Reversible cerebral vasoconstriction syndrome (RCVS),

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Case

- A 28-year-old woman had thunderclap headache (TCH),
- after 7 days she had left hemiparesis.
- She had a history of oral contraceptive and citalopram medications.
Brain magnetic resonance imaging FLAIR (a) and diffusion-weighted (b) sequences showed acute ischemia within the right centrum semiovale. MR angiography demonstrated multiple
• Two probable diagnoses performed
  – primary angiitis of the central nervous system
  – reversible cerebral vasoconstriction syndrome (RCVS).
Outline: Reversible cerebral vasoconstriction syndrome

- Definition
- Epidemiology
- Clinical Presentation
- Complications
- Pathophysiology
- Secondary Causes
- Differential Diagnosis
  - Reversible cerebral vasoconstriction syndrome (RCVS) vs. Posterior Reversible Encephalopathy syndrome (PRES)
- Imaging
- Treatment & Prognosis
Definition

• Severe headaches with or without seizures or neurologic deficits and constriction of cerebral arteries which resolves spontaneously within 1-3 months
Table 1. Summary of Critical Elements for the Diagnosis of RCVS\textsuperscript{a}

<table>
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<th>Elements</th>
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<tr>
<td>1. Transfemoral angiography or indirect (CT or MRI) angiography documenting segmental cerebral artery vasoconstriction</td>
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<td>2. No evidence for aneurysmal subarachnoid hemorrhage</td>
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<tr>
<td>3. Normal or near-normal cerebrospinal fluid analysis (protein level $&lt;80$ mg/dL, white blood cell count $&lt;10\mu$L, normal glucose level)</td>
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<td>4. Severe, acute headache, with or without additional neurological signs or symptoms</td>
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<td>5. The diagnosis cannot be confirmed until reversibility of the angiographic abnormalities is documented within 12 wk after onset, or if death occurs before the follow-up studies are completed, autopsy rules out conditions such as vasculitis, intracranial atherosclerosis, and aneurysmal subarachnoid hemorrhage, which can also manifest with headache and stroke.</td>
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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; RCVS, reversible cerebral vasoconstriction syndromes.

\textsuperscript{a}From Calabrese et al.\textsuperscript{7}
Synonyms or Included Disorders

- Isolated benign cerebral vasculitis or angiopathy
- Call-Fleming syndrome
- CNS pseudovasculitis
- Benign angiopathy of the central nervous system
- Postpartum angiopathy
- Migrainous vasospasm
- Migraine angiitis
- Idiopathic thunderclap headache with reversible vasospasm
- Drug induced cerebral vasculopathy
- Fatal vasospasm in migrainous infarction
Epidemiology

• Females > males (2-10:1)
• Mean age of onset = 45 y.o.
• Incidence unknown -- probably under diagnosed especially purely cephalalgic form
• Up to 60% are “secondary”
Clinical Presentation

- Headache (secondary) - “thunderclap variety”, peaks within one minute and very intense
  - Only symptom in 75%
  - Multiple over 1-4 week period is almost pathognomonic
  - Usually posterior and bilateral
  - Nausea/vomiting, photophobia, phonophobia

- Focal neurologic deficits and seizures in minority of patients
Complications

• Localized cortical SAH (20-25%)
• Ischemic or hemorrhagic stroke (5-10%)
• PRES
• Permanent sequelae of a usually benign entity
Pathophysiology

• Proposed mechanism: transient disturbance of cerebral arterial vascular tone in segmental and multifocal fashion
  – Leads to various areas of constriction and/or dilatation
  – Either idiopathic (primary) or secondary (25-60%)
Secondary Causes

- Vasoactive sympathomimetic or serotoninergic substances
  - Selective serotonic uptake inhibitors, alpha-sympathomimetics (nasal decongestants), some diet pills
  - Illicit drugs: cannabis, cocaine, ecstasy

- Postpartum state
  - Usually 1st week postpartum after normal delivery
  - 50-70% associated with vasoconstrictors used to treat postpartum hemorrhage or inhibit lactation

- Other causes: hypercalcemia, pheochromocytoma, exercise, and sexual intercourse
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<tr>
<th>Vasoactive substances</th>
<th>Predisposing conditions</th>
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<tbody>
<tr>
<td>Recreational drugs: Cannabis, cocaine, ecstasy, amphetamines, LSD, binge drinking</td>
<td>Pregnancy</td>
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<tr>
<td>Sympathomimetics, nasal decongestants: ephedrine, pseudoephedrine</td>
<td>Eclampsia, preeclampsia</td>
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<td>Serotonergic drugs: selective serotonin reuptake inhibitors, triptans</td>
<td>Neoplasia: phaeochromocytoma, bronchial carcinoid, glomus tumour</td>
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<td>Immunosuppressants: tacrolimus, cyclophosphamide</td>
<td>Neurosurgery, head injury</td>
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<td>Nicotine patches</td>
<td>Hypercalcaemia</td>
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<td>Herbal medications: ginseng</td>
<td>Porphyria</td>
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<tr>
<td>Blood products: erythropoietin, immunoglobulin, red cell transfusion</td>
<td>Intracerebral haemorrhage, subarachnoid haemorrhage</td>
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</table>
Differential Diagnosis

• Aneurysmal subarachnoid hemorrhage
  – Correlates with site and severity of vasospasm
  – Rare isolated to convexity

• Cerebral vasculitis, particularly PACNS (Primary angiitis of the central nervous system)
  – More insidious, gradually progressive headache
  – Most have MRI abnormalities: multiple, small infarcts
  – CSF is markedly abnormal
  – Preferentially affects small-to-medium arteries whereas RCVS affects medium-to-large arteries
More DDx for Thunderclap Headache

- Other intracranial hemorrhages (cerebellar and interventricular)
- Cervical and intracranial arterial dissections
- Intracranial venous thrombosis
- Giant cell arteritis
- Pituitary apoplexy
- Non-vascular disorders: acute sinusitis, meningitis and CSF hypotension
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<tr>
<th></th>
<th>RCVS</th>
<th>Cervical artery dissection</th>
<th>PACNS</th>
<th>SAH</th>
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<td><strong>History</strong></td>
<td>Sudden onset headache, often thunderclap</td>
<td>Sudden or subacute, can have thunderclap features</td>
<td>Insidious, constant, progressive, dull headache</td>
<td>Sudden onset headache, often thunderclap</td>
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<tr>
<td></td>
<td>More common in females</td>
<td>No sex predilection</td>
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<td></td>
<td>Age 20–50 years old</td>
<td>Age less than 50 years old</td>
<td>Age 40–60 years old</td>
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<td><strong>Risk factors</strong></td>
<td>Drugs, pregnancy, tumours, neuro injury, idiopathic</td>
<td>Atherosclerosis, cervical trauma, connective tissue disease. Can be idiopathic</td>
<td>Family history Known cerebral aneurysm</td>
<td></td>
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<tr>
<td><strong>Examination</strong></td>
<td>Presence or absence of neurological deficit</td>
<td>Presence or absence of neurological deficit. Important to rule out in younger patients.</td>
<td>Presence or absence of neurological deficit, 5% spinal involvement</td>
<td>Depends on severity of haemorrhage</td>
</tr>
<tr>
<td><strong>CT brain</strong></td>
<td>Majority normal Cortical SAH, ICH</td>
<td>Normal in the absence of cerebral infarct (60%); crescentic intramural haematoma on CTA</td>
<td>Majority abnormal—diffuse, multiple small infarcts</td>
<td>Majority abnormal. SAH, cerebral oedema, hydrocephalus</td>
</tr>
<tr>
<td><strong>CSF studies</strong></td>
<td>Majority normal</td>
<td>Normal</td>
<td>Majority abnormal—raised protein, cell count</td>
<td>Abnormal—xanthochromias, raised red cell count</td>
</tr>
<tr>
<td><strong>MRI brain</strong></td>
<td>Majority normal</td>
<td>MRA may reveal intramural haematoma as well as demonstrate flow abnormalities. More sensitive than CT or early infarction</td>
<td>Nonspecific changes Multifocal, cortical or subcortical infarcts, diffuse white matter changes, or leptomeningeal enhancement</td>
<td>Areas of infarct corresponding to vascular territory involved</td>
</tr>
<tr>
<td><strong>Cerebral angiography</strong></td>
<td>Considered gold standard. Useful in recurrent TCH Diffuse segmental stenosis—medium, large arteries</td>
<td>Long-segmental stenosis, intimal flaps, arterial pseudoaneurysm</td>
<td>Unable to visualise changes in small arteries</td>
<td>Aneurysm, arteriovenous malformation Vasospasm (not multifocal) at Day 4</td>
</tr>
<tr>
<td><strong>CNS biopsy</strong></td>
<td>Not indicated</td>
<td>Gold standard. Skip, segmental vascular lesions</td>
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RCVS and PRES

- Overlap: about 10% of cases of RCVS are associated with PRES, regardless of cause
- Share similar clinical features
- PRES has characteristic findings on MRI
  - Symmetrical white matter edema in posterior cerebral hemispheres, particularly parieto-occipital regions
  - Hypo- or iso-intense on DWI and hyperintense on ADC map distinguishes it from stroke in most patients
Imaging

• Imaging plays a vital role as the condition is defined in part by the reversibility of the cerebral vasoconstriction

• Although rarely used, catheter cerebral angiography is considered the “gold standard”
Non-contrast CT

• In uncomplicated RCVS: usually normal
• May show cortical SAH or intracebral hemorrhage in complicated cases
• Should be followed by lumbar puncture if normal to rule out SAH and inflammatory conditions like infection or cerebral vasculitis
MRI

- Usually normal
- May show evidence of infarctions, especially in “watershed” zones
- May look like PRES
- Parenchymal hemorrhages or cortical SAH
Axial FLAIR & DWI (top & middle left) show high signal from right cerebellar infarct. MRA (bottom left) suggests vasculitis. Lateral (center) ICA injection & frontal (right) vertebral artery injection show typical “sausage” beading of RVCS.
Post partum patient shows convexity SAH on FLAIR (left), small bleed on T2* (center) & beading of arteries (right) especially in the right posterior cerebral artery.
CTA/MRA/Angiography

• Alternating areas of constriction and dilatation – a.k.a. “beading” -- in several vascular territories
• May be seen in large-to-medium-sized arteries of anterior or posterior circulation
• Abnormalities may be absent early but show up on repeat imaging, believed to start distally and move centripetally
• NOT specific for RCVS
• Resolution within 3 months is most specific for RCVS
Fig 3. MR angiography confirmed multiple segmental narrowing of the cerebral arteries [A and B] compatible with RCVS. Comparative MRA during the follow-up [C and D] demonstrated resolution of cerebral arterial vasoconstriction.
Post partum patient shows acute right parietal hematoma on CT (left), SAH on FLAIR (center left), PRES-like cerebellar findings (center right) & beading/thinning of arteries on MRA (right).
Prognosis

- Highly dependent on the occurrence of stroke (6-9%)
- Otherwise, by definition, most resolve completely without any sequelae
Treatment

• Symptomatic (pain, seizures, blood pressure control)
• Trigger avoidance (either activity or vasoactive substances)
• Observation
• Calcium channel blockers
• IV magnesium
• Short-course of steroids?
– TCH contain many potential difficulties. Clinicians should consider the imaging of cerebral arteries, even if computed tomography scan and lumbar puncture are normal in TCH. Potential precipitating factors and triggers should also be known and avoided.
Sources


