Analysis of Characteristics in Patients with Non-Hemorrhagic Reversible Cerebral Vasoconstriction syndrome NH-RCVS

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Background: Reversible vasoconstriction syndrome is a phenomenon where the vasculature of the brain begins to spasm. Although initially thought to only be associated with intracranial and subarachnoid hemorrhage, recently, it has expanded to include non-hemorrhagic states. The etiology and physiology of this type of reversible vasoconstriction syndrome remains to be worked out.

Methods: Our meta-analysis will discuss the demographic, past medical, and concurrent medical history, and imaging characteristics, including CT and conventional angiograms of non-hemorrhagic cases in the literature. This includes prior studies and cases/case series where data of non-hemorrhagic cases where vasospasm was noted. A review of treatments, including endovascular approaches, will also be discussed. Results: Similarities and differences from reversible vasoconstriction syndrome associated with hemorrhage will be noted. A discussion of how patients with nonhemorrhagic reversible vasoconstriction syndrome are managed.

Conclusion: Reversible vasoconstriction syndrome may present differently in patients without associated subarachnoid or intracranial hemorrhage.
WHAT IS NH-RCVS?

- Reversible Cerebral Vasocconstriction syndrome (RCVS) has been proposed as a unifying term for variety of previously named similar syndromes, including Call-Fleming syndrome.

- In literature many sporadic case reports or small analysis of collection of cases of non-hemorrhagic RCVS.
Pathophysiology

RCVS is possibly caused by a transient dysregulation of cerebral vascular tone, leading to multi-focal arterial constriction and dilation.
Aims of this Analytic Study

- RCVS is associated with hemorrhage but no distinguishing data or guidelines exist for diagnosis or predicting the RCVS patients without associated hemorrhage (NH-RCVS)

- Establish NH-RCVS as a distinct clinical phenomenon as no ideal set of common presenting symptoms have been assembled in order to help predict or diagnose NH-RCVS

- Establish potential causal relationships, triggers and associations from sporadic case reports as it has not been so far attempted.
Methods

- Analysis on selected case reports on NH-RCVS published from 2004-2011.
- A total of 66 case reports were included in this Analysis out of a total 335 case reports on Cerebral Vasoconstriction.
METHODS

- Analysis of symptomatology
- Analysis of diagnostic investigations
- Analysis of potential triggers/etiology of NH-RCVS
- Analysis of potential clinical outcome for NH-RCVS being a rare etiologic agent itself.
Methods

**INCLUSION CRITERIA:**

- Sudden thunderclap headache with/without focal signs.
- Evidence of beading pattern on CTA, MRA or Cerebral Angiogram without any evidence of IC bleeding or vessel rupture.
- Established evidence of negative vasculitis workup if ordered.
- Positive response to Calcium Channel blockers on f/u imaging.
- No prior history of steroid exposure.
METHODS:

EXCLUSION CRITERIA

Cases with patients having evidence of:
- Sub-arachnoid hemorrhage
- Intracerebral hemorrhage
- Prior Intracerebral Neurosurgical intervention
Results: Clinical Features

- Mean age of 40.
- All of them presented with acute onset of severe thunderclap headache in the patients with localized headaches.
- 20 had occipital headaches, 11 had diffuse bilateral headaches, 4 had frontal, while 2 patients complained of headaches localized to the vertex.
- 26 patients were found to present with hypertensive crisis while 5 were merely hypertensive.
MALE : FEMALE RATIO (18:48)
RESULTS: Features

- Aura was generally reported to be missing. However, was present in patients with Hx of migraines.

- Headache was reported as non-throbbing.
Motor Symptoms

- Monoparesis: 1
- Hemiparesis: 6
- Quadriparetic: 3
SYMPTOMS

- Impaired vision: 13
- Homonymous hemianopia: 2
- Amaurosis: 1
- Cortical blindness: 5
- Photophobia: 9
- Dysarthria: 3
- Phonophobia: 3
- Hyperacusis: 1

Bar chart showing the number of patients with each symptom.
RESULTS: Symptoms

- Monoparesis: 2
- Hemisensory loss: 1
- Dysphasia: 3
- Neglect: 1
Vitals

- HYPERTENSIVE CRISES : 26
- HTN: 5
- OTHERS: NORMOTENSIVE
Results:

Positive finding on Imaging 12-4-29

No of Patient with positive findings

- MRI
- CTA
- Conventional Angiogram
RESULTS: Investigations

- **CSF/LABS**
  - Out of 42 patients who underwent a spinal tap, 38 had normal CSF, while 4 had abnormal results with elevated proteins but no xanthochromia.

  A vasculitis workup done in 22 of these patients was normal, with ESR, CRP being normal in almost all these cases.
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<thead>
<tr>
<th>Precipitating Factors/Association Factors</th>
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<tbody>
<tr>
<td>Vasoactive drugs and SSRI</td>
<td>SSRI: 7</td>
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<tr>
<td>Hydroxycut: 1</td>
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<tr>
<td>Cyclophosphamide: 1</td>
<td></td>
</tr>
<tr>
<td>Methylergometrine: 1</td>
<td></td>
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<tr>
<td>Vasoactive substance: 16</td>
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<tr>
<td>Bromocryptine: 1</td>
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<tr>
<td>Reproductive Hormonal Fluctuation</td>
<td>Hysterectomy &amp; b/l salpingo-0ophorectomy: 1</td>
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<td>Postpartum angiopathy: 3</td>
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<tr>
<td>Ovarian stimulation and artificial insemination: 1</td>
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<td>Recent child birth: 10</td>
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<td>OCP: 4</td>
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<tr>
<td>Procedure related</td>
<td>Uterine Ar. Embolization</td>
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<td><strong>Stress related: physical and emotional</strong></td>
<td>Extreme Physical exertion: 3</td>
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<tr>
<td>Sexual activity: 2</td>
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<tr>
<td>Orgasm: 6</td>
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<tr>
<td>Emotional stress: 1</td>
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<tr>
<td><strong>Extreme of temperature exposure</strong></td>
<td>Hot Shower: 1</td>
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<tr>
<td>Cold water diving: 2</td>
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<tr>
<td><strong>Autonomic dysfunction</strong></td>
<td>Valsalva maneuver: 1</td>
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<tr>
<td>UTI &amp; autonomic dysfunction: 1</td>
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<tr>
<td>Autonomic dysreflexia: 1</td>
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<tr>
<td><strong>CNS disease</strong></td>
<td>Migraine: 3</td>
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<tr>
<td>SLE: 2</td>
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<tr>
<td>Parangangioma of carotid tumors: 2</td>
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RESULTS: Treatment/Response

- Removal of inciting medication/factors, calcium channel blocker.

- Oral calcium channel blockers can be considered as a preliminary treatment option after removal of the offending agents, with other options including oral steroids or IA Calcium Channel blockers.
Conclusion

- Certain common clinical features may be identified for rapid diagnosis and better treatment of NH-RCVS patients. Do not delay imaging studies to lead to diagnosis of Non-Hemorrhagic RCVS.

- Certain associations if identified are strongly related to NH-RCVS onset and can be potential etiologic agents in various settings.
MRA appears to show vasoconstriction more often than CTA in our review and should be obtained as a preliminary step for patients with a high suspicion; but if negative for any vascular abnormalities, a conventional angiogram is the modality of choice for diagnosis.

If identified early can be rapidly treated with oral or intraarterial CCB with excellent response.
NH-RCVS can be an uncommon cause of headaches with distinct clinical/radiologic features with excellent response to CCB

NH-RCVS can be an uncommon cause of ischemic stroke

NH-RCVS can be an uncommon cause of seizures
CONCLUSION

- Large scale clinical trials are needed to study this increasingly common group of disorders.
TAKE HOME MESSAGE

- Thunderclap headaches with no bleed seen on imaging, or negative CSF, accompanied with nausea and vomiting with/without focal signs should alert the physician to the possibility of NH-RCVS especially if a history of recent childbirth, use of vasoactive drugs, OCPs, SSRIs or other severe emotional stressors are obtained.

- Imaging should not be delayed.
Reference:

2. Case reports on RCVS on pubmed.
7. Reversible Segmental Cerebral Arterial Vasospasm and Cerebral Infarction: Possible Association With Excessive Use of Sumatriptan and Midrin: James F. Meschia, MD; Marc D. Malkoff, MD; José Biler, MD