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Case Report

Reversible Cerebral Vasoconstriction Syndrome with Subarachnoid Hemorrhage and Stroke

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Abstract

Reversible cerebral vasoconstriction syndrome is a complex condition characterized by temporary constriction of the brain's arteries. Diagnosis typically involves a retrospective approach, necessitating repeated imaging to confirm the resolution of cerebral arterial spasms. We describe a case of a 22-year-old female with a history of posterior circulation stroke and recurrent thunderclap headaches. On imaging, evidence of stroke, convexity subarachnoid hemorrhage, and multiple areas of stenosis and dilatation in the posterior circulation associated with normal laboratory parameters were found. The resolution of clinical symptoms and angiographic findings were noted in the follow-up. After other diagnoses are excluded, patients can be reassured about favorable prognosis.

Keywords

- subarachnoid hemorrhage
- cerebral vasoconstriction
- thunderclap headache

Case Presentation

A 22-year-old female presented with a known history of drug illicit addiction. She had an on-off headache for the last 15 days. She presented in our institute on 31.10.2020 with sudden onset altered sensorium, visual disturbance, vomiting, and headache. On examination in emergency posterior circulation stroke was considered with National Institutes of Health Stroke Scale of 5. She had 10 episodes of clonic movement of all four limbs. Noncontrast computed tomography (NCCT) and CT angiography head and neck were performed with stroke protocol. NCCT (►**Fig. 1A**) revealed acute infarct in the left occipital lobe (arrow), left medial thalamus, and left lateral cerebellum involving the middle cerebral peduncle corresponding to left posterior cerebral artery (PCA) territory. CT angiography (►**Fig. 1B**) revealed long segment alternate narrowing beading appearance in bilateral PCA (arrow), distal basilar artery, and distal cortical branches of middle cerebral artery. The patient was managed conservatively. A differential diagnosis was made of vasculitis and reversible cerebral vasoconstriction syndrome (RCVS) was made. Magnetic resonance imaging (MRI; 3T) brain contrast with vessel wall imaging (VWI) was done 10 days later. MRI brain (►**Fig. 1C–E**) revealed a contrast-enhancing subacute infarct in the left PCA territory involving the left occipital lobe, left thalamus, and lateral cerebellum. On diffusion-weighted imaging (►**Fig. 1F**), few discrete foci of acute infarcts were noted in the bilateral splenium of the corpus callosum and right posterior lateral thalamus as shown by arrows. Convexity sulcal flair hyperintensities (►**Fig. 2A**) were noted in right high parietal convexity with susceptibility-weighted imaging (SWI) blooming (►**Fig 2B** and **2C**) in the corresponding region s/o sulcal subarachnoid hemorrhage. On SWI (►**Fig. 2C**), multiple enumerated microhemorrhage foci were noted in convexity sulcal involving the bilateral temporoparietal lobe, left cerebellum, and bilateral occipital lobe. On time-of-flight magnetic resonance angiography (MRA) circle of Willis (►**Fig. 2D**) reveals a long-segment beading appearance with narrowing noted in bilateral PCA and distal basilar artery. On VWI, no abnormal vessel wall thickening or enhancement was seen. On imaging found a diagnosis made up of RCVS in place of vasculitis. Laboratory parameters including rheumatoid factor,

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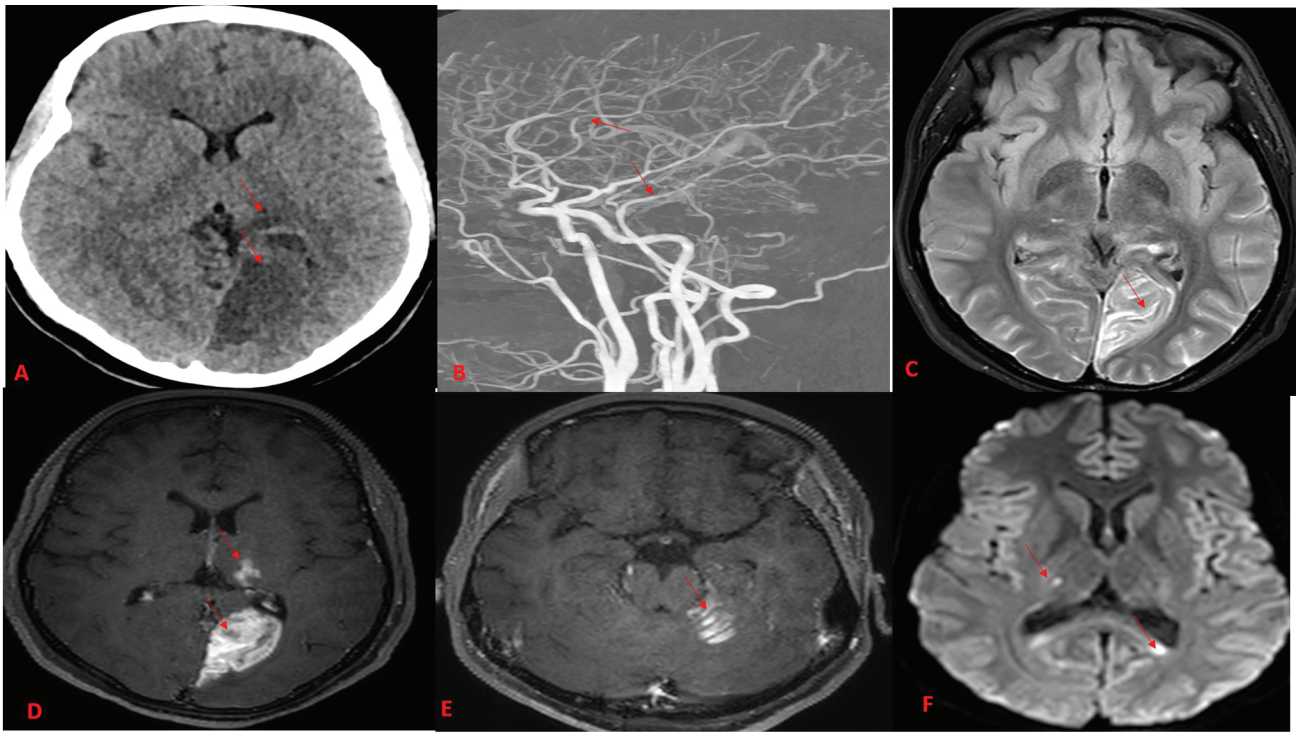

Fig. 1 A 22-year-old girl presented in emergency with a clinically posterior circulation stroke on 31.10.2020. Noncontrast computed tomography (**A**) showing hypodensity in the left occipital lobe and left thalamus (arrow). Computed tomography angio-maximum intensity projection image (**B**) showing a long-segment beading appearance in bilateral posterior cerebral artery, distal basilar artery (arrow), and distal branches of middle cerebral artery. Magnetic resonance imaging brain done 10 days letter reveals fluid-attenuated inversion recovery (**C**) hyperintensity in the left occipital lobe (arrow) with T1 + C images (**D, E**) showing contrast enhancement (in the left occipital lobe, thalamus, and left lateral cerebellum(arrow) s/o subacute infarct. No abnormal vessel wall enhancement was seen. Diffusion-weighted imaging (**F**) showing restriction foci noted in bilateral splenium and right thalamus(arrow) s/o acute infarct.

antinuclear antibody, antineutrophil cytoplasmic antibody, anticardiolipin antibody-immunoglobulin G and immunoglobulin M, anti-ds DNA, C3 level, and cryoglobulin were in the normal range with mild raised erythrocyte sedimentation rate. A follow-up MRI scan was performed on 01.02.2021 (after 3 months of stroke) to confirm the diagnosis. MRI brain (►**Fig. 3**) after 3 months revealed the normal caliber of bilateral PCA (arrow in 3A and 3B) and distal basilar artery with no new infarct or hemorrhage. Resolution of SWI blooming was noted in the bilateral temporoparietal and occipital lobes (3C and 3D). So, patient had no new deficit after 3 months with normalization of MRA suggesting reversible vasoconstriction syndrome as our diagnosis.

Discussion

RCVS refers to a cluster of clinical syndromes that are marked by a profound "thunderclap" headache accompanied by or without neurological impairments. There are various names for this reversible vasoconstriction in the literature, a few of them are as Call-Fleming syndrome, benign arteritis of CNS,[1] benign angiopathy of CNS,[2,3] migrainous vasospasm,[4] postpartum cerebral angiopathy, thunderclap headache with vasospasm, and drug-induced vasospasm.[5]

Focal neurological deficits were present initially in 43% and generalized tonic–clonic seizures occurred in 17%[5] of cases as similar findings in our case. The disease predominantly affects individuals between 20 and 50 years of age.[2] The disease is known to be caused by immunosuppressive and cytotoxic drugs. These syndromes exhibit benign cerebrospinal fluid (CSF) analysis and are characterized by the presence of multiple segmental regions within the cerebral arteries that undergo narrowing or vasoconstriction. Additional laboratory tests including serum analysis to identify inflammation markers like erythrocyte sedimentation rate and C-reactive protein typically yield results that fall within the normal range for patients diagnosed with RCVS.[5,6] The preliminary angiographic assessment results in suspected cases of RCVS may appear unremarkable within the 4 to 5 days following the patient's first clinical presentation. In fact, cerebral vasoconstriction may not be visible in up to one-third of RCVS patients during the initial week following the onset of symptoms.[7] In RCVS, fluid-attenuated inversion recovery (FLAIR) hyperintense vessels can be observed in up to 22% of patients and the presence of hyperintense vessels in RCVS is linked to more severe vasoconstrictions and cerebral hemodynamic disruptions and could signify the onset of ischemic stroke or posterior reversible encephalopathy syndrome.[7]

Typically, these arterial abnormalities subside within a few weeks.[3] This is particularly significant when these imaging findings are encountered in the context of subarachnoid hemorrhage (SAH), as neurointerventionalists may be consulted for their expertise in such cases. The previous literature describes RCVS as classically occurring in the

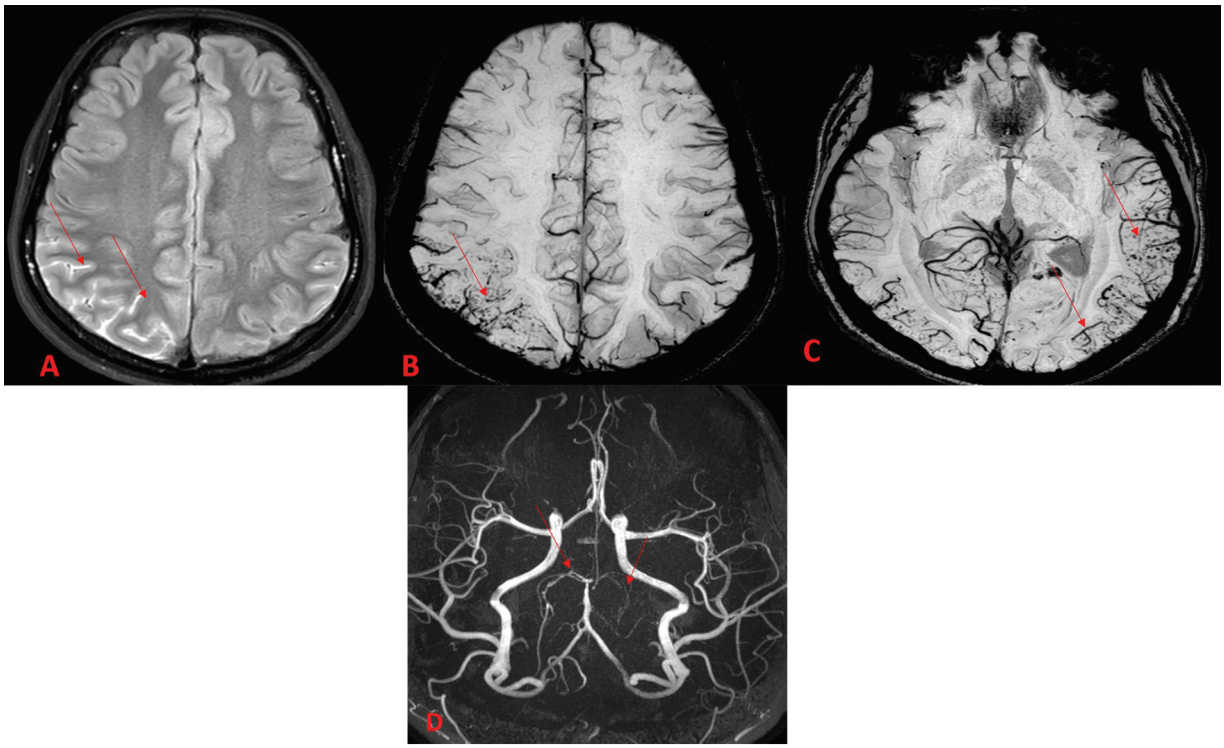

Fig. 2 Continue. Axial fluid-attenuated inversion recovery images (**A**) showing sulcus hyperintensity (arrow) in the right high parietal lobe convexity. Susceptibility-weighted imaging (**B** and **C**) showing multiple blooming foci along the right parietal convexity (arrow in B) and left temporoparietal and bilateral occipital lobe (**C**). Time-of-flight magnetic resonance angiography circle of Willis (**D**) showing a long-segment beading appearance with severe narrowing in bilateral posterior cerebral artery (arrow) and distal basilar artery.

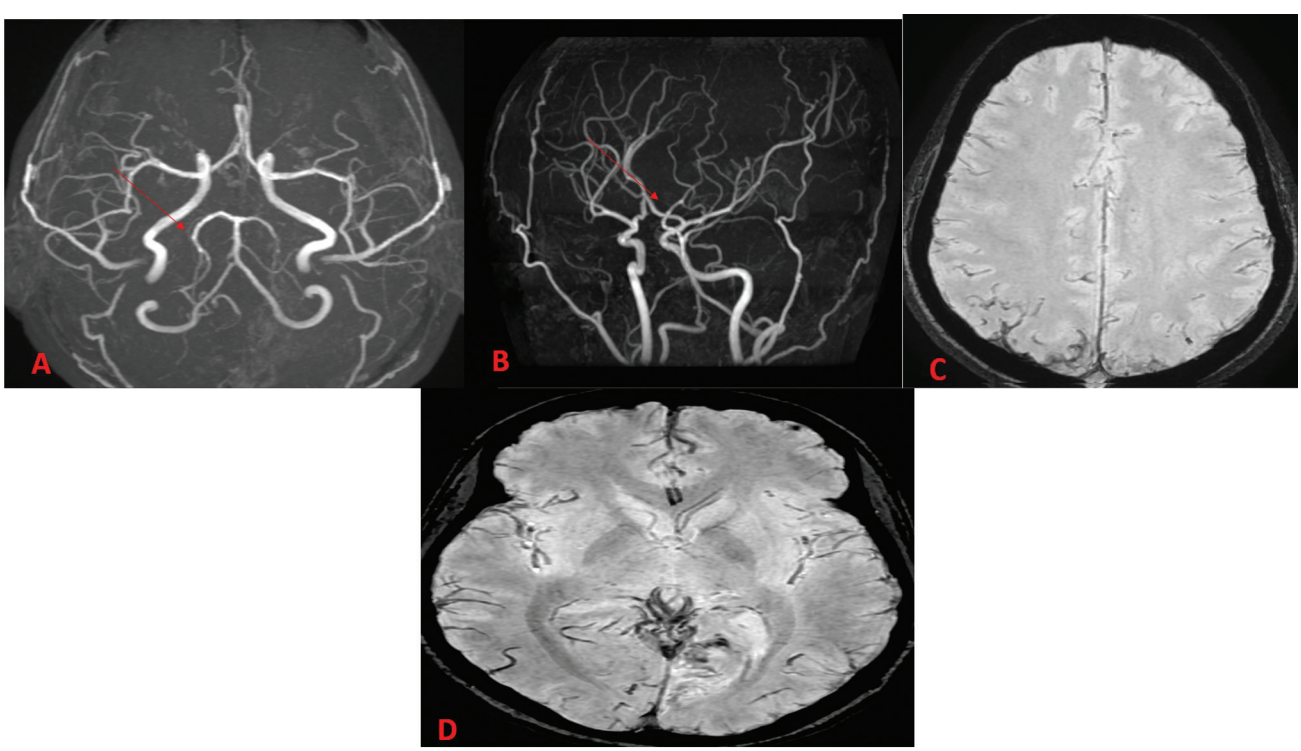

Fig. 3 Follow-up magnetic resonance imaging brain was done after 3 months of initial presentation. Time-of-flight magnetic resonance angiography circle of Willis (**A** and **B**) showing the normal caliber of bilateral posterior cerebral artery (arrow) and distal basilar artery with the disappearance of beading pattern as detected in earlier images at the time of stroke (**B** and **2D**). Susceptibility-weighted imaging (SWI) (**C** and **D**) showing the disappearance of convexity SWI blooming foci as compared with old SWI images (**B** and **C**) at the time of initial presentation. Diagnosis of reversible cerebral vasoconstriction syndrome was made.

absence of SAH with normal CSF analysis[1,3,8]other than isolated case reports.[9,10] Statistically significant risk factors predisposing RCVS patients to hemorrhage included older age, female gender, and patient with a history of migraine.[11] Haji Ali et al[2]and Spitzer et al[12] reported a 13 and 33% chance of SAH in their series of RCVS cases.[6] In more recent studies conducted by Ducros et al,[6,13]it was reported that there is a 22% occurrence of cortical SAH in the largest prospective series of RCVS patients to date. Additionally, their follow-up series involving 89 patients demonstrated a 34% occurrence of intracranial hemorrhage. These findings highlight the significance of monitoring and understanding the potential complications associated with RCVS.

Our case also has convexity hemorrhage and stroke. Patients with RCVS have been shown to delay their presentations (7 days) from the onset of their thunderclap headache,[13] in our case stroke and SAH presented 10 days after the headache. SAH associated with RCVS exhibits a distinct visual pattern, typically appearing as a focal and superficial hemorrhage that overlays the cortical convexity along the cerebral sulci. It is important to note that cortical SAH can sometimes be subtle on imaging and easily overlooked. It may present as just one or two hyperdense sulci on CT scans or as linear areas with high signal intensity on MRI FLAIR sequences. In our case, SAH is evidence only on FLAIR and SWI. MRA is an acceptable alternative for the evaluation of the vasoconstriction in patients with RCVS.

In contrast, vasospasm induced by SAH is usually characterized by long-segmented narrowing of blood vessels, smooth, primarily around the site of the bleeding site. RCVS is frequently misdiagnosed as primary angiitis of the central nervous system (PACNS), leading to unnecessary brain biopsy and long-term treatment involving high-dose steroids and cytotoxic agents, which may have adverse effects. Resolution of vasoconstriction is observed in RCVS through early follow-up angiography. In RCVS, vasospasm is mostly seen in second or third-order intracranial branches but in rare cases, proximal segment vessels can be affected in RCVS and this may represent a temporal progression of distal to proximal vessel vasoconstriction, as described by Ducros et al.[13] Transcranial Doppler (TCD) may have a role in monitoring potential complications of RCVS. In one series, only 13% of RCVS patients met the TCD diagnostic criteria for mild vasospasm[7] however, elevated velocity in TCD was associated with an increased risk of developing posterior reversible encephalopathy syndrome.

RCVS and PACNS can have similar angiographic features, making it difficult to differentiate between the two conditions. However, certain clinical differences can aid in the diagnosis. Calabrese et al[3] have advised to repeat angiography within 12 weeks to document the reversibility of vasospasm. Incomplete resolution of angiographic abnormalities along with progressive clinical worsening would support an alternative diagnosis and warrant further investigation for PACNS. However, angiographic abnormality in PACNS is nonspecific.[14] Patients with PACNS typically present with a history of dull headaches and experience a progressive neurological decline over time. In contrast, RCVS presents with acute headache and is usually a self-limited disease. Analysis of CSF often reveals inflammatory changes in cases of PACNS, including elevated protein levels above 100 mg/dL and leucocytosis; however, none of these findings is specific PACNS.[14] High-resolution MR VWI is a relatively recent technique that is gaining popularity in the assessment of cerebrovascular conditions, such as CNS vasculitis, RCVS, cerebral aneurysms, Moyamoya syndrome, arterial dissection, and intracranial atherosclerosis. In contrast to RCVS, MRI is always abnormal in patients with CNS vasculitis and demonstrating areas of cortical and subcortical ischemia in multiple vascular territories and microhemorrhages and circumferential vessels wall enhancement on contrast MRI.[15,16] Most patients with PACNS will show evidence of multifocal infarcts of different ages upon presentation (90%), in contrast to the initial MR imaging results in patients with RCVS, which are frequently unremarkable.[2] Mandell et al[17] discovered that patients ultimately diagnosed with both RCVS and CNS vasculitis exhibited arterial wall thickening, whereas wall enhancement was solely evident in cases of CNS vasculitis. The authors hypothesized that this discovery aligned with the pathological findings in patients with RCVS who had undergone biopsy, indicating vasoconstriction without underlying inflammatory vessel wall infiltration. Study done by Obusez et al[18] compared VWI findings in RCVS and CNS vasculitis patients with large group of patients. They reveal that 12 of 13 patients of CNS vasculitis demonstrated multifocal, short-segment vessel wall thickening, with 9 having concentric and 3 having eccentric wall enhancement. In comparison of the 13 patients diagnosed with RCVS, 10 demonstrated diffuse uniform wall thickening, of which only 4 had shown mild wall enhancement. Improvement in cerebral artery narrowing following intra-arterial vasodilator therapy has also been proposed as a feature distinguishing RCVS from PACN.[19] The prognosis of RCVS is generally uncertain, but in the majority of patients, the condition tends to be self-limiting. The occurrence of stroke is a significant factor that influences persistent morbidity. Studies have indicated a risk of stroke ranging from 7 to 50% in individuals with RCVS.[20,21]

Conclusion

RCVS-associated SAH is one of the presentations of this condition, and it is important to conduct a diagnostic workup to exclude other potential causes. Once any causative agent is ruled out, patients can be provided reassurance regarding a favorable prognosis, with symptomatic management being the main approach.

Funding
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Conflict of Interest
None declared.

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