Neurological Improvement with Medical Cannabis in a Progressive Supranuclear Palsy Patient: A Case Report

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Keywords

Cannabis · Progressive palsy · Alzheimer's disease · Cannabidiol · Supranuclear

Abstract

Progressive supranuclear palsy (PSP) is a severe, debilitating, and often fatal disease resembling other neurodegenerative disorders, namely Alzheimer's (AD) and Parkinson's (PD) diseases, which have been successfully treated with cannabinoids. We herein report the case of a 71-year-old woman diagnosed with PSP, displaying severe impairment of motor and language functions which progressively improved after treatment with medical cannabis. Before treatment, the patient was unable to move her limbs, was fed soft food, and was unable to speak or move her eyes. The patient has regained horizontal eye movement, is able to walk with assistance, has returned to physiotherapy, started to eat solid food, and has had a remarkable improvement in her speech. The possible mechanisms of this improvement are discussed.

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Introduction

Progressive supranuclear palsy (PSP) is a severe, debilitating, and often fatal disease that has no effective treatment to date. Its clinical and pathological features resemble other neurodegenerative disorders, such as Alzheimer's (AD) and Parkinson's (PD) diseases. The development of new therapies for neurodegenerative disorders has been the subject of intense research in recent years, with several experimental evidence suggesting the possible efficacy of cannabinoids, such as cannabidiol (CBD) and tetrahydrocannabinol (THC) [1]. We herein report the case of improvement in motor and language functions in a patient with PSP after the administration of medical cannabis.

Case Report/Case Presentation

A 71-year-old woman presented to the medical office with a history of 6 years of progressive gait disturbance, parkinsonism, and a severe language disturbance. She had lost the capacity to produce intelligible speech except for moans and unintelligible noises (dysarthria) and displayed ophthalmoplegia. She was also unable to walk and had rigidity of limbs.

Serum levels of folic acid, total calcium, creatinine, iron, ferritin, magnesium, phosphorus, and vitamin B₁₂ were within normal ranges.

A brain MRI was performed and showed (a) mesencephalon-pontine disproportion characterized by marked reduction of the midbrain, with relative preservation of the pons associated with loss of the usual morphology of the midbrain, with dorsolateral concavity and reduction of anteroposterior diameter; (b) reduction of thalamic volume and narrowing of superior cerebellar peduncles, in addition to hypersignal of periaqueductal gray matter on FLAIR and T2WI; (c) signs of neurodegeneration with T2SE-hyposignal mainly of the midbrain and posterolateral aspect of putamens, coinciding with volumetric reduction; (d) large cerebellar fissures, inferring some degree of cerebellar volumetric reduction; (e) enlargement of cortical and cerebellar sulci and brain fissures, predominantly in frontal and insular regions; (f) rare sparse foci with T2/FLAIR hyperintense signal without diffusion restriction on the white matter of the cerebral hemispheres, around the anterior horns and atria of the lateral ventricles, in the semioval nuclei/radiated crown and in the subcortical frontoparietal regions.

A full extract of cannabis oil with the approximate ratios of the main cannabinoids of 0.5% CBD, 2% THC, 10% CBDA (cannabidiolic acid), and 7% THCA (tetrahydrocannabinolic acid) (approximately 11 mg/mL of CBD + CBDA and 9 mg/mL of THC + THCA) was prescribed, beginning with 2 sublingual drops at night and doubling the dose on a weekly basis. The oil was acquired by the patient's family from ABRACE (a non-profit organization founded by relatives of children with refractory epilepsy that benefited from cannabis oil and was conferred the right to grow, extract, and commercialize cannabis products in Brazil). There were no side effects attributable to the oil. After a 3-week period, an improvement in dysarthria was perceived. The patient started to articulate words, although still in an unintelligible manner, attempting to communicate. One week later, she improved word articulation and presented a slight return of gaze function. After 5 weeks of cannabis oil administration, her oral output was further improved, and the family and clinical staff were able to understand the words and the meaning of her speech. She also showed improvement in hand tremor and regained the ability to move her limbs. Finally, the patient was also able to stand on her feet and walk with assistance. Videos displaying the clinical picture and symptom improvement can be found in the online supplementary material (videos 1–5; for all online supplementary material, see www.karger.com/doi/10.1159/000503864).

Discussion/Conclusion

The case presented herein is probably the first report of PSP improvement in scientific literature. PSP is now considered a spectrum of motor and behavioral syndromes associated with a specific four-repeat (4R) tau neuropathology at autopsy. Two general types of tau dysfunction are thought to lead to disease: loss of normal tau function or toxic gain of tau function. Despite some research into how to deal with brain levels of toxic forms of tau or the compensation for loss of tau function [2], there is currently no effective treatment for PSP.

There is evidence of common toxic mechanisms in the etiopathogenesis of neurodegenerative diseases, mainly neuroinflammation, excitotoxicity, mitochondrial dysfunction, and reduced trophic support [3]. There has been substantial evidence of cognitive benefits with the association of Δ^9 -THC and CBD in experimental models of AD, but the role of the endocannabinoid system in the pathophysiology of neurodegenerative disorders and its importance as a potential therapeutic target are beyond the scope of this report and were reviewed elsewhere [4]. Briefly, the endocannabinoid system modulates the release of several neurotransmitters such as dopamine, serotonin, noradrenaline, γ -aminobutyric acid (GABA), glutamate, acetylcholine (ACh), and endogenous opioids [5]. CBD and THC are the two most studied phytocannabinoids and represent potential therapeutic agents for several neuropsychiatric disorders, such as addiction, anxiety, mood, and psychotic disorders as well as movement disorders (PD, Tourette syndrome, spasticity of multiple sclerosis), refractory epilepsy, and chronic pain [6–13]. The efficacy of cannabinoids in neuropsychiatric disorders may be due to their multi-target drug profile and the ensuing modulation of neurotransmitter release by the endocannabinoid system [14, 15]. CBD also decreases neuroinflammation through adenosine A2a receptor stimulation, exerts immunological modulation by reducing leukocyte transmigration and down-regulating the expression of vascular cell adhesion molecule-1, and reduces microglia activation and the expression of chemokine ligands 2 and 5 and interleukin 1 beta, among other effects [16]. In AD studies, CBD inhibited in vitro hyperphosphorylation of tau and reduced A β production by promoting amyloid precursor protein ubiquitination [17]. In addition, in vivo CBD treatment has been shown to reverse cognitive deficits in a double transgenic AD mouse model [18]. Anti-inflammatory and neuroprotective effects of CBD could be due to its ability to reduce the level of iNOS, GFAP, calcium binding protein B, and nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B). These actions may be partially mediated through the PPAR- γ receptor [19]. Moreover, a prospective observational study found improvement in 10 severely demented patients regarding rigidity and behavioral problems treated with a CBD/THC combination [1].

Preliminary studies with CBD on PD have demonstrated that it reduces psychotic symptoms and REM sleep behavior disorder, and it could reverse catalepsy behavior in rodents, probably because of its action on the 5-HT1A receptor [20]. In vivo studies have shown that CBD has neuroprotective effects against MPP+ (a neuro-

toxic protein relevant to PD), increasing mRNA levels of the antioxidant enzyme Cu, Zn-superoxide dismutase in substantia nigra, and preventing the depletion of dopamine and reduction in tyrosine hydroxylase activity in caudate-putamen [21]. CBD may also normalize glutamate homeostasis, reduce microglia activation, and promote neuritogenesis, which is not dependent or additive to nerve growth factor and might involve the activation of tropomyosin receptor kinase A (trkA) receptors and increased expression of axonal and synaptogenic proteins [22]. Moreover, an open-label report of 22 PD patients who used smoked cannabis evidenced improvement in tremor, rigidity, and bradykinesia [23]. Finally, THC exerted a neuroprotective effect against all toxins in a human cell model of PD attributable to activation of PPAR- γ receptors [24].

CBD's multiple sites of action are both an advantage and a challenge for the daily clinical practice, as well as for research. Future research in animal models and observational studies in refractory patients or in patients with diseases with no specific treatment available are warranted. This new treatment might represent some hope to patients suffering from this fatal disease. Research of medical cannabis is still in its beginnings but should be encouraged, especially in refractory patients or those for whom there is no specific treatment

Statement of Ethics

This report was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The guardians of the patient have given their written informed consent to publish their case (including publication of images). The study protocol was approved by the Research Ethics Committee of the Armed Forces Hospital.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.G.H. and M.A.A.V. fully participated in the conception, acquisition, analysis, and interpretation of data for the report, drafting the work and revising it critically for important intellectual content, and final approval of the version to be published.

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