A Rare Case of Idiopathic Reversible Cerebral Vasoconstriction Syndrome

Shezhad Muhamed[1] MD., MBA., Vivien Sehapovic[2] BS., Hardeep Singh[3] PhD, MS., and Louise Jones[3] PhD, M.Ed.

1. Northeast Georgia Medical Center-GME Emergency Medicine, Gainesville, GA
2. Northeast Georgia Medical Center-GME Research Summer Internship Program, Gainesville, GA
3. Northeast Georgia Medical Center- GME Research, Gainesville, GA

Northeast Georgia Medical Center
GRADUATE MEDICAL EDUCATION

Background

Migraines affect 46% of adults and account for ≈3.5 million Emergency Department (ED) visits annually in the United States. Headaches can sometimes manifest as the main symptom in many serious conditions, including reversible cerebral vasoconstriction syndrome (RCVS).

RCVS is a non-inflammatory intracranial vasculopathy classified as a condition of diffuse cerebral artery constriction.

- Complications associated with RCVS can include seizures, hemorrhagic strokes, and transient neurological deficits.
- RCVS is a rare condition, accounting for ≈3 hospitalizations per million adults.

Purpose

The purpose of this case study is to illustrate:

1. The identifying traits of RCVS
2. The diagnostic process
3. The medical management
4. The longitudinal clinical outcomes associated with RCVS

Case Presentation

34-year-old, female who presented to the ED with a chief complaint of a recurrent, severe headache.

Her past medical history was significant for heart murmurs and migraines, occurring about one to two times a month, and were worse in the summer that she attributed to increased stress.

The patient reported that she underwent cryotherapy, for stress-relief, before initial evaluation in the ED. She also reported that she began having recurrent headaches that initially began during cryotherapy. The patient presented to the ED two days after the cryotherapy treatment, twice on the same day. The patient was evaluated then for the third time three days later (see center timeline).

Day 1

- **First ED Visit** for severe headache described as worse than previous headaches. Also photophobia, nausea.
  - Had normal CTA Brain; negative for SARS-COV-2, RSV, Influenza A and B; Non-focal neurological exam; Normal vital signs
  - Patient was treated with dexamethasone, prochlorperazine, diphenhydramine, and ketorolac and discharged home after headache resolved
- **Second ED visit** (4 hours later) for severe headache.
  - No new imaging. Patient stated she used acetaminophen and ibuprofen to some relief before this visit; Non-Focal Neurological exam; Besides elevated BP of 124/100, all other vital signs were normal
  - Diphenhydramine, metoclopramide, and ketorolac were administered in the ED, and upon re-assessment, the patient reported resolution of her symptoms. Discharged home.

Day 4

- **Third ED visit** for headache.
  - Initial vital signs were significant for elevated BP and heart rate
  - In the ED, patient began having tonic-clonic activity of the upper extremities with right eye deviation
  - Emergently intubated, had blood work and lumbar puncture done that was significant for elevated WBC count; Urine drug screen was THC positive.
  - CT Brain showed two focal parenchymal hemorrahages: one in the left parietal lobe and one in the posterior left occipital lobe (See Figure 1)
- **Patient admitted to ICU from the ED due to ongoing concerns for meningitis/encephalitis and for ventilation management. Neurosurgery/Neurology consulted for further management.**

Day 5

- MRI and carotid/cerebral angiography showed no change in intracranial hemorrhages compared to Day 4 (see Figures 2 and 3)
  - RCVS vs Vasculitis remained in differential
- Patient extubated
- Throughout hospital admission stay, patient had labile BP readings, being intermittently hypertensive; was managed by nephrology.
- Meninigitis/Encephalitis panel resulted as being negative, so an infectious process as the etiology was ruled out
- Negative for MTHFR C.1286A>C mutation and was heterozygous for the MTHFR C.665C>T mutation.
- Neurology team's leading diagnosis as patient's initial symptoms began during cryotherapy, which could lead to vasoconstriction

Day 10

- Medications given during hospital admission (days 5-10):
  - Verapamil 80mg PO q8h, topiramate 25mg PO BID, levetiracetam 1000mg BID
- At the time of discharge, the patient was noted to not having any focal neurological deficits and was also advised to discontinue use of herbal supplements and vitamins that she reported as previously having used.
  - Medications prescribed to patient for discharge home:
    - Verapamil 40mg Q8h, topiramate 25mg Q12h (and tapered off), levetiracetam 1000mg BID, lisinopril 10mg daily, melatonin 3mg to take twice nightly, pregabalin 25mg BID

Diagnostic Images

Figure 1A. CT Brain

Figure 1B. CT Brain

Figure 2. MRI Brain

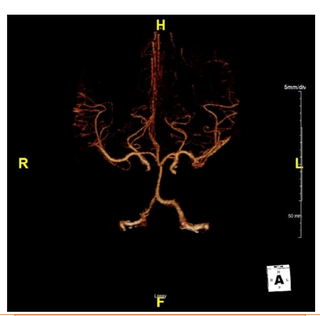

Figure 3. Cerebral Angiography

Figure 4. CT Brain

Discussion

- There are many **challenges in diagnosing** RCVS because the timing between headache onset and abnormal image findings are inconsistent, varying over a period of about 8 days. Though the most affected people with RCVS are female, Caucasian, and have an average age of 45, the patient discussed in this case study was younger and African-American.. The patient did not have a previous history of vascular risk factors usually correlated with a higher risk for RCVS, such as coronary artery disease, hypertension, and diabetes.
- **Prior history of migraines** has been shown to correspond with an increased risk for RCVS as well, which the patient in this study did report. Some studies have also shown a correlation between **COVID-19** and RCVS.
- Though the pathological process of RCVS is unknown, some studies suggest that a dysfunction of cerebral vascular tone and abnormalities in the blood-brain barrier may be the cause of RCVS. However, there are **two factors** that have been linked to a higher risk for RCVS: the use of vasoactive substances and the post-partum state. Vasoactive substances linked to being likely triggers and/or worsening agents of RCVS include adrenergic agents, SSRI/SNRI, blood products, chemotherapy drugs, pseudoephedrine. and even anti-migraines drugs such as ergot derivative drugs, NSAIDS, and triptans.
- Some **recreational drugs** that have also been linked to a higher risk of RCVS, having even led to fatal cases of RCVS when combined with other vasoactive substances, include amphetamines, cannabis, cocaine, ecstasy, and nicotine.
- The patient in this case study had a normal HCG, but the urine rapid drug screen was positive for THC. Emotional stress has also been thought to be a causative factor for RCVS, and this patient did note that she had an increased workload during the time period she had RCVS.
- Earlier studies have shown that the administration of glucocorticoids, NSAIDS, and diphenhydramine, are linked with worsening outcomes in RCVS., which patient was given during the initial two ED studies, unknown if this could have contributed to the worsening of RCVS.
- At the three-month follow-up appointment, a CT of the head was performed was normal (see *Figure 4*). This finding aligns with earlier research, where RCVS resolves within one to three months.

Conclusion

RCVS is an underdiagnosed condition that is characterized by a sudden-onset severe headache that can often be misdiagnosed as a migraine. It is important to note that complications including ICH, SAH, and seizures can arise, not just from other vasculopathies, but from RCVS as well, hence, an early diagnosis is critical. **It is especially important to evaluate further patients who present to the ED for recurrent, severe headaches, even if recent past imaging shows no acute abnormalities.**

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