

ILLUSTRATIVE TEACHING CASES

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Large Subcortical Intracerebral Hemorrhage Because of Reversible Cerebral Vasoconstriction Syndrome

A Case Study

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A 43-year-old man presented with a thunderclap headache, associated with photophobia, phonophobia, and nausea. Aside from the sudden onset of the headache, it felt typical of his migraine headaches. The patient used marijuana earlier in the day. Over the following 2 hours, he developed dysarthria and weakness involving the left face, left upper extremity, and left lower extremity. These symptoms prompted him to seek further evaluation.

The patient has no known medical history apart from migraine headaches without aura and major depressive disorder. He takes escitalopram for depression and uses no other medications. He denied use of any illicit substances except for marijuana.

The patient's blood pressure was 187/84. A noncontrast computed tomography scan of the head revealed a large intraparenchymal hemorrhage involving the right lenticular nucleus (Figure [A]). Over the following hour, the patient became somnolent and was intubated electively for airway protection. A computed tomography angiogram of the head suggested a small asymmetrically prominent and somewhat irregular vessel traversing the medial aspect of the hemorrhage. An arterial catheter cerebral angiogram revealed multifocal stenosis of the supraclinoid left internal carotid artery, pericallosal, callosal marginal, and frontal branches of the left anterior cerebral artery, remote from the site of hemorrhage (Figure [B]). Multifocal stenoses were also seen involving the right supraclinoid internal carotid artery, pericallosal, callosomarginal, frontal branches of the right anterior carotid artery, and multiple branches of

the right middle cerebral artery. Immediate local improvement in stenosis occurred following selective injection of intraarterial verapamil in the left pericallosal artery (Figure [B]). A 1 mm pseudoaneurysm of a right lateral lenticulostriate artery was seen, corresponding to the abnormality suggested on the computed tomography angiogram and representing the source of the hemorrhage (Figure [C]). There was no evidence of branch occlusion, vessel wall irregularity, aneurysm, or arteriovenous shunting. The overall clinical picture was felt to represent reversible cerebral vasoconstriction syndrome (RCVS).

He received nimodipine. Serial head imaging showed expansion of the hemorrhage up to 7.6×5.1×3.7 cm with 8 mm of midline shift, but the patient remained clinically stable and did not undergo any surgical interventions. After a month, the patient was discharged to inpatient rehabilitation and ultimately back home.

About 2 months later, the patient had an elective arterial catheter angiogram that showed complete resolution of the multifocal vasoconstriction as well as interval resolution of the pseudoaneurysm (Figure [D]).

CASE DISCUSSION

This unique case highlights an uncommon presentation of RCVS in which a patient is initially found to have a subcortical intraparenchymal hemorrhage in the setting of hypertension. A subcortical hemorrhage in a patient presenting with hypertension may

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Nonstandard Abbreviations and Acronyms

RCVS	reversible cerebral vasoconstriction syndrome
SAH	subarachnoid hemorrhage

deter further diagnostic studies to address uncommon causes of subcortical hemorrhage, particularly when the hemorrhage seems in a location associated with hypertensive hemorrhages and when a patient's chronic hypertension status is not known. This case provides an opportunity to discuss the utility of vascular imaging in addressing the differential of intracerebral hemorrhage, to attempt to reconcile the meaning of a pseudoaneurysm in the context of a subcortical intraparenchymal hemorrhage, and to review the approach to using calcium channel blockers to evaluate multifocal vascular stenoses. This patient without chronic hypertension had multiple potential triggers for RCVS, presented with an atypical subcortical hemorrhage given his lack of chronic hypertension, underwent angiography that showed multifocal vasospasm that improved with verapamil, and had complete resolution of vasospasm over time. His clinical presentation, history of known triggers for RCVS, and characteristic angiographic findings provided support for the RCVS diagnosis and helped distinguish it from other causes of vasospasm and intracerebral hemorrhage.

RCVS represents a common presentation of multiple disorders involving thunderclap headache in the setting of reversible vasoconstriction of the cerebral vasculature. The term RCVS originated in 2007 as an acronym to unify various names, terms, and eponyms describing the same clinical-radiographic process.^{1,2} It typically affects men and women 20 to 50 years of age, although it may also occur in children and adolescents.^{2,3} The incidence of RCVS has been increasing, although it remains unclear if this increase represents a true increase in incidence or if it represents better detection because of improved imaging techniques and greater awareness of the syndrome.^{2,3} Its pathophysiology, albeit poorly understood, may relate to sympathetic overactivity, dysregulation of vascular tone, and blood-brain barrier breakdown because of a variety of potential triggers.¹ Although sympathomimetic agents have been most commonly cited as triggers, numerous other precipitants have been identified (Table 1).¹⁻³

RCVS classically follows an acute and self-limited course.¹⁻⁴ Headache, nausea, vomiting, photophobia, and phonophobia may represent the only clinical manifestations.¹⁻⁴ Transient focal neurological deficits may occur in a subset of patients and mimic a migraine aura,⁴ which may complicate the early clinical picture

as it did in this patient with a history of migraine. Diagnosis of RCVS requires acute severe headache, uniphasic course without new symptoms more than 1 month after onset, segmental vasoconstriction of cerebral arteries through angiography, no evidence of aneurysmal subarachnoid hemorrhage (SAH), normal or near-normal cerebrospinal fluid studies, and complete or substantial normalization of the arteries by angiography within 12 weeks of clinical onset.^{1,3-5} These clinical features differentiate it from primary angiitis of the central nervous system, which may seem radiographically similar but follows a more insidious course and lacks a thunderclap headache and uniphasic course.⁶ Other considerations for a multifocal vasculopathy include intracranial atherosclerosis, fibromuscular dysplasia, and infectious arteritis. The unique clinical features outlined above help differentiate these various entities from RCVS. Moreover, a RCVS₂ score has been proposed to identify patients likely to have RCVS based on clinical and noninvasive radiographic data (Table 2).⁵

While the diagnosis of RCVS is typically supported through digital subtraction angiography, we initially performed a computed tomography angiogram to evaluate for vascular pathology. The differential for spontaneous intracerebral hemorrhage is wide and includes hypertensive vasculopathy, cerebral amyloid angiopathy, hemorrhagic conversion of an arterial or venous ischemic infarct, septic embolism, dural arteriovenous fistula, arteriovenous malformation, hemorrhage of an underlying neoplasm, encephalitis, vasculitis, and vasospasm. We initially performed a computed tomography angiogram as a noninvasive strategy to evaluate for some of the above considerations given the patient's lack of chronic hypertension and young age, as well as given the fact some data may suggest a role for noninvasive strategy in patients with atypical hemorrhages.⁷ When we later performed digital subtraction angiography for further evaluation, we found multifocal vascular stenoses and administered intraarterial calcium channel blockers, which caused vessel dilatation. This response does not represent a response specific to RCVS and may occur in other conditions causing vasospasm such as coronary vasospasm or cerebral vasospasm from aneurysmal SAH. However, a response to calcium channel blockers may differentiate RCVS from mimics such as primary CNS angiitis and intracranial atherosclerosis. Thus, the overall constellation of the patient's medical history, the multifocal stenoses seen on the digital subtraction angiography, and the response to verapamil supported the impression of RCVS.

Complications of RCVS include SAH, intraparenchymal hemorrhage, and cerebral infarction. Hemorrhagic complications commonly occur within the first week of RCVS.² SAH is usually small and cortically located and

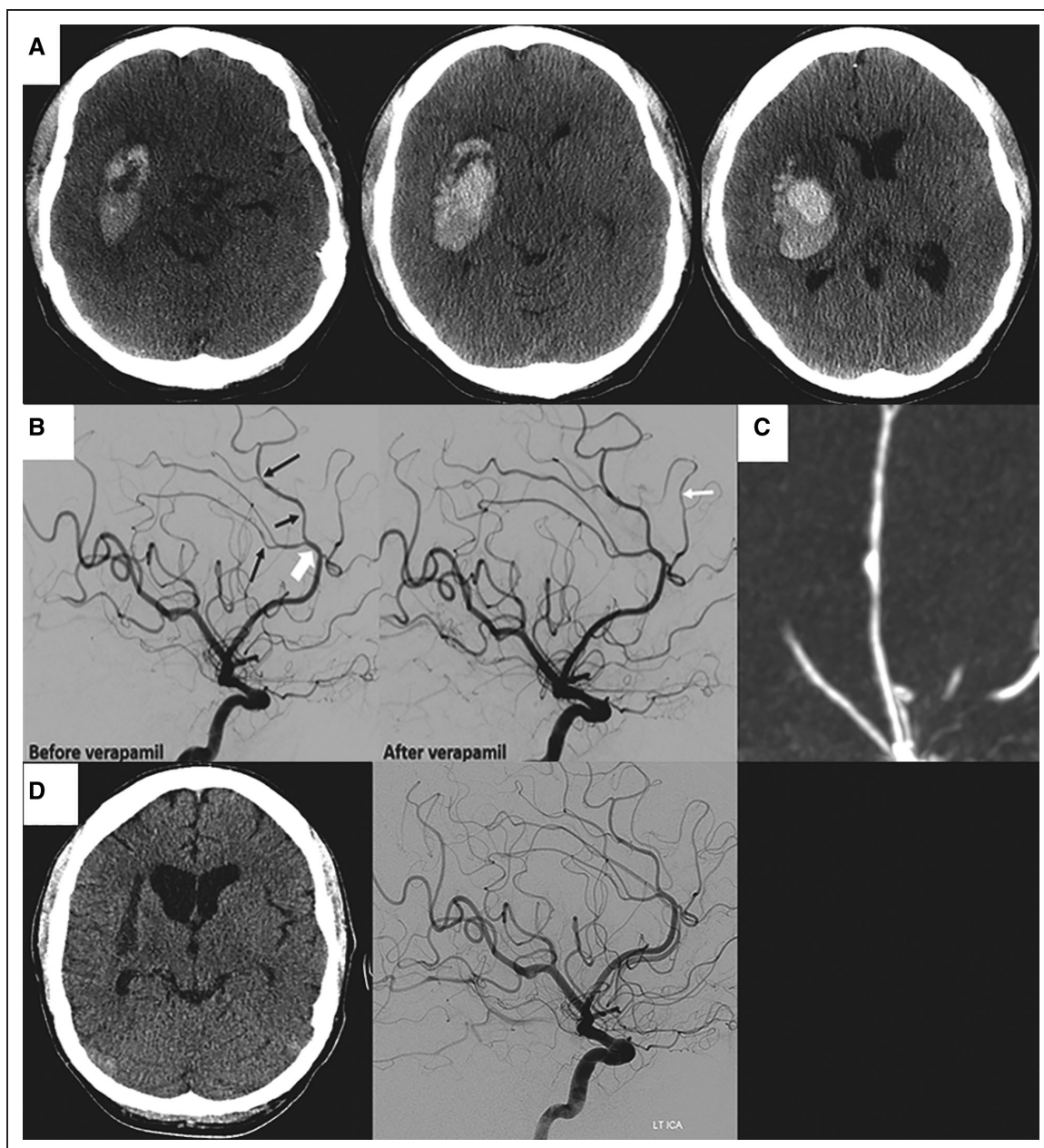


Figure. Case images.

Computed tomography (CT) of the head with axial sections demonstrating a large intraparenchymal hemorrhage centered in the right lenticular nucleus (**A**). Arterial catheter diagnostic cerebral angiogram of the left internal carotid artery before and after injection of verapamil in the left pericallosal artery from microcatheter positioned at large white arrow (**B**). Multifocal areas of stenosis are seen throughout the visualized arteries (black arrows in **B**). Marked improvement is seen following injection of verapamil with persistence of spasm in callosomarginal branch (white arrow in postverapamil angiogram) in which verapamil was not injected given position of microcatheter injection. A pseudoaneurysm in a right lateral lenticulostriate branch was identified as the likely source of the intraparenchymal hemorrhage (**C**). Follow-up CT showing resolution of the hematoma with residual encephalomalacia and catheter diagnostic cerebral angiogram of the left internal carotid artery performed 2 months later demonstrating complete resolution of the spasm (**D**).

is the most frequently observed hemorrhagic complication.⁸ Cortical SAH has been attributed to impaired autoregulation of distal vessels, while lobar and subcortical hemorrhages may relate to severe hypertension and ischemic-reperfusion injury in the setting of rapid changes in arterial caliber.^{9,10} Available reviews detailing hemorrhagic manifestations of RCVS highlight that

lobar hemorrhage occurs more often than subcortical hemorrhage.^{7,8}

Of note, a pseudoaneurysm was identified and considered to represent the site of the subcortical intraparenchymal hemorrhage. When a perforating vessel is involved in the pathogenesis of an intracerebral hemorrhage, such as a lenticulostriate perforator

Table 1. RCVS Triggers¹⁻³

Vasoactive medications
Alpha-sympathomimetic drugs (phenylpropranolamine, pseudoephedrine, ephedrine, norepinephrine)
Recreational drugs (alcohol, amphetamine, cannabis, cocaine, ecstasy, nicotine)
Selective serotonin reuptake inhibitors
Ergotamine
Methergine
Bromocriptine
Triptans
Ginseng
Immunosuppressants
Tacrolimus
Cyclophosphamide
Interferon
Blood products
Blood transfusions
Erythropoietin
Intravenous immunoglobulin
Catecholamine secreting tumors
Pheochromocytoma
Bronchial carcinoid tumor
Glomus tumors
Pregnancy and postpartum states
Migraine headache
Hematologic conditions
Antiphospholipid antibody syndrome
Thrombotic thrombocytopenia purpura
Hemolysis, elevated liver enzyme, low platelet syndrome
Miscellaneous
Carotid dissection
Unruptured cerebral aneurysm
Hypercalcemia
Porphyria
Head trauma
Subdural spinal hematoma
Cerebral venous thrombosis
CSF hypotension
Autonomic dysreflexia
Phenytoin intoxication

CSF indicates cerebrospinal fluid; and RCVS, reversible cerebral vasoconstriction syndrome.

in this case, it is common to see a pseudoaneurysm. It is well accepted angiographically that the appearance of a pseudoaneurysm is related to the site of the hemorrhage and that a pseudoaneurysm may be found when hemorrhage of a damaged vessel is contained by surrounding brain parenchyma. This finding is not specific to RCVS and has been observed in multiple conditions involving a hemorrhage regardless

Table 2. RCVS₂ Score

Criteria	Value
Recurrent or single thunderclap headache	
Present	+5
Absent	0
Intracranial carotid artery involvement	
Present	-2
Absent	0
Vasoconstrictive trigger	
Present	+3
Absent	0
Sex	
Female	+1
Male	0
Subarachnoid hemorrhage	
Present	+1
Absent	0

A score ≥ 5 has a 99% specificity and 90% sensitivity for diagnosing RCVS, and a score ≤ 2 has a 100% specificity and 85% sensitivity for excluding RCVS. RCVS indicates reversible cerebral vasoconstriction syndrome.

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of the etiology of the hemorrhage. Its presence in this case reflects involvement of a perforating vessel, which is consistent with the location of this patient's hemorrhage.

Therapeutic options for the treatment of RCVS include oral, intravenous, and intraarterial medications.² Calcium channel blockers such as nimodipine have been given by oral and intravenous routes and may alleviate the headache associated with RCVS, although evidence has yet to demonstrate that these medications influence the evolution of vasoconstriction or prevent hemorrhagic or ischemic complications of RCVS. Other intravenous medications such as magnesium sulfate, serotonin antagonists, and dantrolene may be considered. Intra-arterial therapies such as nimodipine, nicardipine, papaverine, and milrinone may be considered. Balloon angioplasty has also been proposed as an endovascular treatment for RCVS. In addition to any medical or endovascular intervention, identification and withdrawal of any suspected exogenous trigger is recommended.

Overall, RCVS represents a challenging syndrome to study. Its numerous potential triggers, the heterogeneity of its natural history, and the relative paucity of cases reported make understanding the mechanisms of RCVS challenging. The variety of locations in which hemorrhage occurs may reflect different mechanisms, which may be understood better over time. However, expanding the phenotype of hemorrhagic complications of RCVS is essential so that the diagnosis is not missed. Our case highlights that subcortical hemorrhage is a manifestation of RCVS and that vasoconstriction must

TEACHING POINTS

- Reversible cerebral vasoconstriction syndrome (RCVS) is an under-recognized cause of thunderclap headache and represents a common presentation of multiple disorders involving reversible vasoconstriction of the cerebral vasculature. Ischemic stroke and intracerebral hemorrhage may complicate the course of RCVS.
- The diagnosis of RCVS requires an acute severe headache following a uniphasic course in the setting of segmental vasoconstriction of the cerebral arteries with normalization of vasoconstriction within 12 weeks of clinical onset. A vasodilatory response to intraarterial

calcium channel blockers may differentiate it from other causes of multifocal vasculopathy, but this response is not highly specific to RCVS and may be seen in other conditions such as vasospasm from aneurysmal sub-arachnoid hemorrhage.

- Subcortical intraparenchymal hemorrhage may represent a manifestation of RCVS or other forms of vasculopathy and merits consideration of vascular imaging in patients presenting with hemorrhage without traditional vascular risk factors.

be considered in the diagnostic work-up of cryptogenic subcortical hemorrhages in patients without traditional vascular risk factors.

ARTICLE INFORMATION

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