



A Highly Effective Treatment?

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Abstract

The medical use of cannabinoids, especially in palliative care, is by now well known. Despite clinical data remain limited and inconclusive, cannabinoids may be effective in nausea and vomiting, cancer pain, anorexia and depression or anxiety. A 60-year-old American woman, with an insignificant medical history, was first seen at the out-patient hematology department in July 2016. She presented with intermittent right-sided abdominal pain for several weeks. The pain increased by eating fatty foods.

Introduction

The medical use of cannabinoids, especially in palliative care, is by now well known. Despite clinical data remain limited and inconclusive, cannabinoids may be effective in nausea and vomiting, cancer pain, anorexia and depression or anxiety [1,2]. The therapeutic effect of cannabinoids on cancer is even more controversial, but several preclinical studies suggest cannabinoids may have anti-tumor effects. We present a case of marginal zone lymphoma, with a remarkable response during self-treatment with cannabinoid oil and will briefly discuss some of the anti-tumor effects of cannabinoids.

Case Presentation

A 60-year-old American woman, with an insignificant medical history, was first seen at the out-patient hematology department in July 2016. She presented with intermittent right-sided abdominal pain for several weeks. The pain increased by eating fatty foods. Bowel movements were varying for several weeks. There were no signs of gastro-intestinal blood loss. These symptoms were manageable with dietary changes. She had lost 10 kg in weight, but there were no night sweats or fever. Upon physical examination a splenomegaly was noted. Lymph nodes were not palpable. Routine laboratory investigation showed a modest anemia (hemoglobin 10.96 g/dL). Results were otherwise unremarkable. A CT-scan revealed limited abdominal lymphadenopathy and a splenomegaly of 19 cm. A lymph node biopsy demonstrated a nodal marginal zone lymphoma. Since patients' complaints disappeared spontaneously and disease burden was limited a wait-and-see policy was followed. A year and a half later, in January 2018, the lymphoma progressed with troublesome splenomegaly (23 cm) and progressive lymphadenopathy (largest lymph node - portacaval - 49 mm × 33 mm, Figure 1). The hemoglobin concentration decreased to 8.06 g/dL. Patient was advised to start treatment with immunochemotherapy (rituximab, cyclophosphamide, vincristine and prednisolone). She refused the proposed treatment, as well as blood transfusions. Patient claimed to have to travel to the USA to arrange some financial aspects of her life. She was advised to have regular medical check-ups in the USA. In December 2018, patient returned to the out-patient clinic. Her abdominal complaints and hemoglobin value (11.76 g/dL) had improved. Patient told us that she treated herself

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Figure 1: CT-scan, January 2018 showing progressive lymphadenopathy. Shown in figure is the portacaval lymph node measuring 49 mm × 33 mm.



Figure 2: CT-scan, June 2019 showing further decrease in lymphadenopathy. Shown in figure is the portacaval lymph node measuring 15 mm × 10 mm.

with cannabis and cannabinoid oil. A CT scan revealed a significant decrease in size of all the previously enlarged lymph nodes and of the splenomegaly (14 cm). On a CT scan 6 months later, in June 2019, a further decrease in size of the lymphadenopathy (portacaval lymph node 15 mm × 10 mm, Figure 2) and splenomegaly (13 cm) was seen. On the most recent CT-scan in December 2020 progressive disease was seen (portacaval lymph node 22.2 mm × 12.4 mm), with new lymphadenopathy. Spleen size is stable at 13 cm. Patient however remained asymptomatic. A wait-and-see policy was again advised. She will continue the cannabinoid oil.

Discussion

The endocannabinoid system and the effect on cancer

The Endocannabinoid System (ECS) consists of Cannabinoid (CB) receptors; CB1 and CB2, endogenous cannabinoids (also referred to as endocannabinoids) and enzymes involved in their synthesis, transport and degradation [2-5]. The CB receptors are widely spread throughout the body. The ECS is involved in several processes including embryogenesis, immune response and energy balance. Alterations of CB receptor expression, different levels of endocannabinoids and different expression of endocannabinoid degradative enzymes have been found in cancer and in some cases seem to be related to prognosis. However these alterations are not consistent and vary between tumor types [3,5].

Apart from the endogenous cannabinoids, cannabinoids can also be found in Cannabis plants. The main phytocannabinoids are Cannabidiol (CBD) and delta-9-Tetrahydrocannabinol (THC). In contrast to THC, CBD has mainly non-psychoactive effects and is one of the agents of interest in its effect on cancer. Vast arrays of synthetic cannabinoids are also available [2,6,7].

Several preclinical studies have evaluated the anticancer effect of cannabinoids. The administration of cannabinoids or inhibition of degradative enzymes has been shown to have an effect on tumor proliferation, neovascularization, invasion, chemotherapy resistance and induction of apoptosis [3-6]. In addition several studies show an anti-invasive effect of cannabinoids [4,5].

The endocannabinoid system and hematological malignancies

Several studies have investigated the expression of CB receptors and the effect of cannabinoids specifically in hematological malignancies. In most B-cell non-Hodgkin lymphomas higher mRNA levels of CB receptors type 1 and type 2 can be found, when compared to reactive lymphoid tissue, however at a highly variable level [7,8].

In Mantle Cell Lymphoma (MCL) cannabinoid receptors type 1

and 2 are over expressed, when compared to reactive tissue. Ligation of these receptors with endocannabinoids or synthetic cannabinoids inhibits cell proliferation and induces cell death in MCL cell lines. Mice with human MCL cell lines had slower growing and smaller tumors when injected with endocannabinoids [7,9].

In Hodgkin lymphoma an over expression of CB1 is seen in the Reed-Sternberg cells, while the surrounding reactive tissue is largely negative for CB1 receptors. Treating Hodgkin lymphoma cell lines with a CB1 receptor agonist resulted into a decreased viability of these cell lines [10].

Conclusion

In this letter to the editor, we described a patient with a nodal marginal zone lymphoma, who showed an objective decrease in lymphadenopathy and splenomegaly, after self-administration of cannabinoids.

To the best of our knowledge this is a first case report describing a clinical effect of cannabinoids on non-Hodgkin's lymphoma. We addressed only a limited selection of data concerning the endocannabinoid system and its effect on cancer, however, it is clear that there is emerging evidence that cannabinoids play a role in the pathophysiology of cancer and therefore, in the future, might have a place in the treatment of different types of cancer.

In addition, patients become more and more articulate, and often do their own research. Given the upcoming reporting of 'cannabis and cancer' we think it is important to have some knowledge about the current scientific status of this topic.

References

1. Agar M. Medicinal cannabinoids in palliative care. *Br J Clin Pharmacol.* 2018;84(11):2491-4.
2. Turgeman I, Bar-Sela G. Cannabis for cancer - illusion or the tip of an iceberg, a review of the evidence for the use of Cannabis and synthetic cannabinoids in oncology. *Expert Opin Investig Drugs.* 2019;28(3):285-96.
3. Fraguas-Sanchez A, Martin-Sabrose C, Torres-Suarez A. Insight into the effect of the endocannabinoid system in cancer: A review. *Br J Pharmacol.* 2018;175(13):2566-80.
4. Hinz B, Ramer R. Anti-tumor actions of cannabinoids. *Br J Pharmacol.* 2019;176(10):1384-94.
5. Ramer R, Hinz B. Antitumorigenic targets of cannabinoids - current status and implications. *Expert Opin Ther Targets.* 2016;20(10):1219-35.
6. Kis B, Ifrim F, Buda V, Avram S, Pavel I, Antal D, et al. Cannabidiol - from plant to human body: A promising bioactive molecule with multi-target effects in cancer. *Int J Mol Sci.* 2019;20(23):5905.
7. Wasik A, Christensson B, Sander B. The role of cannabinoid receptors and the endocannabinoid system in mantle cell lymphoma and other non-Hodgkin lymphomas. *Semin Cancer Biol.* 2011;21(5):313-21.
8. Gustafsson K, Wang X, Severe D, Eriksson M, Kimby E, Merup M, et al. Expression of cannabinoid receptors type 1 and type 2 in non-Hodgkin lymphoma: Growth inhibition by receptor activation. *Int J Cancer.* 2008;123(5):1025-33.
9. Flygare J, Gustafsson K, Kimby K, Christensson B, Sander B. Cannabinoid receptor ligands mediate growth inhibition and cell death in mantle cell lymphoma. *FEBS Lett.* 2005;579(30):6885-9.
10. Benz A, Renne C, Maronde E, Koch M, Grabiec U, Kallendrusch S, et al. Expression and functional relevance of cannabinoid receptor 1 in Hodgkin lymphoma. *PLoS One.* 2013;8(12):e81675.