Unilateral Basal Ganglia Hemorrhage and Lateral Rectus Palsy: An Unusual Association in Marijuana-Induced Reversible Cerebral Vasoconstriction Syndrome

Sir,

Reversible cerebral vasoconstriction syndrome (RCVS) is a clinic-angiographic syndrome characterized by sudden severe headache, with or without other acute neurological symptoms, and segmental constriction of cerebral arteries with spontaneous resolution within 12 weeks.[1] The underlying pathophysiology has been attributed to endothelial dysfunction and brief disturbance of the regulation of cerebral arterial tone, which could be idiopathic or precipitated by conditions including the postpartum period, exposure to blood products, vasoactive drugs, migraines, hypertension, neoplasms, trauma, pregnancy.[2] Intracranial hemorrhage (ICH) in RCVS is usually subarachnoid, but may be intraparenchymal in 3–10% of cases.[3] Women and migrainers have been shown to have a predisposition to develop ICH and in turn have persistent severe focal neurological deficits.[3] Often under-recognized, cerebral edema in RCVS can be secondary to infarcts, hemorrhages, vasospasm, hydrocephalus, or disruption of the blood–brain barrier, often refractory to need emergent surgical decompression in the few cases reported.[4,5] We report a unique case of marijuana induced RCVS unilateral basal ganglia hemorrhage and a right lateral rectus palsy which completely resolved with medical management.

A 29-year-old man presented with severe holocranial throbbing headache for 7 days with nausea and vomiting. He also complained of painless binocular diplopia with horizontally separated images, for far more than near objects, worsening in the right lateral gaze. He was a habitual daily cannabis smoker for the past 10 years and his last use of marijuana had been 4 days prior to admission. On presentation, the patient was alert and oriented with blood pressure was 130/90 mm of Hg and Mini Mental Status Examination (MMSE) was 30. There was right lateral rectus palsy with abduction restriction. Fundus examination revealed no abnormality and the visual fields were normal. Rest of the neurological examination and systemic examination revealed no abnormality. MRI brain demonstrated a left basal ganglia subacute hematoma with magnetic resonance angiogram (MRA) showing segmental constriction and dilatation of anterior cerebral arteries with no large vessel occlusion or cerebral venous abnormality [Figure 1a-e]. Bilateral abducens nuclei and nerves were normal [Figure 1d]. Complete blood count, liver and renal functions, C – reactive protein (2.91 mg/l), and ESR (20 mm/h) were normal. Serum IgG4, anti-nuclear antibody, anti-dsDNA, ANCA, HIV, Hepatitis B and C serology, and VDRL were negative. Coagulopathy evaluations were unremarkable [Table 1]. Toxicology screening from the urine was positive for cannabinoids. Electroencephalogram, echocardiography, electrocardiogram were unremarkable. Cerebrospinal fluid (CSF) showed an opening pressure of 390 mm of Hg with no other abnormality. With a background of marijuana abuse and angiogram findings with raised intracranial tension, cannabis-related RCVS was suspected, and treatment with oral nimodipine 30 mg thrice a day along with acetazolamide 250 mg thrice a day was initiated on second day of hospital stay. His headache and diplopia improved over the next week of hospital stay. The MR angiogram performed after 4 weeks demonstrated normal cerebral arteries [Figure 1f]. At 90-day follow-up, the patient had completely stopped marijuana use and had no recurrence of headache without any neurological deficits.

Use of vasoactive substances has been associated with RCVS, compatible with its pathophysiology of endothelial dysregulation and transient disturbances in cerebral arterial tone secondary to the induced vasospasm.[6] In a retrospective review comparing RCVS among marijuana users and non-marijuana users, it was found that the former occurs predominantly in younger men and is known to present with variable degrees of headache, in contrast to the sudden severe "thunderclap" headache described in RCVS.[6] Our patient had throbbing headache, albeit not severe enough to qualify as thunderclap headache, short duration and associated cranial nerve involvement pointed towards a secondary etiology. Postulated mechanisms for marijuana induced RCVS include cerebral vasospasm, vasculitis and impaired cerebral autoregulation suggested by transcranial Doppler studies.[7]

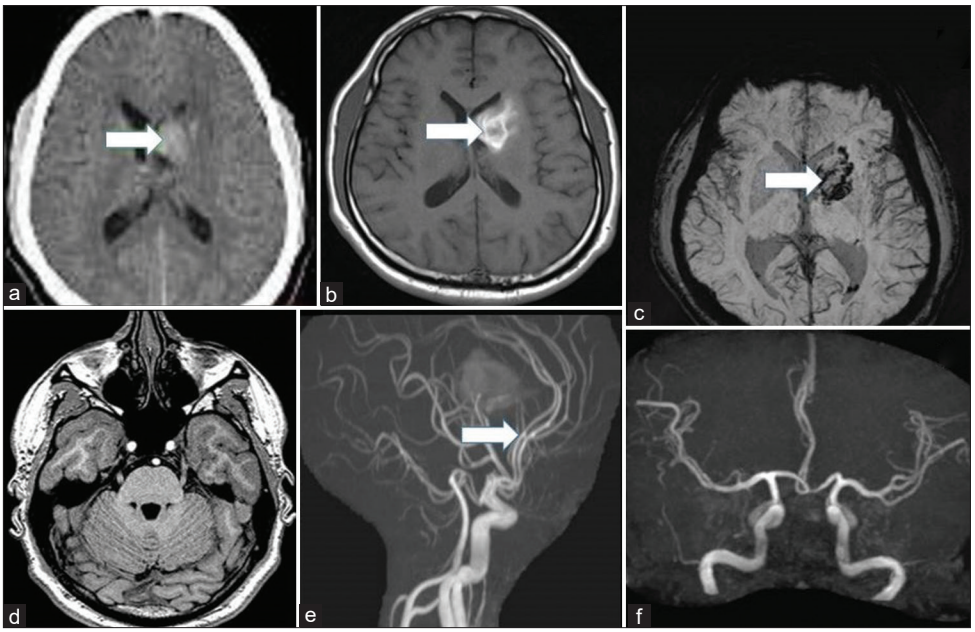

Figure 1: (a) Computed tomography showing hematoma in left caudate nucleus with intraventricular extension. (b and c) magnetic resonance imaging (MRI) showed subacute hematoma in left caudate nucleus. (d) T2 FLAIR image showing bilateral normal abducens nuclei. (e) MR Angiogram showing constriction in bilateral anterior cerebral arteries. (f) Normal MR Angiogram of intracranial vessels at 4 weeks of follow-up

Table 1: Laboratory blood investigations

Parameter	Value obtained	Reference Range
Hemoglobin	15 gm/dl	13–18 gm/dl
Total leucocyte count	7900/cumm	4000–11000/cumm
Platelet count	4.31 lakhs/cumm	1.5–4.5 lakhs/cumm
Erythrocyte sedimentation rate	20 mm/hour	<20 mm/hour
Urea	32 mg/dl	16–48 mg/dl
Creatinine	0.3 mg/dl	0.7–1.2 mg/dl
Prothrombin time (PT)	10.2 seconds	12 seconds
International normalized ratio (INR)	1.1	<1.2
Activated partial thromboplastin time (APTT)	33.4 seconds	28–38 seconds
Total bilirubin	0.29 mg/dl	<1.2 mg/dl
AST	26 U/L	<50 U/L
ALT	24 U/L	<41 U/L
ALP	38 U/L	40-129 U/L
Total protein	6.27 gm/dl	6.6–8.7 gm/dl
Albumin	3.6 gm/dl	3.5–5.2 gm/dl
Antithrombin III	107%	80–120%
Protein C	112%	70–140%
Protein S	99%	72.2–123.3%
Vitamin B12	547	191–946
Homocysteine	10.2 umol/L	5.4–16.2 umol/L
Antiphospholipid antibody IgM	1.01 U/ml	<12 U/ml

The prevalence of intraparenchymal hemorrhages in RCVS has been variable in multiple retrospective studies, ranging from 3 to 15%.[2] A large prospective study of 89 patients with RCVS found ICH in 34% of patients including cortical SAH, ICH, and SDH.[3] These hemorrhages are usually single, lobar, associated with another type of stroke (convexity hemorrhage or infarction), usually detected with a concomitant presence of a focal neurological deficit. The initial pathology consists of transient segmental constriction and dilation of angiographically silent small vessels which causes the initial headache and rupture of small vessels. At a later stage, involvement of major intracranial vessels results in ischemic infarctions.[8] Our patient although presented early with ICH, it was purely cephalalgic with an isolated left basal ganglia hemorrhage.

There have been scarce reports of cranial nerve involvement in RCVS. A report of pupil involving third nerve palsy as the presenting feature of RCVS postulated focal vasospasm and local hyperperfusion to be the likely pathogenesis.[9] Theorizing similar mechanisms in pre-eclampsia causing a sixth nerve palsy, the authors hypothesized multiple pathomechanisms including nerve infarction, inflammation of nerve fascicles, displacement of the nerve due to cerebral oedema.[10] Lateral rectus palsy has not been reported earlier in RCVS. Without any other associated focal neurological deficit and rapid reversibility with ICP lowering therapy, the lateral rectus palsy in our case was hypothesized to be as a consequence of raised ICP. However, nerve infarction secondary to vasospasm as a pathophysiological possibility cannot be excluded, regardless of a normal structural imaging of the sixth nerve.

Refractory intracranial hypertension in RCVS needing surgical decompression has been documented in few case reports. The pathophysiology of cerebral edema in RCVS is multifactorial; secondary to ischemic and hemorrhagic strokes, vasospasm with subclinical ischemia or disruption of the blood–brain barrier.[4,5]

Drugs targeted at vasospasm such as nimodipine, verapamil and magnesium sulphate have been tried to relieve arterial

narrowing, however, prospective and retrospective large studies suggest no change in the time course of cerebral vasoconstriction.[1] Our patient had good response to nimodipine and acetazolamide.

This case highlights an atypical presentation of marijuana induced RCVS. Moreover, our patient had a mild, persistent headache in contrast to the typical severe, recurrent headache of RCVS. Lateral rectus palsy in this patient could be secondary to multiple mechanisms: cerebral edema, focal vasospasm and hypoperfusion.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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