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Tumor Response to Neratinib Plus High Dose Vitamin C with Nutritional and Spiritual Support in Metastatic Her2+ Breast Cancer: Case Report and Literature Review

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Abstract

44 y/o Puerto Rican female patient with right breast invasive ductal carcinoma, poorly differentiated, ER/PR negative, Her2+, with axillary lymphadenopathy (T3N3) confirmed by PET/CT scan. She underwent Herceptin and then bilateral mastectomies. A repeated PET/CT scan revealed uptake at the right mastectomy scar plus right axillary lymph nodes. She received Herceptin. Serum tumor markers became high and CXR and CT scan of the chest revealed right pleural effusion requiring insertion of a chest tube for drainage.

In view of recurrence, we began treatment with Neratinib also she received ~~a~~ high dose intravenous vitamin C (50g 2 to 3 x W) plus oral vitamins/supplements. She followed spiritual support with meditation and prayer techniques. Her symptoms went away, and she was re-evaluated with PET/CT scan and tumor markers which turned normal indicative of free of disease regarding metastatic breast cancer. She was free of disease but kept on Neratinib as a maintenance and preventive approach. She should have been on continuous nutritional (metabolic correction) protocol, but she quit, and her disease recurred with risen tumor markers and recurrent moderate to large left pleural effusion~~.~~ We are presenting this case as the first one reported in the medical literature with complete response to an integrative medicine approach (Neratinib Plus High Dose intravenous Vitamin C, Nutritional (Metabolic Correction), and Spiritual Support in Metastatic Her2+ Breast Cancer after failure to Trastuzumab. This case is indicative of the importance of keeping the integrative oncology approach to sustain the disease-free survival also called relapse-free survival. We encourage the physicians to be more comprehensive in the multidisciplinary management of these patients with an integrative medicine approach.

Keywords

Tumor; Neratinib; Vitamin C; Metastatic; Her2+; Breast cancer; Trastuzumab; Nutritional Support; Metabolic Correction Protocol; Spiritual Support; Disease-free survival.

Introduction

Breast cancer (BC) is the most common cancer in women and an estimated 281,550 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S. [1-2]. About 43,600 women in the U.S. are expected to die in 2021 from BC. The overall death rate from BC decreased by 1% per year from 2013 to 2018 [1-2]. These decreases are notion to be the result of cure advances and beforehand detection via screening. BC became the most common cancer globally as of 2021, accounting for 12% of all new annual cancer cases worldwide, according to the World Health Organization [3]. Hormone receptor-positive (HR+) means that tumor cells have receptors for the hormone estrogen or progesterone, which can promote the growth of HR+ tumors. Human epidermal growth factor receptor 2 (HER2+) means that tumor cells make high levels of a protein called HER2/neu, which is associated with certain aggressive types of breast cancer. The breast cancer subtype HR+/HER2- is the most common subtype with an age-adjusted rate of 88.1 new cases per 100,000 women, based on 2014–2018 cases [4].

Breast most cancers are divided into molecular subtypes with applicable prognostic and predictive implications for scientific practice. In HER2-positive BC, adjuvant therapy with trastuzumab improves outcomes. One year of trastuzumab remains the most common option for treatment [5]. Disease-free survival has often been used as the primary endpoint in adjuvant trials of breast cancer, although in one study [5], disease-free survival was found to be an acceptable surrogate for overall survival in the adjuvant setting. These results, which apply mainly to the adjuvant use of trastuzumab for 12 months, indicate levels of association, both at the patient and at the trial level, that are promising from the point of view of replacing a final endpoint such as overall survival [5]. Her2 BC patients have a high rate of recurrence with metastatic disease and therapeutic options are available. One of those options is neratinib. The efficacy of neratinib with capecitabine was investigated in NALA (NCT01808573), a randomized, multicenter, open-label clinical trial in 621 patients with metastatic HER2-positive breast cancer who

received two or greater prior anti-HER2 primarily based regimens in the metastatic setting. Median PFS was 5.6 months for patients who received neratinib with capecitabine and 5.5 months for those receiving lapatinib with capecitabine. The PFS rate at 12 months was 29% vs 15%, respectively [6]. Median OS was 21 months for patients receiving neratinib with capecitabine compared to 18.7 months for those receiving lapatinib plus capecitabine. The ORR was 32.8% vs 26.7%, respectively. The median response duration was 8.5 vs 5.6 months, respectively [6]. The most common adverse reactions of any grade (>5%) in the neratinib plus capecitabine arm were diarrhea, nausea, vomiting, decreased appetite, constipation, fatigue/asthenia, weight decreased, dizziness, back pain, arthralgia, urinary tract infection, upper respiratory tract infection, abdominal distention, renal impairment, and muscle spasms [6]. The recommended neratinib dose for advanced or metastatic breast cancer is 240 mg (6 tablets) given orally once daily with food on days 1-21 of a 21-day cycle plus capecitabine (750 mg/m2 given orally twice daily) on days 1-14 of a 21-day cycle until disease progression or adverse reactions [6].

Because of the adverse reactions of the chemotherapeutic agents, cancer patients are looking for complementary alternative medicine (CAM) approaches or integrative oncology (IO) toattaina better quality of life and health [7-9]. Cancer patients may require professional support for nutrition and the use of CAM before they start their therapies. High-dose intravenous vitamin C is also proven to benefit cancer patients [10-12]. Nutritional support and metabolic correction are especially important in cancer patients. The altered strength metabolism of tumor cells affords a conceivable goal for aunhazardous chemotherapeutic approach. An increased glucose consumption rate has been observed in malignant cells [13]. The respiratory process of malignant cells is impaired and the transformation of a normal cell into malignant is due to defects in the aerobic respiratory pathways [13]. Cancer may originate from insufficient availability of oxygen [13]. Oxygen by itself has an inhibitory action on malignant cell proliferation by interfering with anaerobic respiration (fermentation and lactic acid production). Interestingly, during cell differentiation (where the cell energy level is high) there is an increased cellular production of oxidants that appear to provide one type of physiological stimulation for changes in gene expression that may lead to a terminally differentiated state. The failure to maintain high ATP production (high cell energy levels) may be a consequence of the inactivation of key enzymes, especially those related to the Krebs cycle and the electron transport system[13]. A distorted mitochondrial function (transmembrane potential) may result. This factor ought to be suggestive of an essential mitochondrial involvement in the carcinogenic procedure in addition to imparting it as a viable therapeutic goal for most cancers. Intermediate metabolic correction of the mitochondria is postulated as a possible non-toxic therapeutic approach for cancer.

The term “metabolic correction” is used to describe a biochemical–physiological process that improves cellular biochemistry as a means of achieving metabolic or physiological optimization [14]. Metabolic correction, through the increase of cofactors, can supply unmet enzyme needs and compensate for nutritional deficiencies/insufficiencies induced by improper nutritional intake or by the increased demand for nutrients caused by genetics, disease, medications, or physical or environmental stressors. Nutrient insufficiencies are inflicting an expand in morbidity and mortality, at super value to our society. Metabolic correction can have a significant impact on the reduction of morbidity and mortality and their financial cost to our society and contribute to improving health and wellbeing [14].

Spirituality also provides support and healing to cancer patients [15-17]. It has been cautioned that spirituality is related with greater well-being, due to the fact it provides social support, improves the relationship with the partner, offers meaning, and reduces self-focus and worry. A qualitative study was done among ten people with cancer, using the Consensual Qualitative Research method for the analysis of semi-structured interviews [17]. Support was found for the mechanisms of meaning provision and reduction of self-focus and worries. Participants also mentioned emotion-focused roles of spirituality: Feeling supported by a transcendental confidant, expressing negative emotions (in prayer), accepting, allowing feelings of misery, and viewing problems from a distance. There was once no point out of a contribution of spirituality to adjustment thru accelerated social assist per se or a greater first-class of the relationship with the associate. The results of the study indicate that the role of spirituality in emotion regulation deserves attention in understanding how spirituality helps cancer patients to adjust to their disease. In this case, we demonstrated the efficacy and disease-free survival of Neratinib Plus High Dose Vitamin C with Metabolic Correction Protocol and Spiritual Support in Metastatic Her2+ Breast Cancer after failure to Trastuzumab.

Case Report

44 years old Puerto Rican female patient whom by April 2017 was diagnosed with invasive ductal carcinoma, poorly differentiated, with focal ductal carcinoma in situ solid type, high nuclear degree with central necrosis, with Her2 receptor positive and metastasis to the axillary lymph nodes on the right side. By June 2017 she began treatment with Trastuzumab immunotherapy and by July 2017 the Vitamin C per vein of 50grams 3 times per week along with a metabolic correction with Dr. Miguel J.Berdiel and Dr. Michael J.Gonzalez. By November 2017, the sono mammography finding was a slight decrease in neoplasm and a slight decrease in the size of lymphadenopathy. Trastuzumab treatment was maintained until August 2018.

By November 2018 she had bilateral mastectomy and 21 lymph nodes were removed which 19 were positive. In February 2019, PET/CT scan was performed reflecting metastatic disease to several lymph nodes. Tumor markers were:CA27.29 of 7.10 and CA 15.3 of 9.40. She continued injecting vitamin C 2 times a week until May 2019 then started Trastuzumab treatment again with Dr. Raúl Morales Borges. Since the scores began to rise CA27.29 of 11.30 and CA15.3 of 14.60 finished treatment with Trastuzumab in November 2019 with CA15.3 of 12.89. By March 2020 began to feel fatigued and her liver enzymes rose along with platelets and homocysteine. A chest CT indicated a right sided pleural effusion. She required a thoracentesis in April 2020, with pleural fluid biopsy, leaving this positive for malignant cells. Her markers CA15.3 of 55.99 CA27.29 of 73.35. No getting improvement, a placement of chest tube with a pleurodesis was done in May 2020. CT SCAN was repeated and a soft tissue mass-like injury within the anterior chest wall with a diameter of approximately 7 x 2 cm was found. For May 2020 started a treatment of 3 times per week intravenous vitamin C and Neratinib tablets 3 of 40mg daily. By June 2020 she was tested for follow-up treatment showing decrease in tumor markers, CA 15.3 of 13.11, CA 27.29 of 14.60. By August 2020, a PE/CT scan was normal. The latest treatment follow-up study August 31, 2020 with tumor markers CA 15.3 of 9.09 and CA 27.29 of 10.90 (Table 1). Today she remains active in treatment with Neratinib 40mg 3 tablets daily, but she was not compliance with the metabolic correction protocol.

Dates	Antigens	
	CA15.3	**CA27.29**
	(0-25 U/mL)	**(0-42 U/mL)**
Feb-19	9.5	7.1
May-19	14.6	11.3
Nov-19	12.89	-
Apr-20	55.99	73.35
Jun-20	13.11	14.6
Aug-20	9.09	10.9

Table 1: Cancer Antigens CA15.3 and CA27.29.

Metabolic Correction Protocol

The affected person was once dealt with higher doses of intravenous vitamin C. At the beginning of the treatment 25g of Vitamin C was given twice a week (2 weeks) after that 50g three times per week which continued for a year. The patient began a Paleolithic Diet that consisted of organic fruits (berries), cruciferous vegetables, nuts, grass-fed meat, free-range poultry, and wild-caught fish. This diet excluded processed food and sugar. The affected person used to be given a dietary supplementation protocol (metabolic correction therapy) consisting of a excessive efficiency multivitamin and mineral, CoQ10 a hundred mg tid, R-alpha lipoic acid 300 mg bid, Acetyl L-Carnitine five hundred mg bid, Magnesium Citrate five hundred mg bid, Omega-3's 1 g tid, Mixed phospholipids 100 mg qd, Vitamin D3 10,000 IU qd. No adverse or negative secondary effects of treatment were reported.

Spiritual Support Protocol

First, select an area to provide calm and peace, proper light, and avoiding sounds that disturb her. She should be sitting back or lie down comfortable. Patient was encouraged to do deep breathing relaxation exercises. We always encouraged the patient to opens each individual session with prayer or a meditation, reflect upon the good things of life and what God has given to us, open her heart and mind, do not problem-solve, analyze, criticize, or go into her own issues deeply. She should center on her concerns regarding her faith journey, work in the world, contemplative life and practice, or any other issue as it relates to her own embodied spirituality. She should do this session for 10-15 minutes daily basis.

Follow up and Actual Status of her disease

The patient continued taking neratinib 120 mg daily without interruptions, but she was not compliance with metabolic correction protocol including high dose vitamin C and diet. She was asymptomatic until late April 2021 when began complaining orthopnea and felt palpable left neck lymphadenopathy. She had elevated serum tumor marker such as CA 27.29 of 57.36 u/mL in January and 81.89 u/mL in April 2021. CT scan of the chest from June 2021 revealed mild lymphadenopathy related to the aortic arch and large left pleural effusion from recurrent BC. She was free of disease from June 2020 to January 2021 for 7

months. She had a chest tube drainage of her effusion by Summer 2021 and re-adjustments in her metabolic correction protocol. In view of recurrence, she received treatment with Ado-Trastuzumab Emtansine 3.6 mg/Kg IV every 3 weeks from September. 9 to December 1 of 2021 for 5 cycles plus integrative medicine with L-taurine 1000 mg oral twice a day, but she developed brain metastasis by January 2022 and the treatment was changed to oral Lapatinib 1,250 mg daily on days 1-21 continuously since February 2022. She is also receiving radiotherapy, but she is being referred for gamma knife surgery. She is receiving the metabolic correction protocol described before.

Discussion

Treatment of breast cancer continues to evolve with less morbidity, more effective systemic therapy, and a better understanding of the biology of breast cancer. It's important to know that a multidisciplinary group is needed to be involved as in the presented case. The widespread introduction of a multidisciplinary team (MDT)-work for breast cancer management has in part evolved due to the increasing complexity of diagnostic and treatment decision-making (18). An MDT approach aims to bring together the range of specialists required to discuss and agree with treatment recommendations and ongoing management for individual patients. Multidisciplinary groups (MDTs) are resource-intensive, but we lack robust (randomized managed trial) proof of their effectiveness. Clinical consensus is typically favorable on the advantages of high-quality expert MDT work. Breast most cancers nurses have a key position in assessing holistic needs, and their professional contribution has additionally been related with expanded affected person trip and excellent of life. Evidence is regarded inside a context of developing most cancers incidence at a time of expanded economic restraint, and it may additionally now be necessary to reevaluate the shape and fashions of MDT work to make sure that MDTs are an environment friendly use of resources.

As every patient is different, cancer care must be tailored to each patient based on a holistic needs assessment [19]. It's important to explore how support can be provided from the perspectives of the healthcare providers, family members, and caretakers. Examples of universal practices at healthcare establishments global as properly as supportive care furniture through assist agencies are discussed. The desires of breast cancer sufferers lengthen past the decision of most cancers as a disease, and the restoration of fitness as long way as feasible is a quintessential element of healing. Understanding the complex issues involved in the journey of breast cancer will aid healthcare providers to be better equipped to sensitively address their concerns and focus on healing the patient holistically.

Patients with breast cancer typically use complementary and integrative treatment options as supportive care throughout most cancers therapy and to manipulate treatment-related facet results [20].

However, proof aiding the use of such remedies in the oncology placing is limited. A record supplied up to date medical exercise hints from the Society for Integrative Oncology on the use of integrative remedies for unique medical warning signs throughout and after breast most cancers treatment, such as anxiety/stress, depression/mood disorders, fatigue, fantastic of life/physical functioning, chemotherapy-induced nausea and vomiting, lymphedema, chemotherapy-induced peripheral neuropathy, pain, and sleep disturbance [20]. Music therapy, meditation, stress management,

and yoga are endorsed for anxiety/stress reduction. Meditation, relaxation, yoga, massage, and track remedy are endorsed for depression/mood disorders. Meditation and yoga are encouraged to enhance the exceptional of life. Acupressure and acupuncture are encouraged for decreasing chemotherapy-induced nausea and vomiting. Acetyl-L-carnitine is now not encouraged to forestall chemotherapy-induced peripheral neuropathy due to the opportunity of harm. No sturdy proof helps the use of ingested dietary supplements to control breast most cancers treatment-related aspect effects. In summary, there is a developing physique of proof aiding the use of integrative therapies, specifically mind-body therapies, as nice supportive care techniques at some stage in breast most cancers treatment. Many integrative practices, however, continue to be understudied, with inadequate proof to be definitively advocated or avoided. There are many gaps in providing individual-centric, holistic care [21]. Integrative medicine refers to the use of traditional medicine alongside conventional preventive or therapeutic interventions (allopathic medicine) as comprehensive, individual-centered, evidence-based care [21].

The three pillars of complementary remedy (lifestyle modifications, mind-body practices, and use of herbal products) have the practicable for most cancers prevention and enhancing quality-of lifestyles and even remedy response in most cancers sufferers when blended with traditional oncology care.

In our case, it is pointed out that nutritional and spiritual support is vital in the oncologic management of breast cancer. Therefore, continued research into integrative therapies is required to extend the benefits to a broader patient population and improve outcomes in breast and other common cancers.

Conclusion

Integrative oncology seems effective in management of patients with breast cancer. In the presented case, it was shown that the need for continuum care integrating nutritional and spiritual care to cancer patients had a positive outcome. Also, this is a first case reported in Hispanics using neratinib plus high dose vitamin C with nutritional and spiritual support in metastatic Her2+ breast cancer after failure to trastuzumab. Further research and case reports are encouraged.

References

1. https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html.
2. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf.
3. https://www.reuters.com/article/health-cancer-int/breast-cancer-overtakes-lung-as-most-common-cancer-who-idUSKBN2A219B
4. https://seer.cancer.gov/statfacts/html/breast-subtypes.html
5. Saad ED, Squifflet P, Burzykowski T, Quinaux E, Delaloge S, et al. (2019) Disease-free survival as a surrogate for overall survival in patients with HER2-positive, early breast cancer in trials of adjuvant trastuzumab for up to 1 year: a systematic review and meta-analysis. Lancet Oncol. 20(3):361-70.
6. Saura C, Oliveira M, Feng YH, Dai MS, Chen SW, et al. (2020) NALA Investigators. Neratinib Plus Capecitabine Versus Lapatinib Plus Capecitabine in HER2-Positive Metastatic Breast Cancer

Previously Treated with ≥ 2 HER2-Directed Regimens: Phase III NALA Trial. J Clin Oncol. 38(27):3138-49.

7. Irmak Z, Tanrıverdi Ö, Ödemiş H, Uysal DD. (2019) Use of complementary and alternative medicine and quality of life of cancer patients who received chemotherapy in Turkey. Complement Ther Med. 44:143-150.

8. Gerson-Cwilich R, Serrano-Olvera A, Villalobos-Prieto A. (2006) Complementary and alternative medicine (CAM) in Mexican patients with cancer. Clin Transl Oncol. 8(3):200-7.

9. Moyad MA. (2001) The prevalence and effectiveness of complementary and alternative medicine: what has been learned and what it may be telling us about our patients, ourselves, and conventional medical treatment. Semin Urol Oncol. 19(4):257-69.

10. González MJ, Miranda-Massari JR, Mora EM, Guzmán A, Riordan NH, et al. (2005) Ortho molecular oncology review: ascorbic acid and cancer 25 years later. Integrative cancer therapies. 4(1):32-44.

11. Morales-Borges RM. (2018) Orthomolecular Medicine, Micronutrients, High Dose Vitamin C, and Cancer: Why it Should be Revisited. J Altern Complement Integr Med. 4:53.

12. González MJ, Berdiel MJ, Cintrón IV AV. (2017) High Dose IV Vitamin C and Metastatic Breast Cancer: A Case Report. J Orthomol Med. 32(6).

13. González MJ, Miranda Massari JR, Duconge J, Riordan NH, Ichim T, et al. (2012) The bio-energetic theory of carcinogenesis. Med Hypotheses. 79(4):433-9.

14. González MJ, Miranda Massari JR. (2012) Metabolic Correction: A Functional Explanation of Orthomolecular Medicine. J. Orthomol. Med.. 27(1).

15. Morales-Borges RH, Rodríguez-Díaz M. (2019) Role of Spiritual Medicine as Integrative Medicine in Patients with Cancer. J Altern Complement Integr Med. 5:086.

16. Morales-Borges AH. (2021) Christianity, Neurotheology & Cancer-Oncologic Christian Neuro Theology: New Era, Needs more attention. J Altern Complement Integr Med 7: 172. of. 2021; 3:2.

17. Garssen B, Uwland-Sikkema NF, Visser A. (2015) How spirituality helps cancer patients with the adjustment to their disease. Journal of religion and health. 54(4):1249-65.

18. Taylor C, Shewbridge A, Harris J, Green JS. (2013) Benefits of multidisciplinary teamwork in the management of breast cancer. Breast Cancer (Dove Med Press). 5:79-85.

19. Ng ZX, Ong MS, Jegadeesan T, Deng S, Yap CT. (2017) Breast Cancer: Exploring the Facts and Holistic Needs during and beyond Treatment. Healthcare (Basel). 5(2):26.

20. Greenlee H, DuPont-Reyes MJ, Balneaves LG, Carlson LE, Cohen MR, et al. (2017) Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J Clin. 67(3):194-32.

21. Basu P, Tripathi R, Mehrotra R, Ray K, Srivastava A, et al. (2021) Role of integrative medicine in the continuum of care of breast cancer patients in the Indian context. Cancer Causes Control. 32(5):429-40.