

CLINICAL VIGNETTE

Reversible Cerebral Vasoconstriction Syndrome Presenting with Thunderclap Headaches, Non-Aneurysmal Subarachnoid Hemorrhage and a Grossly Abnormal Lumbar Puncture

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A 53-year-old female with history of pancreatic bifida presented to the Emergency Department (ED) with history of thunderclap headaches. The headaches were associated with photophobia and vomiting. She had been evaluated in the ED on multiple occasions for the above symptoms in the week prior to admission. A Computed Tomography (CT) scan of the head without contrast one week prior showed no acute issues. Six days prior to admission, she re-presented to the ED and CT scan with angiography of the head and neck was performed which was also normal. Four days prior to admission, she was reevaluated in the ED for intractable headaches and underwent a brain magnetic resonance imaging (MRI) with and without contrast, which showed no abnormalities despite her ongoing severe headaches.

On the day of admission, she returned to the ED with worsening headaches and a lumbar puncture was performed, which appeared bloody with numerous red blood cells (RBC) on analysis. Specifically, RBC count was 141,500/mcL and 78,000/mcL in tube #1 and tube #4 respectively. White blood cell (WBC) count, glucose and protein levels from the cerebrospinal fluid were normal. Another CT scan performed on the same day now showed subarachnoid hemorrhages (SAH) not previously noted on her earlier CT scans. Her vital signs and physical examination, including neurological exam, were normal as were the rest of her laboratory tests.

The patient was evaluated by Neurosurgery and a cerebral angiogram was recommended, which revealed diffuse vasculopathy with evidence of intracerebral arterial narrowing in multiple vessels without evidence of aneurysms. Verapamil 10mg was administered intravenously, which resulted in significant improvement in areas of significant narrowing (Figures 1 and 2).

The patient had a thorough infectious and autoimmune work-up which were all negative. At this point, she was diagnosed with reversible cerebral vasoconstriction syndrome (RCVS) and started on a 21-day course of nimodipine. This was effective at decreasing the severity and frequency of her headaches. On the day of discharge from the hospital, she was ambulatory with full use of all her limbs without sensory deficits or coordination problems.

On follow-up visits, she only complained of minor headaches which have not been as severe as her presentations in the prior

months. A subsequent CT cerebral angiogram and MRI of the head 1 month later, showed complete resolution of all subarachnoid bleeding and the absence of the previously noted intracerebral arterial narrowing.

Discussion

The exact trigger of RCVS in this patient is not clear. The patient had a grossly positive CSF analysis with elevated RBC count. Radiographic, clinical and laboratory data initially ruled out non-aneurysmal causes of SAH such as trauma, vasculitis, venous thrombosis, use of sympathomimetic agents and other medications. The SAH in this case can be attributed to RCVS because of the absence of aneurysms on cerebral angiograms in the presence of intracerebral arterial narrowing in multiple vessels. What is unique about this case is the presence of a grossly abnormal lumbar puncture which is uncommon and has rarely been reported in the literature.

Reversible cerebral vasoconstriction syndrome is a rare disorder only recently described in the last 40 years. Most patients present with recurrent severe thunderclap headaches which may be associated with minimal to severe neurologic deficits.^{1,2} Other non-specific symptoms may include vomiting, photophobia and other visual changes. The distinguishing characteristic of this syndrome is the presence of a characteristic “string and beads” appearance on cerebral angiogram, which is the reversible segmental vasoconstriction observed in large and medium cerebral arteries.³⁻⁵ Multiple risk factors have been identified with this syndrome. These include recent postpartum status, acute and severe blood pressure elevation and use of certain medications with serotonergic or sympathomimetic properties.⁴ RCVS is more commonly diagnosed in women than men in a 3:1 ratio and the peak incident is between 20 to 50 years.⁶ The pathophysiology of RCVS is not well understood but it is suspected that disturbances in cerebral vascular tone is the most important aspect of this disorder.^{4,7} It is suspected that similar causes of vasospasms exist for both aneurysmal subarachnoid hemorrhage and RCVS. These include the presence of catecholamine, serotonin, nitrous oxide, and endothelin-I, which have been documented as causes of vasoconstriction.⁸

RCVS is partly a diagnosis of exclusion once other etiologies or precipitants are excluded. Definitive diagnosis of RCVS is made by cerebral angiography which demonstrates the

aforementioned alternating areas of arterial stenosis and dilation (the “string on beads”) with subsequent reversibility of the vasoconstriction. Because RCVS is generally transient, repeat cerebral angiography within 3 months should show complete resolution.^{3,4} For most cases of RCVS, blood and CSF findings are normal or near-normal in non-aneurysmal RCVS.⁵ This case report is one of a few to show a grossly abnormal cerebrospinal fluid analysis can also be seen in RCVS. Other modalities that may aid in diagnostic evaluation include magnetic resonance angiography and use of serial transcranial Doppler.^{9,10}

Due to the absence of randomized controlled trials, the current treatment of RCVS is largely based on expert opinion and experience detailed in several case series.⁶ Patients are encouraged to stop the use of all medications and illicit drugs that may be associated with RCVS. The most common class of medications used in the treatment RCVS are calcium channel blockers such as nimodipine, verapamil and nifedipine. A common regimen is the use of oral nimodipine at 60 mg every 4 hours tapered over several weeks.⁵ Endovascular therapies involving direct intra-arterial instillation of calcium channel blockers such as nimodipine and use of intracranial angioplasty have been successful in treating some refractory cases of vasoconstriction in patients who deteriorate.¹¹

In conclusion, RCVS is becoming more and more understood though continues to remain largely underdiagnosed. It is important for this syndrome to be considered in the differential diagnoses of all severe headaches by the Emergency Medicine physician. Rapid diagnosis is warranted to allow immediate withdrawal of any precipitating agents and initiation of therapies that will provide a chance for an improved outcome.

Figures

Figure 1. Multifocal intracranial narrowing most prominent in the right MCA territory but present in all intracranial vascular territories affecting the medium to small arterial vessel.

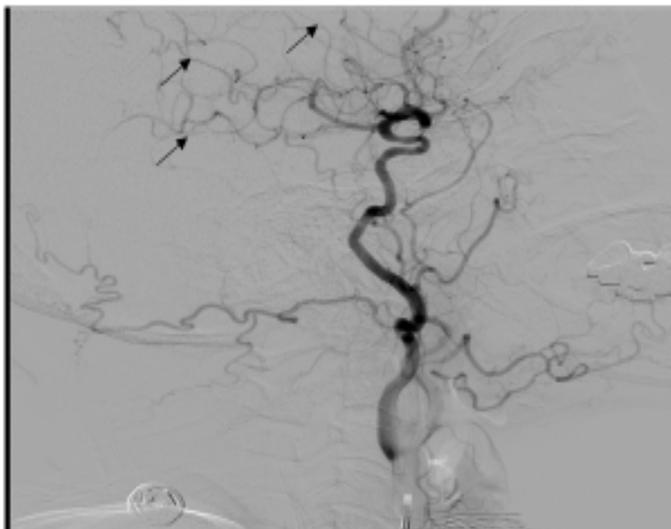
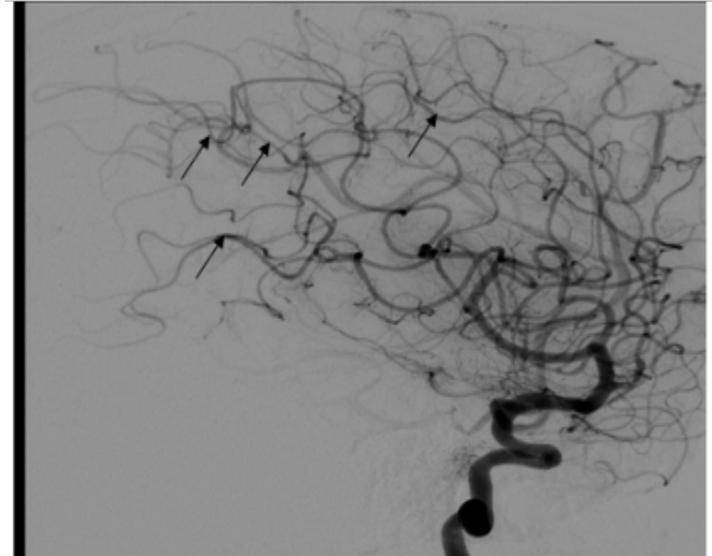


Figure 2. The most prominent areas of narrowing demonstrate significant improvement after infusion of 10 mg verapamil.



REFERENCES

1. **Dodick DW, Brown RD Jr, Britton JW, Huston J 3rd.** Nonaneurysmal thunderclap headache with diffuse, multifocal, segmental, and reversible vasospasm. *Cephalalgia*. 1999 Mar;19(2):118-23. PubMed PMID: 10214538.
2. **Chen SP, Fuh JL, Lirng JF, Chang FC, Wang SJ.** Recurrent primary thunderclap headache and benign CNS angiopathy: spectra of the same disorder? *Neurology*. 2006 Dec 26;67(12):2164-9. PubMed PMID: 17190937.
3. **Ducros A.** Reversible cerebral vasoconstriction syndrome. *Handb Clin Neurol*. 2014;121:1725-41. doi: 10.1016/B978-0-7020-4088-7.00111-5. Review. PubMed PMID: 24365443.
4. **Calabrese LH, Dodick DW, Schwedt TJ, Singhal AB.** Narrative review: reversible cerebral vasoconstriction syndromes. *Ann Intern Med*. 2007 Jan 2;146(1):34-44. Review. PubMed PMID: 17200220.
5. **Ducros A, Boukobza M, Porcher R, Sarov M, Valade D, Boussier MG.** The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain*. 2007 Dec;130(Pt 12):3091-101. Epub 2007 Nov 19. PubMed PMID: 18025032.
6. **Singhal AB, Hajj-Ali RA, Topcuoglu MA, Fok J, Bena J, Yang D, Calabrese LH.** Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Arch Neurol*. 2011 Aug;68(8):1005-12. doi: 10.1001/archneurol.2011.68. Epub 2011 Apr 11. PubMed PMID: 21482916.
7. **Ducros A, Boussier MG.** Reversible cerebral vasoconstriction syndrome. *Pract Neurol*. 2009 Oct;9(5):256-67. doi: 10.1136/jnnp.2009.187856. Review. PubMed PMID: 19762885.
8. **Bain J, Segal D, Amin R, Monoky D, Thompson SJ.** Call-Fleming syndrome: headache in a 16-year-old girl.

Pediatr Neurol. 2013 Aug;49(2):130-133.e1.
doi:10.1016/j.pediatrneurol.2013.05.005. PubMed
PMID: 23859861.

9. **Chen SP, Fuh JL, Chang FC, Lirng JF, Shia BC, Wang SJ.** Transcranial color doppler study for reversible cerebral vasoconstriction syndromes. *Ann Neurol.* 2008 Jun;63(6):751-7. doi: 10.1002/ana.21384. PubMed PMID: 18496847.
10. **Chen SP, Fuh JL, Wang SJ, Chang FC, Lirng JF, Fang YC, Shia BC, Wu JC.** Magnetic resonance angiography in reversible cerebral vasoconstriction syndromes. *Ann Neurol.* 2010 May;67(5):648-56. doi: 10.1002/ana.21951. PubMed PMID: 20437562.
11. **Ioannidis I, Nasis N, Aghianniotaki A, Katsouda E, Andreou A.** Reversible cerebral vasoconstriction syndrome: treatment with multiple sessions of intra-arterial nimodipine and angioplasty. *Interv Neuroradiol.* 2012 Sep;18(3):297-302. Epub 2012 Sep 10. PubMed PMID: 22958768; PubMed Central PMCID: PMC3442303.

Submitted August 7, 2017