphasize the ways in which the E.N.T. specialist can improve the approach of Larynx tumors:

1. Radio necrosis assessment by systemic and surgical treatment

2. Assessment of on acceptable deglutition and respiration

Materials and methods:

We reviewed the chart from 122 patients with Larynx cancer. All cases enlisted in this paper are provided by the high energy radiotherapy laboratory of the emergency hospital Baia Mare for a period of 3 years. (2005-2008)

A. Surgical procedures: - necrosis debridement followed by adequate local treatment similar to that applied for leg ulcers;
- vascular flap has been tailored and inserted in the defect, when possible.

B. Systemic treatment: - Vitamin E 1000/day in association with 400 mg SR Pentoxifilin for at least 2 years (the same treatment is recommended also of those patient submitted to high energy doses in order to prevent to recurrences.

A 2 year follow up is always necessary to evaluate the efficacy of the above mention treatment (patients with/without the associations between systemic and surgical treatment).

Study stages:

Two major cohorts with patients of complicated Larynx cancers have been evaluated:

- one from the Oncology Institute Cluj Napoca
- one from The Emergency Hospital of Baia Mare

Cases have been assessed by 3 levels of severeness:

-sclerosis and superficial atrophy but with now functional distortions chronic lesions with several periods of acute symptoms such as inflammation (condritis, dermatitis, lymphangitis) or superficial wounds on the skin and mucosa which can disappear after adequate local treatment. Such lesions often associate uncomfortable functional disorders.

Long lasting necrosis with different extensions and persistent functional disorders for respiration and deglutition requiring Tracheostomy and Gastrostomy.

This study is proposing a long follow up of those patients in whom the above mentioned therapeutic options have been applied; the follow up period was 2 years.

Results:

The second patient cohort (Emergency Hospital of Baia Mare) has been submitted to Cobalt Therapy with an Elite 1000 device functioning since 2003 (the total number of patients was 122, with 15 cases following palliative radiotherapy and 105 cases following curative radiotherapy. Only 17 cases following radiotherapy or radiotherapy and Chemotherapy have been selected for this paper.

Other 35 patients have been submitted to postoperative radiotherapy combined with Cisplatin chemotherapy.

All these patients have been radically treated at the Oncology Institute Cluj Napoca.

Discussion:

Of the total number from 122 patients in the study, 14 patients experienced relapse in the first 2 years. Disaggregated by the 3 anatomic levels were 10 cases of laryngeal glottic floor, 4 was in the supraglottic floor. From these 14 cases were irradiated adjuvant after total laryngectomy. In 9 cases total doses were 72 Gy and in 5 cases the total doses were 50 Gy. Reported to prevail disease stage with 8 cases (57%) stage IV followed by 4 cases of stage III (28,5%) and only 2 cases with stage II (14%). Apparently inexplicable nodal metastases occurred in the 2 cases of stage II

According to a study published in The New England Journal of Medicine, total of 547 patients were randomly assigned to one of the three study groups. The median follow-up period was 3.8 years. At two years, the proportion of patients who had an intact larynx after radiotherapy with concurrent cisplatin (88 percent) differed significantly from the proportions in the groups given induction chemotherapy. In this trial, the overall survival among patients with stage III or IV laryngeal cancer was excellent (75 percent at two years) and did not differ significantly according to the treatment. Laryngeal preservation was best achieved with radiotherapy plus concurrent cisplatin; induction chemotherapy followed by radiotherapy was not significantly better than radiotherapy alone. With concurrent therapy, there was an absolute reduction in the rate of laryngectomy of 43 percent⁶.

Conclusions:

The number of radiotherapy complications has significantly decreased in the last twenty years, due to the substantial improvement of radiotherapy devices as well as to the new knowledge in the field of radiobiology.

Though, when such complications occur several symptoms provoke deep sufferings to the patients and are very difficult to treat by the physicians.

On the other hand the so called surgical salvage procedures for the remaining tumors as well as for the lymph nodes metastasis have become an every day practice.

Late complications percentage has also decreased and the most part of such lesions can be managed either by local conservative treatment or by reconstructive surgery using vascularized flaps.

Actual development of radiotherapy techniques and also of radiobiology and does new evaluation gives now on accurate administration of optimal radiation doses.

This E.N.T. tumors and Larynx cancer specially can now be treated with high energy doses with less late complications using regular Cobalt devices because are usually superficial and really very extensive.

That is why radiotherapy can be complete with surgery in all early stages of Laryngeal tumors, offering beside this the best options for 3 and 4 A late stages (but in this stages salvage surgery) is essential for accurate management of tumor and Lymph node metastasis.

In several cases it is difficult to make separation between the side effects of radiotherapy and those of chemotherapy (especially with CysPlatin, because this drug is now a standard protocol in association with radiotherapy).

Because there is a slight difference between normal and neoplastic cells concerning cells response to irradiation control doses can't overcome 80 Grey without an a significant increase of the number of late complications.

For this reason of most part of radiotherapists make a "therapeutic compromise" giving a total dose of 70 Grey fractionated in daily doses of 2 Grey 5 days/week.

This gives an optimal low rate of late complications and of recurrences as well. (all recurrences may be better managed by long and accurate follow up for at least 3 years.