Critical Reviews in Oncology/Hematology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Role of radiation therapy in melanomas: Systematic review and best practice in 2016

Magali Fort[a], Saada Guet[a], Shan Husheng[a], Elie Calitchi[a,b], Yazid Belkacemi[a,b,*], On behalf of AROME (Association of Radiotherapy & Oncology of the Mediterranean arEa ; www.aromecancer.org) and TRONE (Transatlantic Radiation Oncology NEtwork

[a] *Radiation Oncology Department of Henri Mondor University Hospital and University Paris-Est Creteil (UPEC), Créteil, France*
[b] *Henri Mondor Breast Center and University of Paris-Est Creteil (UPEC), Créteil, France*

Contents

ARTICLE INFO

Article history:
Received 10 August 2015
Received in revised form 2 December 2015
Accepted 16 January 2016

Keywords:
Melanoma
Chemoradiation
Chemotherapy
Radiotherapy

ABSTRACT

Radiotherapy has been used for skin cancers since early after the discovery of X-rays. The introduction of sophisticated surgery techniques and information of the general population on potential late radiation-induced toxicity and carcinogenesis have led to limiting indications in the dermatologist community. However, radiotherapy (RT) has undergone considerable developments, essentially including technological advances, to sculpt radiation delivery, with demonstration of the benefit either alone or after adding concomitant cytotoxic agents or targeted therapies. Although side effects due to high doses and/or the use of old RT techniques have been significantly decreased, the risk of atrophic scars, ulcerations or secondary cancers persist. In this systematic review, we aim to discuss indications for

* Corresponding author at: Hôpitaux Universitaires Henri Mondor, 51 avenue Mal De Lattre de Tassigny, 94010 Créteil, France. Fax: +33 1 4981 2589.
E-mail address: yazid.belkacemi@aphp.fr (Y. Belkacemi).

http://dx.doi.org/10.1016/j.critrevonc.2016.01.016
1040-8428/© 2016 Elsevier Ireland Ltd. All rights reserved.

Please cite this article in press as: Fort, M., et al., Role of radiation therapy in melanomas: Systematic review and best practice in 2016. Crit Rev Oncol/Hematol (2016), http://dx.doi.org/10.1016/j.critrevonc.2016.01.016

Radiosensitivity
Preoperative
Targeted therapies

RT in melanomas with focus on new advances that may lead to rehabilitating this treatment option according to the tumor radiosensitivity and clinical benefit/risk ratio. Melanomas have been considered as radioresistant tumors for many years.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Radiotherapy (RT) has been used for skin cancers since early after the discovery of X-rays. The introduction of sophisticated surgery techniques and information of the general population on potential late radiation-induced toxicity and carcinogenesis have led to limiting indications in the dermatologists community. Although side effects due to high doses and/or the use of old RT techniques have been significantly decreased, the risk of atrophic scars, ulcerations or secondary cancers persist. Concurrently, RT techniques are less taught for skin cancers in Europe, North America and Australia (Hernández-Machin et al., 2007).

In this systematic review, we aim to discuss the indications for RT in melanoma skin cancers and focus on new advances that may lead to rehabilitating this treatment option according to the tumors' radiosensitivity and the clinical benefit/risk ratio.

2. Methods

To conduct this review, a literature search was performed on the MEDLINE database between 1976 and 2015. All reports, including preclinical studies of skin tumors radiosensitivity, clinical trials and reviews relative to the management of melanoma skin cancers involving RT in a curative intent were selected. We used the following key words for skin tumors: « melanoma AND radiotherapy »; « melanoma AND radiobiology »; « BRAF inhibitor AND radiotherapy »; « radiotherapy AND melanoma AND targeted therapy »; « immunotherapy AND melanoma AND radiotherapy » and « ipilimumab AND radiotherapy ». Only reports written in English were reviewed in detail. Publications in all other languages were examined for the presence of an abstract written in English and/or data presented in tabular form. The remaining reports written in a non-English language that lacked an abstract translated into English and numerical data presented in tabular form were excluded. All study types (case reports; case series; clinical trials and retrospective reviews); regardless of sample size; were reviewed.

3. Results

3.1. Radiobiology: from experimental data to clinical response

3.1.1. Radiosensitivity

Melanomas and gliomas are among the most resistant cells to radiation (Kumala et al., 2003). Knowing that cancer cells may undergo an unlimited number of divisions and even a single cell may be a source of a proliferating clone, successful cancer therapy aims to eliminate all clonogenic tumor cells from the organism. Most *in vitro* investigations of the response of tumor cells to radiation involve two endpoints: studies of rapid cell killing due to apoptosis, or longer-term studies of the clonogenic cell survival.

Cells having surviving fractions of 2 Gy (SF2) less than 0.35 are considered as radiosensitive, while those with values greater than 0.35 are regarded as radioresistant (McIlwrath et al., 1994). SF2 values illustrating radiosensitivity of low passage melanoma cell lines derived from clinical melanoma specimens express a whole variety of values ranging from 0.36–0.93. It was noticed that the decrease of radiosensitivity is related to the increase of melanin produced by different melanoma cells (Marshall et al., 1994).

Proton irradiation has a larger capacity to inactivate HTB140 melanoma cells than γ-rays. Within the first 48 h after irradiation, protons eliminate cells mostly by apoptosis, while γ-rays express high survival levels, implying the lack of apoptotic cell death. At 7 days, both protons and γ-rays reduce cell numbers, most probably by the expression of the induced irreparable DNA damage, also including genomic instability genesis with the more pronounced effect in the case of γ-rays than in the case of protons (Petrović et al., 2006).

On the other hand, oncogenes activation by radiation exposure may alter the sensitivity of cells to ionizing radiation. Pomp et al. evaluated the influence of the oncogenes NRAS and MYC on the radiation sensitivity of cells of a human melanoma cell line. Single-dose experiments showed decreased survival after transfection with MYC, wild-type NRAS or mutated NRAS. Co-transfection with MYC and mutated NRAS decreased survival up to 4 Gy, whereas no shift in radiosensitivity was seen with higher doses. Transfection with NRAS or MYC alone increased radiation sensitivity, while transfection of cells containing NRAS with MYC restored resistance to higher doses of radiation exposure (Pomp et al., 1996).

3.1.2. Dose and fractionation (Table 1)

When RT is chosen for melanoma treatment, there is no difference between standard fractionation and hypofractionation schedules. In a retrospective analysis conducted between 1980 and 2004 with 56 high-risk melanoma patients treated with adjuvant hypofractionated or ($n = 41$; 73%) or conventional RT ($n = 15$; 27%), no difference in terms of disease control was observed. However, 2 patients (4%) had severe late complications, such as osteoradionecrosis of the temporal bone or radiation plexopathy (Chang et al., 2006).

One phase III randomized trial was published in 1991 by the Radiation Therapy Oncology Group (RTOG 83-05). The objective was to test high dose per fraction and hypofractionation to increase tumor radiosensitivity. In 137 patients with measurable melanomas, the authors compared 32 Gy in 4 fractions (of 8 Gy) delivered over 21 days *versus* a standard scheme delivering 50 Gy in 20 fractions (of 2.5 Gy) delivered 5 days a week over 26–28 days. The trial demonstrated an overall response rate of 57–60%, but failed to show any difference between the 2 fractionation regimens. Furthermore, the overall response rate was lower than that previously reported (about 97%) with 3 fractions of 9 Gy or 8 fractions of 5 Gy delivered twice a week (Sause et al., 1991).

3.1.3. Radiation-induced toxicity in melanomas

The concern after skin irradiation is acute and late toxicity that depends on total dose, fractionation, dose per fraction and intrinsic radiosensitivity of the patient. Beside skin, lymphatic irradiation can induce lymphedema and significant morbidity and quality of life deterioration. Additionally, the risk is increased in the adjuvant setting where surgery itself has been recognized as a risk factor for lymphedema. In a single arm phase II trial, Burmeister et al. (2002) prospectively evaluated the toxicity of RT in 130 patients treated with 48 Gy in 20 fractions over 4 weeks. With such a lower dose per fraction, they showed no severe late effects, with a very low

Please cite this article in press as: Fort, M., et al., Role of radiation therapy in melanomas: Systematic review and best practice in 2016. Crit Rev Oncol/Hematol (2016), http://dx.doi.org/10.1016/j.critrevonc.2016.01.016

Download English Version:

https://daneshyari.com/en/article/6113595

Download Persian Version:

https://daneshyari.com/article/6113595

Daneshyari.com