Reversible cerebral vasoconstriction syndrome: the importance of follow-up imaging within 2 weeks

Kiyomitsu Fukaguchi (fukaskgh@gmail.com)
Shonan Kamakura General Hospital https://orcid.org/0000-0003-2262-1898
Tadahiro Goto
Tokyo University
Hiroyuki Fukui
Shonan Kamakura General Hospital
Ichiro Sekine
Shonan Kamakura General Hospital
Hiroshi Yamagami
Shonam Kamakura General Hospital

Original research

Keywords: thunderclap headache, reversible cerebral vasoconstriction syndrome, emergency department, follow-up imaging

Posted Date: May 17th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-28609/v1

Version of Record: A version of this preprint was published at Acute Medicine & Surgery on January 1st, 2020. See the published version at https://doi.org/10.1002/ams2.559.

Abstract

Background: In patients with thunderclap headache, reversible cerebral vasoconstriction syndrome (RCVS) should be considered as a differential diagnosis. However, RCVS diagnosis in the emergency department (ED) remains challenging. This study described the clinical features of RCVS, determined the factors related to RCVS diagnosis, and suggested treatment strategies for its management.

Methods: We retrospectively identified eight patients diagnosed with RCVS and reviewed their medical records. From January 2010 to March 2019, eight patients with RCVS (ages 18-69 years, 5 females) were identified.

Results: The median duration from the ED visit to RCVS diagnosis was 6 days (range, 1-11 days). Of the eight patients, seven were middle-aged, six had apparent triggers, six had subarachnoid haemorrhage (SAH), five had high systolic blood pressure, and none had any specific abnormality observed upon physical examination. At the ED visit, RCVS was diagnosed in only one patient with a history of RCVS. In other patients, SAH was diagnosed in two patients, and primary headache was diagnosed in four patients with negative computed tomography (CT) findings. Based on the follow-up imaging, seven of eight patients with convexal SAH were diagnosed as having RCVS (as the cause of SAH) using angiography (e.g., magnetic resonance angiography).

Conclusions: RCVS with negative CT findings at the ED visit was likely to be misdiagnosed as primary headache. In patients with thunderclap headache and negative CT findings, physicians should consider RCVS as a differential diagnosis, inform patients of the risk of RCVS and the likelihood of a negative image evaluation early in the course of the disease, and carry out follow-up imaging within 2-weeks of the visit.

Introduction

Headache is one of the most frequent symptoms among patients presenting at the emergency department (ED). In particular, the sudden intense headache called “thunderclap headache,” is widely known as an important symptom suggesting several critical conditions including aneurysmal subarachnoid haemorrhage (aSAH). While aSAH is a most critical condition that should be differentiated, recent studies have underscored the importance and prevalence of reversible cerebral vasoconstriction syndrome (RCVS) among patients with thunderclap headache [1–3].

RCVS is a relatively new disease concept, defined by Calabrese et al. in 2007 [4–6] and included in the *International Classification of Diseases, 10th revisio*n (ICD-10). Representative symptoms of RCVS include thunderclap headache, sometimes involving minor bleeding (like SAH), and focal neurological symptoms caused by reversible segmental spasms in the cerebral blood vessel [6]. While RCVS was thought to be a common, benign condition, recent studies have reported that RCVS causes premature stroke and recurrent headache, which could be responsive to interventions [7]. Despite the clinical importance, there are few ED-based clinical studies and no optimal strategy to manage patients with suspected RCVS in the ED [8].

To address the knowledge gap in the literature, we described the clinical features and course of RCVS among eight patients presenting at the ED who were ultimately diagnosed with RCVS. We also determined factors related to RCVS diagnosis, and reported the strategy to manage patients suspected of having RCVS at the ED.

Methods

This is a case-series using hospital data at one of the largest tertiary care hospital in Japan, with 42,000 annual ED visits and 14,000 emergency transportations. The observation period was from January 2010 to March 2019. We retrospectively identified patients who were diagnosed as RCVS using the ICD-10 code. We then reviewed their medical records to report patient characteristics, medical history (e.g., triggers of headache), clinical features, diagnostic tests performed at the first ED visit, imaging findings at the ED visits and the time of diagnosis, the number of days from the onset of headache to diagnosis, and the number of days from confirmation of vasospasm. This study was approved by the hospital's Institutional Review Board, and the requirement of written informed consent was waived.

Results

Patient characteristics and clinical features at the ED visit

The patient characteristics and clinical features of the eight RCVS cases are summarised in Table 1. The median age was 55 years (range, 18–69 years), and 5 patients were female. Six patients visited the ED in the summer or autumn. Seven patients visited the ED for thunderclap headache, while one patient visited for headache with syncope. Based on their medical history, varying causes were thought to be triggers of RCVS, including sexual intercourse, beating of drums at a festival, physical or emotional stress (e.g., dietary restriction and school examinations, and the death of a daughter), exertion, and urinary tract infection. Three patients had comorbidity with migraine or chronic headache, and one patient had a history of RCVS.

Table 1
Clinical features of eight patients with reversible cerebral vasoconstriction syndrome in the emergency department

Case number	Age, sex	Visit season	Chief complaints	Potential trigger	Comorbidities	Pulse rate, per min	Blood pressure, mmHg	Physical examinations, including neck stiffness	Initial imaging findings	Initial ED diagnosis	Dispositi
1	60 F	Autumn	Thunderclap headache	Sexual intercourse	Chronic headache	97	159/104	No abnormality	No specific CT findings	Primary headache (RCVS was not suspected)	Home
2	66 F	Summer	Thunderclap headache, vomiting	Beating drums	None	75	160/95	No abnormality	Finding of cSAH by CT	cSAH	Hospital
3	18 M	Autumn	Thunderclap headache, vomiting	Physical and emotional stress (dietary restriction and school exam)	RCVS (2 years ago), migraine	99	95/57	No abnormality	No specific CT findings. Peripheral cerebral vasospasm of the left MCA by MRA	RCVS	Hospital
4	51 F	Spring	Thunderclap headache	Unknown	Hypertension, cerebral infarction	92	132/84	No abnormality	No specific CT and MRI findings	Primary headache (RCVS was not suspected)	Home
5	58 F	Summer	Thunderclap headache	Emotional stress (death of her daughter)	Migraine, insomnia	56	148/76	No abnormality	No specific CT findings	Primary headache (RCVS was not suspected)	Home
6	51 F	Winter	Thunderclap headache, nausea	Exertion (ran in a hurry)	Menopausal disorder	72	159/97	No abnormality	No specific CT findings	Primary headache (RCVS was not suspected)	Home
7	65 M	Summer	Headache, syncope	Unknown	Diabetes	85	162/89	No abnormality	Finding of cSAH by CT	cSAH	Hospital
8	69 M	Autumn	Thunderclap headache, fever	Urinary tract infection	Diabetes, chronic kidney disease	92	112/81	No abnormality	No specific CT and MRI findings	UTI, Primary headache (RCVS was not suspected)	Hospital

Abbreviations: ED, emergency department; F, female; CT, computed tomography; RCVS, reversible cerebral vasoconstriction syndrome; cSAH, convexal subarachnoid haemorrhage; M, male; MRI, magnetic resonance imaging; DSA, digital subtraction angiography; MRA, magnetic resonance angiography; CTA, computed tomography angiography; MCA, middle cerebral artery; PCA, posterior cerebral artery;

UTI, urinary tract infection;

The mean pulse rate was 84 beats per minute (range, 56–99), the mean systolic blood pressure was 141 mmHg (range, 95–162 mmHg), and the mean diastolic blood pressure was 85 mmHg (range, 57–104 mmHg). All patients had no specific findings (including neck stiffness) at physical and neurological examinations. In all cases, head computed tomography (CT) was taken at the ED visit, but there were no abnormalities observed except in two patients with SAH. In three patients, magnetic resonance imaging (MRI) was further performed, with no specific findings.

The initial diagnosis at the ED was that of primary headache in five out of eight patients. In these five patients, there were no medical records suggestive of RCVS, and four patients were discharged home without further instructions on RCVS. In the remaining three patients who were not diagnosed with primary headache, SAH was diagnosed in two, and RCVS was diagnosed in one. The RCVS patient diagnosed at the ED visit was the patient with a history of RCVS; this patient showed vasospasm on MRI.

Follow-up and RCVS diagnosis

Among the seven patients who were not diagnosed with RCVS at the initial ED visit, follow-up imaging was performed within 2 weeks (range, 2–11 days; Table 2). Based on the follow-up imaging, all seven undiagnosed cases revealed SAH with a slight pericortical hematoma as a complication of RCVS. These seven patients were diagnosed with RCVS following further assessment of SAH using angiography. The diagnostic devices for vasospasm were magnetic

resonance angiography (MRA), CT angiography (CTA), and digital subtraction angiography (DSA) in five, one, and two patients, respectively. The sites of vasospasm were the middle cerebral artery and the diffuse and multiple vessels in three and five patients, respectively. Improvement in vasospasm was later confirmed in seven patients. One patient died of a reason other than an intracranial disease.

Table 2
Clinical courses of eight cases of reversible cerebral vasoconstriction syndrome (RCVS)

Case number	Days from the initial ED visit to RCVS diagnosis (Days from onset of headache)	Diagnostic device	Imaging findings and the site of spasm	RCVS-related complications	Prognosis
1	2 (7)	MRA	Spasm of the right MCA (M1)	Frontal lobe cSAH (MRI)	Confirmed the improvement of spasm 3 months later by CTA
2	5 (10)	DSA	Spasm of the segmental diffuse cerebral artery	Parietal lobe cSAH (CT)	Confirmed the improvement of spasm 3 months later by MRA
3	1 (1)	MRA	Spasm of the peripheral cerebral artery of the left MCA (M2)	None	Confirmed the improvement of spasm 1 month later by MRA
4	9 (9)	MRA	Spasm of the cerebral artery of the right MCA (M2)	Frontal lobe cSAH (MRI)	Confirmed the improvement of spasm 6 months later by MRA
5	7 (10)	DSA	Spasm of both sides of the PCA and right MCA	Occipital lobe cSAH (MRI)	Confirmed the improvement of spasm 3 months later by MRA
6	6 (6)	MRA	Spasm of the peripheral cerebral arteries of the fornix and posterior circulation	Parietal lobe cSAH (MRI)	Confirmed the improvement of spasm 3 months later by MRA
7	11 (13)	MRA	Spasm of both sides of MCA	Left temporal lobe cSAH (CT)	Confirmed the improvement of spasm 6 months later by MRA
8	6 (6)	CTA	Spasm of both sides of PCA	Occipital lobe cSAH (CT)	Not checked Death

Abbreviations: ED, emergency department; cSAH, convexal subarachnoid haemorrhage; CT, computed tomography, MRI, magnetic resonance imaging; DSA, digital subtraction angiography; MRA, magnetic resonance angiography; CTA, computed tomography angiography; MCA, middle cerebral artery; PCA, posterior cerebral artery;

UTI, urinary tract infection; M1, M1 segment (Horizontal / Sphenoidal part) of MCA; M2, M2 segment (insular part) of MCA;

Discussion

From the eight patients in our study, we found two important points for managing patients with suspected RCVS. First, RCVS may likely be misdiagnosed as primary headache in patients with no complications such as SAH. Second, in thunderclap headache with negative CT findings, RCVS should be considered as a differential diagnosis and the patient should be followed-up with imaging (e.g., MRI, MRA) within 2 weeks of the visit. At our hospital, in seven out of eight patients, the condition was not diagnosed as RCVS at the ED visit. Although RCVS diagnosis is obviously difficult at the ED, the ED management of these patients should be an important basis for emergency care.

Characteristics and management at the initial ED visit

RCVS characteristics in in-hospital or outpatient settings have been reported in several studies [6–7,9]. For example, RCVS typically occurs in the middle-aged population along with thunderclap headache involving nausea/vomiting [7]. Similar to other cardio- or cerebrovascular diseases, a key history may be the presence of triggers. RCVS triggers that have been previously reported include the prescription of vasoactive drugs such as triptans and selective serotonin reuptake inhibitors [9–11], bathing [12], and sexual activity [13]. In our study, the reported characteristics of the eight patients with RCVS are consistent with those described in previous reports and are very similar to those of aSAH – middle-aged patients (n = 7/8) that visited the ED for thunderclap headache with nausea/vomiting (n = 7/8), apparent triggers (n = 6/8), SAH (hypertension, diabetes, migraine) risk (n = 6/8), high systolic blood pressure (≥ 140 mmHg) at the ED visit (n = 5/8), and no specific abnormality during the physical examination (n = 8/8). However, in contrast to the characteristics of patients with aSAH, there were no specific CT findings in six out of eight patients with RCVS at the ED visit. These results indicate the difficulty in diagnosing RCVS based on the present illness, vital signs, and physical findings, although the apparent triggers may be somewhat beneficial. Therefore, in the case of thunderclap headache with negative CT findings, physicians should consider RCVS as a differential diagnosis, inform the patient of the potential risk of RCVS, and record the potential diagnosis in the patients' medical chart for further review at a follow-up visit. Indeed, four patients who were discharged to their homes did not receive appropriate follow-up instructions.

The timing of imaging and the diagnosis of RCVS

The most important point that makes RCVS diagnosis difficult is the inconsistency in the duration between the onset of headache and the vasospasm imaging findings. RCVS imaging features are often normal in the early stages of severe headache (e.g., at the ED visit). Consistent with observations reported in previous studies [7–10], an average of 8 days was required to confirm vasospasm in this study. Previous studies revealed that vasospasm occurred over time from the peripheral side to the central side of the cerebral artery [7, 14–16], and the appropriate timing of the image evaluation is considered to be 1–2 weeks after the onset of headache [8]. However, by this time, the headache tends to improve [7], and thereafter, the patients no longer visited the hospitals.

Complications and prognosis of RCVS

While studies have reported that the prognosis of RCVS was generally good, recent studies have demonstrated the risk concurrent with SAH, as well as other complications in patients with RCVS [6–7,9]. Reported complications of RCVS include SAH in 22–34%, cerebral haemorrhage in 6–12%, and cerebral infarction in 4–10% [9,17–18]. These cerebrovascular complications are likely to occur at an early stage [9]. Due to no RCVS-specific findings for the presenting illnesses, or upon physical examination, laboratory testing, and CT imaging, these cerebrovascular complications may be the key to RCVS diagnosis at an early stage. Indeed, in our cases, the SAH complication led to RCVS diagnosis in seven out of eight patients. Conversely, because cerebrovascular complications are reported in 20–30% of RCVS, approximately 70–80% of RCVS patients without complications are likely to be misdiagnosed as having primary headache or other conditions.

In our study, there were four patients with slight hematoma that was not detected at CT, and required further imaging using MRI. Although MRI is an expensive test, it may be helpful to distinguish SAH and RCVS from other common, non-life-threatening conditions at the ED, if available.

An accurate RCVS diagnosis can improve the patients' outcomes. Triggers have been reported in about 50% [19] of patients with RCVS, and some of these triggers may be avoidable in the patients' daily lives. In addition, the recurrence rate of RCVS has been reported at 5% within 5 years [20]. Patients with undiagnosed RCVS are at risk of frequent ED visits and of receiving inappropriate therapy (e.g., triptan for migraine). Therefore, the accurate diagnosis of RCVS may reduce unnecessary ED visits and tests and lead to appropriate therapy.

Conclusion

Based on eight cases of RCVS presenting at an initial ED visit, there were no specific findings including the presenting illness, vital signs, physical examination, and CT imaging that would allow for diagnosis of RCVS at the ED. RCVS without specific CT findings at the ED visit was likely to be misdiagnosed as primary headache. Since prompt diagnosis of RCVS is difficult at the ED, for patients with thunderclap headache and negative CT findings, physicians should consider RCVS as a differential diagnosis, inform patients of the risk of RCVS, and perform the follow-up imaging (e.g., MRA) within 2-weeks of the ED visit. This practice could facilitate early diagnosis of RCVS, resulting in improved patient outcomes and the reduction of unnecessary ED visits and related resources.

Abbreviations

aSAH, aneurysmal subarachnoid haemorrhage; cSAH, convexal subarachnoid haemorrhage; CT, computed tomography; CTA, computed tomography angiography; DSA, digital subtraction angiography; ED, emergency department; MCA, middle cerebral artery; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; PCA, posterior cerebral artery; RCVS, reversible cerebral vasoconstriction syndrome; SAH, subarachnoid haemorrhage; SSRI, selective serotonin reuptake inhibitors; UTI, urinary tract infection

Declarations

Ethics approval and consent to participate

This study was approved by the hospital's Institutional Review Board, and the requirement of written informed consent was waived.

Consent for publication

Not applicable, as the requirement of written informed consent was waived by the hospital's Institutional Review Board.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

Kiyomitsu Fukaguchi takes responsibility for the paper as a whole. Kiyomitsu Fukaguchi, Hiroyuki Fukui, Ichiro Sekine, and Hiroshi Yamagami conceived the study. Tadahiro Goto, Hiroyuki Fukui, Ichiro Sekine, and Hiroshi Yamagami supervised the conduct of the study. Kiyomitsu Fukaguchi and Tadahiro Goto drafted the manuscript, and all authors contributed substantially to its revision.

Acknowledgements

Not applicable.

References

[1] Edlow JA. Managing Patients With Nontraumatic, Severe, Rapid-Onset Headache. Ann Emerg Med. 2018;71(3):400.

[2] Ducros A, Bousser MG. Thunderclap headache. BMJ. 2013;346:e8557.

[3] Schwedt TJ. Clinical spectrum of thunderclap headache. Expert Rev Neurother. 2007 Sep;7(9):1135-44.

[4] Call GK, Fleming MC, Sealfon S, et al. Reversible cerebral segmental vasoconstriction. Stroke. 1988 ;19:1159–70.

[5] Singhal AB, Caviness VS, Begleiter AF, et al. Cerebral vasoconstriction and stroke after use of serotonergic drugs. Neurology. 2002;58(1):130.

[6] Calabrese LH, Dodick DW, Schwedt TJ, et al. Narrative review: reversible cerebral vasoconstriction syndromes. Ann Intern Med. 2007;146(1):34-44.

[7] Ducros A. Reversible cerebral vasoconstriction syndrome. Lancet Neurol. 2012;11(10):906-17.

[8] Chen SP, Fuh JL, Wang SJ, et al. : Magnetic resonance angiography in reversible cerebral vasoconstriction syndromes. Ann Neurol. 2010;67(5):648-56.

[9] Ducros A, Boukobza M, Porcher R, et al. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. Brain. 2007;130:3091–101.

[10] Chen SP, Fuh JL, Chang FC, et al. Transcranial color doppler study for reversible cerebral vasoconstriction syndromes. Ann Neurol. 2008;63:751–57.

[11] Chen SP, Fuh JL, Wang SJ. Reversible cerebral vasoconstriction syndrome: an under-recognized clinical emergency. Ther Adv Neurol Disord. 2010;3:161–71.

[12] Wang SJ, Fuh JL, Wu ZA, et al. Bath-related thunderclap headache: a study of 21 consecutive patients. Cephalalgia. 2008;28:524–30.

[13] Hu CM, Lin YJ, Fan YK, et al. Isolated thunderclap headache during sex: Orgasmic headache or reversible cerebral vasoconstriction syndrome? J Clin Neurosci. 2010;17:1349–51.

[14] Miller TR, Shivashankar R, Mossa-Basha M, et al. Reversible Cerebral Vasoconstriction Syndrome, Part 1: Epidemiology, Pathogenesis, and Clinical Course. AJNR Am J Neuroradiol. 2015;36:1392-9.

[15] Miller TR, Shivashankar R, Mossa-Basha M, et al. Reversible Cerebral Vasoconstriction Syndrome, Part 2: Diagnostic Work-Up, Imaging Evaluation, and Differential Diagnosis. AJNR Am J Neuroradiol. 2015 ;36:1580-8.

[16] Shimoda M, Oda S, Hirayama A, et al. Centripetal Propagation of Vasoconstriction at the Time of Headache Resolution in Patients with Reversible Cerebral Vasoconstriction Syndrome. AJNR Am J Neuroradiol. 2016;37:1594-8.

[17] Sattar A, Manousakis G, Jensen MB. Systematic review of reversible cerebral vasoconstriction syndrome. Expert Rev Cardiovasc Ther. 2010 ;8:1417–21.

[18] Singhal AB, Hajj-Ali RA, Topcuoglu MA, et al. Reversible cerebral vasoconstriction syndromes : analysis of 139 cases. Arch Neuro1. 2011;68:1005-12.

[19] Ducros A, Wolff V. The Typical Thunderclap Headache of Reversible Cerebral Vasoconstriction Syndrome and its Various Triggers. Headache 2016;56:657-73.

[20] Chen SP, Fuh JL, Lirng JF, et al. Recurrence of reversible cerebral vasoconstriction syndrome : a long-term follow-up study. Neurology. 2015;84:1552-8.