Multiple Cerebral Infarcts in a Young Patient Associated With Marijuana Use

Leila Costa Volpon, MD, Camila Lacerda Muniz de Melo Sousa, MD, Silvia Keiko Kavaguti Moreira, MD, Sara Reis Teixeira, MD, and Ana Paula de Carvalho Panzeri Carlotti, MD

Cerebrovascular events associated with marijuana use have been reported previously. This association is plausible, but not well-established yet. A 14-year-old girl, long-term heavy cannabis user, presented with generalized tonic-clonic seizures and decreased level of consciousness a few hours after smoking cannabis. Brain magnetic resonance imaging showed multiple areas of acute, subacute and chronic ischemic lesions in the left frontal lobe, basal ganglia, and corpus callosum. History of other illicit drug use and other known causes of stroke were ruled out. Cannabis might cause stroke through direct effects on the cerebral blood circulation, orthostatic hypotension, vasculitis, vasospasm, and atrial fibrillation. Long-term daily use of marijuana in young people may cause serious damage to the cerebrovascular system.

Key Words: adolescence, cannabinoids, stroke

CASE REPORT

Marijuana is a preparation obtained from the Cannabis plant, which contains both psychoactive and nonpsychoactive chemical compounds. Diverse groups of compounds derived from the plant are referred collectively as cannabinoids. The most important of these in terms of biological activity and recreational use is delta-9-tetrahydrocannabinol (THC) (Thanvi and Treadwell, 2009). Cannabinoids exert their effects at cannabinoid receptors (CB1 and CB2) in the brain and periphery, regulating neurotransmitter release as a part of the recently described endocannabinoid system, which is considered a major modulator of cerebral blood flow (Latorre and Schmidt, 2015).

Regular cannabis use is defined as using 10 to 19 times in a month, whereas heavy use is defined as using ≥20 times a month; both have been associated with a range of chronic health problems, such as anxiety, depression, and neurocognitive alterations (Hall and Degenhardt, 2009). Evidence accumulated over the past decades supports a link between cannabis and stroke (Geller et al., 2004; Westover et al., 2007; Thanvi and Treadwell, 2009; Wolff et al., 2011; Singh et al., 2012; Bernson-Leung et al., 2014; Inal et al., 2014; Oyinloye et al., 2014; Wolff et al., 2014; Hackam, 2015; Rumalla et al., 2016). This association is plausible, but still not well-established.

Herein, we report case of a heavy daily cannabis user adolescent who developed multiple cerebral infarcts. This case report was approved for publication by the patient and her family.

A 14-year-old girl, with a 2-year history of daily cannabis use (8–10 cigarettes per day), presented with generalized tonic-clonic seizures for about 5 minutes. Her blood pressure was 90/60 mm Hg, pulse rate 160 beats/min, pulse amplitude was weak, and her axillary temperature was 40°C. At the Emergency Room, diazepam, phenoxytoin, dipyrone, and a bolus of normal saline were administered. After seizure control, Glasgow Coma Scale was 4 and pupils were equal. She was intubated and transferred to the pediatric intensive care unit (PICU). Two hours earlier, she had used marijuana and alcohol. She had no history of trauma, fever, nausea, vomiting, or headache. Her past medical history was unremarkable. She was a full-term baby born by vaginal delivery in good condition, with a birth weight of 3500 g. Her mother experienced an uncomplicated pregnancy and she reached normal development milestones during childhood. She denied tobacco use. Her mother also had been using cannabis daily for the past 3 years. There was no family history of stroke or cardiovascular disease.

On examination, in the PICU, the patient remained with a Glasgow Coma Scale score of 4 and had another seizure soon after admission. Her blood pressure was 110/65 mm Hg, pulse rate 115 beats/min, and pulse amplitude was normal. She was treated with phenobarbital and midazolam. Neurological examination showed equal pupils and reactive to light, absence of neck stiffness, normal bilateral patellar reflex and cough reflex, plantar skin reflex in bilateral flexion, and absence of vestibulo-ocular reflex. Soon after administration of phenobarbital and midazolam, she had cold extremities, and her blood pressure dropped to 67/24 mm Hg, which improved after a continuous infusion of dopamine and epinephrine. Initial laboratory studies showed lactic acidosis and hyperglycemia. Head computerized tomography scan was normal. Electroencephalography (EEG) monitoring was not
available; however, an EEG was performed the day after admission and ruled out status epilepticus. Serum electrolytes, complete blood count, and coagulation studies were normal. Toxicological screening was positive for cannabis (THC) and negative for alcohol, amphetamines, tricyclic antidepressants, cocaine, and ecstasy. Magnetic resonance imaging (MRI) of the brain showed multiple ischemic infarcts in the left frontal lobe, basal ganglia, and genu of corpus callosum, which had both chronic and acute features (Fig. 1), with a normal angiogram. Further investigation for differential diagnosis showed negative markers for autoimmune disease, normal transthoracic echocardiogram, normal cerebral spinal fluid analysis, and negative serological tests for syphilis and HIV.

The patient was weaned off mechanical ventilation, hemodynamic support was discontinued, and she was transferred to the neurology ward 6 days later. She remained drowsy and disoriented for 10 days. Neurological reflexes were normal and there were no motor or sensory deficits. Also, she had dysphagia and stridor. Airway assessment showed subglottic stenosis, so she underwent a tracheostomy and was discharged home for rehabilitation. However, the patient did not attend an outpatient appointment for screening of coagulopathies and thrombophilia. Twelve months later, her tracheostomy tube was withdrawn and dysphagia improved. She was lost to neurological follow-up and denied seizures, but complained about chronic headache. Her family is being followed up by social workers and currently is marijuana and alcohol-free. She went back to school, but has learning disabilities. Moreover, she has been on psychiatric treatment due to suicidal ideation and depression.

**DISCUSSION**

Marijuana is certainly the most widely used illicit drug among teenagers. Adolescent marijuana users may be more vulnerable to neural dysfunction and other deleterious consequences than adults, since the brain undergoes dramatic changes in gross morphology characterized by loss of gray matter paralleled by an increase in white matter during this period of life (Rubino and Parolaro, 2016). The first reported case of neurological deficits related to cannabis use was in 1964 (Mohan and Sood, 1964). Since then, there have been some case reports of ischemic and hemorrhagic stroke, and transient ischemic attacks in cannabinoid users that are inconclusive (Geller et al., 2004; Singh et al., 2012; Bernson-Leung et al., 2014; Inal et al., 2014; Oyinloye et al., 2014; Wolff et al., 2014; Hackam, 2015). Westover et al. found that cannabis use was a significant risk factor for ischemic stroke in a controlled epidemiology study (Westover et al., 2007). In a population-based analysis of hospitalized patients in the United States, Rumalla et al. concluded that, among younger adults, recreational marijuana use is independently associated with a 17% increase in the likelihood of acute ischemic stroke hospitalization (Rumalla et al., 2016). It is postulated that cannabis might produce stroke through direct effects on the cerebral vasculature, and also orthostatic hypotension, vasculitis, vasospasm, and atrial fibrillation (Thanvi and Treadwell, 2009). Reversible cerebral vasoconstriction syndrome, which is characterized by severe headaches with or without other symptoms, and segmental constriction of cerebral arteries that resolves within 3 months have been reported in association with cannabis use (Wolff et al., 2011, 2014). This increasingly recognized syndrome must be considered as a possible pathophysiology mechanism of stroke in marijuana users, especially in patients with multiple areas of infarction. It is also possible that cannabis, being an illegal drug not subject to sanitary control, may be mixed with other substances that could increase the risk of stroke. It is often mixed with tobacco, even though nicotine was not screened in this...
cannabis and cerebrovascular events, and found that this association is relatively robust (Hackam, 2015). There seems to be a predilection for the basal ganglia in strokes associated with cannabis consumption and substantial stroke recurrence (Oyinloye et al., 2014; Hackam, 2015). A case series of patients with ischemic stroke who were cannabis users showed a higher prevalence of infarcts in the posterior circulation. However, in this series, as in our case, no evidence of structural vasculopathy was found (Singh et al., 2012).

The patient was admitted at the Emergency Room with signs of shock, probably owing to prolonged seizures. During her PICU stay, hemodynamic support was necessary which could be related to the adverse effects of phenobarbital and midazolam. However, evidence suggests that there are cardiovascular effects of cannabis presumably resulting from loss of basic autonomic and homeostatic functions secondary to presynaptic inhibition of noradrenaline release (Kunos and Bátkai, 2001). Cerebrovascular effects are less well-understood (Singh et al., 2012).

This young patient remained in critical condition for some days. Geller et al. reported 2 cases of adolescent males with cannabis-associated cerebellar infarction that developed an acute syndrome of cerebellar, brainstem dysfunction, and death (Geller et al., 2004). To the best of our knowledge, this is the first report of such a young patient (14 years old) with cannabis-associated multiple ischemic infarcts.

Our patient has been treated in the psychiatric department for depressive disorder. Indeed, evidence indicates that heavy cannabis use per se during adolescence may represent a risk factor for the development of psychiatric disorders (Rubino and Parolaro, 2016). Also, she has developed a learning disability, probably due to cognitive sequelae of cerebral infarcts. Nevertheless, there is evidence suggesting that repeated exposure to cannabis during adolescence might have deleterious effects on intelligence and cognitive function (Squeglia and Gray, 2016).

In conclusion, long-term daily use of marijuana in young people may cause serious damage to the cerebrovascular system. Raising awareness about the risks of cannabis use seems crucial. Toxicology screening should be done in young patients with stroke and no obvious cause, or if suggested by history or physical examination.

REFERENCES