Ortiz MR, et al., J Altern Complement Integr Med 2022, 8: 244
DOI: 10.24966/ACIM-7562/100244

HSOA Journal of
Alternative, Complementary & Integrative Medicine

Case Report

High Dose Intravenous Ascorbic Acid (Vitamin C) and Glutathione as Integrative Therapy in a Patient with Diffuse Large B-Cell Lymphoma: Case Report

Mizael Ramos-Ortiz[1], Raúl H Morales-Borges[2]* and Michael J González[3]

[1]Department of Interdisciplinary Studies, Natural Sciences Faculty, University of Puerto Rico Rio Piedras Campus, Rio Piedras PR, USA

[2]Department of Medicine of Ashford of Presbyterian Community Hospital, PSC and Division of Hematology/Oncology, Integrative Optimal Health of Puerto Rico, San Juan PR, USA

[3]Department Human Development, Nutrition Program, Medical Sciences Campus, School of Public Health, University of Puerto Rico, San Juan PR , USA

Abstract

Diffuse Large B-Cell Lymphoma is the most common Non-Hodgkin's Lymphoma. Given its prevalence, there is an interest in studying the treatments available and how these can be improved. The standard treatment is a chemotherapeutic regimen known as R-CHOP. The goal of this paper is to inform of an integrative approach to R-CHOP, implementing high dose intravenous Vitamin C (AA) with glutathione (GSH). In the case presented herein, the patient attained complete remission with a minimal toxicity profile and an excellent performance status. These results present a possible viable approach for patients suffering of Diffuse Large B-Cell Lymphoma. In this paper, we also briefly review the literature available on the aforementioned treatment.

Keywords: Ascorbic Acid; Diffuse Large B-Cell Lymphoma; Glutathione; Integrative Medicine; Integrative Oncology; Vitamin C

***Corresponding author:** Raúl H Morales-Borges, Department of Medicine of Ashford of Presbyterian Community Hospital, PSC and Division of Hematology/Oncology, Integrative Optimal Health of Puerto Rico, San Juan PR, USA, Tel: +1 787220412; Fax: +1 7877230554; E-mail: raul.morales.borges@gmail.com; raul@nairesearch.org

Citation: Mizael Ramos-Ortiz, Raul Morales-Borges, González MJ (2022) High Dose Intravenous Ascorbic Acid (Vitamin C) and Glutathione as Integrative Therapy in a Patient with Diffuse Large B-Cell Lymphoma: Case Report. J Altern Complement Integr Med 8: 244.

Received: April 13, 2022; **Accepted:** April 18, 2022; **Published:** April 25, 2022

Resumen

El linfoma difuso de células b grande es el linfoma de tipo no-Hodgkin's más común. Dado su prevalencia, existe un interés en investigar sus tratamientos y como estos pueden ser mejorados. El tratamiento estándar es un régimen quimioterapéutico conocido como R-CHOP. El objetivo de este artículo es informar sobre un método integrativo en donde se implementan dosis altas de vitamina C intravenosa y glutatión al R-CHOP. En el caso presentado, un paciente de Linfoma Difuso de Células B Grande alcanzó remisión completa con un perfil de toxicidad mínimo y una evaluación física excelente. Los resultados revelan una posible vía para atender este tipo de caso. Adicional, en este artículo también se revisa brevemente la información disponible acerca del tratamiento mencionado

Introduction

In the case presented herein, we discuss the effects of high dose intravenous Vitamin C (IV AA) with glutathione (GSH) integrated with chemotherapy on Diffuse Large B-Cell Lymphoma (DLBCL). This cancer accounts for 30% common Non-Hodgkin's Lymphoma, making it the most common of such cases [1]. In general, 63.2% of patients diagnosed survive 5 years or more [2]. This percentage is directly proportional to the stage in which it's found (the earlier the stage, the higher the chances of survival). The common approach is to apply systemic chemoimmunotherapy, R-CHOP being the standard treatment [1]. In this case, R-CHOP was integrated with doses of IV Vitamin C and Glutathione.

Studies have revealed that high dose IV AA has cytotoxic effects on cancer cells [3-6]. This is primarily due to its pro-oxidant activity via the production of H_2O_2 in addition to other biochemical mechanisms. AA primarily acts as an electron donor in biosynthetic pathways, such as the synthesis of collagen. Its co-enzymatic activity is also known to play a role in cholesterol metabolism and neurotransmitter synthesis (non-specified), among others [3]. Other case reports have demonstrated this treatment's effectivity in treating cancer cells and improving the patient's condition [7,8]. One of the two cases mentioned (García et al.) tells the story of a late-stage prostate cancer patient, which within a year of treatment with IV AA and a change in diet improved in physical condition (loss of pain and recovery of limited capabilities) and mental improvement (decreased dementia state).

Glutathione (GSH), an antioxidant abundant in the human body, can have different effects on cancer cells. If GSH is present in a cancer cell line, it provides it with chemo-resistant properties. However, if administered intracellularly, GSH can have cytotoxic effects in the tumor. This antagonistic effect can be explained via GSH conjugates which in fact detoxify cells and are formed by the interaction of GSH and electrophilic species [9]. Another way to approach GSH is to remove it; depletion of GHS augments chemosensitivity in cancer cells. Adding GSH analogues to interact with Glutathione-S-Transferase could also deplete tumor chemoresistance [10]. GSH mechanisms are still speculative and warrant more research.

The combination of antioxidants and chemotherapy is a controversial area in the practice of oncology. A study with mice demonstrated that coadministration of exogenous GSH significantly attenuated doxorubicin-induced cardiotoxicity and hepatotoxicity by increasing intracellular GSH levels [11]. Another study showed a possible involvement of glutathione as an important intracellular protective agent in cisplatin-induced genotoxic effects in the mice bearing ascites Dalton's lymphoma [12]. There was no clinical experience published using GSH to minimize side effects of chemotherapeutic agents when we reviewed the medical literature.

To our knowledge, there is no published case on using Vitamin C and Glutathione integrated with chemotherapy to treat Diffuse Large B-Cell Lymphoma. In this report we are advancing the cause for integrative medicine and the use of Vitamin C in cancer patients.

Case Report

History, Exam and Diagnostic Studies

The patient is a 64-year-old white male from Puerto Rico who visited his doctor feeling pain in his left flank region. A CT scan revealed he had retroperitoneal lymphadenopathy. Standard laboratory resulted with a serum-ß-2-microglobulin of 0.15 mg/dL, sed rate of 1.00 mm/hr.; lactic acid dehydrogenase (LDH) of 136 U, a negative C-Reactive Protein (CRP), and a normal Glucose-6-Phosphate dehydrogenase count (347.49 U/RBC). Nuclear PET/CT scan depicted bilateral axillary lymphadenopathy, right upper cervical and left lower cervical enlarged nodes of 3.7 x 3.5 cm and multiple splenic masses. A CT guided biopsy of the left paraaortic node revealed that the patient had Diffuse Large B-Cell Lymphoma.

Prior to this diagnosis, the patient had not experienced other diseases. He did not smoke, nor was he exposed to irritants (such as asbestos). He had no known drug allergies, no known use of illegal drugs and drank occasional wine. Pertinent surgical history includes right knee meniscus surgery and nasal septum surgery. Physical exams showed he had splenomegaly.

Treatment

The patient was submitted to an integrative regimen of R-CHOP supplemented with high dose AA IV and GSH IV a day before each chemo cycle. The cycles were scheduled to be administered with at least 28 days in between each treatment, the last two being five months apart. The patient was given four cycles of R-CHOP, which included: 1200mg of Cyclophosphamide IV, 100mg of Doxorubicin IV, 2mg of Vincristine IV, 100mg of Prednisone Oral, and 735mg of Rituximab IV. The day before each of the first four cycles, the patient was infused with 20g of AA, and 200mg of GSH. The last two cycles were of consolidation, ensuring that the patient was cancer free. In these last two cycles, the patient was only infused with 25g of AA the day before, and 735mg Rituximab IV.

Post-treatment

The treatment was well tolerated with minimal side effects such as: stomatitis, neutropenia, fatigue, peripheral neuropathy, and constipation. All of these were grade 1, manageable, and the patient recovered from them all. After treatment completion he was reevaluated as following. The PET/CT scan found marked metabolic response to treatment with no metabolically active residual disease at present time. Repeated laboratories were negative with negative CRP, a sed rate of 2 mm/hr.; LDH of 132 U, and a serum-ß-2-microglobulin of 0.12 mg/dL. He is currently asymptomatic, with normal physical exam results and an excellent performance status.

Discussion

Rituximab-CHOP (R-CHOP) is the standard treatment for DLBCL. One study reveals that rituximab on combined with artesunate may act in a complementary manner and eventually synergize in tumor cell killing [13]. Rituximab is a monoclonal antibody that targets CD20 antigen usually used as standard treatment for Non-Hodgkin's Lymphoma and works as a sensitizer of B-cell lymphoma cells to standard anticancer drugs. Artesunate is an anti-malarial drug, which also exerts profound activity towards cancer cells. While rituximab alone was minimally cytotoxic, it increased cytotoxicity when combined to artesunate in Ramos cells. Although the introduction of rituximab to CHOP has increased the quality of the treatment, there is still much room to grow [14]. Only 30-50% of the patients survive, 30% relapse after treatment is complete, and there is no firm knowledge on alternatives for treatment-resistant cancers or relapsing patients [15]. Therefore, it is of importance to identify improvements to this chemotherapeutic scheme whilst new drugs are developed.

It has been reported that high intracellular concentrations of AA have cytotoxic effects on tumor cells [3]. AA exerts an antioxidant effect extracellularly, inhibiting free radicals and reactive oxygen and nitrogen species; all whilst having prooxidant effects inside tumor cells. Its usefulness comes also due to its harmless nature towards non-cancer cells. Normal cells have antioxidant enzymes which eliminate H_2O_2 and other reactive species [16]. Its chemo-selectivity is due to its similarities to glucose, the main source of energy for tumor cells. Aside from being an efficient chemotherapeutic agent, IV AA has also been shown to improve patients' quality of life by alleviating cancer treatment side effects such as fatigue, insomnia, nausea, and others [17]. AA decreases oxidative stress produced by chemotherapy, which may reduce fatigue. AA also participates in the synthesis of neurotransmitters, like serotonin, which are involved in patient mood (Tables 1 & 2).

Drug	Amount
Cyclophosphamide IV	1200mg
Doxorubicin IV	100mg
Vincristine IV	2mg
Prednisone Oral	100mg
Rituximab IV	735mg

Table 1: Chemotherapy regimen of Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP every 28 days for 4 cycles.

IV = Intravenously

R-CHOP chemotherapy is a standard treatment for non-Hodgkin lymphoma. R-CHOP is most often given in cycles 3 to 4 weeks apart. It is a systemic therapy that consists of five separate drugs. These are:

- (R) rituximab (Rituxan)
- (C) cyclophosphamide
- (H) doxorubicin hydrochloride
- (O) vincristine (Oncovin, Vincasar PFS)
- (P) prednisone

Date	22/08/18	9/19/2018	10/16/2018	11/14/2018	1/9/2018	3/19/2019
Concentrations of AA	25g	25g	25g	25g	25g	25g
Concentrations of GSH	200mg	200mg	200mg	200mg	200mg	200mg
Date	7/11/2019	12/10/2019				
Concentrations of AA	25g	25g				
Concentrations of GSH	0	0				

Table 2: High dose Ascorbic Acid and Glutathione (AA & GSH) cycles.

AA = Ascorbic Acid (Vitamin C)

GSH = Glutathione

g = grams

mg = milligrams

High-dose Vitamin C (AA) modulates infiltration of the tumor microenvironment by cells of the immune system and delays cancer growth in a T cell-dependent manner. GSH is a promising drug for the prevention of chemotherapy-induced toxicity, and that it does not reduce the clinical activity of those agents. That is the rationale of adding them to the standard regimen of chemotherapy in this case.

Regarding Glutathione (GSH), its content in cancer cells is particularly relevant in regulating mutagenic mechanisms, DNA synthesis, growth, and multidrug and radiation resistance. Higher GSH levels are associated with multidrug and radiation resistance in malignant tumors, as compared to with normal tissues. Thus, approaches to cancer treatment based on modulation of GSH should control possible growth-associated changes in GSH content and synthesis in these cells. Despite the potential benefits for cancer therapy of a selective GSH-depleting strategy, such a methodology has remained elusive up to now. Estrela, Ortega and Obrador [18] made an excellent review focusing on an analysis of links among GSH, adaptive responses to stress, molecular mechanisms of invasive cancer cell survival and death, and sensitization of metastatic cells to therapy. Experimental evidence shows that acceleration of GSH efflux facilitates selective GSH depletion in metastatic cells.

Applying these concepts to our case, and being the only one published in medical literature, we postulate that adding GSH as a therapeutic tool to R-CHOP regimen is synergistically killing the lymphoma cells in addition to minimizing the toxicity profile. The outcome of this case, although clearly not sufficient, demonstrates the viability of this approach combining known chemotherapeutic treatments with new supplements, such as AA and GSH. One case report is always limited by its nature, one patient's success is never enough to fulfill the rigorous standard for establishing treatments. Our report does however call for more research into the biochemistry of GSH and AA, and how these can be applied safely to other cancer patients.

Conclusion

This is the first case describing potential uses of vitamin C and glutathione, both integrated with chemotherapy, to treat Diffuse Large B Cell Lymphoma. The result of this treatment was a cancer free asymptomatic patient. This case report adds to the literature that states Vitamin C's utility as an adjuvant treatment, functioning in two ways: inducing tumor reduction and improving patient quality of life. Treatments involving GSH administration, as the one in this case presented, have potential uses in facilitating, or supplementing chemotherapy and warrant further research. Implementation of R-CHOP with high dose AA and GSH is a viable approach for patients suffering of DLBCL. Finally, this paper advocates the implementation of various treatments to achieve a higher grade of medicine.

Acknowledgement

The authors would like to acknowledge and thank the oncology nurse Nelmarie Álvarez Rodríguez for her collaboration in patient care and during the transfusions.

References

1. Abraham J, Gulley J L (2019) The Bethesda Handbook of Clinical Oncology. Wolters Klewer, USA.
2. NIH (2022) Cancer Stat Facts: NHL - Diffuse Large B-Cell Lymphoma (DLBCL). NIH, USA.
3. González MJ, Massari JRM, Mora EM, Guzmán A, Riordan NH, et al. (2005) Orthomolecular oncology review: ascorbic acid and cancer 25 years later. Integrative cancer therapies 4: 32-44.
4. Cameron E, Pauling L (1974) The orthomolecular treatment of cancer. I. The role of ascorbic acid in host resistance. Chem Biol Interact 9: 273-283.
5. Cameron E, Pauling L, Leibovitz B (1979) Ascorbic Acid and Cancer: A Review. Cancer Res March 39: 663-681.
6. Padayatty SJ, Levine M (2000) Reevaluation of ascorbate in cancer treatment: emerging evidence, open minds and serendipity. Journal of the American College of Nutrition 19: 423-425.
7. Garcia KM, Jesus CD, Berdiel MJ, Miranda JR, Duconge J, et al. (2016) Intravenous Vitamin C and Metabolic Correction as Adjuvant Therapy for prostate Cancer: a Case Report. J Cancer Prev & Curr Res 5: 1-3.
8. González MJ, Berdiel MJ, Cintrón AV (2017) High Dose IV Vitamin C and Metastatic Breast Cancer: A Case Report. J Orthomolec Med 32: 1-4.
9. Balendiran GK, Dabur R, Fraser D (2004) The Role of Glutathione in cancer. Cell Biochem and Funct 22: 343-352.
10. Traverso N, Ricciarelli R, Nitti M, Marengo B, Furfaro AL, et al. (2013) Role of Glutathione in Cancer Progression and Chemoresistance. Oxidative Med and Cell Longevity 10: 1-10.
11. Shen BY, Chen C, Xu YF, Shen JJ, Guo HM, et al. (2019) Is the combinational administration of doxorubicin and glutathione a reasonable proposal? Acta Pharmacol Sin 40: 699-709.
12. Khynriam D, Prasad SB (2003) Cisplatin-induced genotoxic effects and endogenous glutathione levels in mice bearing ascites Dalton's lymphoma. Mutat Res 526: 9-18.
13. Sieber S, Gdynia G, Roth W, Bonavida B, Efferth T (2009) Combination treatment of malignant B cells using the anti-CD20 antibody rituximab and the anti-malarial artesunate. Int J Oncol 35: 149-158.
14. Sehn LH (2010) A decade of R-CHOP. 116: 5-6.
15. Coiffier B, Sarkozy C (2016) Diffuse large B-cell lymphoma : R-CHOP failure — what to do ? Hematology 2016: 366-378.
16. Shilpi S, Shivvedi R, Singh A, Saraogi GK, Jain V, et al. (2018) Vitamin-C: properties, functions, and application in cancer therapy. J Cancer Prev & Curr Res 331: 331-335.
17. Carr AC, Vissers MCM, Cook JS (2014) The effect of intravenous vitamin C on cancer- and chemotherapy-related fatigue and quality of life. Front in Oncol 4: 1-7.
18. Estrela JM, Ortega A, Obrador E (2006) Glutathione in cancer biology and therapy. Crit Rev Clin Lab Sci 43: 143-181.

HERALD

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752