

# Triptan-induced Reversible Cerebral Vasoconstriction Syndrome: Two Case Reports with a Literature Review

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## Abstract

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We encountered two patients with sumatriptan-induced reversible cerebral vasoconstriction syndrome (RCVS). The present patients were taking sumatriptan for the first time because they had been tentatively diagnosed with a migraine. On reviewing the literature, we found nine other cases of triptan-induced RCVS, predominantly among women aged 30 to 40 years. RCVS has been precipitated by triptan at the first ever use, after daily use, and even with long-term use at a normal dose. Patients with acute onset of severe headache should be thoroughly evaluated, and triptan should be administered appropriately. If triptan-induced RCVS is suspected, vascular imaging should be repeated after several days.

**Key words:** reversible cerebral vasoconstriction syndrome, triptan, migraine, thunderclap headache

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## Introduction

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Reversible cerebral vasoconstriction syndrome (RCVS) is a clinical entity characterized by severe headaches with or without acute neurological symptoms, the radiological features of which include multifocal segmental constriction of the cerebral arteries that resolves spontaneously within three months (1-4). RCVS is considered a rare syndrome, but the growing use of vasoactive drugs combined with the more frequent use of non-invasive neurovascular imaging has increased the incidence (4). Triptan is one of the drugs that triggers RCVS (2, 4), but triptan-induced RCVS cases are relatively rare. We herein describe two cases of sumatriptan-induced RCVS and review the clinical features of triptan-induced RCVS.

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## Case Reports

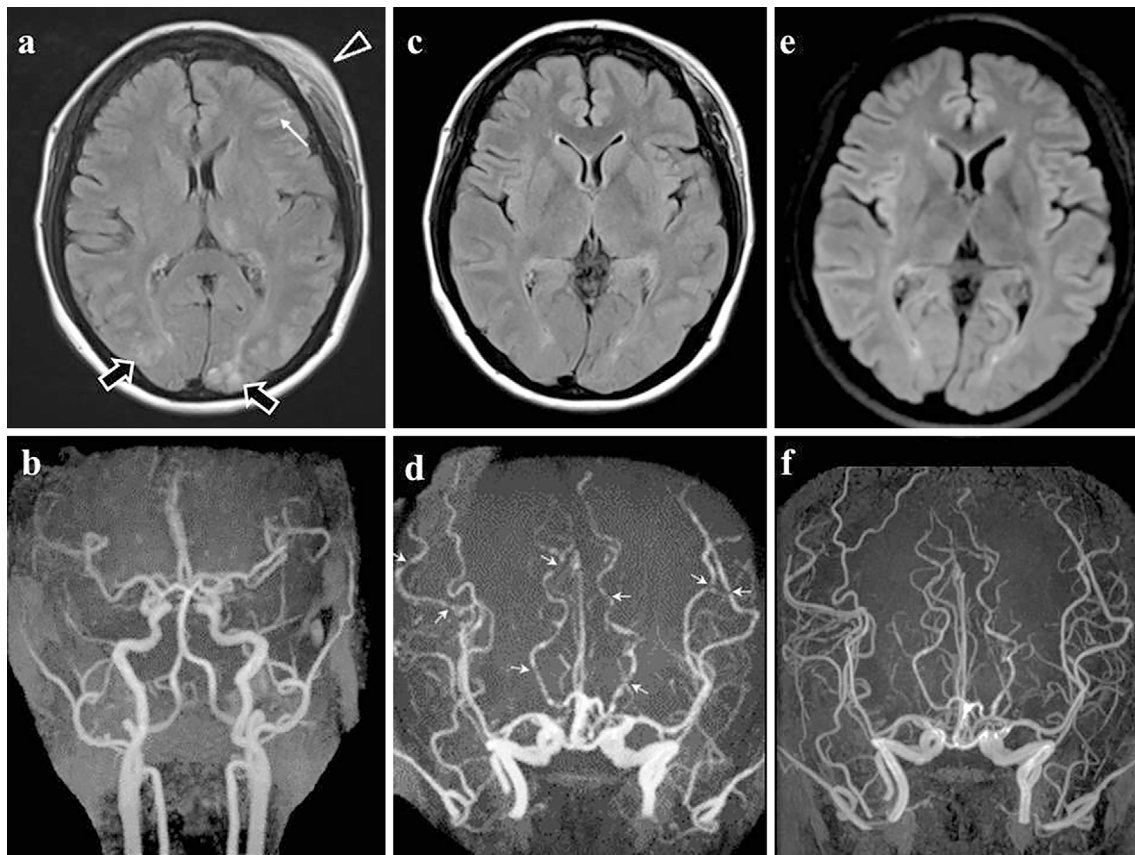
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### Case 1

A 43-year-old woman with a history of uncontrolled hypertension began suffering from a bifrontal-throbbing headache every other day, associated with neither nausea, photo-

phobia, nor phonophobia. Three weeks later, she sought medical attention when over-the-counter medications failed to relieve the headaches. The results of a computed tomographic (CT) scan of the head were normal, and she was prescribed oral sumatriptan. One hour after taking the drug, she experienced a sudden exacerbation of her headache, followed by a seizure, which caused her to fall and hit her head against the floor. She was subsequently admitted to our institute.

On admission, her blood pressure was 171/72 mmHg, and she was afebrile. Shortly thereafter, she again experienced a generalized epileptic seizure that was treated by intravenous administration of diazepam and phenytoin. The laboratory findings, including a blood count, coagulation parameters, and the results of liver and renal tests, were normal. Magnetic resonance imaging (MRI) of the brain using fluid-attenuated inversion recovery (FLAIR) revealed a left parietal cortical subarachnoid hemorrhage (SAH) (Fig. 1a, small white arrow) and multiple high-intensity lesions in the bilateral occipital lobes (Fig. 1a, large black arrows). Diffusion-weighted MRI and magnetic resonance angiography (MRA) revealed no abnormalities (Fig. 1b). On Day 6, MRA showed narrowing of the bilateral middle and posterior cerebral arteries (Fig. 1d, white arrows), although the lesions on



**Figure 1.** a: FLAIR-MRI on admission showing a left parietal cortical subarachnoid hemorrhage (small white arrow), multiple lesions on the bilateral occipital lobes (large black arrows), and traumatic scalp hematoma (black arrowhead). b: MRA on admission showing no abnormalities. c: FLAIR-MRI on Day 6 showing the resolution of the occipital lesions. d: MRA on Day 6 showing a beaded appearance of the bilateral middle and posterior cerebral arteries (white arrows). e: FLAIR-MRI on Day 14 showing no additional findings. f: MRA on Day 14 showing the resolution of the narrowing vessels.

the occipital lobes had improved (Fig. 1c). Her blood pressure was controlled within a normal range through administration of first amlodipine and then lomerizine. On Day 14, her headache had improved, and findings on MRI and MRA were normal (Fig. 1e and f). She was diagnosed with a headache attributed to arterial hypertension before sumatriptan administration, and RCVS associated with posterior reversible encephalopathy syndrome (PRES). The cortical SAH might have been due either to the head trauma or to RCVS.

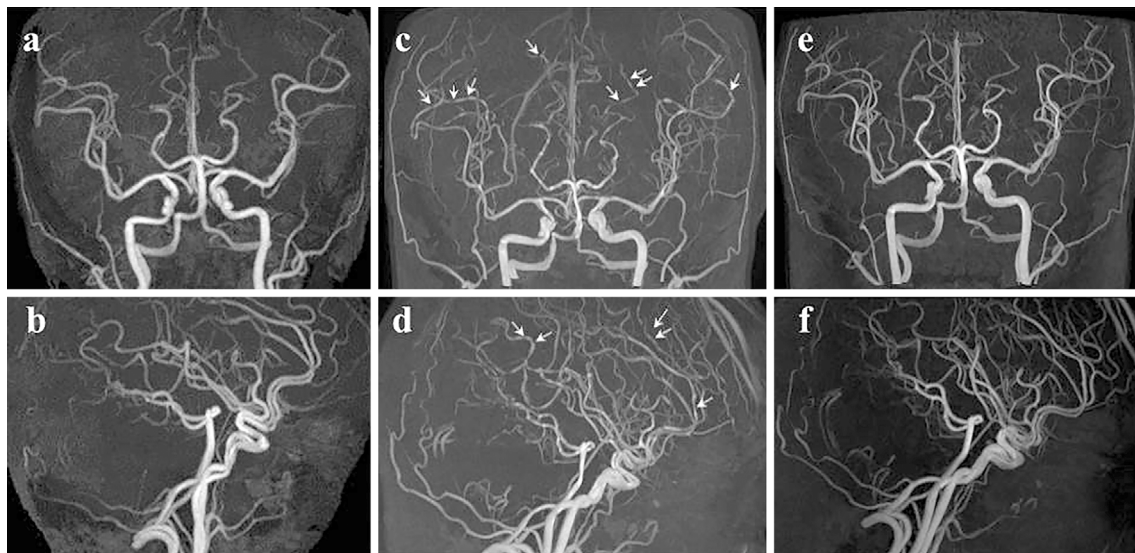
## Case 2

A 30-year-old woman developed a bifrontal-throbbing headache 4 days after spontaneous delivery. The pregnancy had been uneventful, and she never had signs of eclampsia. She had no remarkable medical history. On admission, had blood pressure was 180/104 mmHg. The findings from a neurological examination and initial CT scan were normal. The brain MRI with MRA findings were also normal (Fig. 2a and b). She was treated with nasal sumatriptan, but the headaches initially showed no response. The headaches then gradually resolved following the administration of

acetaminophen over a few days, and the patient was discharged. A repeat MRI with MRA performed on Day 6 after her discharge showed narrowing of the bilateral anterior, middle, and posterior cerebral arteries (Fig. 2c and d, white arrows), which were normalized on Day 25 (Fig. 2e and f). In this case, the headache peaked during the first few days following sumatriptan administration and disappeared before the peak of cerebral vasoconstriction. She was retrospectively suspected of having had a postpartum headache before starting sumatriptan administration.

## Discussion

Sumatriptan is often used to treat migraines and occasionally induces cerebral vasoconstriction. Our two patients were taking sumatriptan for the first time because they had been tentatively diagnosed with a migraine. It was difficult to show any clear evidence of sumatriptan-induced RCVS in both of these cases. Sumatriptan seemed to play a primary role in Case 1, but a secondary role or even an incidental role due to the postpartum period in Case 2. However, sumatriptan likely either induced or exacerbated RCVS in both



**Figure 2.** a, b: MRA on admission showing no abnormalities. c, d: MRA on Day 7 showing a diffuse, beaded appearance of the intracranial vasculature (white arrows). e, f: MRA on Day 25 showing the complete resolution of the narrowing vessels.

**Table.** Case Reports of RCVS and Triptan Use.

Reference	Age/sex	Trigger drug	Postpartum period	Subarachnoid hemorrhage	Stroke	Headache characteristics	Clinical outcome
9	43M	Sumatriptan† (T), Midrin†	No	No	Ischemic	Bioccipital-throbbing	Recovery
10	20F	Sumatriptan* (I), Ergotamine*	Yes	No	Ischemic	Severe frontal and occipitounuchal	Recovery
11	37F	Sumatriptan† (I), Ergotamine†	No	No	Hemorrhage	Frontal throbbing	Impairment
12	34M	Sumatriptan (I) †	No	No	Ischemic	Nonconscious	Recovery
13	12M	Eletriptan (T)	No	Yes	No	Severe acute	Recovery
14	39F	Naratriptan (T) †, SNRI, SSRI	No	Yes	No	Severe bifrontal-throbbing	Recovery
7	68F	Sumatriptan (?)	No	No	Ischemic	Thunderclap	Death
Present case 1	44F	Sumatriptan* (T)	No	Yes	PRES	Thunderclap	Recovery
Present case 2	30F	Sumatriptan* (N)	Yes	No	No	Bifrontal-throbbing	Recovery

(T) Tablet, (N) Nasal spray, (I) Injection, \* First ever use, † Abuse or daily use, SNRI: serotonin norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, PRES: posterior reversible encephalopathy syndrome

cases.

The recent literature reflects a growing interest in RCVS. Four studies including more than 10 cases have been published (5-8). However, only nine cases in the literature have described the association between triptans and RCVS in detail (Table) (7, 9-14). The mean age among these 9 cases was 36 years, and 6 (66.7%) were women. Sumatriptan, administered either subcutaneously, orally, or nasally, was the most commonly implicated drug. RCVS was precipitated at the first ever use, or after daily use of one or several drugs, or even after long-term use of triptan at normal doses. Two patients presented with RCVS within the first week after delivery, suggesting that triptans must be used carefully in patients with headache in the postpartum period. The most frequent finding on cerebral imaging was ischemic stroke (four cases). Only two patients presented with thunderclap head-

ache. Most patients had good recovery, but severe stroke seemed to induce poor outcomes.

The underlying mechanisms of RCVS are unknown. Triptan can precipitate RCVS when administered to susceptible patients. An individual's susceptibility to developing RCVS may be influenced by genetic predisposition (e.g., brain-derived neurotrophic polymorphism, female gender) and precipitating factors (e.g., vasoactive substances, pregnancy/postpartum) (15). Triptan-induced RCVS may be more frequent than previously thought. Regardless of the presence of a migraine, patients presenting with acute onset of severe headache should be thoroughly evaluated, and triptan should be administered carefully, as it could precipitate RCVS or aggravate cerebral vasoconstriction. If triptan-induced RCVS is suspected, vascular imaging should be performed after several days.

**The authors state that they have no Conflict of Interest (COI).**

## References

1. Calabrese LH, Dodick DW, Schwedt TJ, Singhal AB. Narrative review: reversible cerebral vasoconstriction syndromes. *Ann Intern Med* **146**: 34-44, 2007.
2. Ducros A. Reversible cerebral vasoconstriction syndrome. *Lancet Neurol* **11**: 906-917, 2012.
3. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* **33**: 629-808, 2013.
4. Yancy H, Lee-Iannotti JK, Schwedt TJ, Dodick DW. Reversible cerebral vasoconstriction syndrome. *Headache* **53**: 570-576, 2013.
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* **130**: 3091-3101, 2007.
6. Singhal AB, Hajj-Ali RA, Topcuoglu MA, et al. Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Arch Neurol* **68**: 1005-1012, 2011.
7. Robert T, Kawkabani Marchini A, Oumarou G, Uské A. Reversible cerebral vasoconstriction syndrome identification of prognostic factors. *Clin Neurol Neurosurg* **115**: 2351-2357, 2013.
8. Katz BS, Fugate JE, Ameriso SF, et al. Clinical worsening in reversible cerebral vasoconstriction syndrome. *JAMA Neurol* **71**: 68-73, 2014.
9. Meschia JF, Malkoff MD, Biller J. Reversible segmental cerebral arterial vasospasm and cerebral infarction: possible association with excessive use of sumatriptan and Midrin. *Arch Neurol* **55**: 712-714, 1998.
10. Granier I, Garcia E, Geissler A, Boespflug MD, Durand-Gasselien J. Postpartum cerebral angiopathy associated with the administration of sumatriptan and dihydroergotamine: a case report. *Intensive Care Med* **25**: 532-534, 1999.
11. Nighoghossian N, Derex L, Trouillas P. Multiple intracerebral hemorrhages and vasospasm following antimigrainous drug abuse. *Headache* **38**: 478-480, 1998.
12. Singhal AB, Caviness VS, Begleiter AF, Mark EJ, Rordorf G, Koroshetz WJ. Cerebral vasoconstriction and stroke after use of serotonergic drugs. *Neurology* **58**: 130-133, 2002.
13. Yoshioka S, Takano T, Ryuji F, Takeuchi Y. A pediatric case of reversible cerebral vasoconstriction syndrome with cortical subarachnoid hemorrhage. *Brain Dev* **34**: 796-798, 2012.
14. Ba F, Giuliani F, Camicioli R, Saqqur M. A reversible cerebral vasoconstriction syndrome. *BMJ Case Rep* **2012**: bcr0920114841, 2012.
15. Chen SP, Fuh JL, Wang SJ, Tsai SJ, Hong CJ, Yang AC. Brain-derived neurotrophic factor gene Val66Met polymorphism modulates reversible cerebral vasoconstriction syndromes. *PLoS One* **6**: e18024, 2011.

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