

Cannabis-Related Stroke: Case Series and Review of Literature

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Marijuana, or cannabis, is one of the most commonly used illicit drugs worldwide. Although there are some case reports of stroke associated with cannabis use, there is no information on a causal role of cannabis in stroke. We identified 14 patients admitted to St Louis University Hospital between January 2004 and July 2007 with ischemic stroke who had documented clear exposure to cannabis during or before symptom onset and a positive urine screen for cannabis. We report this series, along with 3 cases previously reported by our group, for a total of 17 patients (13 men and 4 women), with a mean age of 41 years (range, 15-63 years). Nine patients were under age 45 years, 4 had a history of hypertension, and 10 sustained stroke in the posterior circulation. Headache, dysarthria, and ataxia were the most common presenting symptoms. Five patients had recurrent stroke with reexposure to cannabis. No patient had a prothrombotic state or cardiac source of embolism. Autopsy performed in 2 patients revealed hemorrhagic infarct with no evidence of vasculitis or embolus. The absence of other vascular risk factors in most of our patients, the temporal relation of symptom onset to cannabis exposure, and the recurrence of symptoms in a few patients with reexposure suggest a causal role of cannabis in these cases of ischemic stroke. However, this causal association cannot be definitely ascertained, given the descriptive nature of our series. More research is needed to explore this possible causal association. **Key Words:** Cannabinoids—ischemic stroke—vasospasm.

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After alcohol, marijuana, or cannabis, is the most commonly used recreational drug in Australia and the United States. In the Australian national drug strategy household survey, 33% of subjects aged 20-29 years reported a lifetime use of cannabis.¹ In the United States, the percentage of young adults aged 18-25 who had ever used cannabis increased from 5.8% in 1965 to 50% in 2002.² Cannabis is generally regarded as safe. In 2000, an estimated 76% of America's 14.8 million illicit drug users used cannabis alone (59%) or in conjunction with other illicit drugs

(17%).³ Approximately 7 million people in the US population use cannabis at least weekly.

Limited information exists on the frequency, risk factors, mechanisms, and final outcomes of ischemic strokes associated with illicit drug use. Illicit drug use is a suspected risk factor for stroke in young adults, reportedly associated with 2%-39% of cases of ischemic stroke.⁴ Although cannabis is the most widely used illicit drug, there are only a few case reports of cannabis-related stroke. The support for a link between cannabis use and stroke has come primarily from case reports and some animal studies. Evidence accumulated over the last several decades supports a link between cannabis and stroke. Human imaging and postmortem examinations, as well as laboratory models, suggest that cannabis might produce stroke through direct effects on the cerebral circulation, orthostatic hypotension, central nervous system vasculitis, vasospasm, and atrial fibrillation.⁵⁻⁷

With the fairly recent discovery of the endogenous cannabinoid system and extraordinary scientific advances that followed, the development of useful cannabinoid-based medicines is an important area of investigation that may

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prove useful for a variety of health conditions. Indeed, pharmaceutical drugs have been developed that either contain or have similar chemicals as those found in the cannabis plant, some of which are currently in phase II and phase III FDA-approved trials. Here we report 17 patients with cannabis-related stroke who presented to the St Louis University Hospital between 2004 and 2007, including 3 patients reported by Geller et al in 2004.⁸

Materials and Methods

This retrospective case study was approved St Louis University's Institutional Review Board. We reviewed 831 patients who were admitted to St Louis University Hospital's stroke unit between January 2004 and July 2007 and identified 14 patients with acute stroke and a clear history of exposure to cannabis and a positive urine screen for cannabis. We also included 3 adolescent males with cerebellar infarction and a history of acute marijuana use who were reported in 2004.⁸ Complete hematologic, biochemical (including a lipid panel, homocysteine, and hemoglobin A1c), and cardiac evaluations (electrocardiography, Holter monitoring for at least 48 hours, and transthoracic echocardiography [TTE] with bubble study), along with vascular studies (neck and brain carotid duplex/magnetic resonance angiography [MRA]) and neuroimaging studies (brain stroke protocol magnetic resonance imaging [MRI], brain computed tomography [CT]) were done in all patients except cases 14 and 15, who had an incomplete workup. Urine drug screen was done by fluorescence polarization immunoassay for 11 drugs, including cannabis, cocaine, heroin, barbiturates, ethanol, phencyclidine, amphetamines, LSD, methadone, benzodiazepines, and propoxyphene. Patients under age 45 years were also screened for hypercoagulable states and underwent transesophageal echocardiography (TEE). Two of the 3 patients reported previously underwent brain autopsy and cerebrospinal fluid evaluation.

All clinical data were gathered from medical records review, MRI reports, and various imaging and laboratory test results. Baseline demographic data and information on past medical history (ie, transient ischemic attack [TIA] and stroke; cardiovascular diseases, including atrial fibrillation; tobacco use; hyperlipidemia; and hypertension), use of other drugs, family history of stroke, and follow-up, including recurrence of symptoms with reexposure, were collected. The history of cannabis smoking and interval between cannabis smoking and onset of stroke symptomatology were documented in each patient.

Results

We evaluated 17 patients (13 men and 4 women), with a mean age of 41 years (range, 15-63 years). The patients' clinical characteristics are summarized in Table 1. Three patients had a history of smoking less than 1 pack of

cigarettes per day (cases 5, 11, and 14). All patients except 3 adolescents (cases 1, 2, and 3) had a long-standing history of cannabis use of more than 2-3 cigarettes per week. Thirteen patients had smoked cannabis for several hours and were smoking at the time of symptom onset. In 3 patients, stroke symptoms started within 30 minutes of the last exposure to cannabis (cases 6, 9, and 15), and in 1 patient, symptom onset was 24 hours after exposure (case 2). Four patients noticed transient confusion, slurred speech, or frank dysarthria and gait ataxia before stroke (cases 4, 8, 12, and 16). Four patients had a history of hypertension (cases 11, 12, 15, and 17). Five patients had a history of alcohol use (cases 4, 9, 10, 11, and 12), although alcohol was not detected in blood samples, and 2 had a history of cocaine use (cases 16 and 17). Three patients had history of stroke occurring within 5 years before admission (cases 15, 16, and 17), and 5 others experienced recurrent stroke during reexposure to cannabis (cases 4, 8, 12, 13, and 16). Two patients had symptomatic orthostatic hypotension on admission (cases 12 and 15). The stroke occurred in the posterior circulation in 58% of cases and in the anterior circulation in 42% of cases. One patient had internal carotid artery (ICA) occlusion (case 11).

Illustrative Cases

Case 1

A 15-year-old male presented with acute-onset headache, dysarthria, and gait ataxia within 30 minutes after using cannabis. Brain MRI revealed a right cerebellar infarct (Fig 1), and cerebral angiography and brain biopsy findings were normal. He was discharged to rehabilitation with partial resolution of his neurologic symptoms.

Case 7

A 37-year-old male presented with acute-onset global aphasia and right hemiparesis. He was smoking cannabis at the time of symptom onset. Brain MRI revealed an infarct in the left middle cerebral artery (MCA) distribution (Fig 2). Head and neck MRA showed no vascular lesions, and TEE demonstrated no cardiac source of embolism. A vasculitis panel (including sedimentation rate, antinuclear antibodies, double stranded DNA, antiphospholipid antibody, cytoplasmic antineutrophil cytoplasmic antibody and perineuclear antineutrophil cytoplasmic antibody and a workup for hypercoagulable state (protein culture and sensitivity, and factor V Leiden) were negative. He was discharged to rehabilitation and did not experience any recurrence over 1 year of follow-up.

Case 12

A 50-year-old man presented with acute-onset dizziness and imbalance. MRI revealed multiple small, scattered foci

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