JOURNAL OF ORTHOMOLECULAR MEDICINE

OPEN ACCESS

VOLUME 33, NUMBER 4

PUBLISHED: AUGUST 2018

CASE REPORT

High-Dose Vitamin C Helps Prevent Recurrence of Stage IV Ovarian Cancer: A Case Report

Author(s): Yuen Chuen Fong Raymond, BSc, MBBS, MMedSc, M Med(OM), FAMS[1], Stephanie Anne Loke Mun See, BA, BA (Hons)[2], Yuen Tin Wei[3]

1. Principal Doctor, Hosanna Clinic, 2. Researcher, Hosanna Clinic, 3. Medical Student, National University of Singapore

Abstract. *Introduction: Stage IV ovarian cancer has a high recurrence rate of 90%-95%. High dose intravenous vitamin C (IVC) therapy administered with nutritional supplements helps prevent recurrence of cancer.*

Case Description: The stage IV ovarian cancer patient began IVC therapy soon after completion of conventional treatments. The patient started with a consecutive 28-day program at a dosage of 25g/day, increasing gradually to 75g/day. Following this, the frequency declined gradually from twice a week over twelve months and slowly reduced to once every three to four weeks at 75g/day. The patient also adopted a ketogenic diet with supplements, exercise and detoxification. Progress was monitored via blood tests and scans every three to six months.

Discussion: Despite the initial poor prognosis and high relapse rate of late-stage ovarian cancers, this patient is cancer-free five years after diagnosis and enjoys a good quality of life. High dose IVC is documented to enhance the cancer patient's recovery and prolonged survival. Recent research has shown that it enhances cancer-killing effects of radiation and chemotherapy and helps to induce the epigenetic modulation of blood cancer cells. It is effective in killing chemo-resistant cancer stem cells.

Recommendations: High-dose IVC is safe and cost-effective with good anti-inflammatory and potential anti-cancer properties. It is recommended that cancer patients consider high-dose IVC therapy upon the completion of conventional oncology treatment to maintain a good quality of life and potentially prolong survival.

Objective

This is a single case report that documents the benefits of high-dose intravenous vitamin C (IVC) therapy in keeping high recurrence of late stage ovarian cancer at bay.

Introduction

Ovarian cancer is the fifth most common type of cancer in Singapore (National Registry of Diseases Office, 2017) and has the seventh highest cancer mortality rate in females in 2010-2014 (NRDO, 2015). Incidence rates of ovarian cancer in Singapore are higher than that of Australia, Japan, China and India but lower than the United Kingdom (NRDO, 2015).

Ovarian cancer often has no symptoms in its early stages. Four in five ovarian cancer patients (Alteri et al., 2018) in the United States are diagnosed at the advanced stages where the

 ISSN 0317-0209

disease has already spread into the abdominal cavity. Although the five-year survival rate for patients diagnosed with ovarian cancer is 47.4 percent (2008-2014) in the United States (Noone et al., 2018), late-stage patients have a disproportionately high rate of recurrence with stage III and IV patients recording 70 to 90 percent and 90 to 95 percent recurrence rates respectively (Ovarian Cancer Research Fund Alliance).

In the United States, there is no lack of medical research documenting the beneficial effects of IVC therapy as a form of cancer treatment. Its use is increasing in popularity amongst integrative, functional and orthomolecular medicine practitioners.

IVC therapy was first applied on cancer patients by Linus Pauling (Cameron & Campbell, 1974). IVC therapy has a controversial history, due in part to subsequent clinical trials conducted at the Mayo Clinic which failed to demonstrate any benefit (Moertel et al., 1985; Creagan, Moertel & O'Fallon, 1979). However, it was later discovered that although the similar doses were used in both the Pauling-Cameron and Mayo Clinic studies, the former administered the vitamin C (ascorbic acid) intravenously while the latter administered the vitamin C orally, leading to drastically different outcomes (Cameron, 1991; Padayatty, Sun & Wang, 2004).

Studies undertaken by the United States of America National Institute of Health showed that vitamin C demonstrated cytotoxicity in cancer cells at high serum levels and is achievable only through intravenous administration (Padayatty, 2004). Furthermore, studies have also shown that oral administration of large doses of vitamin C increases serum levels to a maximum of 220 µmol/L while serum levels can reach 14,000 µmol/L via intravenous administration (Padayatty, 2004). Concentrations of 1,000 to 5,000 µmol/L are selectively cytotoxic to tumour cells in vitro (Padayatty, 2004; Chen, Espey, & Krishna, 2005).

In Singapore, IVC therapy is better known as a form of aesthetic treatment for skin whitening and rejuvenation rather than as a type cancer therapy primarily due to a lack of supporting data from controlled clinical trials. Many Singaporean cancer patients are well aware of the negative side effects of conventional cancer treatment, causing some to opt for alternative treatments such as Chinese medicine, herbal medicine, acupuncture, bio-resonance therapy, Gerson therapy, macrobiotic diets and raw food diets to complement conventional cancer treatments (Yuen, Chong & Lim, 2016). Since many of these alternative treatments are not well documented, their effectiveness remains unknown.

Patient Adopted High-Dose IVC Therapy Right After Surgery and Chemotherapy

The patient, a 48-year-old Chinese woman, was diagnosed with stage IV ovarian cancer in March 2013. A well-defined rounded lesion with mild enhancing rim was found situated in a posterolateral manner to the left submandibular gland and lateral to the left carotid vessels. Soon after diagnosis, the patient underwent oophorectomy and hysterosalpingectomy surgeries, followed by six cycles of chemotherapy and radiotherapy. Post-treatment, blood tests conducted on September 21, 2013 indicated that her tumour markers were within the normal range, while her haemoglobin levels stood at 9.7g/dL (12.0-16.0g/dL) and white blood cell count at 2.9x109/L (4-10x109/L).

Although in remission, her oncologist warned that late-stage ovarian cancer patients have a 70 percent probability of a relapse within the first year. The despondent patient was determined not to give up, and in a bid to prevent a relapse, she decided to give IVC therapy a try in November 2013 to repair and restore her immune system.

The patient underwent an initial daily program of high-dose IVC starting from a dosage of 25g and progressively increasing up to 75g per day over a period of 28 days. Subsequently, the patient maintained an IVC regiment of 75g per day, two times a week for a period of twelve months and reduced to once a week for six months. After this, the treatment was further reduced to one dose every two weeks for another six months and finally to a maintenance dose every three or four weeks until five years post-operation.

To complement the IVC treatment, the patient adopted a plant-based diet, drank raw vegetable juices and consumed additional nutritional supplements (Yuen et al., 2016). In addition, the patient adopted the modified Gerson protocol for liver detoxification and exercised two to three times per week.

Her progress was monitored every three to six months by her oncologist and Dr Yuen via pelvic ultrasounds, blood tests for ovarian cancer markers, renal and liver functions, complete blood profiles as well as inflammation markers.

Results

A blood test conducted in March 2015 showed an increase in haemoglobin levels to 11.3 g/dL, while white blood cell count increased to 5.8x109/L. Even though the red and white blood cell counts were in the lower end of the reference range, the patient's health improved and she experienced a better quality of life.

A pelvic ultrasound conducted in March 2015 showed no pelvic mass or free fluid with an unremarkable urinary bladder status. A subsequent blood test on April 20, 2015 showed normal CA125 tumour marker (cancer antigen) of 6.1 U/mL (<36 U/mL). On April 12, 2018, she had a CA125 of 3.0 U/mL, while MRI scans showed no cancer growth and no abnormal pelvic mass was observed.

 ISSN 0317-0209

It has been more than five years since her completion of conventional cancer treatment, and the patient has not experienced a relapse of cancer. She currently enjoys a good quality of life and has certainly beaten the odds.

Discussion

Pharmacology: Vitamin C is a water-soluble antioxidant that is important for the proper functioning of the immune system. Dr Hugh Riordan, who founded the Riordan Clinic in 1975, noted that in high doses vitamin C has positive effects on many chronic illnesses (Riordan,1988; Carr & McCall, 2017).

It is undisputed that cancer cells absorb glucose at much higher rates than normal cells. PET and CT scans – common cancer diagnostic tools – involve injecting radioactive glucose into patients to identify and evaluate cancer metastases in their bodies.

The molecular structure of vitamin C is remarkably similar to glucose. When high-doses of vitamin C are administered intravenously, it becomes a pre-oxidant and cancer tumour cells mistakenly absorb vitamin C as its food source. There is increasing evidence that IVC is selectively toxic to some types of tumour cells by inducing tumour cell apoptosis, inhibiting angiogenesis and reducing inflammation (Riordan Clinic Research Institute, 2015). Vitamin C at normal physiological concentrations is a water-soluble antioxidant (Riordan Clinic Research Institute, 2015). However, at high concentrations (350-450 mg/dL), vitamin C dissociates in the extracellular fluid to become an ascorbate radical (AscH−), causing iron to be reduced to the ferrous form (AscH− + Fe3+ → _Fe2+ + AscH− + H+). The ferrous iron then reacts with oxygen, producing a superoxide anion (O2−), which reacts with hydrogen to form H_2O_2 (Riordan Clinic Research Institute, 2015). As the concentration of H_2O_2 increases in these tumour cells, they are vulnerable to the cytotoxic effects of H_2O_2, and hence inducing apoptosis and tumour cells are killed (Chen et al., 2005; Fritz et al., 2014; Putchala et al., 2013; Deubzer et al., 2010).

Under the Riordan IVC protocol, the Riordan Clinic advocates a concentration of 0.1 to 1.0g of ascorbic acid per kilogram of body mass (Riordan Clinic Research Institute, 2013b).

Effects of IVC Therapy: IVC therapy is relatively safe compared to radiotherapy and chemotherapy.

The patient experienced temporal healing reactions such as mild fever and vomiting during and up to two hours after the IVC therapy. Endotoxins produced by the necrosis of harmful cells create healing responses similar to the Jarish-Herzheimer reaction (Pound & May, 2005). Such healing responses may manifest as fever, chills, strong body odour and pimples on the body. These reactions occur within two hours after IVC therapy, are transient, reversible and are typically resolved after two to three hours.

By contrast, the patient sustained prolonged side effects such as dryness in the mouth, eyes, and nose, muscle and bone aches, toothache, hair loss, loss of taste, frequent nosebleeds, lethargy, weakness, and low immunity during her prior chemotherapy and radiotherapy protocols.

Against the odds of a 90 to 95 percent recurrence rate for stage IV ovarian cancer within the first year, the patient did not experience a relapse. As of May 2018 - five years after her initial diagnosis – blood tests and scans indicate that her cancer did not relapse and she is in complete remission. The patient now enjoys a good quality of life, loves travelling and is gratefully living out a purposeful new lease of life.

Such results can be attributed to the benefits of IVC therapy and is not a coincidence.

Benefits of High-dose Vitamin C as an Anti-cancer Agent: High-doses of vitamin C has been widely documented to effect cytotoxic and anti-metastatic actions on malignant cell lines (Chen et al., 2005) and can enhance chemotherapy by reducing chemo toxicity in ovarian cancer (Yan et al., 2014).

The treatment improves the quality of life for cancer patients (Kuiper et al., 2014; Carr, Vissers & Cook, 2014; Yeom, Jung & Song, 2007), prolongs survival (Cameron & Pauling, 1976; Cameron & Pauling, 1978), potentiates chemotherapy and reduces the side effects of chemotherapy (Jung et al., 2016; Hoffer et al., 2015).

It is proven safe even in high-doses (Schoenfeld et al., 2017; Stephenson, Levin, Spector & Lis, 2013) and enhances the immune systems of cancer patients to fight against cancer (Maggini et al., 2017; Carr and Maggini, 2017; Pavlovic, 2010; Strohle et al., 2011). It also raises the host resistance against cancer (Gonzalez & Miranda-Massari, 2014), prevent the cancer from further spreading (Schleich et al., 2013). It is an epigenetic modulator of genes with a key role in cancer development (Shenoy, Bhagat & Nieves, 2017; De Francesco et al., 2017; University of Salford, 2017).

Conclusion

Compared to conventional chemotherapy and radiotherapy, IVC therapy, in combination with a diet and supplement regimen, appears to help prevent the recurrence of stage IV ovarian cancer. The combined use of IVC therapy, diet and supplemental nutrition reduces inflammation, improves sur-

 ISSN 0317-0209

vival rate, enhances quality of life and prolongs life expectancy in ovarian cancer patients without all the negative side effects that accompanies conventional cancer treatment.

IVC therapy has also been co-administered with conventional therapy without impairing the response. It is safe for most patients and relatively inexpensive. IVC therapy has the potential to become an important chemotherapeutic method to combat cancer. This, however, can take place only through further research and clinical study.

Authors' Notes

This article was written as an observational study of one patient.

Declaration of Conflicting Interests: The authors declare there are no conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding: The authors did not receive any paid honoraria, financial support nor external grants for the research, authorship and/or publication of this article from any pharmaceutical companies nor any other organizations.

Acknowledgements: The authors extend our heartfelt thanks to the ovarian patient and her husband for permitting us to publish and share her medical information. We also wish to acknowledge participants in the Hosanna Clinic Cancer Patients' Support Group for their encouragement to continue the pursuit of safe and less invasive cancer therapies and to spread the word. Finally, our gratitude and appreciation goes to the dedicated staff of Hosanna Clinic - Sujeewa, Lynn, Tharidu and Shalika - who tirelessly and patiently provided much needed care, support and love to our cancer patients.

References

Alteri R, Brooks D, Chambers W, Chang E, Cotter J, Desantis C, Drope J, Fedewa S, Gansler T, Gapstur S, Gaudet M. (2018) *Cancer Facts & Figures 2018,* pp 28. American Cancer Society.

Cameron E, Campbell A (1974). The orthomolecular treatment of cancer. II Clinical trial of high-dose ascorbic acid supplements in advanced human cancer. *Chem Biol Interact,* 1974; 9(4): 285-315.

Cameron E. (1991) Protocol for the use of vitamin C in the treatment of cancer. *Med Hypotheses,* 1991;36(3):190- 194.

Cameron E, Pauling L (1976) Supplemental ascorbate in the supportive treatment of cancer: Prolongation of survival times in terminal human cancer. *Proc Natl Acad Sci USA,* 1976; 73(10): 3685-3689.

Cameron E, Pauling L (1978) Supplemental ascorbate in the supportive treatment of cancer: Re-evaluation of prolongation of survival times in terminal human cancer. *Proc Natl Acad Sci USA*,1978; 75(9): 4538-4542.

Carr AC, McCall C. (14 April 2017) The role of vitamin C in the treatment of pain: new insights. *J Transl Med,* 2017;15(1):77. DOI: 10.1186/s12967-017-1179-7

Carr AC, Vissers MC, Cook JS (16 Oct 2014) The effect of intravenous vitamin C on cancer and chemotherapy-related fatigue and quality of life. *Front Oncol,* 2014;4: 283. DOI: 10.3389/fonc.2014.00283

Carr AC and Maggini S. (3 Nov 2017) Vitamin C and Immune Function. *Nutrients,* 2017; 9(11). pii: E1211. DOI: 10.3390/nu9111211.

Chen Q, Espey MG, Krishna MC, Mitchell JB, Corpe CP, Buettner GR, Shacter E, Levine M. (2005) Pharmacologic ascorbic acid concentrations selectively kill cancer cells: Action as a pro-drug to deliver hydrogen peroxide to tissues. *PNAS,* 2005; 102(38):13604–13609.

Creagan ET, Moertel CG, O'Fallon JR, et al. (1979) Failure of high-dose vitamin C (ascorbic acid) therapy to benefit patients with advanced cancer: a controlled trial. *N Engl J Med,* 1979; 301(13): 687-690.

De Francesco EM, Bonuccelli G, Maggiolini M, Sotgia F, Lisanti MP. (9 Jun 2017) Vitamin C and Doxycycline: A synthetic lethal combination therapy targeting metabolic flexibility in cancer stem cells (CSCs). *Oncotarget,* 2017 Jun 9; 8(40): 67269-67286. DOI: 10.18632/oncotarget.18428. eCollection 2017 Sep 15.

Deubzer B, Mayer F, Kuci Z, et al. (2010) H_2O_2-mediated cytotoxicity of pharmacologic ascorbate concentrations to neuroblastoma cells: potential role of lactate and ferritin. *Cell Physiol Biochem,* 2010; 25: 767-774.

Fritz H, Flower G, Weeks L, et al. (2014) Intravenous vitamin C and cancer: a systematic review. *Integr Cancer Ther,* 2014; 13: 280-300.

Gonzalez MJ, Miranda-Massari JR (2014) Anticancer Mechanisms of Vitamin C. In: *New Insights on Vitamin C and Cancer.* SpringerBriefs in Cancer Research, Springer, New York, NY.

Hoffer LJ, Robitaille L, Zakarian R, Melnychuk D, Kavan P, et al. (2015) High-dose intravenous vitamin C combined with cytotoxic chemotherapy in patients with advanced cancer: a phase I-II clinical trial. *PLoS One,* 2015; 10(4): e0120228.

Jung SA, Lee DH, Moon JH et. al (Jun 2016) L-Ascorbic acid can abrogate SVCT-2-dependent cetuximab resistance mediated by mutant KRAS in human colon cancer cells. *Free Radic Biol Med,* 2016 Jun; 95:200-208. DOI: 10.1016/j.freeradbiomed.2016.03.009. Epub 22 Mar 2016.

Kuiper C, Dachs GU, Munn D, Currie MJ, Robinson BA, Pearson JF, Vissers MC. (4 Feb 2014) Increased tumor ascorbate is associated with extended disease-free survival and decreased hypoxia-inducible factor-1 activation in human colorectal cancer. *Front Oncol,* 2014 Feb 4;4:10. DOI: 10.3389/fonc.2014.00010. eCollection 2014.

Maggini S, Maldonado P, Cardim P,Newball CF, Latino ERS (2017) Vitamins C, D and Zinc: Synergistic Roles in Immune Function and Infections. *Vitam Miner,* 2017;6:3 DOI: 10.4172/2376-1318.1000167

Moertel CG, Fleming TR, Creagan ET, Rubin J, O'Connell MJ, Ames MM. (1985) High-dose vitamin C versus placebo in the treatment of patients with advanced cancer who have had no prior chemotherapy; a randomized double-blind comparison. *N Engl J Med,* 1985;312:137- 141

National Registry of Diseases Office (NRDO) (19 June 2017). *Singapore Cancer Registry Annual Registry Report, 2015.*

National Registry of Diseases Office (NRDO) (26 May 2015). *Singapore Cancer Registry Interim Annual Report, Trends in Cancer Incidence in Singapore 2010-2014*.

Noone AM, Howlader N, Krapcho M, Millder D, Brest A, Yu M, Ruhl J, TatalovichZ, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). (April 2018) *SEER Cancer Review,* 1975-2015, National Cancer Institute. Bethesda, MD. https://seer.cancer.gov/statefacts/html/ovary. html

Ovarian Cancer Research Fund Alliance (n.d.). https://ocrfa.org/patients/about-ovarian-cancer/recurrence.

Padayatty SJ, Sun H, Wang Y, et al. (2004) Vitamin C pharmacokinetics: implications for oral and intravenous use. *Ann Intern Med,* 2004; 140(7): 533-537.

Pavlovic V (2010) A short overview of vitamin C and selected cells of the immune system. *Cent Eur J Med,* 8:1-10.

Pound MW, May DB. (2005) Proposed mechanisms and preventative options of Jarisch-Herxheimer reactions. *J Clin Pharm Ther,* 2005; 30(30): 291-295.

Putchala MC, Ramani P, Sherlin HJ, Premkumar P, Natesan A. (2013) Ascorbic acid and its pro-oxidant activity as a therapy for tumours of oral cavity: a systematic review. *Arch Oral Biol,* 2013; 58(6): 563-574.

Riordan Clinic Research Institute. (2013) *The Riordan IVC Protocol for Adjunctive Cancer Care: Intravenous Ascorbate as a Chemotherapeutic and Biological Response Modifying Agent.* 2013: 21.

Riordan Clinic Research Institute. (2013) *The Riordan IVC Protocol for Adjunctive Cancer Care: Intravenous Ascorbate as a Chemotherapeutic and Biological Response Modifying Agent.* 2013: 1.

Riordan HD. (1988) *Medical Mavericks, Vol. I,* Bio-Communications Press, Wichita, KS, 1988.

Schleich T, Rodemeister S, Venturelli S, Sinnberg T, Garbe C, et al. (2013) Decreased plasma ascorbate levels in stage IV melanoma patients. *Metab Nutr Oncol,* 2013; 1: e2-e6.

Schoenfeld JD, Sibenaller ZA, et al (18 Feb 2017) O2 and H 2O2 – Mediated Disruption of Fe Metabolism Causes the Differential Susceptibility of NSCLC and GBM Cancer Cells to Pharmacological Ascorbate. *Cancer Cell,* 2017; 31(4): 487-500. DOI: 10.1016/j.ccell.2017.02.18

Shenoy N, Bhagat T, Nieves E. (21 Jul 2017) Upregulation of TET activity with ascorbic acid induces epigenetic modulation of lymphoma cells. *Blood Cancer J.* 2017 Jul;7(7): e587. Published online 2017 Jul 21. DOI: 10.1038/bcj.2017.65

Stephenson CM, Levin RD, Spector T, Lis CT. (2013) Phase I clinical trial to evaluate the safety, tolerability, and pharmacokinetics of high-dose intravenous ascorbic acid in patients with advanced cancer. *Cancer Chemother Pharmacol,* 2013 Jul; 72(1):139-146.

Strohle A, Wolters M, Hahn A (2011) Micronutrients at the interface between inflammation and infection-ascorbic acid and calciferol: part 1, general overview with a focus on ascorbic acid. *Inflamm Allergy Drug Targets,* 2011;10(1): 54-63.

University of Salford. (8 Mar 2017) Vitamin C effective in targeting cancer stem cells. *Science Daily.*

Yan Ma, Julia Chapman, Mark Levine, Kishore Polireddy, Jeanne Drisko, Qi Chen. (5 Feb 2014) High-Dose Parenteral Ascorbate Enhanced Chemosensitivity of Ovarian Cancer and Reduced Toxicity of Chemotherapy. *Science Transl Md,* 2014 Feb 5;6(222): 222ra18

Yeom CH, Jung GC, Song KJ. (Feb 2007) Changes of Terminal Cancer Patients' Health-related Quality of Life after High Dose Vitamin C Administration. *J Korean Med Sci,* 2007 Feb; 22(1):7-11.

Yuen CFR, Chong SLG, Lim KM. (2016) Effects of high doses of vitamin C on cancer patients in Singapore: nine cases. *Integrative Cancer Therapies,* 2016; 15(2):197–204.

 ISSN 0317-0209