

[CASE REPORT]

Marijuana-related Reversible Cerebral Vasoconstriction Syndrome

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Abstract:

The legalization of recreational marijuana in some countries has been accompanied by an increased number of case reports of serious cardiovascular and cerebrovascular complications. However, there have been few studies describing the detailed clinical course of reversible cerebral vasospasm syndrome (RCVS) associated with marijuana use. We herein report a unique case of recurrent bi-fronto-parietal subcortical (watershed) infarction in the setting of chronic daily marijuana use for several years, with evidence of bilateral anterior cerebral artery vasoconstriction. The quick resolution of symptoms with treatment and the normalization of cerebral vasoconstriction on follow-up imaging lend high certainty to the diagnosis of RCVS.

Key words: RCVS, cannabinoid, marijuana

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Introduction

The legalization of recreational marijuana has been accompanied by an increased number of case reports of serious cardiovascular and cerebrovascular complications (1). However, there have been few studies describing the detailed clinical course of reversible cerebral vasospasm syndrome (RCVS) associated with marijuana use.

We herein report a case of marijuana-related RCVS in a patient with a history of recurrent stroke.

Case Report

A 42-year-old woman presented with a 4-day history of headache, nausea and vomiting and a 14-hour history of left-sided weakness and numbness. She was a habitual daily cannabis smoker, and her last use of marijuana had been four days prior to admission.

The patient's medical history was notable for an initial diagnosis of stroke at an outside hospital 14 months prior, when she presented with acute onset of right-sided weakness, gait imbalance and tingling in both hands that was associated with headache, nausea and vomiting. Her only re-

markable medical history at the time was being an active smoker of tobacco cigarettes and marijuana, which she had smoked daily for eight years. Imaging studies, including magnetic resonance imaging (MRI) and a computed tomography (CT) angiogram (CTA), revealed bilateral subcortical centrum semiovale fronto-parietal infarction with no evidence of stenosis or occlusion of the intra- and extracranial vessels. The diagnostic workups, including a transesophageal echocardiogram and hypercoagulable blood panel, were unremarkable, so an implantable loop recorder was placed. She was placed on antiplatelet therapy and statin therapy, with which she was compliant. Her symptoms gradually improved over the course of rehabilitation in the subsequent few weeks. While she stopped smoking tobacco, she continued to smoke marijuana on a daily basis. She had had other intervening hospitalizations and reported that she had recently been admitted about two months earlier with a possible seizure, at which time MRI had demonstrated bi-parietal vertex stroke. She had been prescribed levetiracetam but never taken it. She had had no further seizure-like events.

On presentation to our emergency room, the patient was alert and oriented to her name, age and current month but not the name of the hospital. She was easily distractible

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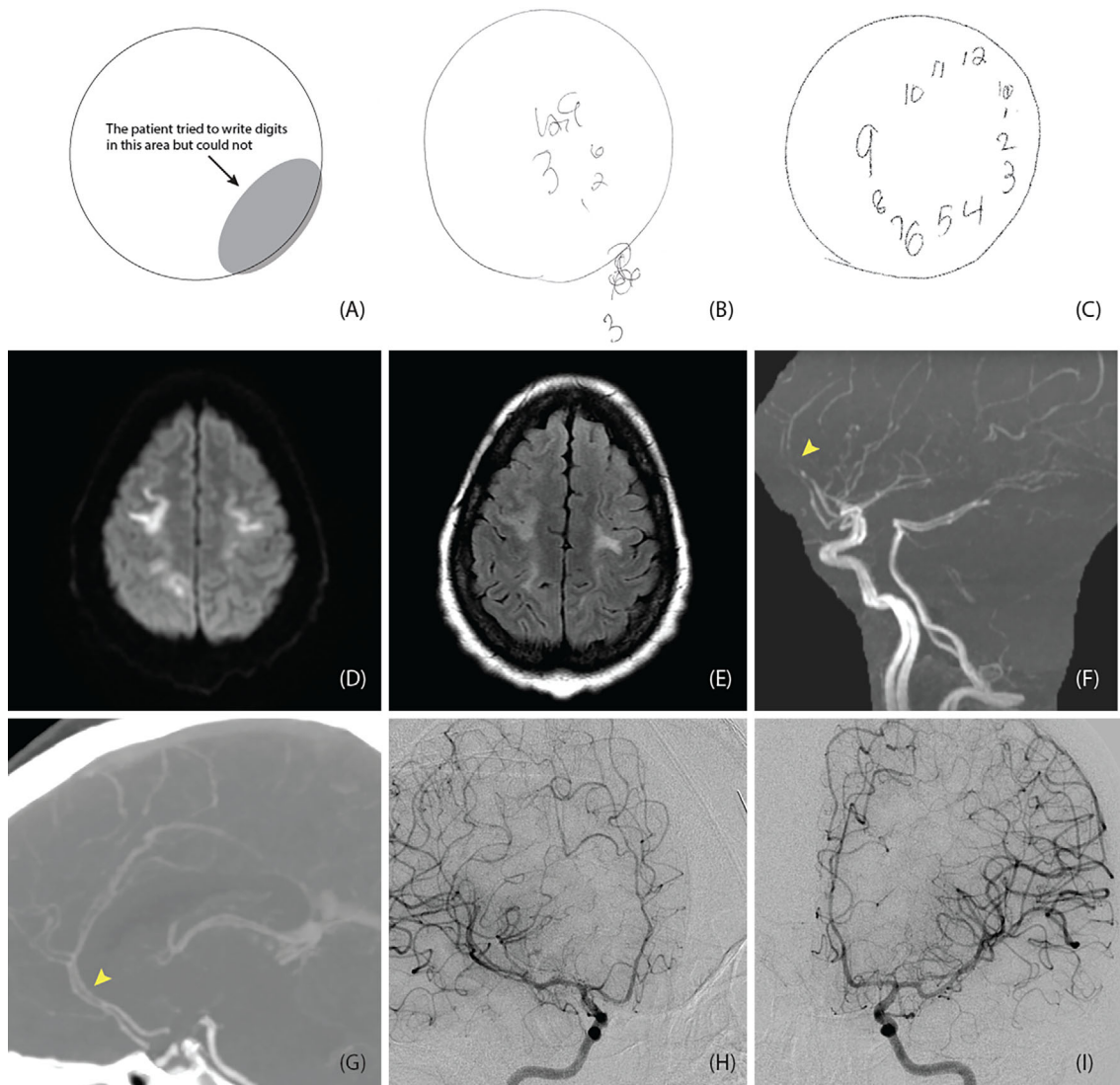


Figure. Clinical and imaging presentation of marijuana-induced RCVS. The patient initially presented hemispatial neglect on clock-drawing test (A), followed by improvement after the initiation of verapamil on hospital day 2 (B, day 3; C, day 5). Brain MRI demonstrated restricted diffusion (D) and increased fluid attenuated inversion recovery signals (E) at the bilateral high convexity subcortical area of the parietal lobes. A magnetic resonance angiogram (F) and CT angiogram (G) were notable for diffuse vasoconstriction of the cerebral arteries, especially in the anterior cerebral arteries (shown with yellow arrowhead). The cerebral angiogram performed on hospital day 6 showed normal cerebral arteries [H, branches of the right internal carotid artery (ICA); I, branches of the left ICA].

with limited attention. Her language function was intact, and her speech showed no dysarthria. Her visual fields were full. A motor examination was notable for left-side-predominant bilateral weakness (right limbs showing antigravity with drift, left arm showing no movement against gravity, left leg drifting and falling to the bed). There was left-sided spatial and personal inattention (see also clock-drawing test; Figure A-C) and left-right confusion. Sensation to a pin was decreased on the left side, but sensory extinction was not present. Coordination was intact in the right limbs and left leg but not testable in the left arm due to the degree of weakness. Her initial National Institutes of Health Stroke Scale (NIHSS) score was 8.

Initial CT findings were notable for bilateral frontal cen-

trum semiovale hypodensity, with the left side more significantly affected than the right. The findings from a magnetic resonance angiogram (MRA) and CTA were notable for diffusely narrowed cerebral arteries, particularly the anterior cerebral arteries (ACAs), with no large vessel occlusion (Figure F, G). MRI demonstrated restricted diffusion (Figure D) and increased fluid attenuated inversion recovery signals (Figure E) at the bilateral high convexity subcortical areas of the frontal and parietal lobes (right-side predominant). Laboratory tests, including autoimmune and coagulopathy evaluations, were unremarkable except for mildly elevated C 4 (64 mg/dL). Urine toxicology screening was positive for cannabinoids. Magnetic resonance venography, an electroencephalogram, an electrocardiogram, and transthoracic echo-

Table. Characteristics of Patients with RCVS Associated with Marijuana.

Type of RCVS	Cannabis-related	Not related to cannabis use
Age [median (IQR)]	Younger [27 (20-38)]	Older [51 (38-56)]
Sex (female, %)	Predominantly male (33%)	Predominantly female (77%)
Thunderclap headache (%)	Less frequent (33%)	More frequent (71%)

The data was collected from a retrospective cohort study by Jensen J. et al. (4) RCVS: reversible cerebral vasoconstriction syndrome, IQR: interquartile range

cardiography were unremarkable. Interrogation of the implanted loop recorder revealed no episodes of atrial fibrillation since implantation in 2018.

Given the MRA and CTA findings of bilateral ACA stenosis, cannabis-related RCVS was suspected, and treatment with verapamil was initiated on hospital day 2. Her headache and neurologic deficits, including hemi-spatial neglect dramatically improved after the initiation of verapamil (Figure B, C). The cerebral angiogram performed on hospital day 6 demonstrated normal cerebral arteries (Figure H, I). At 90-day follow-up, the patient had been compliant with cessation of marijuana use and had no recurrence of headache, with only minimal residual left foot clumsiness when walking.

Discussion

The patient's clinical features of headache, bilateral watershed infarctions on MRI, bilateral reversible cerebral artery stenosis, and improvement of neurological deficits after initiation of verapamil were all compatible with RCVS (2). The patient's history of stroke was also considered to be secondary to marijuana-related RCVS given the same clinical symptoms and the similar imaging findings.

Although most patients with RCVS present with "explosive-onset, worst-ever" headaches, or thunderclap headaches, 15% of patients do not follow this typical presentation (3). The characteristics of patients with marijuana-related RCVS and differences from non-marijuana-related RCVS from a previous retrospective study are described in Table (4). Marijuana-related RCVS occurs predominantly in younger men and in particular is known to present with variable degrees of headache (5). Even patients who have ischemic stroke secondary to marijuana-related RCVS might not report headache (6). Recently, multifocal intracranial stenosis has been suggested as a potential cause of cannabis-related stroke, which is more common among young marijuana users than among older ones (7). Patients with RCVS may have a variety of neurologic symptoms depending on the area affected by ischemia or brain edema, including higher brain dysfunction, with Balint syndrome-like features of simultanagnosia, optic ataxia and ocular apraxia reported (3). The present marijuana-related RCVS case was unique in that 1) the patient was a woman, and 2) her headache was rather mild in severity, was associated with recurrent stroke, and was accompanied by the rapid resolution of higher brain dysfunction following treatment.

Several mechanisms of action underlying marijuana-induced brain ischemia have been reported, including vasospasm due to increased oxidative stress through formation of reactive oxygen species and hyperadrenergic state, a reduced oxygen supply secondary to the increase in carboxyhemoglobin levels after inhalation, and a pro-coagulant or pro-thrombotic state (1). The pathophysiology also underlies vasospasm and thrombosis of coronary artery, resulting in cannabinoid-associated acute myocardial infarction, especially in young men using cannabis.

There is no standard treatment for cannabis-related RCVS, and the mainstay treatments are supportive. Clinical and angiographic resolution take place spontaneously (8). If clinical symptoms do not improve spontaneously, as we observed in this case, pharmacologic interventions for vasoconstriction with calcium channel blockers, such as nimodipine and verapamil, are considered options (4). In our case, after starting verapamil, we observed the significant improvement in clinical symptoms and resolution of intracranial vasoconstriction on follow-up imaging.

The findings of our case describe the diverse phenotypic spectrum of cannabis-associated RCVS. The early recognition of cannabis-induced RCVS may help patients avoid unnecessary additional diagnostic testing and lead to better outcomes.

Written informed consent regarding the paper was obtained from the patient.

The authors state that they have no Conflict of Interest (COI).

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