Acta Scientific Pharmacology

Volume 3 Issue 3 March 2022

Short Communication

Factual Basis of Conventional Therapies in Metastatic Cancer Treatment - An Overview

K Ramalingam[1]* and P Karnan[2]

[1]Mediclone Biotech Research Centre, Chennai-48, Dr. Rai Memorial, Medical Centre (Cancer Treatment and Research), I.E.C Member, India

[2]Associate Professor, GRT College of Education, Tiruttani, India

***Corresponding Author:** K Ramalingam, Mediclone Biotech Research Centre, Chennai-48, Dr. Rai Memorial, Medical Centre (Cancer Treatment and Research), I.E.C Member, India.

Received: January 01, 2022

Published: February 16, 2022

Abstract

Cancer research towards the goal of Ehrlich's magic bullets has become an all time exciting and salubrious subject due to novel mechanisms involved in cancer cells which tilt the balance towards their success of survival and failure of novel drugs in the armamentaria of chemotherapy. Still the disease cancer remains as untreatable one beyond the metastatic stage. Both conventional and non conventional bio therapies became in vain futile attempts in rescuing a metastatic cancer patients who is defenseless with poor immune potential and weak and fragile to tolerate further the impacts of cyto-toxic chemotherapy and its side-effects. A meta-analysis of both conventional and non conventional therapies could bring new insights in the research of oncology towards the accomplishment of real-magic bullets. The subtle question that remains is why chemotherapy and radiation fail and why phytotherapy was unrecognized for cancer treatment by FDA USA. This is the utmost important goal in view of the fact (WHO) that almost 50 percent of global population will suffer from cancer disease in the near future.

Keywords: Chemotheraphy; Monoclonal Abs; Interleukines; Neuropeptides; Magic Bullets; Phytochemicals

Introduction

Cancer is a disease of multiple etiology, which manifest outwardly with visible symptoms after a long latent period of ten to fifteen years. Cancer research has become an all time exciting research because cancer disease remains untreatable after a specific stage when metastatic cancer cells invade distant sites to increase their secondary population tremendously that it becomes unstoppable even by the modern chemotherapeutic medicines. The death of the patient with organometastatic cancer cells becomes the reality as they become antagonistic to all human in built immune mechanisms and also to the modern drugs used in cancer treatment. Though the therapeutic research has come out with more toxic chemotherapeutic drugs and biological agents, all these became futile agents in a cancer patient who is defenseless with least immune potential and very weak and fragile to tolerate further the toxicity of modern drugs of conventional therapy. It is because the host-tumour relationship is upset and secondly the balance of power is tilted towards the tumour side. One can expect all immune defense mechanisms to function in an agile person but may not be expected in a patient, whose cancer reached the metastatic phases. This is the apt explanation for the first reason of tumour- host relationship becoming upset. For the second reason, the explanation in brief is the overwhelming antagonistic mechanisms of cancer cells which acquire various intricate cellular and molecular mechanisms of survival. In the metastatic cancer patients cancer cells become the fittest cells to survive which never allow either the drugs to act or the immune systems to function, make the patient(host) unfit for survival and drive the patient to death ultimately by such com-

plications as cachexia, ascites built up and immunological nudity etc. [1].

In cancer treatment the biological approach is far from complete. The above approach comprises three modes viz.,

- Agents acting on the host to boost defenses against the tumour eg.
    - The lymphokine IL-2(N.S) and Tumoric cell vaccine(S)
- Agents acting to kill the tumour cancer cells directly and e.g.
    - Tumour Necrosis factors is non-specific Anti tumour mabs are tumour specific.
- Agents acting to alter tumour biology.

Among these the first two agents are both tumour non-specific and tumour specific. The third category includes agents that interfere with tumour biology like the retinoids, lymphokines, leukoregulin and anti-metastatic agents.

Though in modern cancer therapeutics a number of chemical cytotoxic agents and biological agents are in vogue, both of them proved futile due to problems associated with these agents viz., innumerable side effects, altered or broken self tolerance and autoimmune destructive reaction.

In his book "PRUDENT PROXIES" Ramalingam [2,3] has mentioned the importance of phytochemical compounds acquired through food supplements, vegetables, fruits, Vitamins minerals etc. as the natural elixirs to prevent cancer as well as to cure cancer.

The non conventional phyto-therapeutic agents were prevented for clinical use by the FDA due to the assumption that the size of their therapeutic index is not being known. In the clinical trials stipulated by FDA, the phase I trial determines the maximum tolerant dose of the drug. The phase II trial determines the antitumour activity of the maximal tolerated dose in a variety of malignancies and the phase III trial integrates the drug into combinations of drugs and compare them to the standard therapies.

Ehrlich's magic bullet concept was visualized by the oncologists consequent to the development of hybridoma technology and the manufacture of monoclonal antibodies [4], that specifically binds to the cancer cells. However several obstacles were observed clinically while testing the efficacy of these monoclonal antibodies or their conjugates [5]. Despite these about one hundred monoclonal antibody drugs are in clinical use.

Cancer cells are more superior than our normal tissue cells in their response to any types of therapeutic armamentaria. Their responses only have prevented the realization of the enormous potentials of therapeutic drugs, (systemic) antibodies, or the conjugating drugs, toxins, isotopes and/or cytokines etc. The various anticancer mechanisms of Cancer cells include:

- Unlike the microbial pathogens which are alien to the body and easily recognized by the reportoires of the immune system, cancer. cells being the variant forms of normal counter parts with some original naive antigenic receptors, they escape from the immediate surveillance of the host/man/patient's immune system, which is and of heterogenous nature and potencies.
- Though targeted drugs are prepared with unique specificity for a specific tumour surface receptor, cancer cells develop target negative variants by their antigenic modulation through their genic- batteries.
- Cancer cells by secreting the surface antigens or shedding them into circulation may enhance the natural humoual antibody/formation, Ag-Ab Complex formation which may become a barrier to the administered antibody from reaching the tumour.
- Drug - Conjugated Anti bodies of monoclonal type as functional magic bullets has become a false notion and conceptually weak as they are cleared by the Reticulo- endothelial system, their concentrations reaching the target is often less compared to the chemotherapeutic free drugs administered systemically and are less toxic in action than the free cytotoxic drugs.
- Resistant metastatic cancer cells encoded with multidrug resistance genes will emit or vomit the drugs out of the cells and thus prevent their cytoplasmic uptake e.g. p170 glycoprotein.
- Metastatic cancer cells invasion or movement and their entry into the neo-angiogenic blood capillaries is an important episode of them, before their entry to distant sites or organs. Liotta., *et al*. (1984) have revealed that metastasizing Cancer cells express receptors for the basement membrane protein "laminin" for binding to it and also express an autocrine motility factor that allow them to move through the pores they make in the basement membrane and gain access to the blood stream.

- Recently in a special type of Prostate cancer, neuro-endocrine cells become embedded in the prostate tissue was noticed. The significance the neural and cancer tissue connection has not been considered pertinent towards cancer cells survival as well as their destruction. However previous literature on CNS has revealed that endorphins and encephalins and some neuropeptides can interact with various peripheral tissues and also that renal cells, adrenal cells, Pancreatic cells and peripheral blood lymphocytes all possers surface receptors to these brain neural peptides and proteins [6]. In addition bone marrow is also demonstrated to be the stimulator of anti body producers (SAPS) and their binding to specific receptors on lymphoid cell surfaces, modulate immune functions. These modulating peptide proteins of the brain, hypothalamus, bone marrow and nervous tissues have far reaching implications in imunomodulation, immunostimulation and immune-potentiation and in the therapeutic treatment of cancer disease [7]. Towards the above line, as early as in 1967, Eisen et.al have identified a myeloma protein with antibody activity is of interest to special mention.

In a recent article Ramalingam (2019) has mentioned that chemotherapy should have to go a long way in targeting the cancer cells by circumventing the formidable obstacles which the cancer cells employ and promote their survival and unstoppable growth, He has also revealed that about thirteen types of cancer cell mechanics have to be surpassed by some novel multi- hit agents like that of phyto chemicals of various kinds Viz., Polyphenols, Flavonoids, Saponins, Triterpenes, Alkaloids, Carotenoids etc., which have been demonstrated to enhance, cancer cell death in vitro and promise to do the same in vivo without side effects unlike that of other conventional therapies. So the options for phytotherapeutic medicines have far reaching implications towards cancer cure and hope that miracles can happen [8-10].

Bibliography

1. De Vita V., *et al*. "Cancer: Principles and practice of oncology". Lippincott. Philadelphia USA (1993).

2. Ramalingam K. "The Prudent Proxiex to Prevent Cancer-II Personal Publication, Chennai" (2018).

3. Ramalingam K. "The Prudent Proxies to prevent cancer I Personal Publication, Chennai" (2015).

4. Kohler G and Milstein C. "Continuous cultures of fused cells secreting antibody of predefined specificity". *Nature* 256 (1975): 495-497.

5. Epenetos AA., *et al*. "Limitations of radio-Rebelled monoclonal antibodies for localization of Human neo plasoms". *Cancer Research* 46 (1986): 3183-3191.

6. Petrov RV., *et al*. "Control and Reguelation of the immune response". Meditsina, Leningrad (in Russian) (1981).

7. K Ramalingam and UD Bharathi Rajan. "An analysis of the current knowledge about crustacean immunity and diseases with an overview of vertebrate system". *Uttar Pradesh Journal of Zoology* 27.2 (2007): 135-158.

8. Barsky SH., *et al*. "Laminin molecular domains which alter metastasis murine modal". *Journal of Clinical Investigation* 74 (1984): 843-884.

9. Eisen HN., *et al*. "A myolema protein with antibody activity". *Cold Spring Harbor Symposia on Quantitative Biology* 32 (1967): 75-97.

10. Port CB., *et al*. "Octapeptides deduced from the neuropeptide receptor like pattern of antigen T4 in brain potently inhibit Human imuno deficiency virus. Receptor binding and T-cell infectivity". *Proceedings of the National Academy of Sciences of the United States of America* 83 (1985): 9254-9258.