Reversible cerebral vasoconstriction syndrome (RCVS),

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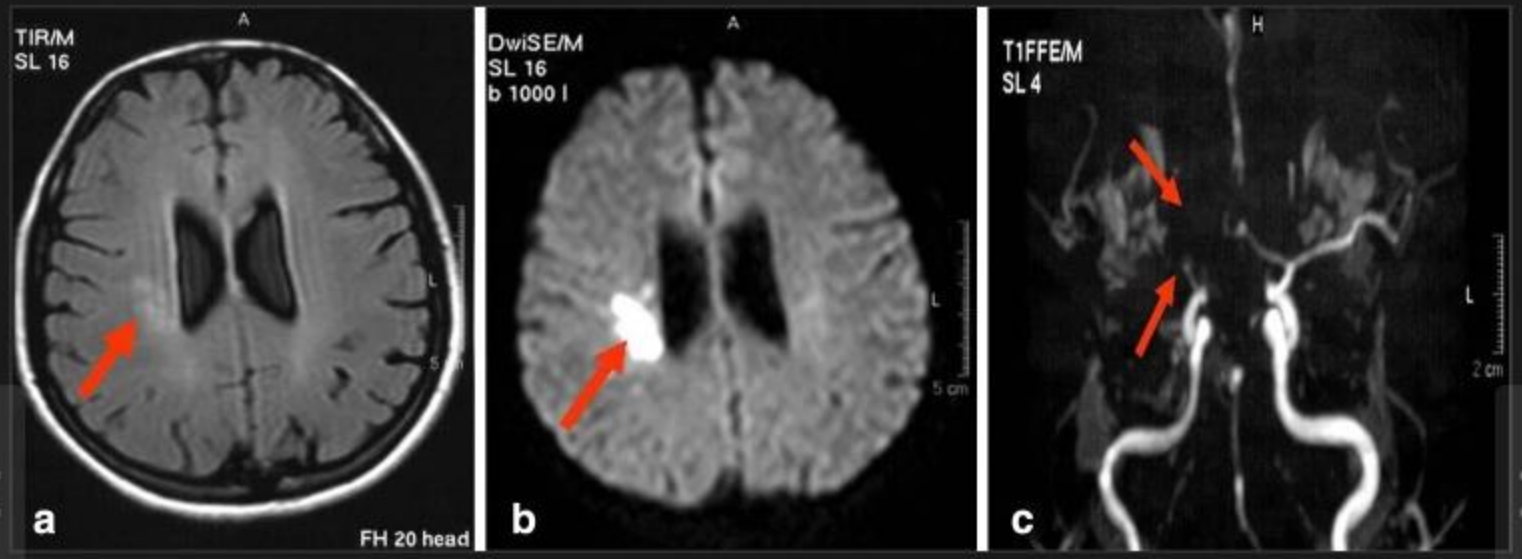
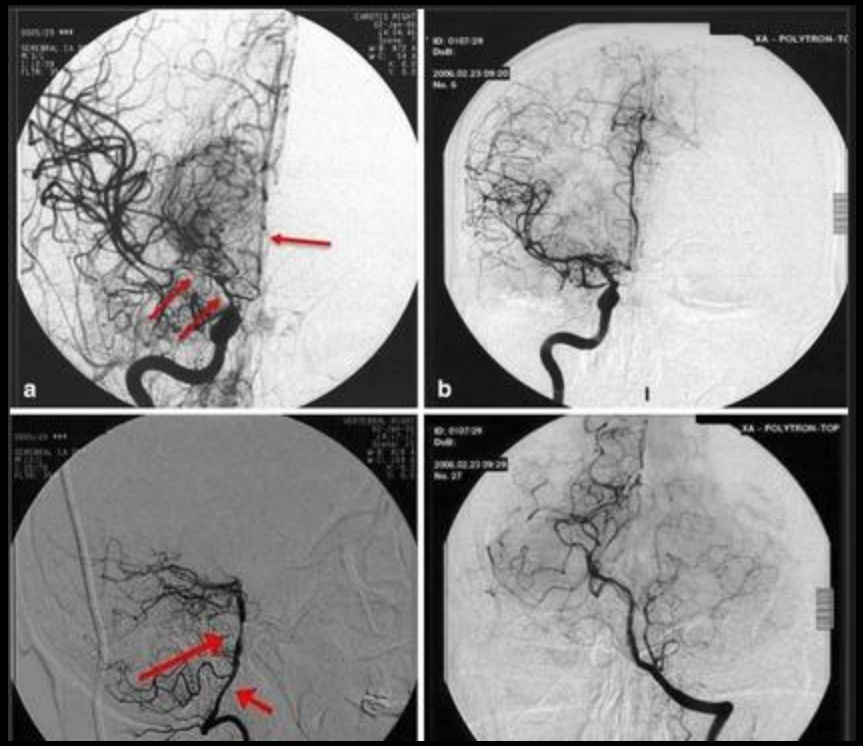
Case

- 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


a
b

- 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[a]

Elements
1. Transfemoral angiography or indirect (CT or MRI) angiography documenting segmental cerebral artery vasoconstriction
2. No evidence for aneurysmal subarachnoid hemorrhage
3. Normal or near-normal cerebrospinal fluid analysis (protein level <80 mg/dL, white blood cell count <10/μL, normal glucose level)
4. Severe, acute headache, with or without additional neurological signs or symptoms
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.

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; RCVS, reversible cerebral vasoconstriction syndromes.
[a] From Calabrese et al.[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 diagnozed especially purely cepahalalgic 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

Table 2: Secondary precipitants of RCVS [9–12].

Vasoactive substances	Predisposing conditions
Recreational drugs: *Cannabis*, cocaine, ecstasy, amphetamines, LSD, binge drinking	Pregnancy
Sympathomimetics, nasal decongestants: ephedrine, pseudoephedrine	Eclampsia, preeclampsia
Serotonergic drugs: selective serotonin reuptake inhibitors, triptans	Neoplasia: phaeochromocytoma, bronchial carcinoid, glomus tumour
Immunosuppressants: tacrolimus, cyclophosphamide	Neurosurgery, head injury
Nicotine patches	Hypercalcaemia
Herbal medications: ginseng	Porphyria
Blood products: erythropoietin, immunoglobulin, red cell transfusion	Intracerebral haemorrhage, subarachnoid haemorrhage

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

Table 3: Distinguishing features of RCVS, cervical artery dissection, PACNS and SAH [9].

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

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

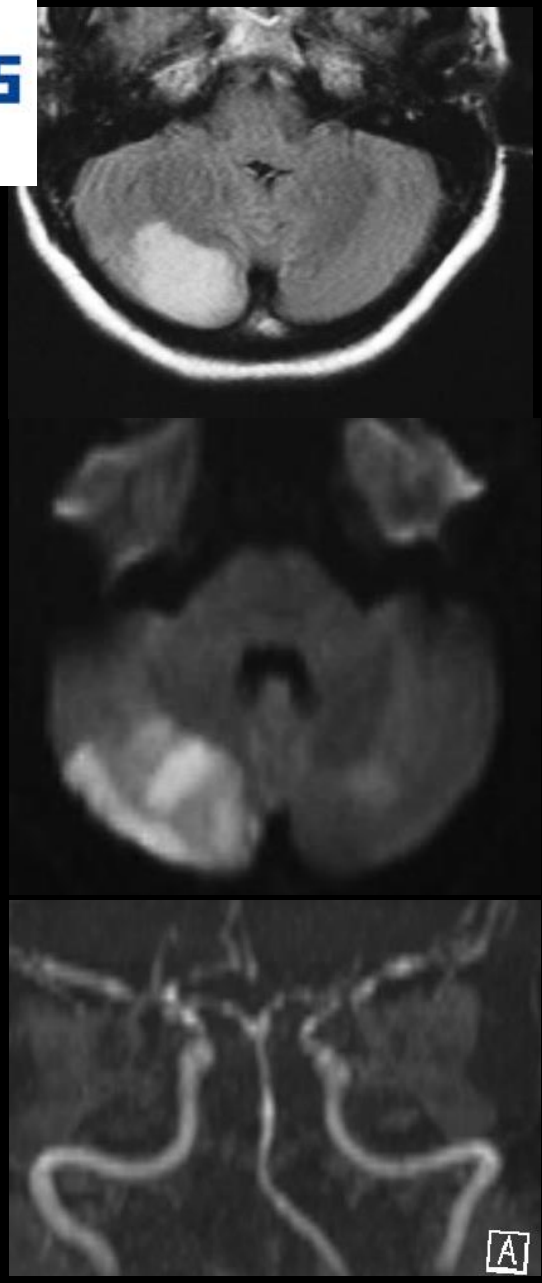
- Imaging plays a vital role as the condition is defined in part by the reversibility of the cerebral vasoconstriction
- Although rarely used, catheter cerebral angiography is considered the “gold standard”

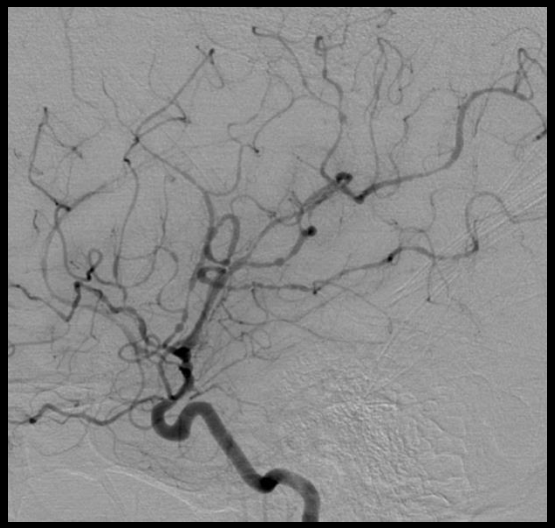
Non-contrast CT

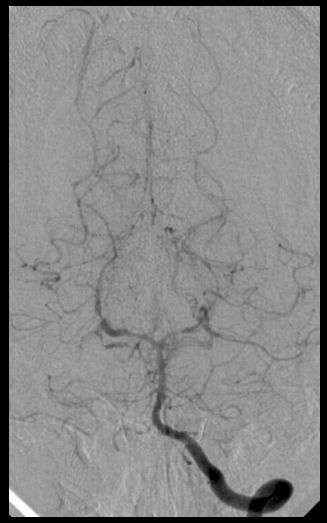
- In uncomplicated RCVS: usually normal
- May show cortical SAH or intracebral hemorrhage in complicated cases
- Should be followed by lumbar puncture if normal to rule out SAH and inflammatory conditions like infection or cerebral vasculitis

MRI

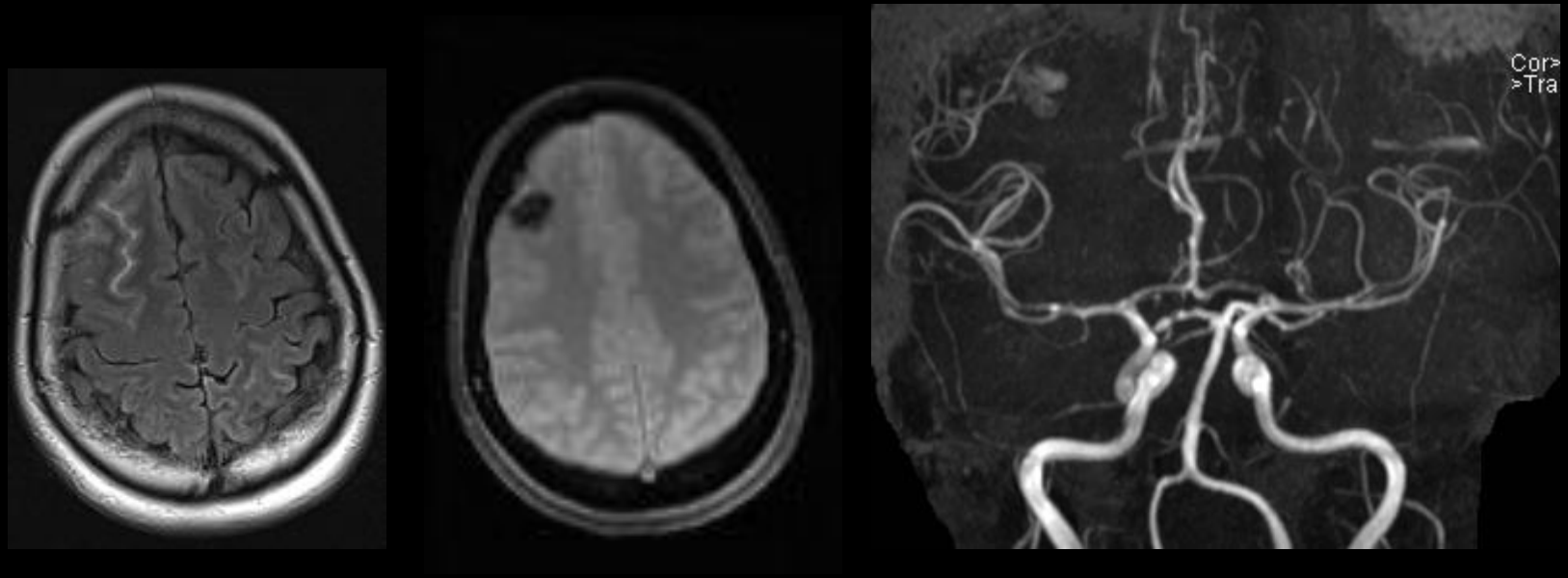
- Usually normal
- May show evidence of infarctions, especially in “watershed” zones
- May look like PRES
- Parenchymal hemorrhages or cortical SAH







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 distallyand move centripetally
- NOT specific for RCVS
- Resolution within 3 months is most specific for RCVS

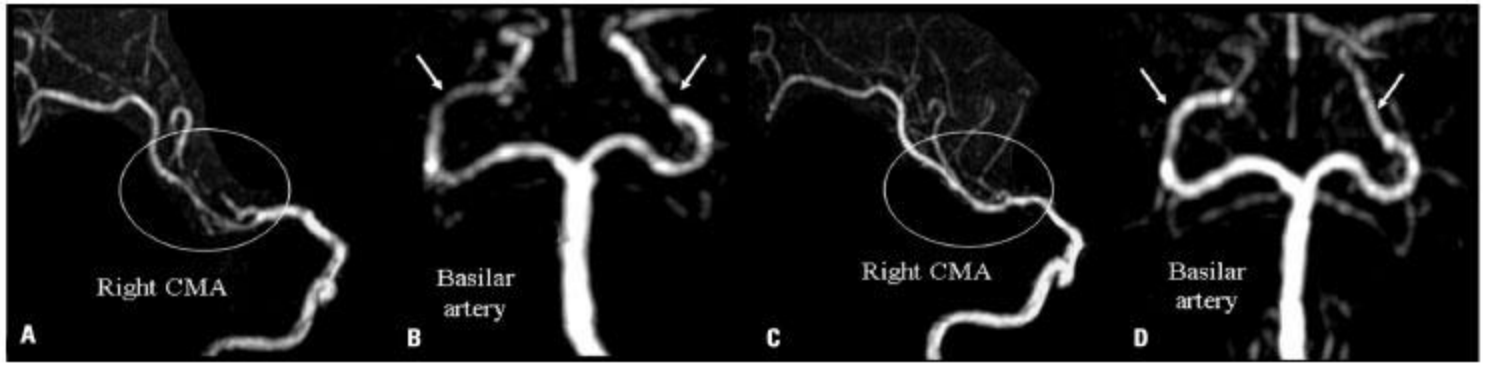
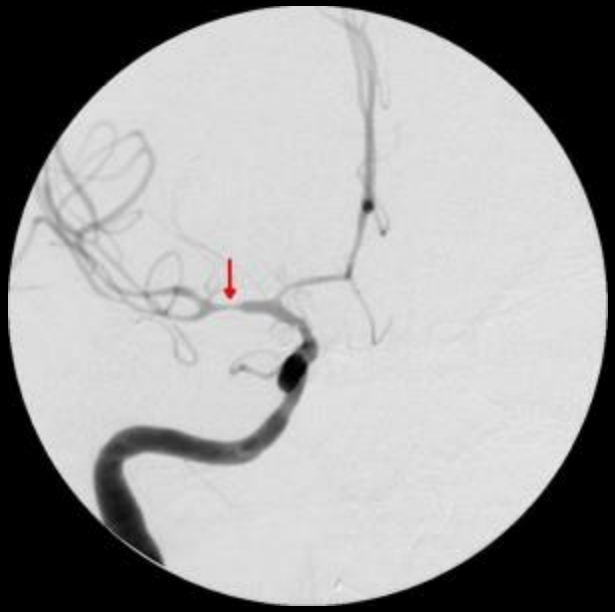
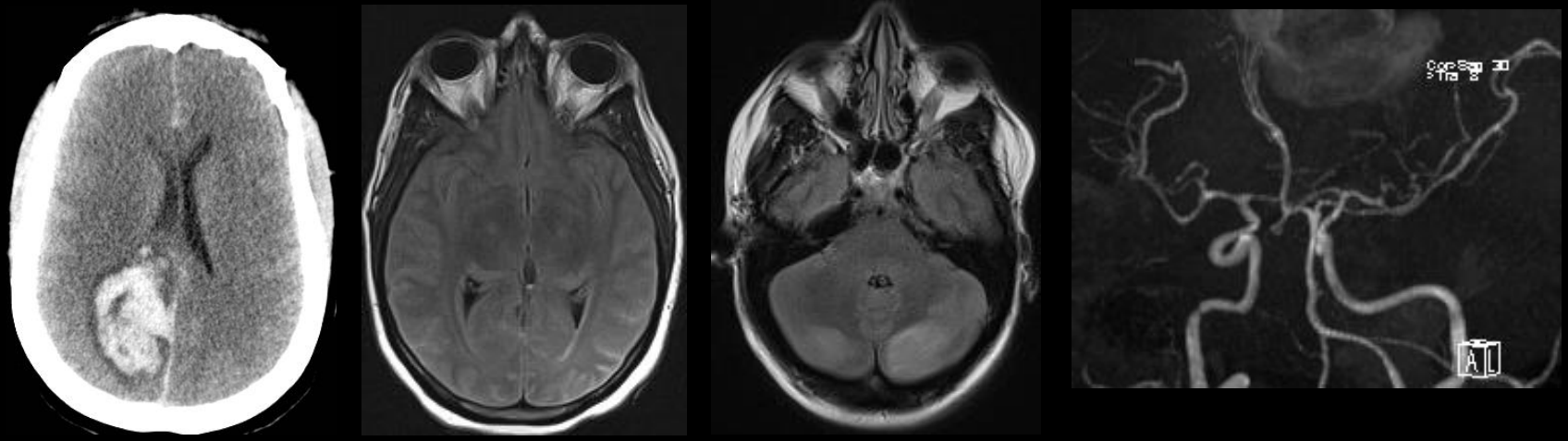


Fig 3. MR angiography confirmed multiple segmental narrowing of the cerebral arteries [A and B] compatible with RCVS. Comparative MRA during the follow-up [C and D] demonstrated resolution of cerebral arterial vasoconstriction.





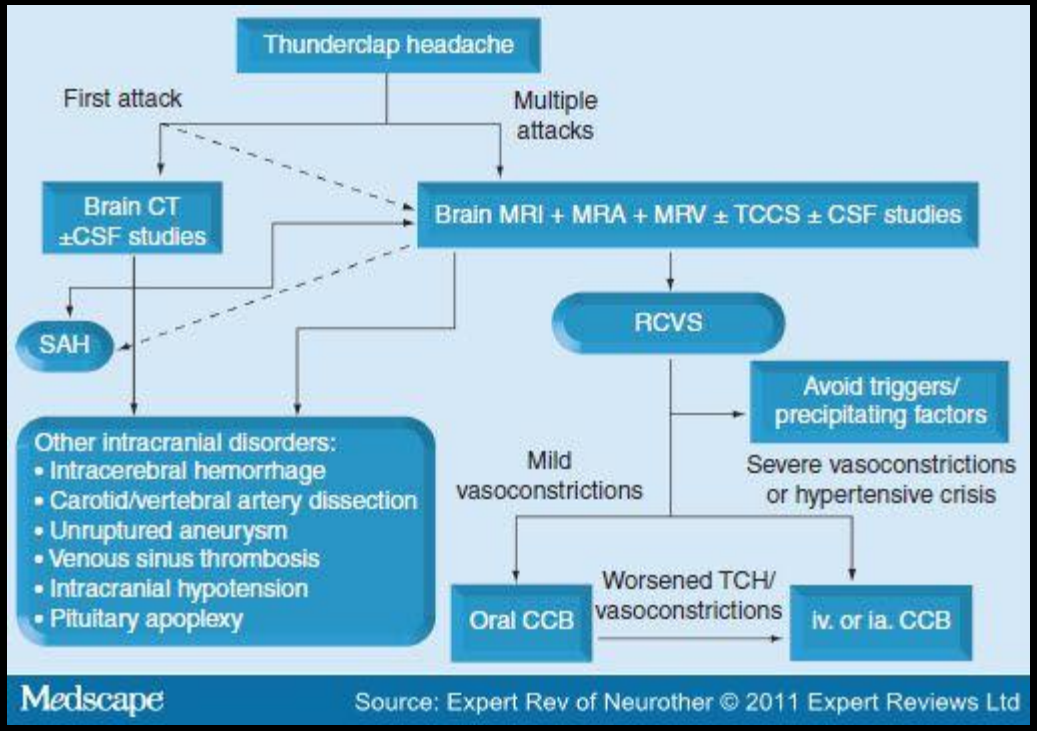
Post partum patient shows acute right parietal hematoma on CT (left), SAH on FLAIR (center left), PRES-like cerebellar findings (center right) & beading/thinning of arteries on MRA (right).

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?


Thunderclap headache
First attack
Multiple attacks
Brain CT ±CSF studies
Brain MRI + MRA + MRV ± TCCS ± CSF studies
SAH
RCVS
Avoid triggers/ precipitating factors
Other intracranial disorders:
• Intracerebral hemorrhage
• Carotid/vertebral artery dissection
• Unruptured aneurysm
• Venous sinus thrombosis
• Intracranial hypotension
• Pituitary apoplexy
Mild vasoconstrictions
Severe vasoconstrictions or hypertensive crisis
Worsened TCH/ vasoconstrictions
Oral CCB
iv. or ia. CCB
Medscape
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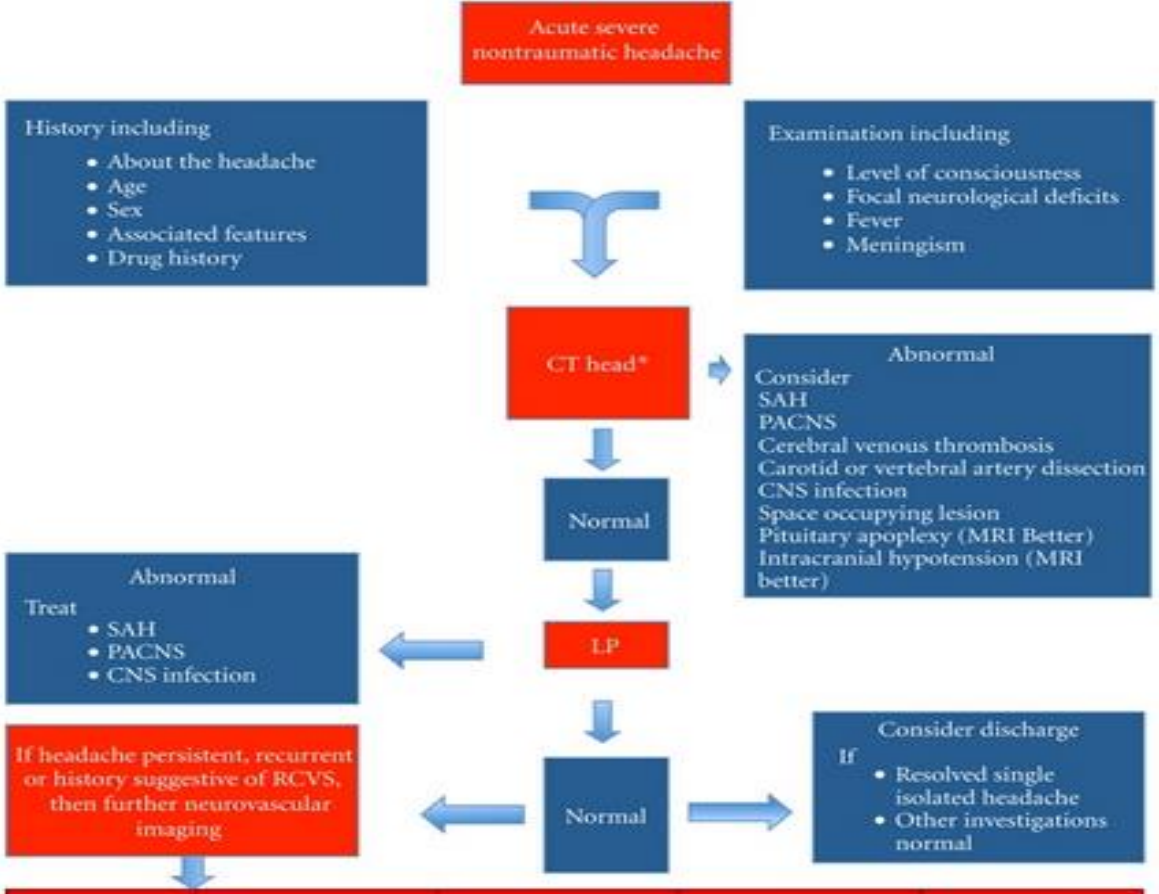
- TCH contain many potential difficulties. Clinicians should consider the imaging of cerebral arteries, even if computed tomography scan and lumbar puncture are normal in TCH. Potential precipitating factors and triggers should also be known and avoided.



	CTA	MRI/A	DSA	TCD
Advantages	Less time consuming than DSA or MRA Readily available Not affected by flow-related inhomogeneites (MRA)	Better brain parenchyma visualisation Better to diagnose: PRES Pituitary apoplexy Small infarcts/haemorrhage Intracranial hypotension	Diagnostic gold standard Best small vessel imaging Dynamic flow assessment	Non-invasive No contrast Repeatable
Disadvantages	Poor visualization of small vessels Ionizing radiation Less information on flow velocity and flow direction Contrast-related complications Different imaging required for specific conditions	Availability Speed Claustrophobia General anaesthetic Contrast-related complications Potentially affected by flow-related inhomogeneites	Invasive Neurological complictions Cannulation site complications No soft tissue imaging Does not differentiate between PACNS and RCVS Ionizing radiation Contrast-related complications	Only assesses large vessels Availability varies Operator dependence Need same operator each time

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