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Case report

Tsunu-associated rapé use as a novel trigger in reversible cerebral vasoconstriction syndrome of synergistic vasoactive exposure: a case report

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Abstract

Introduction
Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by recurrent thunderclap headaches and transient segmental narrowing of cerebral arteries, often precipitated by exposure to vasoactive substances. While several pharmacological and recreational agents have been implicated, traditional indigenous preparations such as tsunu-based rapé remain unexplored.

Case presentation
A 29-year-old man presented with 20 days of recurrent thunderclap headaches, including sex-triggered episodes. Neuroimaging revealed segmental vasoconstriction in the left anterior cerebral artery and right middle cerebral artery M1 segment. Exposures included escitalopram, methylphenidate, cannabis, sumatriptan, and regular tsunu-containing rapé, first headache during rapé inhalation.

Conclusion
Although direct causality cannot be established, this case raises the hypothesis that tsunu-based preparations, particularly when combined with other vasoactive substances, may contribute to cerebral vascular dysregulation. This report highlights the importance of recognizing non-conventional exposures in the evaluation of RCVS and suggests a potential novel trigger that warrants further investigation.

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Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is an increasingly recognized neurovascular disorder characterized by sudden, severe headaches—often described as thunderclap—and reversible multifocal narrowing of cerebral arteries (1–5). The condition has been associated with a wide range of triggers, most notably vasoactive medications, illicit drugs, and physiological stressors. Among these, serotonergic agents, sympathomimetics, and cannabis have been consistently reported as contributing factors in susceptible individuals (6–9).

Despite heightened awareness of common pharmacological triggers, limited attention has focused on traditional or culturally significant substances that may exert comparable vascular effects (10,11). Rapé, a powdered snuff used by Indigenous South American communities, typically combines *Nicotiana rustica* L. a potent nicotine source with alkaline plant ashes such as tsunu (derived from *Platycyamus regnellii* Benth. bark). Administered intranasally, these preparations induce rapid systemic effects, including autonomic activation and potential vasoconstriction (1,8,12).

To date, there is no established literature directly linked tsunu-based rapé to cerebrovascular disorders (13–15). However, characterized by high nicotine content and enhanced mucosal absorption via alkaline ash, suggests a plausible role in cerebral vascular tone modulation. In contemporary settings, where such traditional substances often coexist with prescription medications and recreational agents, synergistic vasoactive interactions become clinically pertinent (16,17).

This case raises the hypothesis that tsunu-containing rape, when combined with established vasoactive agents, may represent an additional and previously underrecognized exposure associated with RCVS. report describes a case of RCVS in a young man with concurrent exposure to multiple vasoactive substances, including habitual use of tsunu-containing rapé. The temporal association during rapé inhalation and the onset of symptoms, combined with established triggers, suggests a cumulative effect on cerebral vasculature. This case introduces tsunu as a potential, previously underrecognized contributor to RCVS and underscores the importance of comprehensive exposure assessment in patients presenting with thunderclap headache (12).

Case presentation

A 29-year-old male presented with a 20-day history of recurrent, abrupt-onset headaches of severe to extreme intensity, described as explosive and reaching peak intensity within seconds, bifrontal with right-sided predominance, and frequently accompanied by marked agitation. Several episodes fulfilled the clinical pattern of thunderclap headache, including six events triggered by sexual activity or masturbation.

The first episode occurred while inhaling tsunu-containing rapé, a substance used regularly in Indigenous rituals for focus and cleansing. Over the preceding six months, he had been taking escitalopram 20 mg daily, approximately 15 days before symptom onset, methylphenidate 36 mg daily was initiated, he also reported near-daily cannabis use and intermittent sumatriptan 100 mg for headache relief. Physical examination revealed normal vital signs, no focal neurological deficits, and mild photophobia, with no family history of cerebrovascular disease.

Given the severity and recurrence, urgent CT angiography was performed, revealing segmental vasoconstriction involving the left anterior cerebral artery and the M1 segment of the right middle cerebral artery, without evidence of subarachnoid hemorrhage.

Cerebrospinal fluid (CSF) examination was performed and revealed an opening pressure of 23 cm H_2O, protein concentration of 20 mg/dL, 1 leukocyte/mm^3, glucose level of 61 mg/dL, chloride concentration of 726 mg/dL, negative VDRL, and gamma globulin level of 16.6%.

Diagnostic challenges included multiple concurrent vasoactive triggers obscuring primary etiology, with differentials encompassing primary thunderclap headache, sentinel subarachnoid bleed, and pituitary apoplexy. The presentation met ICHD-3 criteria for RCVS recurrent thunderclap headaches, angiographic evidence of multifocal narrowing, and expected reversibility with favorable prognosis upon trigger removal.

Management entailed immediate withdrawal of methylphenidate, cannabis, rapé/tsunu, and sumatriptan. At four-week follow-up, headaches had fully resolved (patient-assessed VAS 0/10), with normal clinical examination. Follow-up CT angiography performed one month later demonstrated reversal of the previously observed arterial luminal narrowing, thereby confirming the diagnosis of reversible cerebral vasoconstriction syndrome (Figure 1 and Table 1).

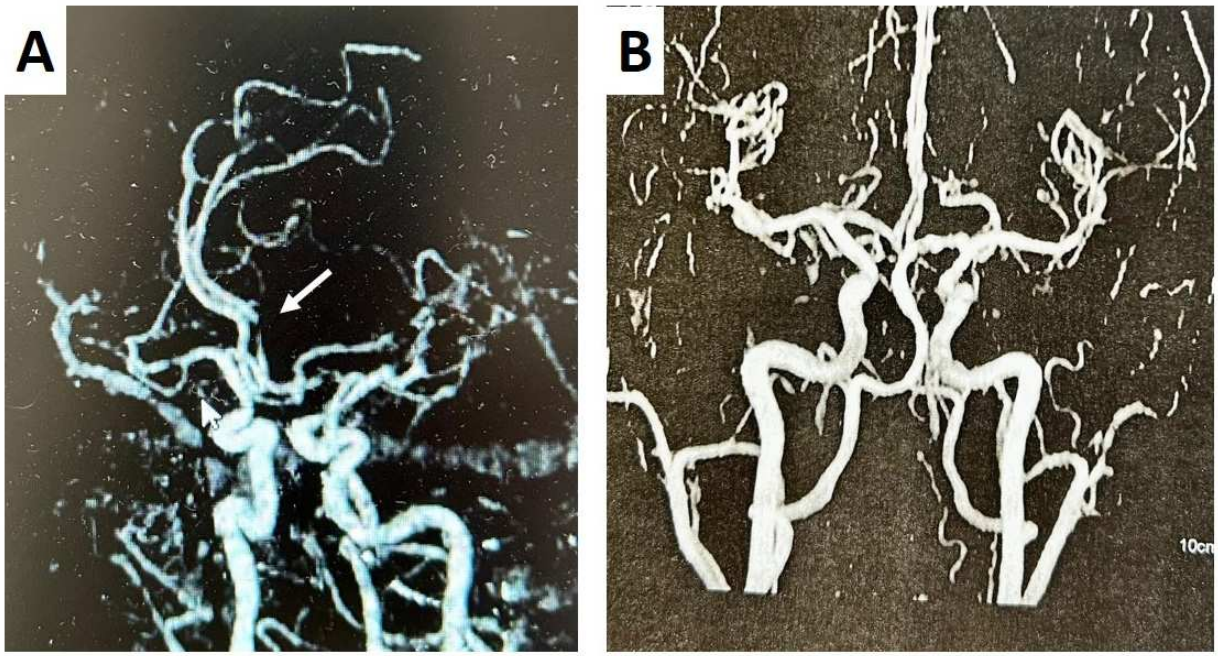


Figure 1. CT angiography performed a few days after the onset of thunderclap headaches demonstrated vasoconstriction of the A2 segment of the left anterior cerebral artery (small arrow) and the M1 segment of the right middle cerebral artery (large arrow). Follow-up CT angiography performed one month later showed complete reversal of the vasoconstriction, consistent with the diagnosis of reversible cerebral vasoconstriction syndrome (RCVS) (Right panel).

Table 1. Timeline

Date/Event	Key Developments
6 months prior	Escitalopram initiated.
15 days prior	Methylphenidate started; ongoing cannabis/rapé use.
Day 0	First thunderclap headache during tsunu/rapé inhalation.
Days 1-20	Recurrent headaches (20+ episodes, including sex-triggered); sumatriptan used intermittently.
Presentation (day 20)	CT angiography: segmental vasoconstriction (left ACA, right MCA-M1).
Post-presentation	Triggers withdrawn.
4-week follow-up	Symptom resolution; Follow-up CT angiography was normal.

Discussion

There is currently no robust scientific literature directly linking tsunu-based rapé to cerebrovascular events such as stroke. However, this absence of evidence should not be interpreted as evidence of safety, particularly when tsunu is used in combination with other vasoactive substances.

Rapé contains *Nicotiana rustica*, with higher nicotine levels than comercial tobacco. Nicotine is a well-established vasoactive compound, inducing sympathetic activation, transient hypertension, and cerebral vasoconstriction. The addition of alkaline plant ash, such as that derived from tsunu, may further enhance mucosal absorption and accelerate systemic effects. Although the specific pharmacological profile of tsunu ash remains poorly characterized, its role in facilitating rapid nicotine delivery is likely relevant.

More importantly, the clinical context in polypharmacological involves exposure to multiple agents known to influence cerebral vascular tone. Cannabis has been increasingly associated with cerebrovascular events, including ischemic stroke and RCVS, particularly in young individuals. Sympathomimetic agents, such as methylphenidate, are also recognized for their potential to induce vasoconstriction and elevate stroke

risk. In addition, serotonergic medications, including selective serotonin reuptake inhibitors such as escitalopram, and serotonin receptor agonists such as sumatriptan, may further modulate vascular reactivity (1,2,7,8,18,19).

RCVS is strongly associated with vasoactive substances exposure, especially when multiple agents are involved resulting in transient cerebral arterial tone dysregulation, segmental vasoconstriction, recurrent thunderclap headaches, and risks of ischemic/hemorrhagic complications (6,7).

In the present case, the temporal relationship between the initiation of methylphenidate and the onset of symptoms, combined with ongoing exposure to nicotine (via rapé), cannabis, escitalopram, and intermittent sumatriptan use, suggests a cumulative and possibly synergistic effect on cerebral vasculature. Rather than attributing causality to a single agent such as tsunu, it is more plausible that the interaction among multiple vasoactive compounds created a permissive environment for the development of RCVS (12,19).

This case highlights the importance of comprehensive exposure assessment in patients presenting with thunderclap headache. It also underscores the need for greater awareness of traditional and recreational substances, such as rapé, which may not be routinely considered in clinical evaluation but can contribute to significant neurovascular effects when combined with other pharmacological agents.

Conclusion

This case exemplifies RCVS diagnostic features and emphasizes the role of combined vasoactive exposures in its pathophysiology. It also serves as a reminder to consider this diagnosis in young patients with thunderclap headache and compatible imaging findings, especially when clear precipitating factors.

Primary take-away lessons

This case underscores comprehensive toxin/exposure screening in thunderclap headache, including traditional substances like tsunu/rapé. Cumulative vasoactive effects likely drive RCVS in polyexposed youth; prompt withdrawal optimizes outcomes and averts complications.

Informed consent

The patient provided written informed consent for publication, confirming de-identification and data use.

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