Chapter 4
Print ISBN: 978-93-91882-09-9, eBook ISBN: 978-93-91882-20-4

New-Competitive- Principal of Tumor Control by Low Dose Radiation

A. N. Shoutko[1*], L. E. Yurkova[2], K. S. Borodulya[2] and L. P. Ekimova[1]

DOI: 10.9734/bpi/nfmmr/v12/12422D

ABSTRACT

In order to verify the principle of indirect control a tumor on the base of morphogenic cells distraction from it, the 114 patients with advanced ovarian carcinoma (stage III-56, stage IY-21, relapse 37), were treated with subtotal half-body (low part) irradiation at low doses (0,1 Gy x 10 for 3 weeks or 3Gy x 3 daily), and obtained data were compared with that for 190 patients (stage III-66, stage IY-25, relapse-99) received conventional local irradiation of the tumor (2 Gy x 23 daily). The surgery and chemotherapy components were equalized in both groups. The 34% and 11% of 5-years survival was obtained at low dose half body irradiation for primary and relapsed patients in comparison with conventional local radiotherapy (7% and 0%). It is concluded, that reparation /regeneration processes being provoked artificially in normal tissues of cancer host are capable to compete remotely with tumor for the morphogenic/feeding cells originated from bone marrow and circulating with the blood.

Keywords: Low dose radiotherapy; advanced ovarian carcinoma; indirect restriction of cancer growth.

1. INTRODUCTION

Conventional medicine recognizes a selective killing of tumor cells as only way of fighting with cancer. This way has brought some doubtless benefits in the past, but in the last decades the effectiveness of traditional treatment progresses more slowly, than it would be desirable [1]. The general nonsense of conventional therapy is the recognition of anti-cancer immunity on one side and the use of cytotoxic treatments leading inevitably to lymphocytopenia on another side. The life span of mammals at normal conditions and irradiation as well depends on limit of proliferative capacity of bone marrow given at the birth [2]. As we argued since the 1998 year, the renewing of all tissues in the body, including malignant ones, *consumes* young lymphoid cells, *exhausting* lymphopoietic potency and thus shortening the life span gradually [3]. The number of lymphocytes in the tumor opposes its stage [4], manifesting the level of frailty inducible by malignant growth as such [5]. Despite this, a strong mielodepression follows inevitably palliative chemo- and radiotherapy of cancer *additionally*. The myelosuppression / lymphocytopenia at “therapeutic” treatment-range leads to temporary restrictions a morphogenic cells activity, in particular, inside a tumor [2,6]. The morphogenic cells (trophocytes / feeding cells) are presented in the blood by hematopoietic stem cells, pro-lymphocytes, angiogenic T-cells [7-9] and some others, like “regulatory” T-cells [10]. All of them are purely differentiated, being on the scale from “truly naive to exhausted senescent T cells” closer to original than final types [11].

There are two ways to restrict the tumor growth’s support by them: 1) either to provoke a self-repopulation stem cells in bone marrow by its *injuring* with relatively high “hemotoxic” doses of “curative” factor, i.e., traditional/conventional mode, or 2) to *redirect* the circulating morphogenic cells *from feeding of* tumor toward *a reparation/regeneration* of numerous but *nonlethal* injuries of different normal cells, induced by *relatively low* doses of “curative” toxicants [6]. In both cases the mechanism of expected benefit has to be not direct but the *mediated* by rearrangement of the tissue’s renewing’s

[1]Laboratory for Improvement of the Cancer Treatment Methods, Russia.
[2]Devision of Gynecological Oncology, Russia.
**Corresponding author: E-mail: shoutko@inbox.ru;*

balance between the cancer and host body. The purpose our presentation is to demonstrate the reliability of described “competitive” approach of cancer therapy at real clinic conditions.

2. RESULT

Obtained retrospective results (Table 1) prove very clearly the possibility to get best survival without traditional local irradiation of tumor in high, so-called “tumoricidal” total dose 40-50 Gy. These results are quite comparable with modern data published already by National Cancer Institute, USA, and some others for specific-survival [12,13].

Table 1. The comparison of the overall 5-years survival after conventional and “competitive” therapies of advanced ovarian carcinoma (n=301 patients)

Mode of combined treatment and status of cancer	**Conventional**	**“Competitive”**
	Local irradiation (50 Gy*)	Subtotal irradiation (1÷9Gy*)
Primary	6,6%	33,8%
		p<0,01
Relapse	0%	10,8%
		P<0,05

**cumulative doses; p-values according exact Fisher-test.*

3. DISCISSION

The found distinction between “conventional” and “competitive” therapy may be attributed to the features of a radiation component of both combined schemes. During seven decades we have been discussing indirect mechanism of diminishing the cancer activity at the conditions of slightly increased natural background radiation or artificial ones in parallel with low dose total/subtotal radiation therapy. In oppose to idea of radiogenic stimulation of anti-cancer immunity [14,15], the mechanism proposed by us bases on the redistribution of circulating morphogenic cells from tumor to exposed normal tissues [3,16,17,18], and was statistically tested [19-20]. Moreover, it quite explains and approves benefit results of the type of chemotherapy cooled “metronomics” [21]. As a proliferative resource of bone marrow is limited and associated very closely with the life span and the level of lymphopenia [22,23], the HBI with cumulative dose 9 Gy was employed mostly as myelosuppressive one. The HBI with cumulative dose 1 Gy was assumed to be able to divert the circulating morphogenic sells [24] from tumor without diminishing their number. It is obviously, that both regimes cannot provide the tumor growth control by direct killing of malignant cells [25]. They were rather similar with non-selective cytotoxic chemotherapy of cancer, which cannot damage the tumor cells lethally, as the conventional local radiotherapy does. Otherwise, non-selective chemotherapy would be fatal to the organism. Beside this, a myelosuppressive action of modern combined therapy is not the rare, random event, as the 85% of main anti-cancer drugs are myelodepressants, in spite of their diversity and high cost. Hence, the mechanism of any nonselective cytotoxic treatment supposed to be an indirect one also, causing temporary disturbances of cellular reproduction in distant normal tissues [26]. The bone marrow is a main target, being the most sensitive/damaged physiological system among those responsible for preservation of life. Its lymphoid lineage is the most amortized by 3-6 courses of the conventional cytotoxic therapy, depending on the initial impact of lymphopoiesis [27].

4. CONCLUSION

We do not find of any principal objections to continue comprehensive investigation of “competitive” low dose-radiotherapy as a cost-effective and alternative to the nonselective cytotoxic chemotherapy of cancer.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Tinganelli W. and Durante M. Carbon Ion Radiobiology Cancers. 2020; 12:3022. DOI:10.3390/cancers12103022
2. Biological Effects of Ionizing Radiation on Tissues, Organs and Systems. Module VIII-b. - 2. Types of cellular damage. Cell death. repair.
   Available: https://www-pub.iaea.org › PDF › eprmedt › Day_2
3. Shoutko AN, Shatinina NN. Chronic Cancer -Could it be? Coherence. Int. J. of Integrative Medicine (Isr). 1998; 2:36-40.
4. Jimenez-Rodriguez R M., Patil S, Keshinro A, Shia J, Vakiani E, Stadler Z, et al. Quantitative assessment of tumor-infiltrating lymphocytes in mismatch repair proficient colon cancer, OncoImmunology. 2020; 9:1:1841948.
   DOI: 10.1080/2162402X.2020.1841948
   To link to this article: Available: https://doi.org/10.1080/2162402X.2020.1841948
5. Shoutko AN, Ekimova LP. The lifespan hormesis phenomenon I population does not make it helthier. Chapter 9 in book: Chalenges in Diseases and Health Resrearch v5 BPI india, uk. 2020;79-93.
6. Shoutko AN Immunity or morphogenesis in cancer development and treatment Integr Cancer Sci Therap. 2019;6:1-8
   DOI: 10.15761/ICST.1000317
7. Kucia M, Ratajczak J, Ratajczak MZ. Bone marrow as a source of circulating CXCR4+ tissue-committed stem cells. Biol Cell. 2005; 97:133-146. [Crossref]
8. Shoutko A, Ekimova L, Mus V, Sokurenko V. Fluctuations of CD34 cells number in blood of cancer patients during final year of life. MHSJ (Acad Publ Platform). 2012; 13:7-13.
9. Shoutko AN, Gerasimova OA, Fedorov VA, Zherebtsov FK. Non-Invasive Vibration-Stress of the Cirrhotic Liver of Patients Waiting for Transplantation Induces of Circulating CD133+ Stem Lymphocytes Committed Phenotypically toward the Liver. Open Journal of Biophysics. 2019;9: 155-168.
   Available: https://doi.org/10.4236/ojbiphy.2019.93012
10. Ohue Y, Nishikawa H, Regulatory T. (Treg) cells in cancer: Can Treg cells be a new therapeutic target Review Cancer Sci. 2019;110(7):2080-2089.
    DOI: 10.1111/cas.14069. PMCID: PMC6609813
11. Larbi A, Fulop T. From “Truly Naiıve” to “Exhausted Senescent” T Cells: When Markers Predict Functionality. Cytometry Part A. 2014;85A:25-35
12. Colombo N, Van Gorp T, Parma G, Amant F, Gatta G, et al. Ovarian cancer. Crit Rev Oncol Hematol. 2006; 60:159-179. [Crossref]
13. Wright JD, Chen L, Tergas AI, Patankar S, Burke WM, et al. Trends in relative survival for ovarian cancer from 1975 to 2011. Obstet Gynecol. 2015; 125:1345-1352. [Crossref]
14. Sakamoto K. Radiobiological bases for cancer therapy by total or half-body irradiation. Nonlinearity Biol Toxicol Med. 2004; 2:293-316.
    DOI: 10.1080/15401420490900254 [Crossref]
15. Scott BR. Low-dose-radiation stimulated natural chemical and biological protection against lung cancer. Dose Response. 2008; 6:299-318. [Crossref]
16. Shoutko AN, Ekimova LP. The impact of middle age on the viability of patients with nonmalignant and malignant diseases. Cancer Research Journal. 2014; 2:114-120.
17. Shoutko AN, Ekimova LP. Abnormal tissue proliferation and life span variability in chronically irradiated dogs. Radiat Environ Biophys. 2014; 53:65-72. [Crossref]
18. Shoutko AN, Ekimova LP. The effects of tissue regenerative status on hormesis in dogs irradiated during their lifespan. Open Journal of Biophysics. 2017; 7:101-115.
19. Shoutko AN, Yurkova LE, Borodulya KS, Ekimova LP. Lymphocytopenia and cytotoxic therapy in patients with advanced ovarian cancer. Cancer Research Journal. 2015; 3:47-51.

20. Shoutko AN, Yurkova LE, Borodulya KS, Ekimova LP. Protracted half-body irradiation instead of chemotherapy: life span and lymphocytopenia in relapsed ovarian cancer. International Journal of Tumor Therapy. 2016; 5:1-7.
21. Singh Malik P, Raina V, André N Metronomics as maintenance treatment in oncology: time for chemo-switch. Frontiers in Oncology. 2014;4|Article76
DOI: 10.3389/fonc.2014.00076
22. Common terminology criteria for adverse events v3.0 (CTCAE) Publish Date: 9 August 2006, American National Standards Institute; 2003.
23. Rimando J, Campbell J, Kim JH, Tang SC, Kim S. The Pretreatment Neutrophil/ Lymphocyte Ratio Is Associated with All-Cause Mortality in Black and White Patients with Non-metastatic Breast Cancer. Front Oncol. 2016; 6:81. [Crossref]
24. Rennert RC, Sorkin M, Garg RK, Gurtner GC. Stem cell recruitment after injury: lessons for regenerative medicine. Regen Med. 2012; 7:833-850. [Crossref]
25. Heinzerling JH, Cho J, Choy H. The role of radiotherapy in the treatment of metastatic diseases in Laden D, Welch DR, Paola B, Eds. Cancer metastasis: biologic basis and therapeutics. New York, USA; Cambrige University Press. 2011;612-621.
26. Malhotra V, Perry MC. Classical chemotherapy: mechanisms, toxicities and the therapeutic window. Cancer Biol Ther. 2003;2:2-4
27. Shoutko AN, Mus VF, Maystrenko DN. Peripheral Signs of Lymphocytopoiesis in the Prediction of the Terminal Life Span of Cancer Patients Chapter 13 in book: Current Topics in Medical research BPI ISBN: 978-81-947979-3-7, eBook ISBN: 978-93-90206-98-8
DOI: 10.9734/bpi/ctmamr/v5 pp138-154

© Copyright (2021): Author(s). The licensee is the publisher (B P International).

DISCLAIMER
This chapter is an extended version of the article published by the same author(s) in the following journal.
Radiology and Diagnostic Imaging, 1(2): 1-2, 2017.