Diagnosing RCVS Without the CV: The Evolution of Reversible Cerebral Vasoconstriction Syndrome

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Abstract

This is a case of a 52-year-old man with a past medical history of 2 episodes of coital thunderclap headaches as well as recent cocaine, marijuana, and pseudoephedrine use, who presented with sudden, sharp, posterior headache associated with photophobia and phonophobia. His initial magnetic resonance imaging (MRI) of the brain, magnetic resonance angiography (MRA) of the head, and magnetic resonance venography (MRV) of the head were all normal as well as a normal lumbar puncture. Given the multiple risk factors for reversible cerebral vasoconstriction syndrome (RCVS), the patient was treated for suspected RCVS, despite the normal imaging. Repeat MRI brain 3 days after hospital admission demonstrated confluent white matter T2 hyperintensities most prominent in the occipital lobes, typical of posterior reversible encephalopathy syndrome (PRES). Repeat MRA of the head 1 day after discharge and 4 days after the abnormal MRI brain showed multisegment narrowing of multiple arteries. This case demonstrates that RCVS may present with PRES on MRI brain and also exemplifies the need to treat suspected RCVS even if imaging is normal, as abnormalities in both the MRI and the MRA may be delayed.

Keywords

vasospasm, intracranial cerebrovascular disorders, vascular headaches, headache disorders

Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) has become recognized as a frequent cause of thunderclap headache. Reversible cerebral vasoconstriction syndrome, also known as Call-Fleming syndrome, is characterized by prolonged but reversible vasoconstriction of cerebral arteries.¹ It was initially reported under various names, until Drs Call, Fleming, and colleagues' definitive case series titled "Reversible Cerebral Segmental Vasoconstriction."² RCVS is an important mimic for central nervous system (CNS) vasculitis and has been frequently misinterpreted in the past as CNS angiitis³ due to overlapping clinical features such as headache, stroke, and angiographic abnormalities.

The syndrome typically presents with severe, acute-onset thunderclap headaches, nausea, and photophobia.⁴ Headache can occur intermittently for days or weeks and resolves completely in approximately 90% of patients.⁵ A prospective study of 67 cases⁶ showed that thunderclap headache was the only symptom in 76% of patients. RCVS mostly affects individuals in their third to fifth decade of life. It affects more women than men, with a ratio of about 4:1.^{1,5}

Case Description

A 52-year-old man with a past medical history notable for 2 episodes of coital thunderclap headache at age 25 noted a sudden, sharp, posterior headache associated with photophobia and phonophobia while carrying heavy luggage. He took two 60-mg pseudoephedrine tablets once and boarded a plane. Right after takeoff, the headache worsened significantly, and he started acting belligerent, arguing and screaming with flight attendants, which he and his wife attributed to his severe headache. He received intravenous (IV) fluids and diphenhydramine in flight and after landing was brought to a local hospital where a head computed tomography (CT) was normal, after which he signed out against medical advice. The next morning his headache did not improve so he was referred to a neurologist who sent him back to the emergency department

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Figure 1. Initial imaging in emergency department. A, Normal magnetic resonance imaging (MRI) brain on day of admission. B, Normal magnetic resonance angiography (MRA) head, on the day of admission.

(ED). In the ED, his neurological examination was normal including mental status and fundoscopy, and magnetic resonance imaging (MRI) brain (Figure 1a) and magnetic resonance angiography (MRA) head (Figure 1b) were unremarkable. An MRV of the head was normal. Lumbar puncture was notable, with white blood cells of 9 cells/ μ L (38% lymphocytes and 41% neutrophils), red blood cells of 2630 cells/ μ L, protein of 56 mg/dL, and glucose of 62 mg/dL (serum glucose of 92 mg/dL). No oligoclonal bands were detected. A repeat lumbar puncture the next day demonstrated no red cells or xanthochromia and an opening pressure of 11 cm H₂O, with the patient in the lateral decubitus position. Systolic blood pressure was mildly elevated in the 130 to 140 mm Hg range. Intravenous valproic acid and IV steroids were administered for presumed migraine. Upon further questioning, the patient admitted to marijuana and cocaine use 5 days prior to admission. In light of the patient's recent exposure to cocaine, marijuana, pseudoephedrine, and high altitude, RCVS was suspected and the patient was started on nimodipine 60 mg every 4 hours. On the third hospital day, 5 days after the headache began, in the absence of significant improvement, despite opioids and IV methylprednisolone, a repeat MRI brain (Figure 2a) demonstrated confluent white matter T2 hyperintensities, most prominent in the occipital lobes. Of note, systolic blood pressure as an inpatient was generally between 140 and 160 mm Hg, with a peak of 180 mm Hg.

Radiographic evidence of posterior reversible encephalopathy syndrome (PRES) in association with RCVS was diagnosed, and the patient was started on nicardipine and transitioned to verapamil SR 180 mg daily, with improvement in his headaches and normalization of blood pressure to the 120s to 130s/70s to 80s mm Hg range.

A repeat MRA head (Figure 2d) 1 day after discharge, and 3 days after PRES was demonstrated on MRI, showed multi-segment narrowing of the bilateral M1, M2, A1, A2, posterior cerebral artery (PCA), and right superior cerebellar artery (SCA), while the MRI brain (Figure 2b) showed improvement in PRES. Follow-up MRA head (Figure 2e)/MRI brain (Figure 2c) 1 month later showed complete resolution of both PRES and RCVS.

Discussion

In 60% of cases of RCVS, causative factors can be identified, while it appears to be idiopathic in approximately 30% of patients. Associated precipitants⁶⁻⁹ include the third trimester and postpartum period, eclampsia and preeclampsia, use of vasoconstrictive drugs (eg, selective serotonin reuptake inhibitors, pseudoephedrine, triptans, and recreational drugs including cocaine, ecstasy, amphetamine derivatives, and marijuana), high altitude, migraine and other primary headaches, cerebral trauma, hypertensive encephalopathy, and a history of having thunderclap headaches.

Neuroimaging findings in RCVS range from a normal MRI to convexity subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, and PRES-like findings. Singhal⁵ retrospectively analyzed 139 consecutive patients with a diagnosis of RCVS at 2 academic centers. Of the patients, 55% had a normal initial CT or MRI scan, but 81% had visible lesions when imaging was repeated. The frequency of specific imaging findings included infarcts (39%), convexity subarachnoid hemorrhage (34%), lobar hemorrhage (20%), edema (38%), or some combination of the above. In 2010, Ducros et al⁹ performed a prospective study of 89 consecutive patients with angiographically proven RCVS and found that 37% had an

Figure 2. Imaging during and after hospitalization. A, Magnetic resonance imaging (MRI) brain on hospital day 3, demonstrating confluent white matter fluid-attenuated inversion recovery (FLAIR) hyperintensities most prominent in the occipital lobes, indicative of posterior reversible encephalopathy syndrome (PRES). B/D, MRI brain 4 days after previous MRI and 1 day after discharge, which showed improvement in PRES. Corresponding magnetic resonance angiography (MRA) demonstrating multisegment narrowing of intracranial vessels, including the M1 segment of the middle cerebral artery and the A2 segment of the anterior cerebral artery (arrows pointing toward stenosis). C/E, MRI brain 1 month after discharge showing complete resolution of PRES. Corresponding MRA head demonstrating complete resolution of vessel narrowing.

abnormal CT or MRI. Of 30 patients with abnormal imaging, 27 had cortical subarachnoid hemorrhage, 11 had intracerebral hemorrhage, and 2 had subdural hemorrhage. Five cases demonstrated PRES-like imaging that occurred in addition to hemorrhage, while 2 patients had PRES without hemorrhage. Chen et al¹⁰ also performed a prospective study of 77 patients with RCVS, although hemorrhage was an exclusion criterion. In their study, 9% of patients with RCVS had PRES and 8% had cerebral infarction. Looking at the temporal evolution of vasoconstriction, Chen et al found that the highest mean numbers of arterial segment involvement occurred on day 16 ± 9.4 , with the initial MRA performed at a mean of 10.4 ± 7.0 days. The sensitivity of vascular imaging early in the course of RCVS has not been studied and is still unknown, so imaging may not show any abnormalities or only minimal vasoconstriction early in the clinical course. Quartuccio et al¹¹ described a case of RCVS presenting with subarachnoid hemorrhage, where an angiogram on admission and

2 weeks after presentation was normal, while a third angiogram 1 month after presentation demonstrated vasoconstriction.

There have been no randomized trials with regard to treatment of RCVS. Removal of any precipitating or aggravating factors should be immediately done once RCVS is suspected. With regard to medications, treatment is primarily symptomatic. Calcium channel blockers are commonly used, and nimodipine has been shown to improve headaches though does not alter the time course of vasoconstriction.¹ Verapamil may also be effective.⁴

The patient in this case had many of the known risk factors for RCVS, including a history of coital thunderclap headache, cocaine, marijuana, and pseudoephedrine use as well as being in a high altitude. Unlike the majority of patients with RCVS who present with subarachnoid or intracerebral hemorrhage, this patient's MRI solely demonstrated radiographic signs of PRES. Interestingly, the MRA and MRI brain were initially normal, and it was not until days later that both the MRI and

the MRA revealed abnormalities. Despite normal initial imaging, RCVS was suspected, and the patient was started on nimodipine. Repeat MRI brain demonstrated fluid-attenuated inversion recovery changes consistent with PRES, which further reinforced the clinical suspicion, and repeat MRA head 3 days later revealed vasoconstriction. It was not until a repeat MRA head 1 month after discharge demonstrating resolution of the vasoconstriction that a diagnosis of RCVS was confirmed. This case exemplifies the need to suspect RCVS even if imaging is normal, as abnormalities in both the MRI and the MRA may be delayed.

Authors' Note

Marc Dinkin and Joseph Safdieh are equally contributing last authors.

Declaration of Conflicting Interests

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