

Reversible Cerebral Vasoconstriction Syndrome Presenting With Visual Field Defects

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Abstract: A 45-year-old woman with a history of depression and anxiety, treated with selective serotonin reuptake inhibitors (SSRIs), experienced acute, recurrent, and severe bifrontal headaches. Over time, she developed a left homonymous hemianopia and mental status changes. MRA revealed segmental vasoconstriction of cerebral arteries in multiple vascular distributions. She was treated with a calcium-channel blocker and magnesium, and there was resolution of her symptoms and cerebrovascular changes. Her clinical course and neuroimaging findings were consistent with reversible cerebral vasoconstriction syndrome. Although rare, this disorder frequently manifests with visual complaints. Although the prognosis is generally favorable, patients with this syndrome require prompt diagnosis and care directed to avoid complications including stroke, seizure, and subarachnoid hemorrhage.

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In 1988, Call et al (1) reported a series of 19 patients with thunderclap headaches. Some developed permanent neurologic deficits, and all demonstrated evidence of reversible cerebrovascular vasoconstriction. The disorder has been designated as reversible cerebral vasoconstriction syndrome (RCVS) although other names include Call–Fleming syndrome, benign angiopathy of the central nervous system, postpartum angiopathy, thunderclap headache with reversible vasospasm, migraine angiitis, and drug-induced cerebral arteritis or angiopathy (2–4).

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In a prospective case series of 67 patients presenting with RCVS, visual symptoms were common transient neurological deficits (5). At times, permanent visual field loss occurred. We report a patient with visual field loss associated with RCVS, and highlight the clinical, neuroimaging, and laboratory considerations associated with this syndrome.

CASE REPORT

A 45-year-old woman with a history of depression and anxiety was evaluated in the emergency department with severe (10/10) bifrontal headache. The headache started suddenly while straining to have a bowel movement. There had been associated nausea, vomiting, phonophobia, photophobia, and transient blurred vision that had since resolved. Review of symptoms was negative for fever, fatigue, tingling in hands and feet, changes in speech, focal weakness, and loss of consciousness. She denied any history of headaches. Current medications included escitalopram, trazodone, and estrogen supplementation.

On examination, she was alert and oriented, but she appeared very uncomfortable secondary to headache. Her pupils were equal in size and reacted normally. Ocular motility was normal. There were no cranial nerve deficits, and her motor examination showed normal muscle bulk, tone, and strength. She had no difficulties with coordination. The rest of the physical examination was within normal limits.

Laboratory studies, brain computed tomography (CT), and cerebrospinal fluid analysis were normal. The patient's headache improved with narcotics, and she was discharged home.

The patient returned to the emergency department 4 times over the ensuing week with severe headaches precipitated by the Valsalva maneuver. On the first 3 occasions, her headache mildly improved with intravenous fluids and narcotics, and she was sent home. During the fourth visit, she was admitted to

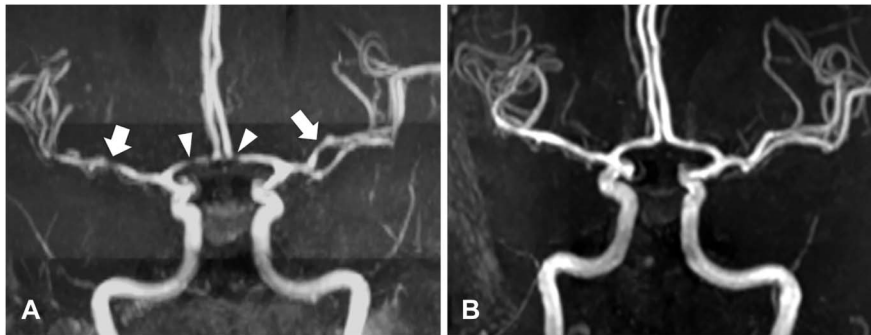


FIG. 1. A. Magnetic resonance angiography reveals areas narrowing of the anterior (arrowheads) and middle (arrows) cerebral arteries. **B.** Six weeks after hospitalization, these vessels appear normal.

the neurology service for further evaluation. CT and magnetic resonance imaging (MRI) of the brain were normal. Nine days later, she developed alternating moments of confusion and lucidity and stated that she had been experiencing vision loss that began minutes to hours after her headaches. Confrontation visual field testing demonstrated left homonymous hemianopia, and positive Babinski and Hoffman signs on the right. Brain MRI was interpreted as showing subtle bilateral parieto-occipital enhancement, and brain magnetic resonance angiography (MRA) was unremarkable.

Five days later, both the mental status changes and homonymous hemianopia resolved. However, the patient had acute worsening of headache with word substitution aphasia and reported decreased vision. MRA revealed multiple sites of small, medium, and large cerebral vascular narrowing and decreased perfusion (Fig. 1A). An emergent MRI revealed bilateral occipital tip abnormalities (Fig. 2). Given the previous negative MRA, the patient was tentatively diagnosed with RCVS secondary to selective serotonin reuptake inhibitor (SSRI) (escitalopram) and estrogen use.

At that time, ophthalmic examination revealed vision of counting fingers in the right eye and 20/200 in the left eye. Pupillary reactions were normal, eye movements were full, and the appearance of the anterior and posterior segments was normal. Because of altered mental status, visual fields could only be performed by the confrontation technique and demonstrated a left homonymous hemianopia.

During the patient's hospital stay, her regular medications were discontinued, and she was treated with nimodipine (60 mg orally every 4 hours), and magnesium (1 g IV once followed by 500 mg orally). Her vision and other symptoms improved over the next 3 days, and she subsequently was discharged on verapamil (80 mg 3 times a day), and magnesium (250 mg twice per day).

MRA performed 6 weeks after discharge revealed increased caliber of the cerebral vessels compared to her previous study (Fig. 1B). Automated visual field testing at 10 and 24 weeks after hospitalization showed no evidence of homonymous visual field loss. The patient's headaches and neurological deficits totally resolved over 8 months of follow-up.

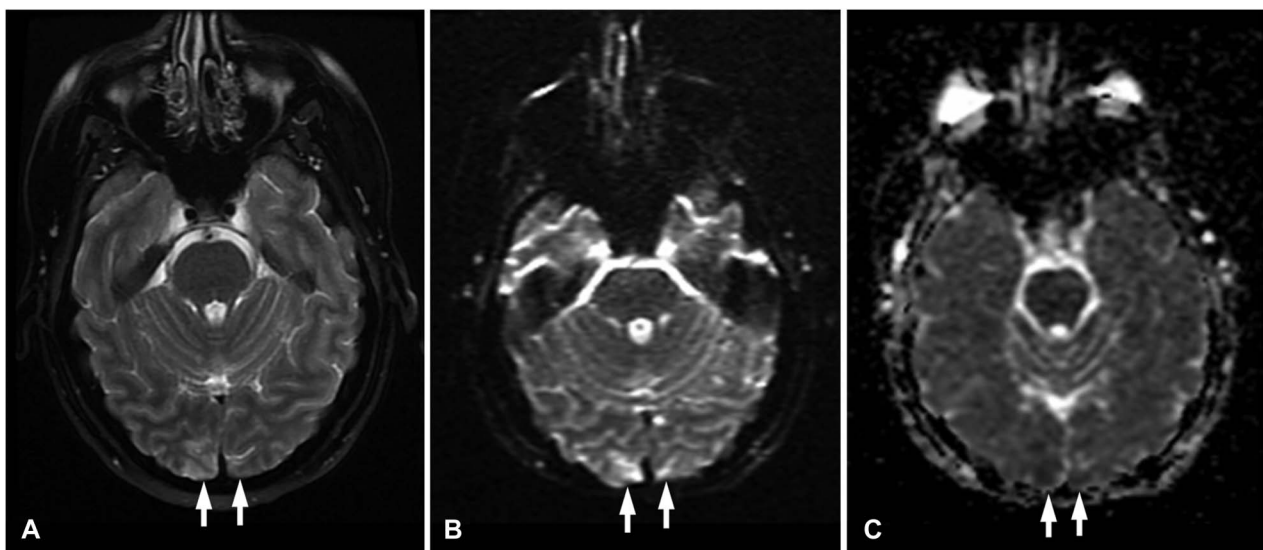


FIG. 2. A. Hyperintense signal is detected in both occipital lobes (arrows) on axial T2 magnetic resonance imaging. Restricted diffusion is confirmed on diffusion-weighted imaging (B) and apparent diffusion coefficient map (C).

TABLE 1. Proposed diagnostic guidelines for Reversible Cerebral Vasoconstriction Syndrome

Acute and severe headache (often thunderclap) reoccurring over 1–2 wk with or without focal deficits and/or seizures
Segmental vasoconstriction of cerebral arteries shown by indirect (e.g., magnetic resonance or computed tomography) or direct catheter angiography showing “strings and beads” appearance
No evidence of aneurysmal subarachnoid hemorrhage
No new symptoms more than 1 month after clinical onset
Normal or near-normal cerebrospinal fluid (protein level <80 mg/dL, leukocytes <10 mm ³ , normal glucose level)
Complete or substantial normalization of arteries shown by follow-up angiography within 12 wk of clinical onset

Adapted from Refs. (2) and (9).

DISCUSSION

RCVS was first reported in 19 patients, many with focal neurological deficits including visual field defects (1). RCVS presents most commonly in women, and typical age of occurrence ranges between 20 and 50 years (2,6–9). In a prospective study of 67 patients with RCVS evaluated over a 3 year period, Ducros et al (5) found that 24% of patients had neurological symptoms, of which 16% were transient, with visual symptoms (hemianopia) being most frequent. One patient developed cortical blindness due to stroke. Singhal et al (10) reported 29% of patients with visual deficits. Robert et al (11) documented that 40% of their patients either had blurred vision or homonymous visual field defects with the majority (75%) experiencing full recovery.

There seems to be an association between RCVS and vasoactive substances. The most common are SSRIs, illicit drugs (including marijuana, cocaine, ecstasy, amphetamines), over-the-counter agents (nasal decongestants, diet pills, pseudoephedrine), and ergot derivatives (4,10,12). These drugs cause serotonergic or adrenergic overactivity, which may play a role in the pathophysiology of RCVS. Additionally, RCVS has been associated with the postpartum state, and immunosuppressive or cytotoxic agents (4). Up to 80% of patients are found to have a trigger that may include sexual activity, straining during defecation, emotional or stressful situations, coughing, physical exertion, or sudden bending down (2–5,13,14). Although uniformly accepted diagnostic criteria are lacking, literature reviews (2,15) and the International Headache Society (9) include guidelines to aid the clinician in establishing the diagnosis of RCVS (Table 1).

Because of the variable presentations of RCVS, the differential diagnosis is very broad. For isolated thunderclap headache, this includes aneurysmal subarachnoid hemorrhage, intraventricular hemorrhage, subdural hematoma, tumor, meningitis, intracranial venous thrombosis, cervical artery dissection, pituitary apoplexy, migraine, and cerebral infarction (3). Disorders that often prove most difficult to be differentiated from RCVS and may have similar neuroimaging findings include cerebral vasculitis, subarachnoid hemorrhage, and arterial dissection (16).

The clinical course and results of testing in our patient were consistent with the diagnosis of RCVS. Her visual deficits were transient and supported by neuroimaging

studies. MRA demonstrated segmental constriction of cerebral arteries, which normalized 6 weeks after hospitalization. Her neuroimaging studies excluded numerous possibilities including intracranial hemorrhage, venous sinus thrombosis, pituitary apoplexy, and arterial dissection. In addition, cerebrospinal fluid analysis was unremarkable, excluding meningitis. She denied any history of migraine.

There are no prospective, randomized, placebo-controlled trials to guide treatment for RCVS. However, there are effective treatment options. Calcium-channel blockers, such as nimodipine, nifedipine, and verapamil have been shown to be beneficial in aborting headaches associated with RCVS (2,11,14,16,17). Magnesium sulfate also has shown favorable results (18). Although glucocorticosteroids have been reported to be independent predictors of a poor outcome and should be avoided (4), there is evidence to support their use at high dose in the short term (19).

In general, patients with RCVS have a good prognosis. RCVS classically has a self-limited course over 1–2 weeks with no new symptoms occurring after 1 month (3,14). Full resolution of signs and symptoms usually occurs and recurrence is infrequent (5). However, significant comorbidities can occur, including ischemic stroke typically in watershed areas, hemorrhagic stroke, transient ischemic attack, brain edema, subarachnoid hemorrhage, seizures, and posterior reversible encephalopathy syndrome (2,3,7,14,17,20).

STATEMENT OF AUTHORSHIP

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REFERENCES

1. Call GK, Fleming MC, Sealton S, Levine H, Kistler JP, Fisher CM. Reversible cerebral segmental vasoconstriction. *Stroke*. 1988;19:1159–1170.

2. **Calabrese LH**, Dodick DW, Schwedt TJ, Singhal AB. Narrative review: reversible cerebral vasoconstriction syndromes. *Ann Intern Med*. 2007;146:34–45.
3. **Ducros A**. Reversible cerebral vasoconstriction syndrome. *Lancet Neurol*. 2012;11:906–917.
4. **Chen SP**, Fuh JL, Wang SJ. Reversible cerebral vasoconstriction syndrome: current and future perspectives. *Expert Rev Neurother*. 2011;11:1265–1276.
5. **Ducros A**, Boukobza M, Porcher R, Sarov M, Valade D, Bousser MG. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain* 2007;130:3091–3101.
6. **Moustafa RR**, Allen CMC, Baron JC. Call-Fleming syndrome associated with subarachnoid haemorrhage: three new cases. *J Neurol Neurosurg Psychiatry*. 2008;79:602–605.
7. **Singhal AB**, Hajji-Ali RA, Topcoglu MA, Fok J, Bena J, Yang D, Calabrese LH. Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Arch Neurol*. 2011;68:1005–1012.
8. **Cvetanovich GL**, Ramakrishnan P, Klein JP, Rao VR, Ropper AH. Reversible cerebral vasoconstriction syndrome in a patient taking citalopram and Hydroxycut: a case report. *J Med Case Rep*. 2011;5:548.
9. **Headache classification subcommittee of the International Headache Society**. The International classification of headache disorders. *Cephalalgia*. 2013;33:705–706.
10. **Singhal AB**, Caviness VS, Begleiter AF, Mark EJ, Rordorf G, Koroshetz WJ. Cerebral vasoconstriction and stroke after use of serotonergic drugs. *Neurology*. 2002;58:130–133.
11. **Robert T**, Marchini AK, Oumarou G, Uske A. Reversible cerebral vasoconstriction syndrome identification of prognostic factors. *Clin Neurol Neurosurg*. 2013;115:2351–2357.
12. **Noskin O**, Jafarimojarrad E, Libman RB, Nelson JL. Diffuse cerebral vasoconstriction (Call-Fleming syndrome) and stroke associated with antidepressants. *Neurology*. 2006;67:159–160.
13. **Chen SP**, Fuh JL, Lirng JF, Chang FC, Wang SJ. Recurrent primary thunderclap headache and benign CNS angiopathy: spectra of the same disorder? *Neurology*. 2006;67:2164–2169.
14. **Ducros A**, Fiedler U, Porcher R, Boukobza M, Stapf C, Bousser MG. Hemorrhagic manifestations of reversible cerebral vasoconstriction syndromes: frequency, features, and risk factors. *Stroke*. 2010;41:250–211.
15. **Sattar A**, Manousakis G, Jensen M. Systematic review of reversible cerebral vasoconstriction syndrome. *Exp Rev Cardiovasc Ther*. 2010;8:1417–1421.
16. **Miller TR**, Shivashankar R, Mossa-Basha M, Gandhi D. Reversible cerebral vasoconstriction syndrome, Part 2: diagnostic work-up, imaging evaluation, and differential diagnosis. *Am J Neuroradiol*. 2015;36:1580–8.
17. **Chen SP**, Fuh JL, Wang SJ. Reversible cerebral vasoconstriction syndrome: an under-recognized clinical emergency. *Ther Adv Neurol Disord*. 2010;3:161–171.
18. **Chik Y**, Hoesch RE, Lazaridis C, Weisman CJ, Llinas RH. A case of postpartum cerebral angiopathy with subarachnoid hemorrhage. *Nat Rev Neurol*. 2009;5:512–516.
19. **Hajji-Ali RA**, Furlan A, Abou-Chebel A, Calabrese LH. Benign angioplasty of the central nervous system: cohort of 16 patients with clinical course and long-term followup. *Arthritis Rheum*. 2007;47:662–669.
20. **Chen SP**, Fuh JL, Wang SJ, Chang FC, Lirng JF, Fang YC, Shia BC, Wu JC. Magnetic resonance angiography in reversible cerebral vasoconstriction syndromes. *Ann Neuro*. 2010;67:648–656.