Chemotherapy and Functional Medicine in a Patient With Metastatic Breast Cancer: A Case Report

Elliot T. Taxman, BA; Erin D. Conlon, BS; Alex Speers, BA; Kristin L. Dismuke, BS; Tonya S. Heyman, MD, FACOG; Thomas L. Taxman, MD, FAAP

Abstract

More than one-half of all cancer patients use some combination of conventional and complementary medicine, but exactly how this is done and what the outcomes include are poorly understood. This case study reports the successful treatment of metastatic invasive ductal breast carcinoma by 2 physician groups with treatments that combined conventional chemotherapy with nutritional support guided by nutritional and digestive laboratory testing. The goal of minimizing side effects and enhancing outcomes was achieved in this patient who did not receive radiation therapy and is almost 3 y posttreatment with no evidence of recurrence.

Elliot T. Taxman, BA; Erin D. Conlon, BS; and Alex Speers, BA, are naturopathic medicine students at the National College of Natural Medicine and master of science in integrative medicine research students at Helfgott Research Institute located in Portland, Oregon; Kristin L. Dismuke, BS, is pursuing her master of science in integrative medical research students at Helfgott Research Institute; Tonya S. Heyman, MD, FACOG, is specializing in gynecology and integrated personalized medicine; and Thomas L. Taxman, MD, FAAP, is a pediatric gastroenterologist and functional medicine practitioner. The physicians are located at the Cleveland Health Institute, Turning Point Pathways to Health program, in Lyndhurst, Ohio.

Corresponding author: Erin D. Conlon, BS
E-mail address: conlon.erin@gmail.com

More than one-half of all cancer patients use some combination of conventional and complementary medicine, but exactly how this is done and what the outcomes include are poorly understood.[1,2] This patient chose to combine conventional oncological treatment, a functional medicine approach guided by comprehensive laboratory testing and intravenous (IV) vitamin therapy. IV vitamin C appears to be safe and has some preliminary evidence for effectiveness in patients with cancer.[3,4] This patient diagnosis and treatment are outlined in the timeline below (Figure 1).

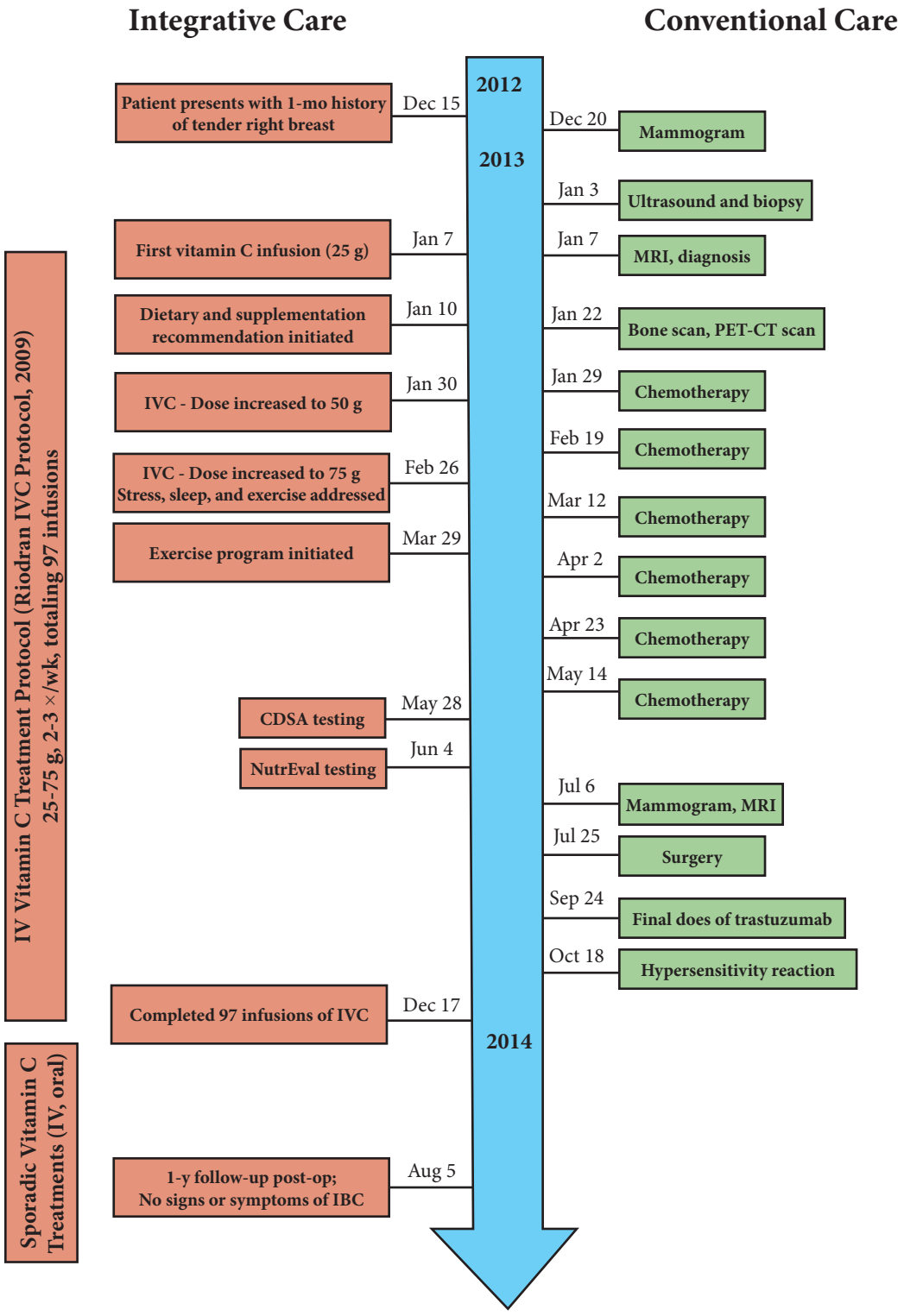
Case

An 80-year-old Caucasian female patient presented to an integrative medicine clinic in December 2012 with a 1-month history of a tender right breast. Her history was significant for arthritis, obesity, hypothyroidism, chronic gastritis, and hypertension. Her current medications included hydrochlorothiazide and triamterene, quinapril hydrochloride, levothyroxine sodium, and esomeprazole. Her family history was positive for breast cancer (daughter at age 46 y and sister at age 70 y). Physical exam revealed an erythematous, warm mass with irregular borders and localized skin thickening palpated across both upper quadrants of the right breast. The mass measured approximately $15 \times 10 \times 5$ cm. In addition, a prominent 1-cm right axillary lymph node was noted.

Diagnostic Testing and Assessment

Mammography revealed increased irregular density in the central upper quadrants of the right breast. A subsequent ultrasound noted a mass in the right breast that was highly suggestive of malignancy and the accompanying guided biopsy concluded invasive ductal carcinoma, grade 3, with involvement of a right axillary lymph node. A magnetic resonance imaging (MRI) on January 7 confirmed the previous diagnosis and indicated that a small mass was found in the left upper outer quadrant of the left breast. A follow-up sonogram and mammogram of the left breast confirmed the MRI findings. She was given a Breast Imaging-Reporting and Data System (BI-RADS) score of 6 and her cancer was concluded to be ER/PR negative and HER2 positive.

Figure 1. Timeline of Patient Care



Abbreviations: MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; IVC, intravenous cholangiogram; CDSA, comprehensive digestive stool analysis; IBC, inflammatory breast cancer; IV, intravenous.

Table 1. Functional Medicine Protocol

Interventions	
Medications	• Levothyroxine sodium: 130 µg QD • Esomeprazole: 40 mg QD • Quinapril hydrochloride: 20 mg QD • Hydrochlorothiazide and triamterene: 37.5/25 QD
Diet	• Low glycemic index • Dairy free • Gluten free • Adequate protein
Supplementation	• Melatonin: 20 mg QHS • Digestive enzymes AC • Probiotics: 60 billion CFU BID ○ *Lactobacillus acidophilus* NCFM ○ *Bifidobacterium animalis* Bi-07 • Medical food shake bid • Vitamin D_3: 5000 IU QD • EPA:DHA: 6000 mg QD • Wheat germ extract: 5.5 g QD • Oral vitamin C: 18-24 g QD • Standardized herbal inflammation relief supplement
Exercise Program	• 10 min of bicycling bid, working toward 30 min/day • Qigong classes
Sleep Program	• Sleep instructions with log to record sleep
Support Recommendations	• Individual counseling • Group support • Part-time caregiver/companion

Abbreviations: QD, once per day; QHS, at bedtime; AC, before meals; CFU, colony-forming unit; BID, twice per day; NCFM, *Lactobacillus acidophilus* NCFM; Bi-07, *Bifidobacterium animalis* Bi-07; IU, international units; EPA:DHA, eicosapentaenoic acid:docosahexaenoic acid.

Table 2. Oncology Protocol

Oncology Recommendations	
Chemotherapy	• 6 doses of DCT given 1× every 3 wk • Docetaxel: 144 mg, dose 1; 112 mg, doses 2 to 6 • Carboplatin: 354 mg, all 6 doses • Trastuzumab: 500 mg average (based on weight)
Surgery	• Mastectomy based on response to chemotherapy
Radiation	• Daily radiation for 6 wk following surgery

Abbreviation: DCT, docetaxel, carboplatin, trastuzumab. .

Treatment

The patient was evaluated at an integrated oncology program that used a functional medicine approach guided by comprehensive, panel-based nutritional and digestive laboratory testing and IV vitamin C. The use of IV vitamin C therapy in cancer remains controversial, although some preliminary trials have shown IV vitamin C to be safe and potentially effective in improving quality of life and fatigue in patients with cancer.[3,4] At this visit, the patient received her first infusion of IV vitamin C (25 g), which was tolerated well. Biweekly infusions were scheduled for the next year. The functional medicine treatment protocol is described in Table 1.

On January 22, 2013, the patient received a bone scan and positron emission tomography-computed tomography (PET-CT) scan of the chest, abdomen, and pelvis, all of which were negative. A medical oncologist recommended the treatment plan, outlined in Table 2.

Chemotherapy began on January 29, after which the patient reported no symptoms. The following day, the dosage of IV vitamin C was increased to 50 g, which the patient tolerated well. The patient was compliant with the nutrition program and had decided to stop taking esomeprazole. A breast exam was performed on February 26 and it was noted that tenderness and erythema of the right breast had remarkably decreased. At this clinic visit, IV vitamin C dosage was increased to 75 g. On March 29, the patient reported fatigue, exacerbated by exercise, as well as alopecia but no other postchemotherapy symptoms were noted. The patient initiated an exercise program at this time, but adherence was poor.

At an April 30 clinic visit, it was noted that the patient's weight had dropped to 78 kg, and her blood pressure had remained steady at 120/60 mm Hg. A decision was made at this time to discontinue all hypertension medications. The patient was experiencing worsening fatigue and blood work was notable for hematocrit of 33%.

Six cycles of chemotherapy were completed by May 31 and a breast exam revealed no palpable mass. A comprehensive digestive stool analysis (CDSA) study and a Nutritional Evaluation (NutraEval) laboratory tests were ordered, the results of which are shown in Tables 3 and 4. A mammogram on June 6 showed increased pleomorphic calcifications posterior to known malignancy and a MRI showed a good overall response to

Table 3. Genova NutraEval Test Results

Malabsorption Markers		
Marker	**Value**	**Reference Range**
Indoleacetic acid (IAA)	<dL	≤4.2
Phenylacetic acid (PAA)	0.10	≤0.12
Bacterial Dysbiosis Markers		
Marker	**Value**	**Reference Range**
Dihydroxyphenylpropionic acid (DHPPA)	11.3	≤5.3
3-Hydroxyphenlacetic acid	5.3	≤8.1
4-Hydroxyphenlacetic acid	19	≤29
Benzoic acid	0.23	≤0.05
Hippuric acid	603	≤603
Yeast/Fungal Dysbiosis Markers		
Marker	**Value**	**Reference Range**
Arabinose	3.6	≤96
Citramalic acid	3.0	≤5.8
Tartaric acid	<dL	≤15
Cellular Energy & Mitochondrial Metabolites		
Carbohydrate Metabolism		
Marker	**Value**	**Reference Range**
Lactic acid	6.4	1.9 to 19.8
Pyruvic acid	2.7	7 to 32
β-OH-Butyric acid (BHBA)	2.5	≤2.8
Energy Metabolism		
Marker	**Value**	**Reference Range**
Citric acid	139	40 to 520
Cis-Aconitic acid	16	10 to 36
Isocitric acid	59	22 to 65
α-Ketoglutaric acid (AKG)	12	4 to 52
Succinic acid	<dL	0.4 to 4.6
Malic acid	1.4	≤3.0
β-OH-β-Methylglutaric acid (HMG)	12	≤15
Fatty Acid Metabolism		
Marker	**Value**	**Reference Range**
Adipic acid	1.4	≤2.8
Suberic acid	1.1	≤2.1
Neurotransmitter Metabolites		
Marker	**Value**	**Reference Range**
Vanilmandelic acid	4.8	0.4 to 3.6
Homovanillic acid	18.2	1.2 to 5.3
5-OH-indoleacetic acid	20.4	3.8 to 12.1
3-Methyl-4-OH-phenyglycol	0.15	0.02 to 0.22
Kynurenic acid	4.8	≤7.1
Quinolinic acid	4.8	≤9.1
Kynurenic/Quinolinic ratio	1.00	≥0.44
Vitamin Markers		
Marker	**Value**	**Reference Range**
α-Ketoadipic acid	0.9	≤1.7
α-Ketoisovaleric acid	1.04	≤0.97
α-Ketoisocaproic acid	0.97	≤0.89
α-Keto-β-Methylvaleric acid	3.1	≤2.1
Formiminoglutamic acid (FIGIu)	0.7	≤1.5
Glutaric acid	0.43	≤0.51
Isovalerylglycine	2.0	≤3.7
Methylmalonic acid	1.2	≤1.9
Xanthurenic acid	0.63	≤0.96
3-Hydroxypropionic acid	13	5 to 22
3-Hydroxyisovaleric acid	12	≤29

Toxin & Detoxification Markers		
Marker	**Value**	**Reference Range**
α-Ketophenylacetic acid (from Styrene)	0.42	≤0.46
α-Hydroxyisobutyric acid (from MTBE)	13.6	≤6.7
Orotic acid	0.77	0.33 to 1.01
Pyroglutamic acid	31	16 to 34
Tyrosine Metabolism		
Marker	**Value**	**Reference Range**
Homogentisic acid	67	≤19
2-Hydroxyphenylacetic acid	0.68	≤0.76
Creatinine Concentration		
Marker	**Value**	**Reference Range**
Creatinine	3.7	3.1 to 19.5 mmol/L
Nutritionally Essential Amino Acids		
Marker	**Value**	**Reference Range**
Arginine	22	10 to 64
Histidine	302	296 to 1136
Isoleucine	35	24 to 58
Leucine	55	30 to 87
Lysine	45	45 to 286
Methionine	93	30 to 82
Phenylalanine	48	26 to 71
Taurine	259	68 to 538
Threonine	136	65 to 252
Tryptophan	87	28 to 111
Valine	40	23 to 61
Nonessential Protein Amino Acids		
Marker	**Value**	**Reference Range**
Alanine	195	146 to 486
Asparagine	103	49 to 182
Aspartic acid	44	35 to 86
Cysteine	60	21 to 78
Cystine	50	26 to 78
γ-Aminobutyric acid	14	≤31
Glutamic acid	25	5 to 21
Glutamine	219	172 to 570
Proline	5	2 to 18
Tyrosine	82	33 to 124
Intermediary Metabolites		
B Vitamin Markers		
Marker	**Value**	**Reference Range**
α-Aminoadipic acid	22	11 to 73
α-Amino-N-butyric acid	30	9 to 49
β-Aminoisobutyric acid	56	22 to 192
Cystathionine	<dL	6 to 33
3-Methylhistidine	252	131 to 318
Urea Cycle Markers		
Marker	**Value**	**Reference Range**
Ammonia	41.8	14.0 to 19.0 mmol/g creatinine
Citrulline	61	12 to 45
Ornithine	11	4 to 21
Urea	371	168 to 465 mmol/g creatinine

Table 3. (continued)

Glycine/Serine Metabolites		
Marker	**Value**	**Reference Range**
Glycine	389	639 to 3306
Serine	296	187 to 568
Ethanolamine	198	208 to 514
Phosphoethanolamine	31	18 to 70
Phosphoserine	46	28 to 63
Sarcosine	34	≤48
Dietary Peptide Related Markers		
Marker	**Value**	**Reference Range**
Anserine (dipeptide)	<dL	7 to 126
Carnosine (dipeptide)	28	10 to 104
1-Methylhistidine	534	92 to 1046
β-Alanine	23	≤21
Markers for Urine Representativeness		
Marker	**Value**	**Reference Range**
Glutamine/Glutamate	9	≥10
Ammonia	41.8	14 to 49 mmol/g creatine
Arginine/Ornithine	2.0	≥1.1
Urine representativeness index	9	5 to 10
Omega 3 Fatty Acids		
Marker	**Value**	**Reference Range**
α-Linolenic (ALA) 18:3	0.12	≥0.09 wt %
Eicosapentaenoic (EPA) 20:5	3.07	≥0.16 wt %
Docosapentaenoic (DPA) 22:5	3.24	≥1.14 wt %
Docosahexaenoic (DHA) 22:6	5.9	≥2.10 wt %
% Omega 3s	12.3	≥3.8
Omega 6 Fatty Acids		
Marker	**Value**	**Reference Range**
Linoleic (LA) 18:2	10.1	10.5 to 16.9 wt %
γ-Linolenic (GLA) 18:3	0.05	0.03 to 0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3	1.18	≥1.19 wt %
Arachidonic (AA) 20:4	17	15 to 21 wt %
Docosatetraenoic (DTA) 22:4	1.41	1.50 to 4.20 wt %
Eicosadienoic 20:2	0.29	≤0.26 wt %
% Omega 6s	29.6	30.5 to 39.7
Omega 9 Fatty Acids		
Marker	**Value**	**Reference Range**
Oleic 18:1	11	10 to 13 wt %
Nervonic 24:1	4.0	2.1 to 3.5 wt %
% Omega 9s	14.9	13.3 to 16.6
Saturated Fatty Acids		
Marker	**Value**	**Reference Range**
Palmitic C16:0	20	18 to 23 wt %
Stearic C18:0	18	14 to 17 wt %
Arachidic C20:0	0.29	0.22 to 0.35 wt %
Behenic C22:0	0.95	0.92 to 1.68 wt %
Tricosanoic C23:0	0.15	0.12 to 0.18 wt %
Lignoceric C24:0	2.0	2.1 to 3.8 wt %
Pentadecanoic C15:0	0.09	0.07 to 0.15 wt %
Margaric C17:0	0.34	0.22 to 0.37 wt %
% Saturated Fats	41.4	39.8 to 43.6

Monounsaturated Fats		
Omega 7 Fats		
Marker	**Value**	**Reference Range**
Palmitoleic 16:1	0.24	≤0.64 wt %
Vaccenic 18:1	1.16	≤1.13 wt %
5-OH-indoleacetic acid	20.4	3.8 to 12.1
Trans Fat		
Marker	**Value**	**Reference Range**
Elaidic 18:1	0.38	≤0.59 wt %
Delta - 6 Desaturase Activity		
Marker	**Value**	**Reference Range**
Linoleic/DGLA 18:2/20:3	8.6	6.0 to 12.3
Cardiovascular Risk		
Marker	**Value**	**Reference Range**
Omega 6s/Omega 3s	2.4	3.4 to 10.7
AA/EPA 20:4/20:5	5	12 to 125
Omega 3 index	9.0	≥4.0
Oxidative Stress Markers		
Glutathione (whole blood)	675	≥669 µmol/L
Lipid peroxides (urine)	8.2	≤10.0 µmol/g creatine
8-OHdG (urine)	23	≤15 µg/g creatine
Coenzymes Q_{10}, ubiquinone (plasma)	1.10	0.43 to 1.49 µg/mL
Elemental Markers (RBCs)		
Nutrient Elements		
Marker	**Value**	**Reference Range**
Copper	0.642	0.466 to 0.721 µg/g
Magnesium	46.1	30.1 to 56.5 µg/g
Manganese	0.041	0.007 to 0.038 µg/g
Potassium	3460	2220 to 3626 µg/g
Selenium	0.73	0.25 to 0.76 µg/g
Zinc	13.4	7.8 to 13.1 µg/g
Toxic Elements		
Marker	**Value**	**Reference Range**
Lead	0.013	≤0.048 µg/g
Mercury	<dL	≤0.0039 µg/g
Antimony	0.002	≤0.002 µg/g
Arsenic	0.032	≤0.071 µg/g
Cadmium	0.001	≤0.001 µg/g
Tin	0.0010	≤0.0009 µg/g
% Saturated fats	41.4	39.8 to 43.6

Table 4. CDSA Test Results

Digestion/Absorption		
Marker	**Value**	**Reference Range**
Pancreatic elastase 1	145	≥201 µg/g
Putrefactive SCFAs (total)	3.1	1.3 to 8.6 µmol/g
Gut Immunology		
Marker	**Value**	**Reference Range**
Eosinophil protein X	1.1	≤7.0 µg/g
Calprotectin	<16	≤50 µg/g
Metabolic		
Marker	**Value**	**Reference Range**
Beneficial SCFAs (total)	36.0	≥13.6 µmol/g
n-Butyrate	4.6	≥2.5 µmol/g
pH	7.0	6.1 to 7.9
β-glucuronidase	5029	337 to 4433 U/g
Secondary Bile Acids		
Marker	**Value**	**Reference Range**
Lithocholic acid (LCA)	2.30	0.65 to 5.21 mg/g
Deoxycholic acid (DCA)	4.04	0.67 to 6.76 mg/g
LCA/DCA ratio	0.57	0.37 to 2.07
Parasitology		
Cryptosporidium	Negative	
Giardia lamblia	Negative	
Entamoebahistolytica/dispar	Negative	

chemotherapy. Surgery was scheduled for July 25. One month before surgery, blood pressure was stable at 130/70 mm Hg without medication and hematocrit was 27.8% and stable.

On July 25, a right modified radical mastectomy was performed with sentinel lymph node excision and complete axillary lymph node dissection. In addition, a left simple mastectomy was performed. The pathology report showed no residual carcinoma in the right breast and skin. Sentinel nodes 1 and 2 were negative for metastatic carcinoma, along with 13 axillary lymph nodes. Fibrocystic changes with microcalcifications and a focal carcinoma in situ were found in the left breast. Postsurgery, the patient refused radiation therapy but continued complying with her functional medicine plan and planned to continue her vitamin C infusions twice per week to complete 1 year of therapy.

The patient received her last dose of trastuzumab on September 24. Two months following surgery on September 30, the patient's hematocrit had returned to baseline levels at 41%. During this time, the patient's blood pressure had begun to rise and her cardiologist placed her on a new hypertension medication. After beginning this medication, the patient experienced a hypersensitivity reaction on October 18 characterized by dermatographism, urticaria, and severely elevated blood pressure. The reaction was treated with methylprednisolone, diphenhydramine, and IV fluids. The patient followed up with cardiology to follow possible cardiotoxicity. At the patient's next functional medicine visit on October 31, it was decided to decrease her IV vitamin C infusions to 50 g.

The patient remained off of hypertension medications and her blood pressure remained stable at 140/70 mm Hg through the end of the year. The year-long IV vitamin C program, consisting of twice-weekly infusions, was completed on December 17 and totaled 97 infusions. The patient continued to improve and began traveling again. At a follow-up visit on January 21, 2014, blood work was normal and the patient reported doing very well. A 1-year post-op clinic visit on August 5, 2014, showed a normal complete blood count (CBC) and comprehensive metabolic panel (CMP) with no signs or symptoms of breast cancer.

This case is unique because of the integrated approach guided in part by nutritional and digestive evaluation (NutrEval) from a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory testing company (Genova Diagnostics, Asheville, NC, USA) that was used in the management of this patient with advanced ductal breast carcinoma.[5] Because this is a case report from the real world practice of medicine, it is not possible to determine the responsibility of the treatments in this patient's success in achieving remission. Nevertheless, the patient survived her cancer with minimal side effects during treatment and is now in her third year of remission. This case study highlights the potential benefits of integrative therapy in the comanagement of patients with invasive ductal carcinoma of the breast.

Patient Perspective

"I was worried about the side effects of chemotherapy but I never had to have a blood transfusion, I only had diarrhea once, and no nausea and vomiting. I had a little bit of fatigue but stayed active and did not have to change my lifestyle very much. I was able to be with my friends and family, and to taste and eat food while I was being treated. I thought that I looked better than the other chemotherapy patients I saw when I went to get treatments. They all looked so sick and so much older than me! The worst thing was losing my hair! I knew that the medications had a long list of side effects and at the beginning I did not understand that they could be minimized, but they were! I had chemotherapy and surgery but never had any radiation. Two years later, I am still cancer free and feel great. I may be healthier now than I was before my diagnosis and treatment."

Author Disclosure Statement

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References

1. Garland SN, Valentine D, Desai K, Li S, Langer C, Evans T, Mao JJ. Complementary and alternative medicine use and benefit finding among cancer patients. *J Alt Complement Med.* 2013;19(11):876-881.
2. Huebner J, Muenstedt K, Prott, FJ, et al. Online survey of patients with breast cancer on complementary and alternative medicine. *Breast Care.* 2014;9(1):60-63.
3. Carr AC, Vissers MCM, Cook JS. the effect of intravenous vitamin c on cancer- and chemotherapy-related fatigue and quality of life. *Front Oncol.* 2014;4:283.
4. Sebastian PJ, Sun AY, Chen C, Espey MG, Drisko J, Levine M. Vitamin C: Intravenous use by complementary and alternative medicine practitioners and adverse effects. *PLoS ONE.* 2010;5(7): e11414.
5. Genova Diagnostics. About us. https://www.gdx.net/about. Accessed November 15, 2015.