DOI: 10.14744/DAJPNS.2020.00113
Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2020;33:437-440

CASE REPORT

Atypical demyelinating lesions due to synthetic cannabinoids: a case report

Zeynep Ozdemir Acar[1], Aysun Soysal[1]

[1]Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Department of Neurology, Istanbul - Turkey

ABSTRACT

Synthetic cannabinoids (SCBs) may cause central nervous system side effects associated with neurological and psychiatric findings. We described a patient with SCBs abuse who presented with confusion. Magnetic Resonance Imaging (MRI) of the brain showed periventricular and subcortical white matter and basal ganglia hyperintensities at T2 and fluid-attenuated inversion recovery sequence with partial rim contrast enhancement on T1-weighted MRI with gadolinium. The patient was treated with high dose methylprednisolone. SCBs can cause serious neurological and psychiatric symptoms. Due to lack of knowledge about these drugs, neuropsychiatric morbidity and mortality are not fully understood.

Keywords: Demiyelination, MRI, synthetic cannabinoids

INTRODUCTION

The possible neuroprotective effects of cannabinoids have been suggested to date in the literature. Two membrane receptors for CBs - CB1 and CB2 receptors- are found in both the central and peripheral nervous systems and non-neuronal cells, including immune cells (1). Based on this, neuroprotective effects have been shown by numerous preclinical and clinical studies. Cannabis preparations are used for spasticity, chronic pain, movement disorders such as Tourette's syndrome or dystonia, glaucoma, epilepsy (2). Despite their medicinal benefits, cannabinoids may be related to ischemic stroke or a hemorrhagic stroke (3,4). Moreover, it has also been suggested that it might be responsible for cognitive impairment and negative changes in brain structure (5,6). Synthetic cannabinoids (SCBs) (spice, K2, bonsai, Jamaica) have recently been abused illegally. These cannabinoids cause systemic and central nervous system (CNS) side effects that occur with neurological and psychiatric findings including behavioral changes (anxiety, paranoia, delirium, stupor, suicidal tendency) (1).

In this case report, we would like to present a patient with atypical demyelinating lesions and a history of SCBs abuse.

CASE

A 34-year-old male patient was admitted to the neurological emergency department and was hospitalized for three days with rapidly increasing difficulty in coordinating movements and speech. On admission, he was presented with slight confusion. He

How to cite this article: Ozdemir Acar Z, Soysal A. Atypical demyelinating lesions due to synthetic cannabinoids: a case report. Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2020;33:437-440.

Correspondence: Zeynep Ozdemir Acar, Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Department of Neurology and Neurosurgery, CEMATEM Unit, Istanbul - Turkey
E-mail: zynp.ozdemir@hotmail.com
Received: September 06, 2020; **Revised:** September 28, 2020; **Accepted:** November 28, 2020

had no previous neurological, psychiatric, or systemic symptoms. The clinical assessment demonstrated a Glasgow Coma Score of 14 with no evidence of meningism and hyperpyrexia (36.8°C). Neurological examination revealed that the patient was confused and had a prolonged reaction time. There was no pathological finding in his motor or sensory functions. His deep tendon reflexes were normal. Routine blood tests at admission were within normal levels. Urine drug screening was positive for cannabinoids (63.7 ng/dL]<50]) and negative for cocaine, amphetamine, benzodiazepines, and barbiturate but at first he and his family denied using illicit drugs. Magnetic resonance imaging (MRI) of the brain demonstrated semi-symmetrical T2/FLAIR hyperintensities in the periventricular and subcortical white matter as well as the basal ganglia with partial rim contrast enhancement (Figure 1). There was a slight restriction in DWI-ADC sequences. Electroencephalography showed a slowdown in both hemispheres in the theta range. Cerebrospinal fluid studies showed 20 lymphocytes, normal glucose, and elevated protein levels (56 mg/dL) normal. High dose intravenous methylprednisolone treatment was initiated. After one week, his consciousness improved depending on this response, steroid therapy was prolonged for 10 days total and followed with oral prednisolone taper. After this cognitive status improved, we could obtained a detailed anamnesis. He had grown up with his family until his adolescence and had used to live with his father and brother after his parent's divorce. He had graduated from high school, completed his military service and had used to work as a carpenter. According to his statement, he had started smoking marijuana 2 years ago and sometimes treid SCBs, but never told how often he used it. He also said he had used to drink 4-pints of beer every day. When he was discharged on hospital on the 21st day, his neurological condition was almost normal except for time disorientation. Follow-up MRI showed improvement in the size of the lesions, no gadolinium enhancement, and no new lesions, 2 months after his admission. Similar to previous ones, no new lesions were seen on follow-up MRI 12 months after his presentation. He has been followed in our out-patient clinic for 5 years, according to his statement he quit smoking and never tried again. There has been no deficiency in his following neurological examination.

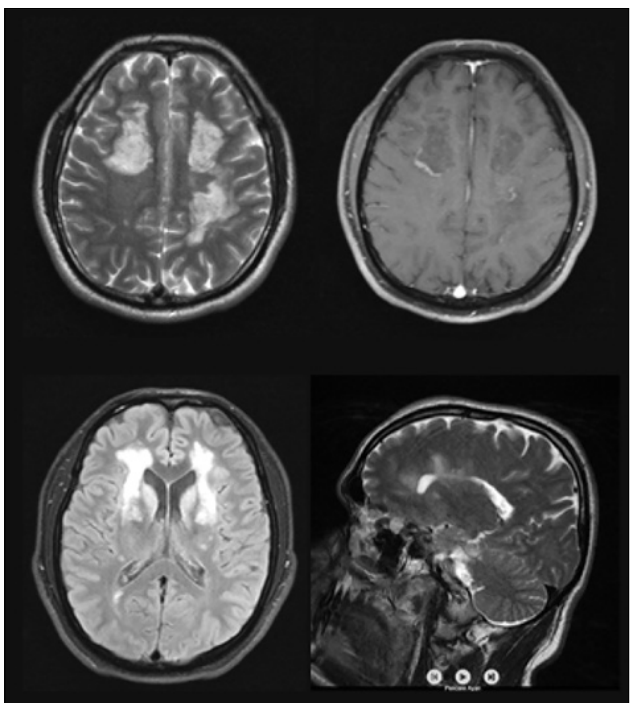

Figure 1. Brain MRI scan showing bilateral hyperdense confluent lesion involving periventricular, subcortical white matter and basal ganglia, with mild peripheral contrast enhancement on T1-weighted imaging.

DISCUSSION

SCBs, called Bonzai, K2, Jamaican gold, black magic, black mamba or spice, etc are derived from marijuana. These are new psychoactive substances and are widely used today due to their low prices. They usually have temporary psychoactive effects including anxiety, agitation, hallucinations, and delirium but they can cause serious metabolic effects such as hypokalemia, rhabdomyolysis, acute kidney injury, myocardial infarction, and death (7). Because of the variable content of these substances, patients may present with various symptoms. The inter and intra-batch variability of SCBs makes these symptoms unpredictable. According to our knowledge, we have two different types of receptors. CB1 receptors, commonly found on neurons in the brain, spinal cord, and peripheral nervous system, are coupled to ion channels. CB2 receptors are peripheral receptors, expressed in immune tissues such as leucocytes, spleen, and tonsils (8). SCBs are lipid-soluble and tend to bind to CBR1 receptors located in periventricular, corticostriatal space, and basal ganglia as well. These are the areas affected in our patient. We were unable to identify the type of SCBs because the patient initially refused to provide a urine sample. Toxic leukoencephalopathy has been well defined following the exposure to heroin, cocaine, and methylenedioxymethamphetamine (or ecstasy) (9-11). Only a few case reports have been published following

the SCB abuse, therefore limited information is available on the pharmacokinetics and toxic mechanisms of SCBs. But it is well known that SCBs are more potent compared to cannabis and have a longer half-life which also means a more prominent toxic effect. According to the radiological images seen in the basal ganglia, the pathology is thought to be secondary to hypoxic-ischemic changes. However, signal enhancement on cortico-subcortical areas such as U fibers and the patient's clinical history suggests that this may be toxic demyelination rather than hypoxic changes. Toxic leucoencephalopathy is well-defined after the appearance of some antineoplastic agents, antimicrobial agents, environmental toxins, and drug abuse like heroin, cocaine, or ecstasy and inflict on the cerebral white matter according to the disease severity. (12) There are some case reports describing toxic changes following illegal drug use, 2C-E, black mamba, but still no consensus on entitling these changes. (9,11,13) Some authors referred to it as toxic leukoencephalopathy or acute disseminated encephalomyelitis (ADEM), but all agree that these changes are myelinopathic changes rather than ischemic changes. The MR images and clinical features of our case are quite similar to ADEM, but we preferred to define it as an atypical demyelinating lesion because it was seen after SBS use. There are no randomly controlled trials for treatment but for the first-line therapy supportive care is considered according to the patient's condition as ventilation support, fever control, electrolyte imbalance regulation etc. If necessary patients should be followed in the intensive care unit. Early immunomodulatory treatments are recommended such as intravenous corticosteroids, immunoglobulins and plasma exchange may also be helpful (14,15). We used 1 gr/day intravenous methylprednisolone for 10 days and the patient was discharged with almost complete recovery without metabolic dysfunction on the 21st day of hospitalization by reducing the dose of 64 mg oral prednisolone.

Kak et al. (16), whose case is very similar to our patient, claim that the side effects of SCBs are dose-dependent and that high doses are essential for toxic leukoencephalopathy. The fact that our patient used SCB in a low doses and at one time may explain the reason for a good prognosis without a neurobehavioral and cognitive deficit in our case.

In recent clinical neurological practice, the increased substance abuse and related CNS side effects are not rare. SCBs are inexpensive and easy to obtain and, unfortunately, are widely abused leading to systemic effects like acute renal failure, cardiac effects including myocardial infarction that all leading to sudden death. When a patient presents with atypical demyelinating lesions and behavioral changes, physicians should be conscious about questioning the patient's history in terms of substance abuse and toxicology screenings should be evaluated.

Contribution Categories		Author Initials
Category 1	Concept/Design	Z.O.A, A.S.
	Literature review	Z.O.A., A.S.
	Data analysis/Interpretation	Z.O.A., A.S.
	Case follow-up (if applicable)	Z.O.A., A.S.
Category 2	Drafting manuscript	Z.O.A.
	Critical revision of manuscript	A.S.
Category 3	Final approval and accountability	Z.O.A., A.S.
Other	Technical or material support	Z.O.A., A.S.
	Supervision	A.S.

Informed Consent: Written informed consent obtained.

Peer-review: Externally peer-reviewed.

Conflict of Interest: There is no conflict of interest.

Financial Disclosure: None declared.

REFERENCES

1. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet 2003; 42:327-360. [CrossRef]
2. Mannucci C, Navarra M, Calapai F, Spagnolo EV, Busardò FP, Cas RD, et al. Neurological aspects of medical use of cannabidiol. CNS Neurol Disord Drug Targets 2017; 16:541-553. [CrossRef]
3. Thanvi BR, Treadwell SD. Cannabis and stroke: is there a link? Postgrad Med J 2009; 85:80-83. [CrossRef]
4. Goyal H, Awad HH, Ghali JK. Role of cannabis in cardiovascular disorders. J Thorac Dis 2017; 9:2079-2092. [CrossRef]
5. Broyd SJ, van Hell HH, Beale C, Yücel M, Solowij N. Acute and chronic effects of cannabinoids on human cognition-a systematic review. Biol Psychiatry 2016; 79:557-567. [CrossRef]
6. Battistella G, Fornari E, Annoni JM, Chtioui H, Dao K, Fabritius M, et al. Long-term effects of cannabis on brain structure. Neuropsychopharmacology 2014; 39:2041-2048. [CrossRef]
7. Zawilska JB. "Legal Highs"--An Emerging Epidemic of Novel Psychoactive Substances. Int Rev Neurobiol 2015; 120:273-300.
8. Lucas CJ, Galettis P, Schneider J. The pharmacokinetics and the pharmacodynamics of cannabinoids. Br J Clin Pharmacol 2018; 84:2477-2482. [CrossRef]
9. Singh R, Saini M. Toxic leucoencephalopathy after 'chasing the dragon'. Singapore Med J 2015; 56:e102-104. [CrossRef]
10. Bianco F, Iacovelli E, Tinelli E, Lepre C, Pauri F. Recurrent leukoencephalopathy in a cocaine abuser. Neurotoxicology 2011; 32:410-412. [CrossRef]

11. Ginat DT. MRI of toxic leukoencephalopathy syndrome associated with methylenedioxymethamphetamine. Neurology 2015; 84:757. [CrossRef]

12. Filley CM, Kleinschmidt-DeMasters BK. Toxic leukoencephalopathy. N Engl J Med 2001; 34:425-432. [CrossRef]

13. Samra K, Boon IS, Packer G, Jacob S. Lethal high: acute disseminated encephalomyelitis (ADEM) triggered by toxic effect of synthetic cannabinoid black mamba. BMJ Case Rep 2017; 2017:bcr2016218431.

14. Scolding N. Acute disseminated encephalomyelitis and other inflammatory demyelinating variants. Handb Clin Neurol 2014; 122:601-611. [CrossRef]

15. Kluger B, Triolo P, Jones W, Jankovic J. The therapeutic potential of cannabinoids for movement disorders. Mov Disord 2015; 30:313-327. [CrossRef]

16. Kak M, Mikhail F, Yano ST, Guan R, Lukas RV. Buzz Juice: Neurological sequelae of synthetic cannabinoids. J Clin Neurosci 2017; 37:43. [CrossRef]