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The Anti-Tumor Effects of Cannabidiol when Administered as a Companion Treatment to Standard Chemotherapy: A Case Study in Breast Cancer

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Abstract

Background: Cannabinoids have been shown to have many palliative effects, including the alleviation of pain and nausea, reduction in anxiety, and inhibition of tumor growth. For cancer patients, these effects are highly desirable, helping to address both the underlying disease and the side effects that too often accompany the diagnosis and treatment regimens.

Case presentation: We report one case of metastatic breast cancer in a patient who was treated with the chemotherapy regimen of palbociclib plus fulvestrant, supplemented with 100 mg of cannabidiol (CBD) daily. At the time of diagnosis, the patient had two bone lesions of considerable size.

Conclusion: The patient responded with a 14% reduction in the size of her bone lesions. A diagnosis- and treatment-matched control patient, on palbociclib plus fulvestrant but not CBD, had her symptoms worsen. This evidence strongly suggests that CBD does indeed have anti-tumor properties and should be strongly considered as a companion treatment for current standard chemotherapy protocols.

Background: Breast cancer is the most common malignancy diagnosed in women worldwide and the second leading cause of cancer-related death in women, with more than 268,000 new cases and 41,000 deaths expected in 2019 [1]. Since 1992, the breast cancer death rate has decreased by approximately one-third [1]. This decrease is largely due to improvements in early detection and therapeutic options, which has resulted in the majority of breast cancer cases being diagnosed at an early localized stage, for which the five-year survival rate is close to 100% [1,2]. However, up to 9% of women present with metastatic disease at the time of diagnosis, with a five-year survival rate of 26%, and nearly 30% of women initially diagnosed with early-stage breast cancer develop metastatic disease, irrespective of treatment [3].

A better understanding of the heterogeneity of the disease has led to a dramatic expansion in the number of treatments that are available to patients with metastatic, or stage IV, breast cancer. These options include endocrine therapies, monoclonal antibodies, antibody-drug conjugates, targeted therapies, and different types of chemotherapy [4]. Yet, metastatic breast cancer remains incurable, and the majority of breast cancer-related deaths remains due to complications from recurrent or metastatic disease [5].

The cannabis plant (*Cannabis sativa L.*) contains a large number of pharmacologically active compounds called phytocannabinoids. The two most abundant of these compounds are Δ9-tetrahydrocannabinol

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(THC) and cannabidiol (CBD), although the amounts and proportions of the various phytocannabinoids in each plant vary by strain and can be adjusted by breeding.

Many cannabinoids, including CBD, have been shown to be non-toxic and to possess anti-tumor activity in multiple cancer types [6]. Numerous mechanisms have been proposed to explain these anti-tumor effects, including the production of reactive oxygen species [7,8], promotion of apoptosis [9], a reduction in inflammation [10], activation of receptors that may inhibit drug transport [11] and tumorigenesis [12], and potentiating the activity of multiple types of chemotherapy [13].

With respect to toxicity, the safety and tolerability of CBD have been investigated in single- and multiple ascending dose studies up to 3,000 mg without any concern [14-31]. The selected daily dose of 100 mg of CBD was therefore well below the limit of concern.

The evidence that CBD is both safe and effective in multiple cancer models is intriguing. We therefore examined the response to CBD of one patient diagnosed with metastatic breast cancer.

Methods

Cannabidiol. A proprietary formulation of CBD was used (bioRenovate™), which comprises CBD isolate (99.25% pure) dissolved in medium-chain triglycerides (MCTs) to a final concentration of 50 mg/ml.

Patient. The patient described in this case study was seen at Southwest Cancer Center (Orlando, Florida). Upon diagnosis with hormone receptor-positive metastatic disease, she was prescribed with the cyclin-dependent kinase inhibitor palblociclib (Ibrance®, Pfizer) plus endocrine therapy with fulvestrant (Faslodex®, AstraZeneca).

Response criteria. The response of patients with solid tumors was measured by CT scan and evaluated using the RECIST (Response Evaluation Criteria in Solid Tumors) guidelines version 1.1 [32].

Results

Case presentation

A 52-year-old woman with no prior history of cancer was diagnosed with metastatic carcinoma of the breast. The tumor was characterized as hormone receptor-positive, HER2-negative. At the time of diagnosis, two metastatic lesions (categorized as non-target lesions by RECIST) were found in the left iliac bone (10.2 cm in size) and femoral neck (12.3 cm in size; Table 1). Initial management included treatment with palbociclib plus fulvestrant according to the following regimen: palbociclib, administered orally at a dose of 125 mg once daily for 21 consecutive days, followed by seven days off in 28-day cycles; and fulvestrant, administered intramuscularly at a dose of 500 mg every 14 days for the first three injections, and then every 28 days [33]. The patient also took CBD, administered sublingually at a dose of 50 mg twice daily.

Three months following the initiation of therapy, the patient was reassessed. Both lesions were found to have decreased in size by an average of 14% (28% and 3%, respectively; Table 1). By RECIST guidelines, the patient was classified as having a non-complete response (non-progressive disease). She was clinically well and continued treatment.

Discussion

Breast cancer is the most frequently diagnosed cancer in the world and the leading cause of mortality in women. The National Cancer Institute estimates 268,600 women will be diagnosed with invasive breast cancer and 41,760 women will die in the United States in 2019 [1]. Since 1991, breast cancer mortality has been decreasing, suggesting a benefit from the combination of early detection and treatment.

The five-year survival rate for women with breast cancer is approximately 90% [1]. That rate drops dramatically for metastatic disease patients, whose five-year survival rate is below 30%. Although this survival rate has improved over the past several decades, we need to make more progress for these patients.

Cannabinoids, and CBD in particular, have been proposed as therapeutic agents for a wide variety of diseases. Although the precise mechanism(s) of action by which cannabinoids exert their effects remain(s) unknown, it has been suggested that the endogenous expression of enzymes, receptors, signaling molecules, and other mediators that comprise the endocannabinoid system render the human body capable of functional responses to this class of compounds.

When taken in conjunction with standard therapy, we found CBD had a significant positive impact, yielding a greater reduction in tumor burden than diagnosis- and treatment-matched control patients.

To our knowledge, this study describes the first observation of CBD being a safe and effective complement to standard therapy for metastatic breast cancer. Our findings indicate patients diagnosed with stage IV disease may benefit significantly from this treatment. Moreover, these results strongly suggest CBD can help potentiate the anti-tumor effects of chemotherapy itself, opening up new avenues of potential research. It is important to note this report is only a

Table 1: Comparison of metastatic breast cancer (stage IV) patient responses in the presence or absence of CBD as part of a standard chemotherapy regimen.

Treatment	Lesion measurements	Patient response to treatment	Category of response
Palbociclib + Fulvestrant	Non-target lesion 1 (media-stinum) 2.4 cm to unknown (pleural effusion found)	(second scan not available)	Progressive disease (based on the presence of pleural effusion)
Palbociclib+ Fulvestrant + CBD	Non-target lesion 1 (left iliac bone): 10.2 cm to 7.3 cm Non-target lesion 2 (femoral neck): 12.3 cm to 11.9 cm	14% reduction in size of lesions	Non-complete response /Non-progressive disease

case study, and so we do not draw any definitive conclusions about the applicability of these results. These observations are potentially important, however, and warrant further exploration in a randomized controlled trial.

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