

Case Report

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Successful Treatment by Mistletoe Viscum Album Extract of a Patient with Recurrent Triple Negative Breast Cancer who declined Chemotherapy



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Abstract

Triple negative breast cancer (TNBC) is an aggressive breast cancer with a high incidence of recurrence and poor prognosis even with the full spectrum of standard oncology treatments. Ever since its introduction about 100 years ago for cancer therapy, mistletoe viscum album extract (VAE) has been widely used in Europe as a popular complementary therapy for many cancers. We present a case of a patient diagnosed with stage 3c (T3N3bM0(i+)) TNBC who declined chemotherapy after a recurrence 2 years later. The patient received subcutaneous, intratumoral as well as intravenous VAE therapy for her recurrence. Her breast masses and lymph node sizes dramatically decreased under ultrasound examination within 2 months. After nearly three years since the tumor resolution, she is currently being managed on weekly subcutaneous VAE as well as intravenous VAE once in 6-8 weeks. She has excellent quality of life, no sign of tumor recurrence or other adverse side effects from her treatments. Though we believe the best outcomes in oncology are by integrating complementary and conventional care together, this case shows that VAE can have standalone effectiveness at least in some cases. Use of VAE to augment conventional treatments should be considered to bolster breast cancer care.

Keywords: Mistletoe; Viscum Album Extract; Breast Cancer; Triple Negative Breast Cancer

Introduction

Breast cancer continues to be the most common cancer diagnosed and the leading cause of death among women globally [1]. Breast cancers that do not express the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) are known as triple negative breast cancers (TNBC). TNBC accounts for 10-15 % of all breast cancer subtypes and is very aggressive, with a high risk of multiple, distant metastasis and recurrence [2]. The median survival for patients with metastatic TNBC is only 13.3 months with treatment [3] and the lack of targeted specific therapy poses challenges to finding cost-effective regimens with minimal side effects that ensure a good quality of life (QOL). Stage 3c TNBC treated only with surgery has an expected median survival of about 30% [4]. Over the years, complementary and alternative medicines (CAM) have been playing more and more significant role in cancer therapy throughout the world. One such CAM is Mistletoe viscum album extract (VAE), which was first introduced for cancer therapy about

100 years ago. An increasing number of studies have reported improvement in QOL and anticancer activity of VAE [5-10]. Cancer trials with VAE are underway to study the overall survival and health related QOL in Europe [11]. Studies outside the USA have shown improvement in breast cancer as well with VAE [12-15].

Here, we report a case of a patient with stage 3c TNBC who declined chemotherapy after her recurrence. She was treated with subcutaneous (SC), Intratumoral (IT) and intravenous (IV) VAE.

Case Report

A 47-year-old woman with a 2-year past history of stage 2 TNBC of the left breast presented with a large 7 cm left breast mass and axillary lymph node enlargement. Her past history was significant for 14 pack years of tobacco, BMI fluctuating between 25 and 30 for past 20 years and she was not on any prescription medications. Her only pregnancy resulted in emergency Cesarean

section and she exclusively breast fed her son for 8 months. After she turned 40 years, she underwent annual screening mammograms for 2 years only. After turning 45, she felt a lump in her left breast. Based on her symptoms and third mammogram, she underwent an excisional biopsy of her breast mass. The pathology report showed a 3 cm triple negative invasive ductal carcinoma, and she was diagnosed with stage 2a TNBC.

She declined further diagnostic, surgical and therapeutic advice from her oncology treatment team. Instead, she traveled to Mexico for a dietary and detoxification program offered at a CAM hospital. While she stayed in Mexico for a period of 28 days, she received daily 30-100 g of IV Vitamin C (IVC). She was also given 4 rounds of Autologous Dendritic cell therapy, Autologous bone marrow stem cell transplant, multiple rounds of Hyperthermia FAR infrared therapy and Hyperbaric oxygen chamber therapy as well as multiple daily herbal supplements along with other CAM treatments. After returning to the US, she underwent periodic laboratory studies and regular mammograms under the care of a local physician. She took weekly IVC and daily CAM supplements. Over a period of 18 months, she remained symptom free and

her Biocept circulating tumor cells had been between 10 and 13. Around her 47th birthday, her mammogram showed suspicious lesion on her left breast. Patient once again declined conventional chemotherapy advised by her oncology treatment team and this time, she opted to come to our clinic instead of CAM hospital in Mexico.

Patients Positron emission tomography computed tomography scan (PET/CT) showed a centrally necrotic 4.2 x 6.7 cm mass with SUV 7.4 in her left breast. Mediastinal and axillary lymph nodes were enlarged with focal intense FDG uptake. She started her IV infusions of VAE as well as IT VAE. As anticipated, a fever response was observed 24 hours after every IT and IV VAE infusions. She tolerated the procedure well. She received a total of 9 IT VAE over a period of about 2 months. The dosage was gradually increased from 10 mg to 200 mg. During this time period she received 7 SC 10-20 mg VAE injections as well as 9 IV VAE. The dosage of IV VAE increased from 60 to 100 mg. Over the course of 2 months the patient felt better vitality and more inwardly settled and her health QOL improved. Her Ultrasound examination revealed the mass on her left breast to have shrunk to 4.3 x 4.8 cm. (Table 1)

Table 1: Table shows amounts of subcutaneous (SC), Intralesional (IL), Intravenous (IV) viscum album extract (VAE) in milligrams (mg) and IV Vitamin C (IVC) in grams (g) given starting from day 1. The 6th column represents patient's comments and notes.

Days	SC VAE (mg)	IT VAE (mg)	IV VAE (mg)	IVC (g)	Patients notes / comments
Day 1	0	10	60		Fever at home of 100.9 F. Lucid dreams about her childhood trauma
Day 3	0	20	80		Fever at home not recorded; breast sore and inflamed
Day 7	10	40	80		Fever at home not recorded
Day 14	10	80	80		Fever at home of 104.3 F
Day 21	10	90	80		Fever at home of 103 F
Day 28	10	110	80		Fever at home not recorded; energy is much better
Day 42	10	140	80		Fever at home of 102.3 F
Day 56	20	180	80		Fever at home of 102.6 F
Day 63	20	200	100		Fever at home not recorded
Day 77					Paused to consult with surgeon. Ultrasound of her breast revealed 4.3 X 4.8 cm mass
Day 98					Lumpectomy performed
Day 112	0	0	200	30	
Day 119	0	0	100	60	
Day 126	0	0	100	90	No fever at home
Day 133	0	0	100	90	No fever at home
Day 134 +	10				Patient taking SC injections at home 3 days a week and 100 mg IV VAE every 6-8 weeks

The VAE injections and infusions were paused for about 2 months in anticipation of surgery. A left breast lumpectomy was performed. The gross pathology report showed a well circumscribed cavity with necrotic center measuring 2.8 x 2.2 cm. Histopathology results showed breast tissue with abscess

cavity, abundant necrosis, numerous histiocytes, dense fibrosis and fibroblast proliferation admixed with recent and old blood. Remaining breast tissue showed fibrocystic changes. There was no evidence of malignancy. Her initial tumor markers, CA 15-3 was 29 U/ml and CA 27.29 was 44 U/ml and her Biocept circulating tumor

cells was 19. One year after her VAE was started, her carcinoma antigens, CA 15-3 were 9 U/ml and CA 27.29 were down to 21 U/ml, remaining stable 3 years later at 7 and 17 respectively. Two months after the 9th dose of IV VAE, she resumed weekly IV VAE for about 4 weeks (**Table 1**). Since there was no tumor, IT VAE was not instituted. Along with her weekly IV VAE the patient also received weekly IVC which was gradually increased from 30 g to 90 g. The patient continued SC VAE after the IV VAE was stopped.

Currently, about 3 years later, the patient injects 10 mg SC VAE 3 days a week and once in 6-8 weeks she receives 100 mg of IV VAE. She undergoes periodic Ultrasound of her breast and axilla. Her latest lymph node ultrasound result indicates that her axillary lymph node sizes have returned to normal. Her lymph nodes continue to be between 1 and 2 cm in their largest diameter. Otherwise, she has been tumor free, symptom free and does not complain of any side effects.

Discussion

Triple negative breast cancer (TNBC) is a very aggressive subtype of breast cancer associated with a high recurrence rate and generally poor prognosis especially when patients don't undergo chemotherapy. Chemotherapy has been the main treatment option and within the past decade repurposed as well as new drugs like polyadenosine diphosphate-ribose polymerase inhibitors are being studied [16-18]. Despite this, the treatment options for TNBC remain limited. When patients undergo aggressive chemotherapy for TNBC practical hurdles such as medication and treatment costs, hospitalizations and treatment associated side effects and reduction in QOL can be frustrating. Not infrequently, patients seek out CAM, sometimes without disclosing that information to their oncology [19,20]. Unrestricted CAM usage could interact in unpredictable ways with conventional therapies. Very few of the thousands of CAM have been studied for safety and efficacy.

VAE was first used for cancer therapy over a 100 years ago as a part of Anthroposophic Medicine [21-24]. Gradually, over a century, numerous *in vitro*, *in vivo* and human studies have been published. Mistletoe lectins are the subject of most studies [25] and have both pro-apoptotic effects as well as a proliferative effect on natural killer (NK) and T Lymphocytes. Viscotoxins are another component that directly causes tumor cell death [26,27]. Other components of VAE have favorable effects on inflammation, endorphins and VEGF and thus impact the broader "terrain" of the patient with cancer.

Although some authors question the survival and QOL advantages to prescribing VAE [28,29] numerous studies and review articles indicate otherwise [30-33]. In breast cancer treatment, VAE has been particularly beneficial in improving QOL and overall survival [11-14,34,35,36]. Up to 75% of cancer patients use VAE alongside their therapy in Europe. VAE is most often used as a SC injected therapy that causes a small ~3cm area of erythema and swelling with each injection. There may be a slight elevation of body temperature of one degree F but usually no other

side effects. Mistletoe Fever Induction Therapy (MFIT) is safe [37] and used routinely by several integrative hospitals in Europe in selected patients who are robust enough to have a high fever up to 104°F [38]. Specific doses and routes of high lectin mistletoe are used in MFIT. Hyperthermia and fever have a known anticancer effect as well as upregulating the immune system. Intratumoral injection of VAE is also performed in selected patients, usually in the setting of MFIT. The unveiling of the tumor during high fever while simultaneously creating a beacon for cancer killing NK and T-cells may be the explanation for several reported local tumor responses as well as abscopal effects, where other distant tumors also responded to this therapy [39,40].

Intratumoral injection of VAE is also performed in selected patients, usually in the setting of MFIT. The unveiling of the tumor during high fever while simultaneously creating a beacon for cancer killing NK and T-cells may be the explanation for several reported local tumor responses as well as abscopal effects [41,42] where other distant tumors also responded to this therapy [43].

Our patient had TNBC that recurred after 2 years. She declined any conventional chemotherapy offered by her oncology treatment team due to her personally held beliefs. She came to our clinic with the intention of using VAE. She responded appropriately to the VAE injections by developing a high fever that lasted for about a day. She noticed improvement in her symptoms by the 3rd dose of VAE injections. Gradually, after 2 months of VAE therapy, her breast mass shrunk dramatically, QOL improved, and her breast became free of disease. She is currently on maintenance VAE injections and has remained cancer free for about 3 years.

Conclusion

We report a case of recurrent TNBC in a patient who declined conventional medicine. It is not very rare to see patients who decline conventional treatments for cancer and request only to be treated with CAM- such cases present an ethical dilemma for clinicians, including the authors. We find that the best ethical solution is to form a bridge for these patients using CAM ideally alongside conventional therapy. With this case we aim to inform clinicians about VAE used widely to treat cancers in other countries especially Germany. In particular this case demonstrates survival and cancer remission as well as improvement in QOL in a patient with recurrent TNBC.

Conflicts of Interest:

The authors declare there is no conflict of interest regarding the publication of this paper.

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