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Striking lung cancer response to self-administration of cannabidiol: A case report and literature review

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Abstract

In spite of new drugs, lung cancer is associated with a very poor prognosis. While targeted therapies are improving outcomes, it is not uncommon for many patients to have only a partial response, and relapse during follow-up. Thus, new drugs or re-evaluation of existing therapies used to treat other non-malignant diseases (drug repurposing) are still needed. While this research both *in vitro* and *in vivo* is being carried out, it is important to be attentive to patients where the disease responds to treatments not considered standard in clinical practice. We report here a patient with adenocarcinoma of the lung who, after declining chemotherapy and radiotherapy, presented with tumour response following self-administration of cannabidiol, a non-psychoactive compound present in *Cannabis sativa*. Prior work has shown that cannabidiol may have anti-neoplastic properties and enhance the immune response to cancer. The data presented here indicate that cannabidiol might have led to a striking response in a patient with lung cancer.

Keywords

Lung cancer, cannabinoid, cannabidiol

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Introduction

The quest to improve the prognosis of lung cancer has led to the development and evaluation of new drugs with mechanisms of action that differ from those of conventional chemotherapy drugs used for many years worldwide. Great effort is now being placed in developing and assessing the potential of targeted therapies and immunotherapy in lung cancer which are leading to improved clinical outcomes.[1] Thus, targeted therapy is replacing conventional chemotherapy as standard treatment for patients with targetable oncogenic drivers.[2] However, it has to be acknowledged that responses to these agents are still partial with tumours recurring during follow-up. In fact, due to tumours' genetic heterogeneity, a complete response in lung cancer patients is very difficult to achieve.[2]

The challenge to improve the outcome of patients with lung cancer is leading to the evaluation of alternative drugs which, alone or in combination, may lead to improved response and survival in patients with lung cancer. Therefore, further development of new drugs or even established therapies previously used to treat non-malignant diseases (drug repurposing) which could have shown an effect on lung cancer *in vitro* and/or *in vivo* are worth pursuing.

One possible example is cannabidiol (CBD), a non-psychoactive compound from *Cannabis sativa*. CBD, which has been used in the management of several non-oncological pathologies,[3] could be a potential drug in the treatment of cancer. CBD has been shown to have anti-neoplastic effects *in vitro* and/or *in vivo* in lung cancer[4–9] and other types of cancer.[10,11] However, although work is needed to better

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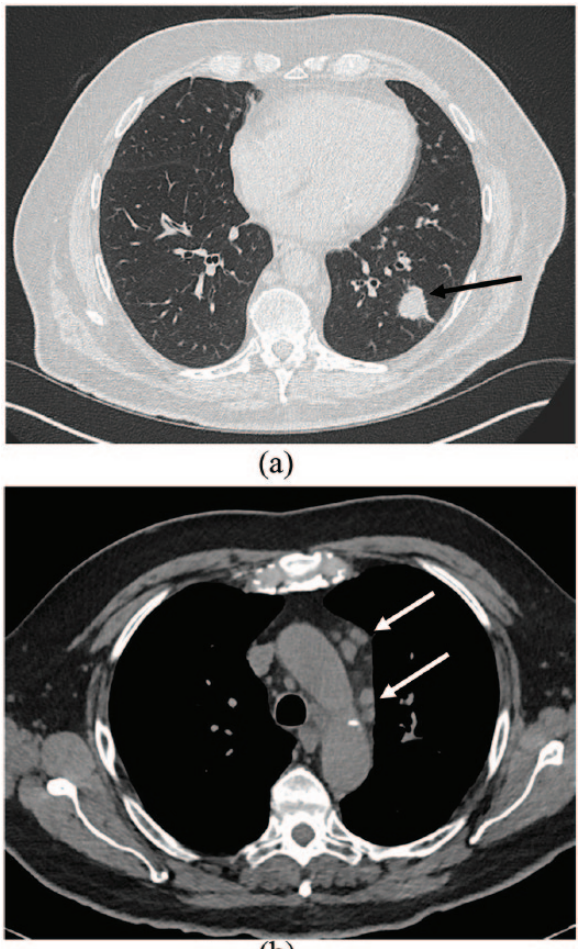

Figure 1. CT scan image at diagnosis: (a) irregular rounded tumour seen in the periphery of left lower lobe, and (b) prominent multiple scattered mediastinal lymph nodes.

understand the mechanism/s of action of CBD both *in vitro* and *in vivo*, it is worth identifying any possible cases of patients with lung cancer whose disease responds to this drug. On this basis, we present here the case of a lung cancer patient whose tumour markedly responded to CBD.

Case

In October 2016, an 81-year-old man with chronic obstructive pulmonary disease (COPD) presented to his general practitioner with a 3-week history of increasing breathlessness but no cough. A chest radiograph identified a shadow in the lower zone in the left lung, and subsequent CT scan confirmed the presence of a 2.5 × 2.5 cm mass in the lower left lung and multiple mediastinal lymph nodes (Figure 1(a) and (b)). The patient underwent an endobronchial ultrasound guided biopsy of the paratracheal lymph nodes which revealed lung adenocarcinoma (T1c N3 M0). Tumour cells were strongly positive for CK7, thyroid transcription factor-1 (TTF-1) and with moderate focal expression of estrogen receptor (ER). They were negative for CK20, S100, PSA, CD56, synaptophysin and chromogranin. The tumour was negative for epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutations.

His previous medical history was COPD, diet controlled diabetes, and cancer of the prostate treated with radical prostatectomy in 2004 and in remission. He was not on regular medication and had no history of drug allergies. He was a retired salesman. There was no previous history of asbestos exposure. He was an ex-smoker (around 18 cigarettes daily for around 15 years) having stopped smoking 45 years ago. His ECOG performance status was 1. Physical examination was unremarkable.

The patient was offered chemotherapy and radiotherapy, but he declined as he was in his 80s and did not want any treatment that could adversely affect his quality of life. The decision was made to follow the patient up but without active treatment.

A CT scan in December 2016 showed that the lung mass had increased in size to 2.7 × 2.8 cm though the mediastinal and left hilar lymph nodes had not changed in size. The patient was offered treatment but again declined. A chest X-ray in July 2017 showed progressive changes in the left lower zone but no significant collapse or effusion evident. The patient had a further CT scan in November 2017 which revealed near total resolution of the left lower lobe mass with only a small area of residual spiculated soft tissue remaining (1.3 × 0.6 cm) and a significant reduction in size and number of mediastinal lymph nodes (Figure 2(a) and (b)). The patient underwent another CT scan in January 2018 which showed stable appearances of the small residual opacity in the left lower lobe and mediastinal lymph nodes.

On further questioning, the patient stated that he had started taking CBD ("MyCBD") oil 2% (200 mg CBD in 10 mL) from the beginning of September 2017. He took two drops (0.06 mL, 1.32 mg CBD) twice daily for a week and then nine drops (0.3 mL, 6 mg CBD) twice daily until the end of September. Following the November 2017 CT scan, the patient started taking nine drops twice daily but had to stop around a week later. The reason behind this was that the patient did not like the taste and caused him slight nausea. He was never physically sick. There were no other changes in the patient's diet, medication or lifestyle from September 2017. Informed written consent was obtained from the patient.

Discussion

The data presented here may indicate that CBD led to a partial tumour response in a patient with histologically proven adenocarcinoma of the lung. Various possible mechanisms of action leading to this objective response might be postulated.

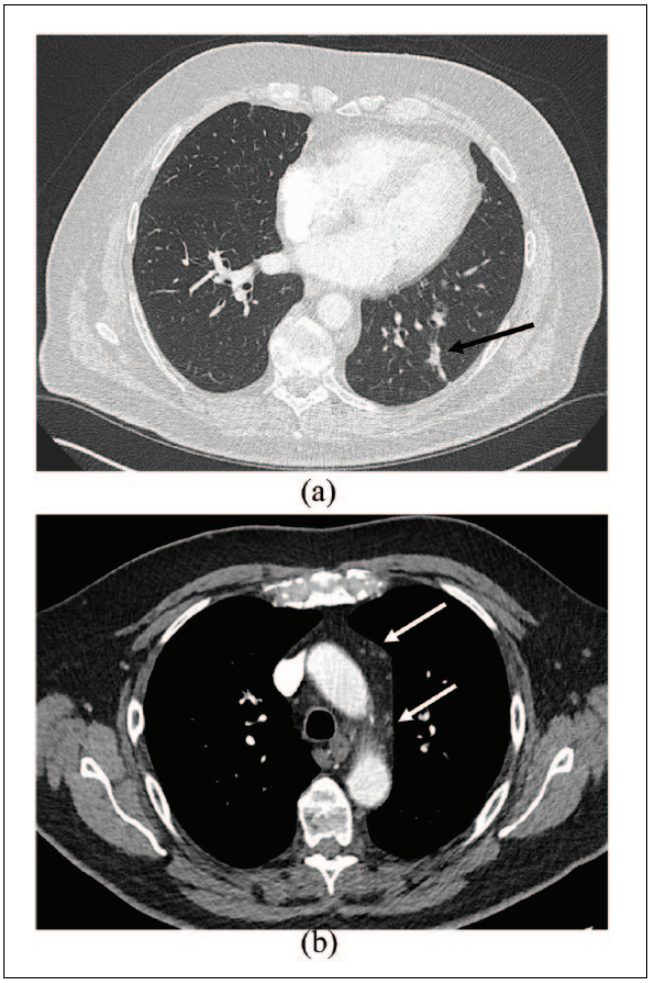

Figure 2. CT Scan image following the patient taking CBD: (a) marked regression of the left lower lobe mass leaving a small irregular residual linear band, and (b) striking regression of the mediastinal lymph nodes.

It has been described that CBD can act on tumour cells, directly or indirectly, through different pathways and that these effects might vary in different tumour cells. CBD acts as an inverse agonist for CB2 receptor and an antagonist for CB1 receptor.[12] However, CBD has low affinity to either CB1 or CB2 receptors.[9] In addition, CBD has anti-cancer effects acting as an agonist for the transient receptor potential vanilloid (TRPV) 1 and 2 leading to changes in intracellular Ca^{2+} levels.[5,13]

It is also reported that CBD can induce apoptosis in cancer cells via the production of reactive oxygen species (ROS), caspase activation[4,13,14] and activation of p53 dependent apoptotic pathways in cancer cells[14,15] and down-regulation of mammalian target of rapamycin (mTOR) and cyclin D1.[16] CBD can also upregulate TNF/TNFR1 and TRAIL/TRAIL-R2 signalling by modulation of both ligand and receptor levels followed by apoptosis.[14] Furthermore, CBD inhibits human umbilical vein endothelial cells (HUVEC) endothelial cells migration, invasion and sprouting in vitro, and angiogenesis in vivo through down-modulation of several angiogenesis-related molecules.[17]

From the immunological point of view, CBD significantly inhibits the recruitment of tumour-associated macrophages (TAM) in primary tumour stroma and secondary lung metastases.[12] CBD enhanced the susceptibility of cancer cells to adhere to and subsequently be lysed by Lymphokine-Activated Killer (LAK) cells, with both effects being reversed by a neutralizing ICAM-1 antibody.[9]

Based on these data, it is clear that several factors may have been involved in this patient's response to CBD. However, although significantly lower potency in non-malignant cells has been described,[18] the effects of CBD on non-malignant cells has yet to be fully assessed.

Conclusion

In summary, the data presented here indicate that CBD may have had a role in the striking response in a patient with histologically proven adenocarcinoma of the lung as a result of self-administration of CBD oil for a month and in the absence of any other identifiable lifestyle, drug or dietary changes. Further work is needed both *in vitro* and *in vivo* to better evaluate the various mechanisms of action of CBD on malignant cells, and its potential application in the treatment of not only lung cancer but also other malignancies.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

The patient described herein had given consent to the use of de-identified patient data for use in research and education. Written informed consent was obtained from the patient for his anonymized information to be published in this article.

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