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Case Report

Acute toxic hippocampal encephalopathy in heavy cannabis users: A case report ☆

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ABSTRACT

Cannabis use is increasing rapidly among young people worldwide despite the deleterious effects of this toxic substance on health. We report a case of acute hippocampal encephalopathy in a heavy cannabis user (8-10 joints/d for 6 years) who presented with a non-febrile status epilepticus. Brain magnetic resonance imaging revealed bilateral and symmetrical high-signal abnormalities in the hippocampal regions. The damage to these regions is often severe, long-lasting, and sometimes irreversible. Therefore, every doctor (emergency doctor, resuscitator, neurologist...) is asked to request a brain MRI in case of neurological signs in a young cannabis user.

Introduction

Accidents related to cannabis intoxication are progressively increasing worldwide, parallel with the legalization of its recreational or medical use. The reported consequences in cannabis users affect the respiratory, cardiovascular, and neurological systems [1,2].

Cannabinoid hyperemesis syndrome is characterized by the association of recurrent episodes of nausea and vomiting and cyclic abdominal pain relieved by hot showers [3]. We report a case of acute hippocampal encephalopathy in a heavy cannabis user who presented with unimproved non-febrile status epilepticus despite treatment.

Case report

A 24-year-old unmarried male with no significant medical or surgical history, is a heavy cannabis user, consuming 8 to 10 joints per day since the age of 18, with no alcohol or tobacco use. He presented to the emergency department in a non-febrile status epilepticus. There is no recent history of travel abroad.

Clinical examination following the critical state (status epilepticus) revealed a Glasgow Coma Scale (GCS) of 8/15, a temperature of 36.8°C, no signs of focalization, stable hemodynamic status with SpO2 at 91%, average capillary blood glucose, and biological signs of inflammation.

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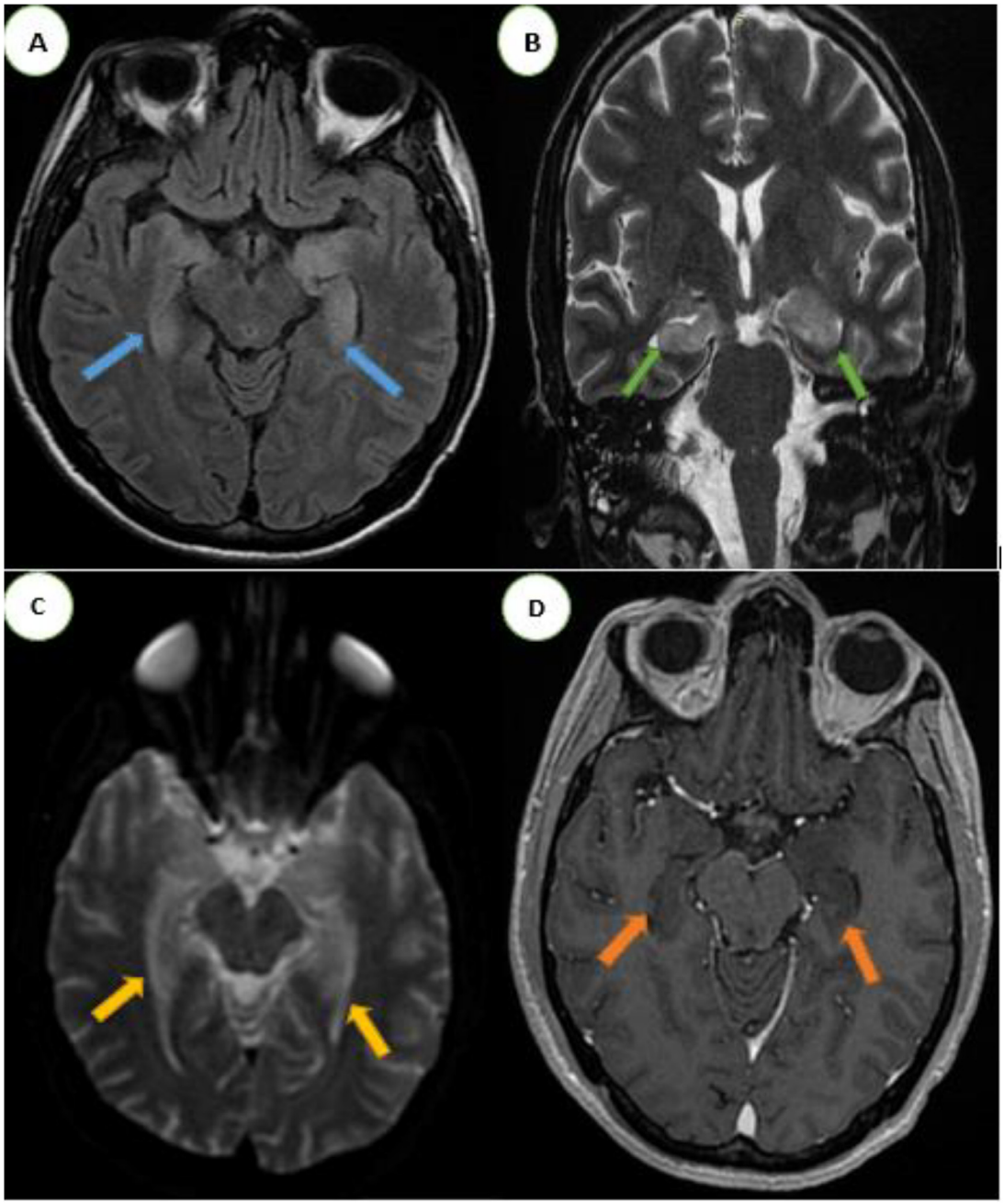

Fig 1 – Cerebral MRI: Axial T2 Flair (A), coronal T2 (B), diffusion (C), and axial T1 with injection of Gadolinium (D): Bilateral and symmetrical hippocampal swelling with hypersignal T2 FLAIR ( ) and T2( ), hypersignal diffusion ( ), not enhanced after injection of PDC ( ).

Initial management included airway clearance, appropriate oxygen therapy, and peripheral venous access. The patient received a short-course treatment with benzodiazepines combined with phenobarbital due to the lack of therapeutic efficacy. The persistence of status epilepticus and worsening of the patient's consciousness prompted intubation and admission to an intensive care unit.

The biological assessment revealed an inflammatory syndrome with a high white blood cell count (25,000/mm^3), a CRP level of 45 mg/L, and a procalcitonin level of 2.65 mg/L. Renal function, lactate, and serum carboxyhemoglobin were within normal ranges. The electroencephalogram showed no abnormalities. The cerebral CT scan did not show any evolving lesions.

Analysis of cerebrospinal fluid showed no particularities: absence of signs of meningitis (less than ten leukocytes/mm^3, no microorganisms, average glucose and protein levels). Antibodies related to autoimmune encephalitis were absent in blood and cerebrospinal fluid analyses.

Blood toxicology testing was positive for cannabis but negative for alcohol and other drugs. A brain MRI revealed bilateral and symmetrical swelling of the hippocampi with high

signal abnormalities in T2 FLAIR and T2 sequences, hyperintense diffusion, and no enhancement after contrast injection (Fig. 1). The diagnosis of acute hippocampal encephalopathy was confirmed.

The patient received intravenous acyclovir (10 mg/kg every 8 h) despite 2 negative PCR tests for herpes simplex virus in cerebrospinal fluid. He also received a bolus of corticosteroids (500 mg/d), empirical antibiotic therapy with third-generation cephalosporin (2 g/d), and gentamicin (1.5 mg/kg every 12 h). Intravenous immunoglobulins (2 g/kg) were administered due to suspicion of autoimmune limbic encephalitis.

The patient's consciousness improved after 3 days of status epilepticus treatment, which allowed for extubation and transfer to a neurology service for etiological exploration and potential therapeutic monitoring. The patient was discharged after ten days with an ambulatory therapeutic protocol based on anticonvulsants, and a follow-up brain imaging control was scheduled for 2 weeks later. The follow-up brain MRI revealed a stable appearance of hippocampal anomalies.

Discussion

Cannabis comprises 2 psychoactive components: Δ-9-tetrahydrocannabinol (Δ-9-THC) and cannabidiol (CBD), both of which have a specific affinity for type 1 cannabinoid receptors (CB1R) found in the neuronal terminals of several brain regions, including the hippocampus [4]. This explains the hippocampal involvement in our patient. They also have a specific affinity for type 2 receptors (CB2R) in immune cells [5].

Cannabidiol has been described as having anticonvulsant properties [6], while Δ-9-tetrahydrocannabinol has been described as proconvulsant [7]. In our case, the onset of the epileptic seizure was preceded by cannabis consumption, suggesting a causal role of cannabis.

In addition to cannabinoid hyperemesis syndrome characterized by severe nausea, recurrent vomiting, and abdominal pain, cannabis encephalopathy may have other manifestations including mental disorders such as depression and anxiety, cognitive impairments like memory and concentration problems. It can also affect the respiratory system through the occurrence of bronchiolitis and respiratory tract infections, and the cardiovascular system through increased risk of cardiovascular disease due to the effect of cannabis on heart rate and blood pressure. Finally, this encephalopathy exposes the risk of cannabis abuse and dependence, in addition to social and legal implications.

Excessive cannabis consumption can lead to acute bilateral hippocampal lesions visible on FLAIR and brain magnetic resonance imaging diffusion sequences.

Other differential diagnoses that can cause bilateral hippocampal lesions were ruled out due to the lack of supporting evidence. These differential diagnoses include herpes encephalitis, autoimmune limbic encephalitis, anoxic encephalopathy, hypoglycemic encephalopathy, or carbon monoxide-related encephalopathy [8].

In cerebral MRI, these encephalitis cases typically present as bilateral symmetric or asymmetric signal abnormalities in T2 and T2 Flair hypersignal, not enhanced after Gado injection. The clinical context, especially the history of exposure to cannabis, herpes infections, carbon monoxide, as well as medical history of known diabetes or neoplasia... and finally, complementary examinations such as cerebrospinal fluid analysis, serological tests, and biopsies help to confirm the diagnosis.

The neurotoxicity of cannabis can explain the long-lasting memory disturbances following episodes of acute encephalopathy in our patient due to the high concentration of CB1R in the hippocampus. Long-term memory deficits have been described in chronic cannabis users [9]. Hippocampal atrophy has also been linked to cannabis consumption [10].

Δ-9-THC may cause these enduring impairments, although CBD may play a neuroprotective role. CB1R deprivation could be responsible for cerebral, cardiac, and renal disorders, while CB2R release could worsen the condition of cannabis users. This explains our patient's condition deterioration after cannabis withdrawal upon admission.

In this regard, studies should be conducted to evaluate the role of the psychoactive components of cannabis, particularly the therapeutic value of cannabidiol.

Conclusion

Cannabis consumption is a pressing public health issue with severe, enduring, and occasionally irreversible side effects. Brain MRI is crucial in diagnosing hippocampal encephalopathy by revealing bilateral hippocampal lesions. Healthcare professionals, including radiologists, neurologists, and intensivists, should remain vigilant for this diagnosis in heavy cannabis users.

This case underscores the importance of recognizing and addressing the health implications of cannabis use, particularly among the youth. It also emphasizes the need for further research to understand better the intricate relationship between cannabis components and their impact on neurological health. By maintaining awareness and conducting thorough assessments, medical practitioners can contribute to the early detection and appropriate management of cannabis-related complications, ultimately improving patient outcomes and public health.

Patient consent

Written informed consent for publication was obtained from patient.

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