Acute Neurologic Syndromes

tPA?

NOT!

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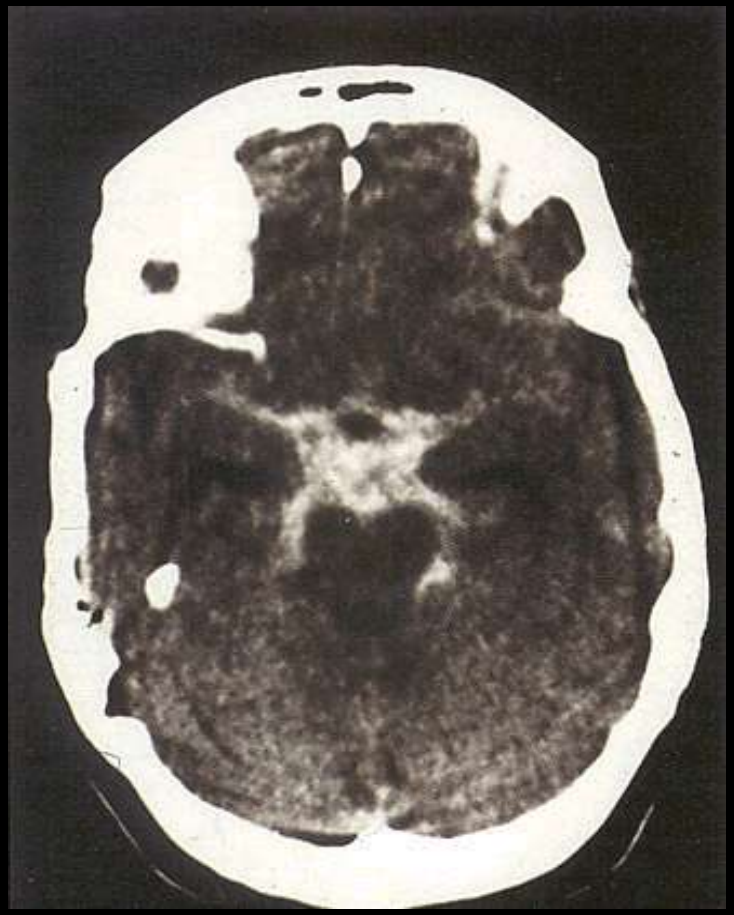
Intravenous t-PA Exclusion Criteria

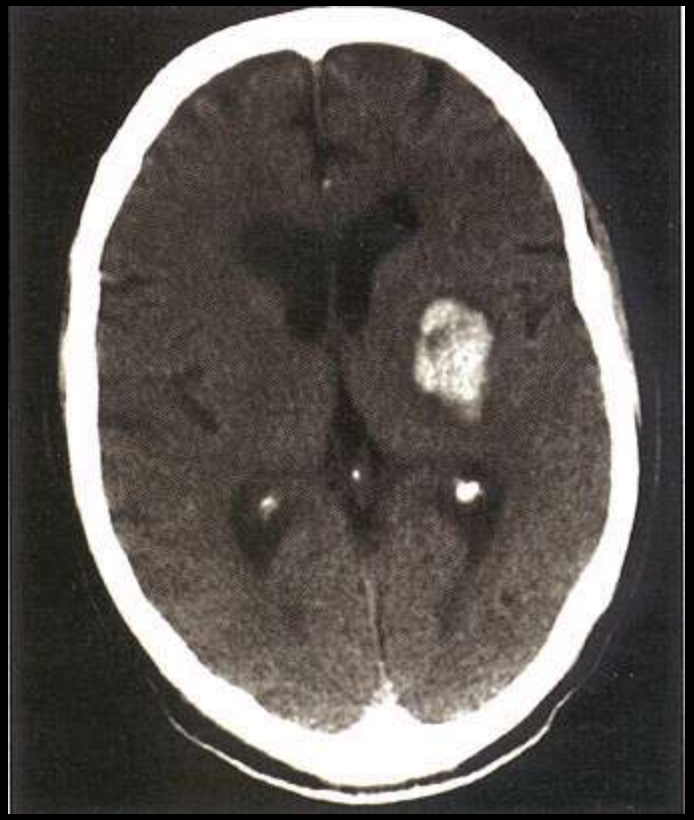
- Time of symptom onset > 180 (or qualified 270) minutes before treatment would begin.
- Evidence of intracranial hemorrhage on pretreatment computer tomography (CT).
- Clinical presentation suggestive of subarachnoid hemorrhage
- Only minor or rapidly resolving stroke symptoms.
- Within 3 months of any intracranial operations, serious head trauma, or previous stroke.
- Major surgery within last 14 days.
- History of gastrointestinal or urinary tract hemorrhage within 21 days.
- Recent arterial puncture at a noncompressible site.
- Recent lumbar puncture.
- On repeated measurements, systolic blood pressure > 185 mm of mercury or diastolic blood pressure > 110 mm of mercury at the time treatment is to begin, or patient requires aggressive blood pressure treatment

This is the worst headache of my life



Subarachnoid Hemorrhage

65 yo man with headache then collapse with right hemiplegia and initial BP of 240/110



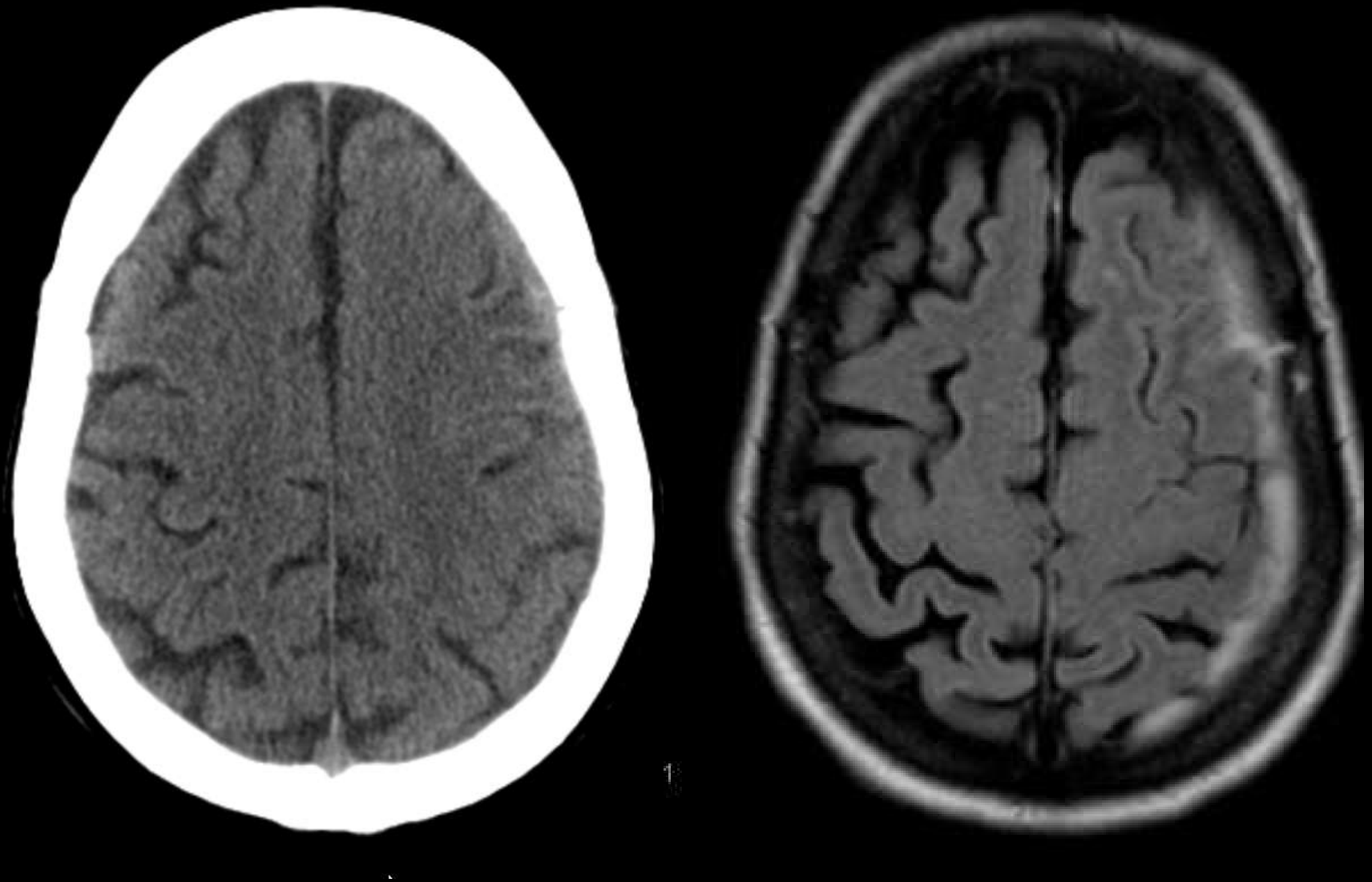
Intracerebral Hemorrhage

CASE #1

- 72 yo old woman with history of atrial fibrillation who present after one hour of progressive aphasia. Exam shows global aphasia but no weakness. Radiologist reports CT negative, all labs negative except INR 2.8

Is she a iv tpa candidate?

Is she an IA tpa candidate?



Subacute Subdural Hematoma

CASE #1
RED FLAGS

72 yo old woman with history of atrial fibrillation who present after one hour of progressive aphasia. Exam shows global aphasia but no weakness. Radiologist reports CT negative, all labs negative except INR 2.8

ALWAYS Look at the scan!!

Acute Ischemic Stroke
Intravenous t-PA Inclusion Criteria

INCLUSION CRITERIA

- Age 18 years or older

- Clinical diagnosis of ischemic stroke causing a measurable neurologic deficit

Objectives

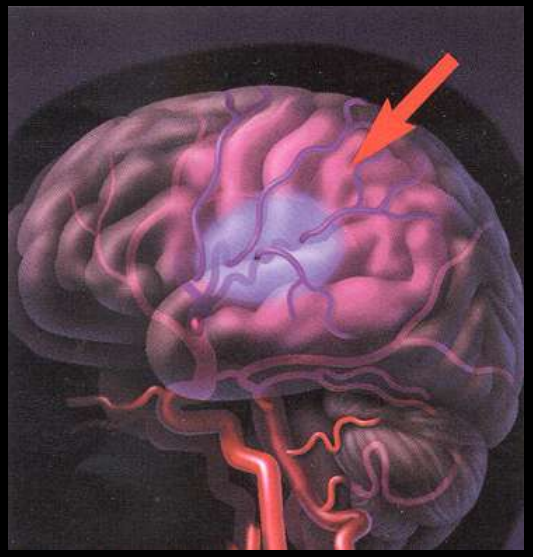
1. Classify common acute stroke syndromes
2. Describe acute non-stroke syndromes including PRES, RCVS, CVT and migraine
3. Distinguish non-stroke neurologic conditions, evaluation and treatment

Disclosures: None

Disclaimer: This is a general clinical pearls talk- there are always exceptions to the rule

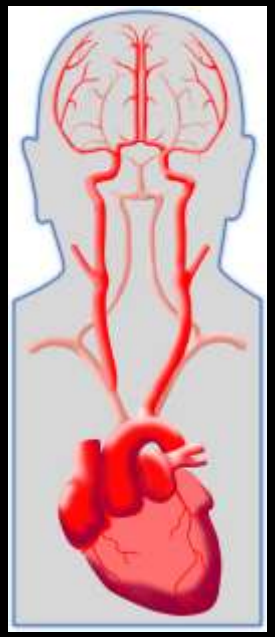
Goal of Therapy in all Neurologic Emergencies

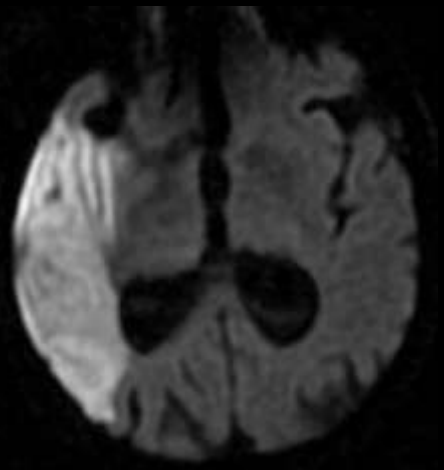
- ACUTE Setting
  - Identify syndrome
  - Take immediate action to reduce disability
  - Minimize Risk
- SUBACUTE setting
  - Understand etiology
  - Prevent second event



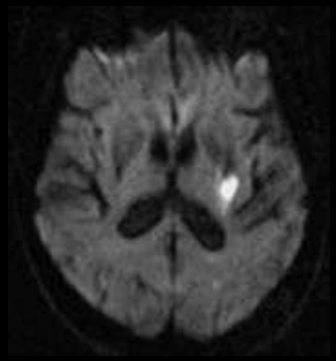
Review of Acute stroke syndromes

- Large artery strokes
  - Right MCA/PCA
  - Right ACA
  - Left MCA/PCA
  - Left ACA
  - Basilar
  - PICA/AICA/SCA (Cerebellar)





- Lacunar syndromes
  - Dysarthria clumsy hand
  - Pure motor
  - Sensorimotor
  - Pure sensory
  - Ataxia hemisensory



Other Acute Non-stroke Syndromes

- High spinal cord lesion (hemorrhage)
- Seizure
- Sudural hematoma (subacute)
- Conversion Disorder
- Unmasking of old deficit (same symptoms, less severe, identified trigger)
- Transient Global anemia
- Hypoglycemia/ Hyperglycemia/Hypocalcemia
- Syncope/presyncope
- Mass lesion
- Radiculopathy/neuropathy
- Multiple sclerosis/ other acute inflammatory disease

Safety of tPA in Stroke Mimics

Table 3. Prevalence and Outcomes of SM Among Patients Treated With IVT Across Different Stroke Registries

Registry	IVT (No.)	SM (No., %)	sICH in SM (No., %)	OE in SM (No., %)	FI in SM (No., %)
Michigan[4]	151	6 (4%)	0	NA	1 (17%)†
Basel[5]	250	7 (3%)	0	0	6 (86%)‡
Houston[6]	512	69 (13%)	0	0	60 (87%)†
Pittsburgh[7]	254	9 (4%)	NA	NA	NA
Phoenix	539	56 (10%)	0	0	54 (96%)†
Overall	1706	147 (9%)	0 (0%)	0 (0%)	121 (83%)
		(95% CI, 7% to 10%)	(95% CI,* 0% to 2.3%)	(95% CI,* 0% to 2.4%)	(95% CI,* 81% to 93%)

SM indicates stroke mimic; IVT, intravenous thrombolysis; sICH, symptomatic intracranial hemorrhage; OE, orolingual edema; FI, functional independence defined as a modified Rankin Scale score of 0 to 1; NA, not available.

*Calculated by the Adjusted Wald method.

†At hospital discharge.

‡At 3 mo.

Of 56 cases

26.5% Conversion Disorder

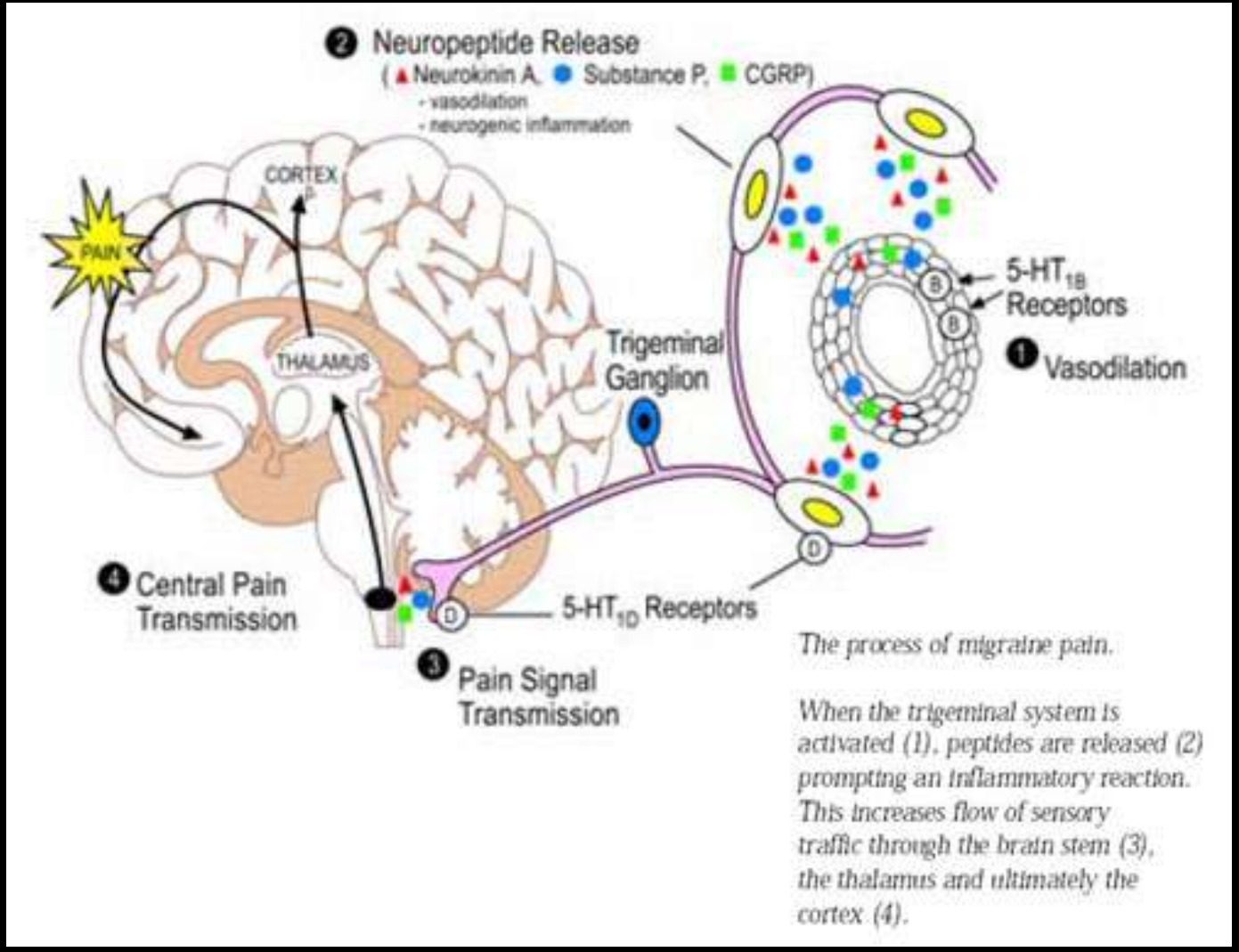
19.5 % Complicated Migraine

19.5% Seizure

Acute Neurologic Syndromes

- Migraine
- Cerebral Venous Thrombosis
- Reversible Cerebral Vasconstriction Syndrome
- Posterior Reversible Encephalopathy Syndrome
- Meningitis with Vasculopathy

Migraine



The process of migraine pain.

When the trigeminal system is activated (1), peptides are released (2) prompting an inflammatory reaction. This increases flow of sensory traffic through the brain stem (3), the thalamus and ultimately the cortex (4).

Features of Stroke

- Sudden onset; maximal on onset and persistent
  - Exceptions: ie stuttering lacunar
- Respects vascular territories (identifiable syndrome)
- Headache is absent or minor feature (simultaneous)
- Usually have vascular risk factors (previously recognized or unrecognized)

Features of Migraine

- Marching progression
- Time course variable
- Numbness and dizziness are prominent features
- May be associated with visual aura, nausea or confusion (does not respect vascular territories)
- Headache often follows neurologic symptoms
- History of migraine (may be remote)

Case #2

- 28 yo male presents with T 38.1 severe headache, nausea and vomiting and right sided numbness. Thirty minutes after arrival to the ED he develops a nonfluent aphasia.
- CT is negative
- Tpa?
- LP
  - WBC 231 (98% Lymphs) CSF glucose and protein normal, GS negative

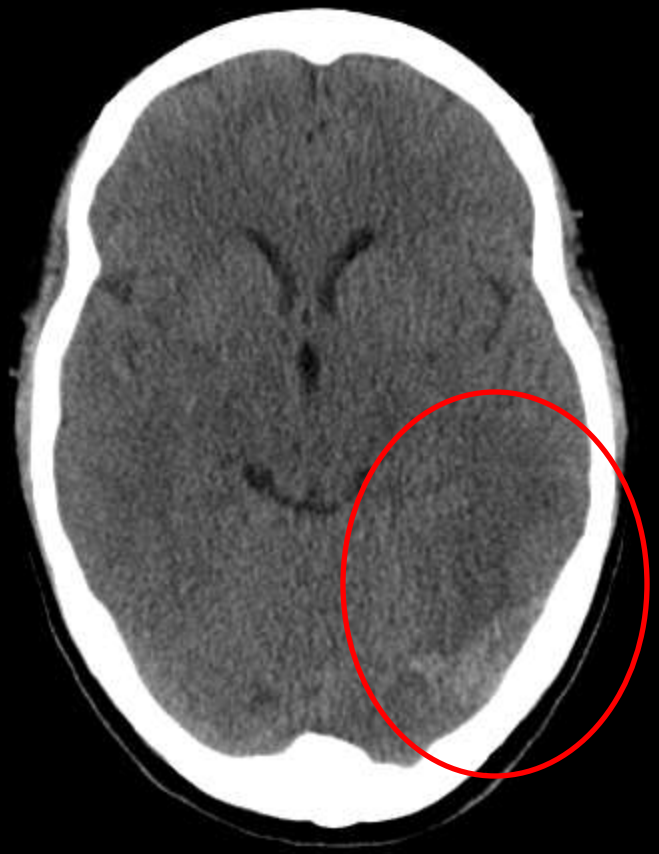
HaNDL
Headache and Neurologic Deficit Lymphocytosis in CSF

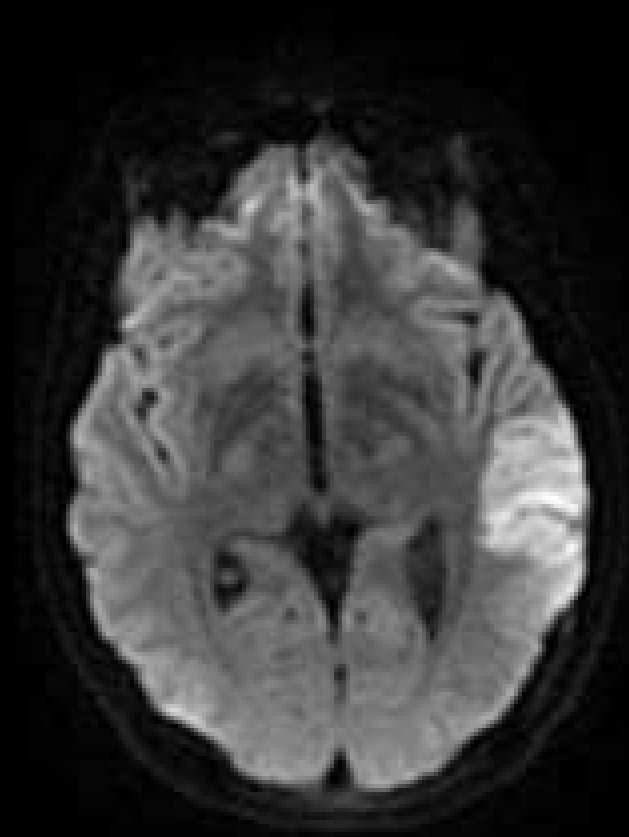
- Also known as Pseudomigraine with temporary neurological symptoms and lymphocytotic pleocytosis (PMP)
- Pathophysiology unknown (infectious or inflammatory)
- Recurrence unlikely after 12 weeks

Case #3

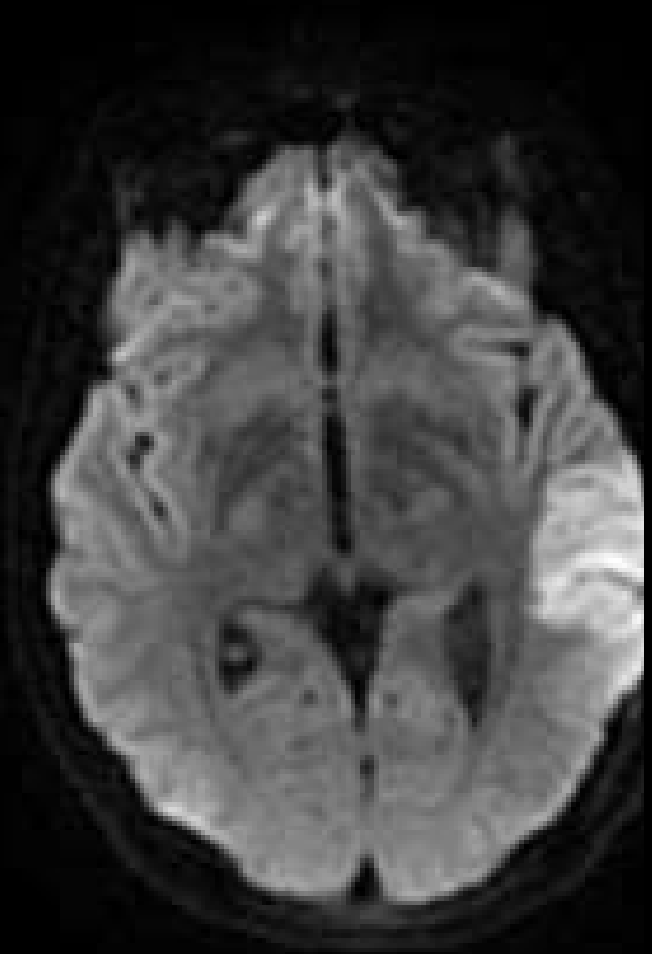
- 52 yo woman with acute onset aphasia. According to her family she is has no vascular risk factors and is generally healthy but suffered from severe diarrhea 10 days ago that resolved except persistent headache. Exam shows fluent aphasia and questionable right visual field cut

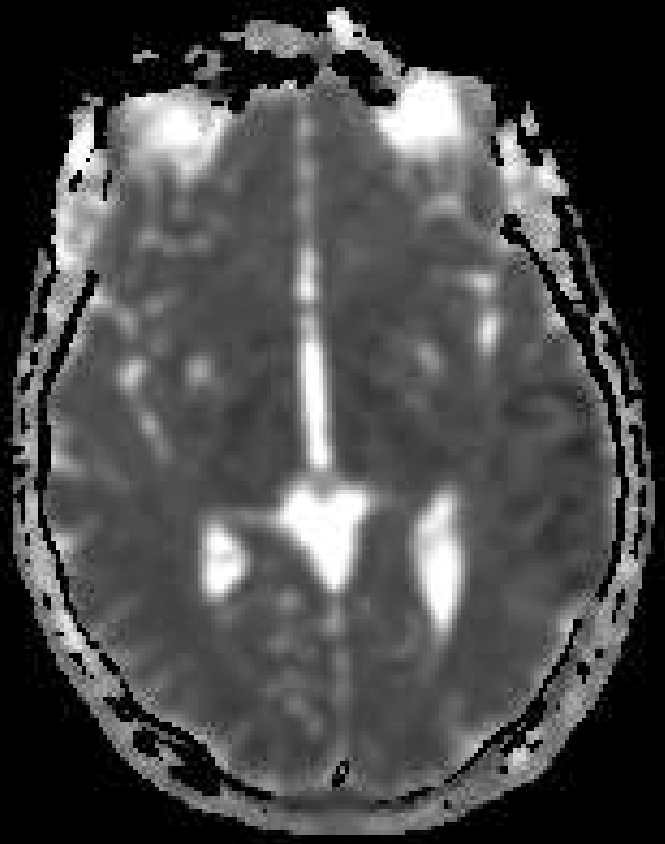
Tpa or not?



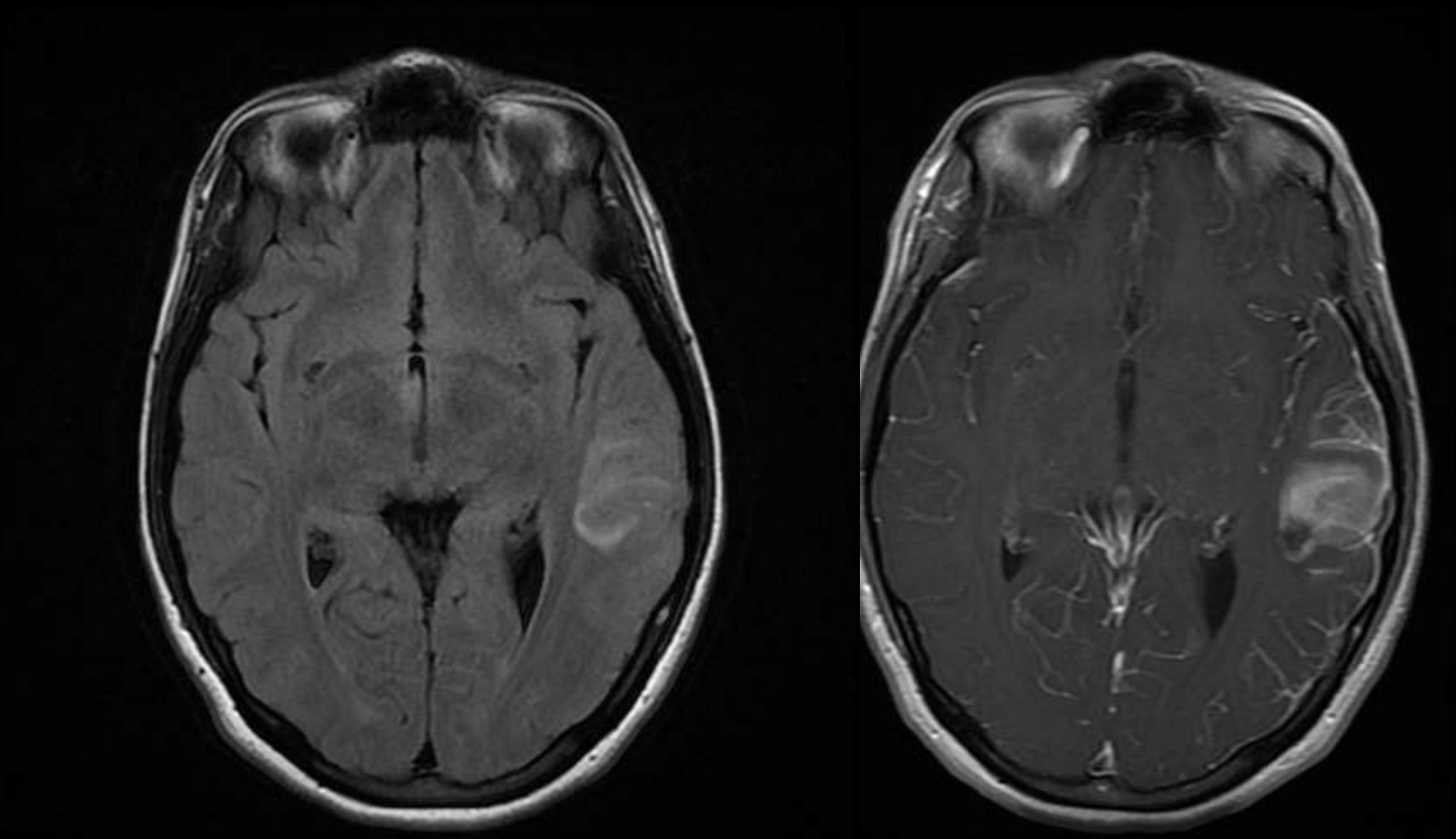


Venous thrombosis

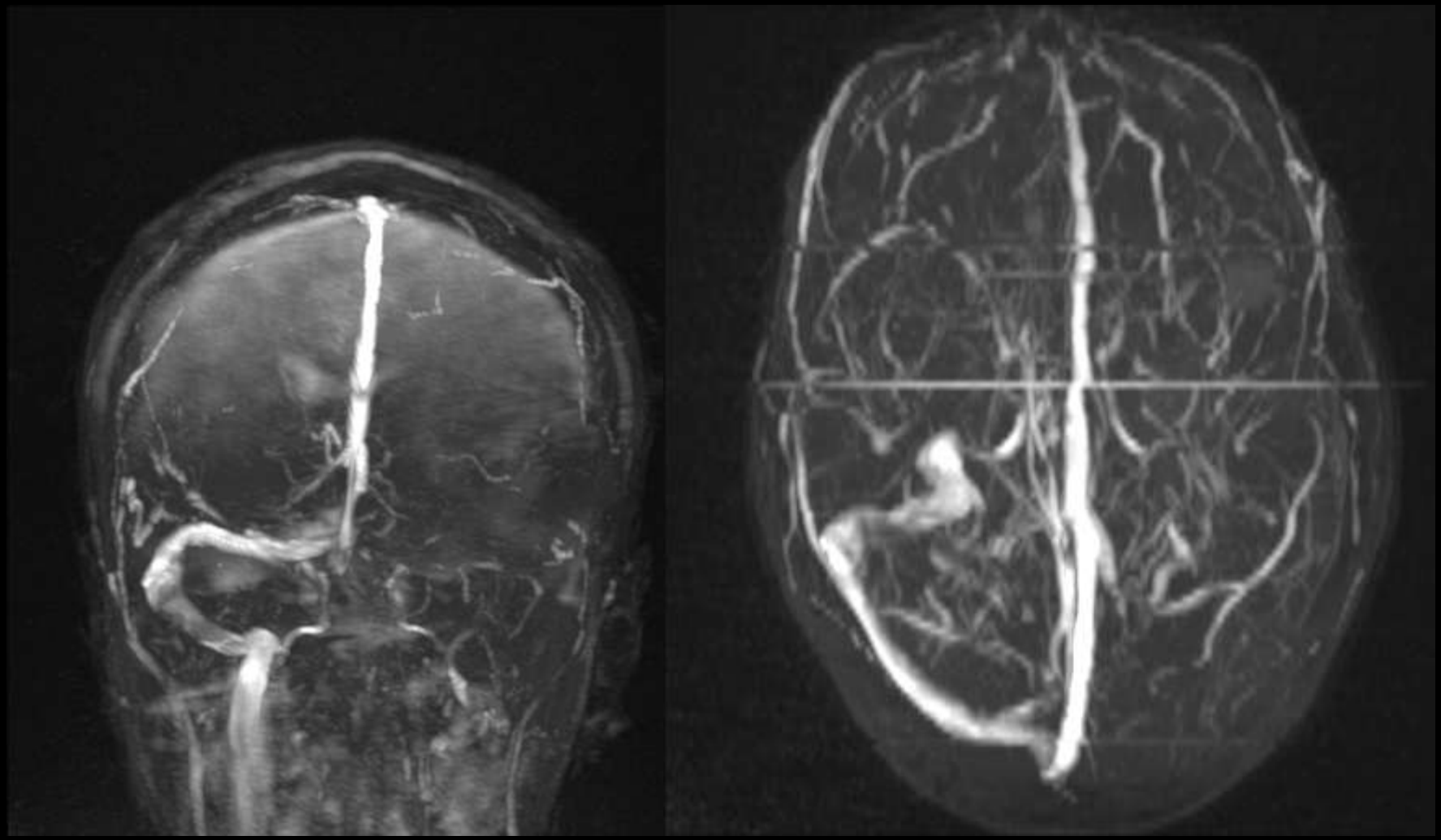




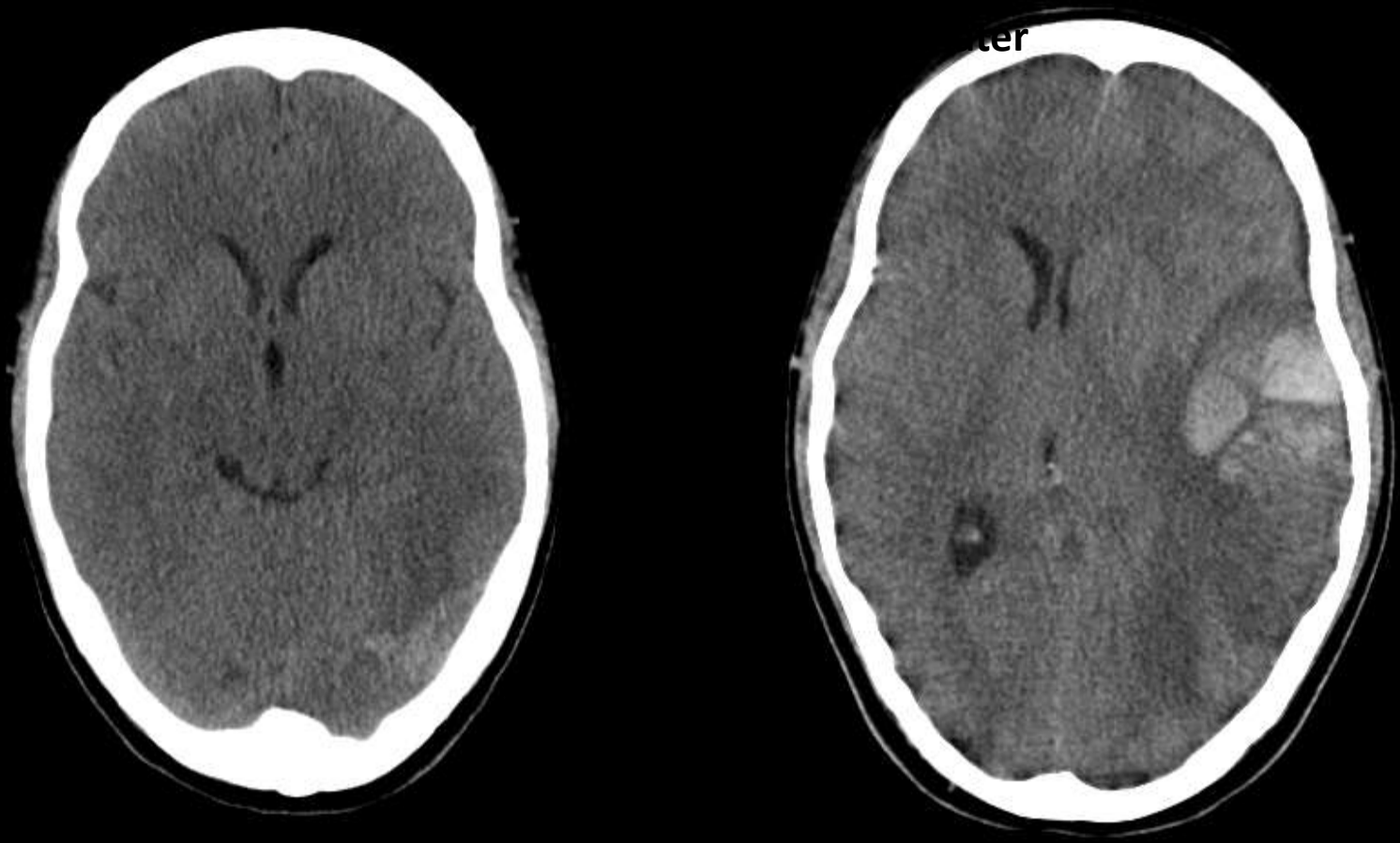
Venous thrombosis misdiagnosed as enhancing tumor



Venous thrombosis

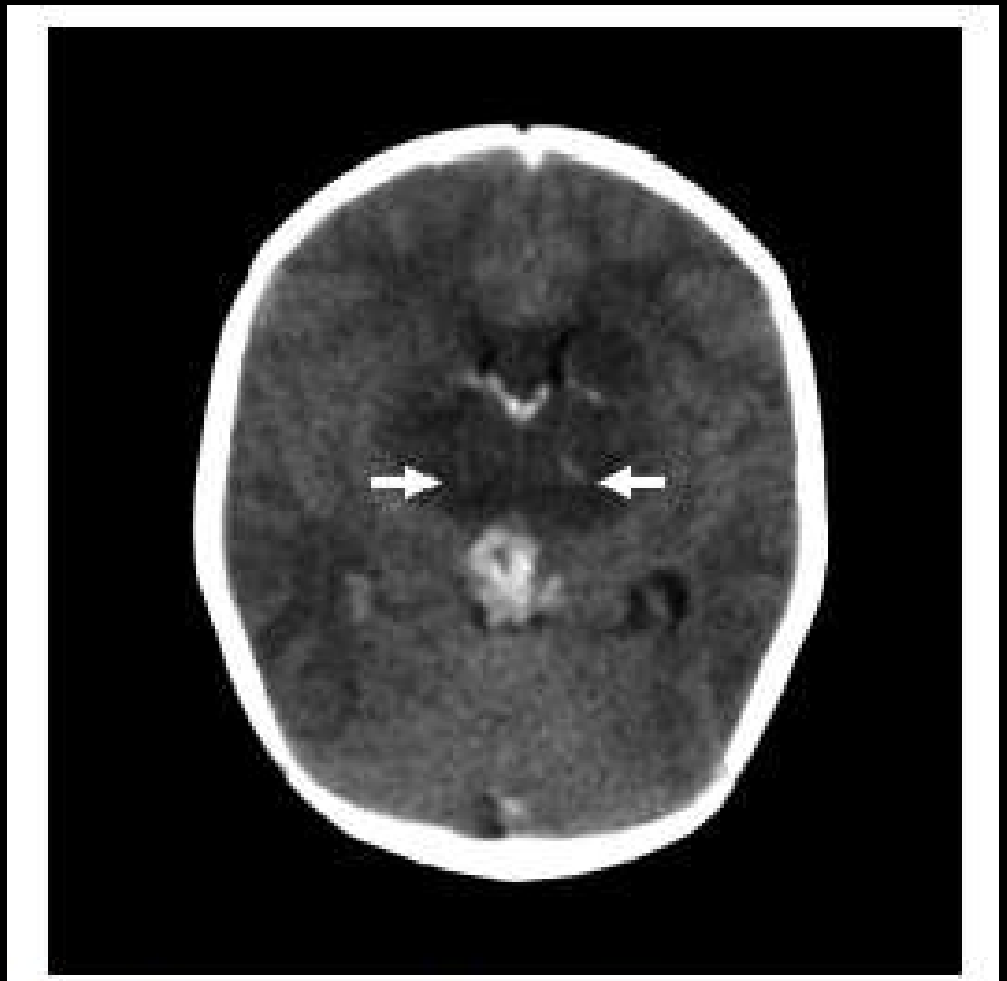


Patient undiagnosed and treated



Decline in LOC but may not develop weakness

Deep Venous thrombosis presents with alteration of consciousness without focal finding



CVT
Age and Sex Distribution

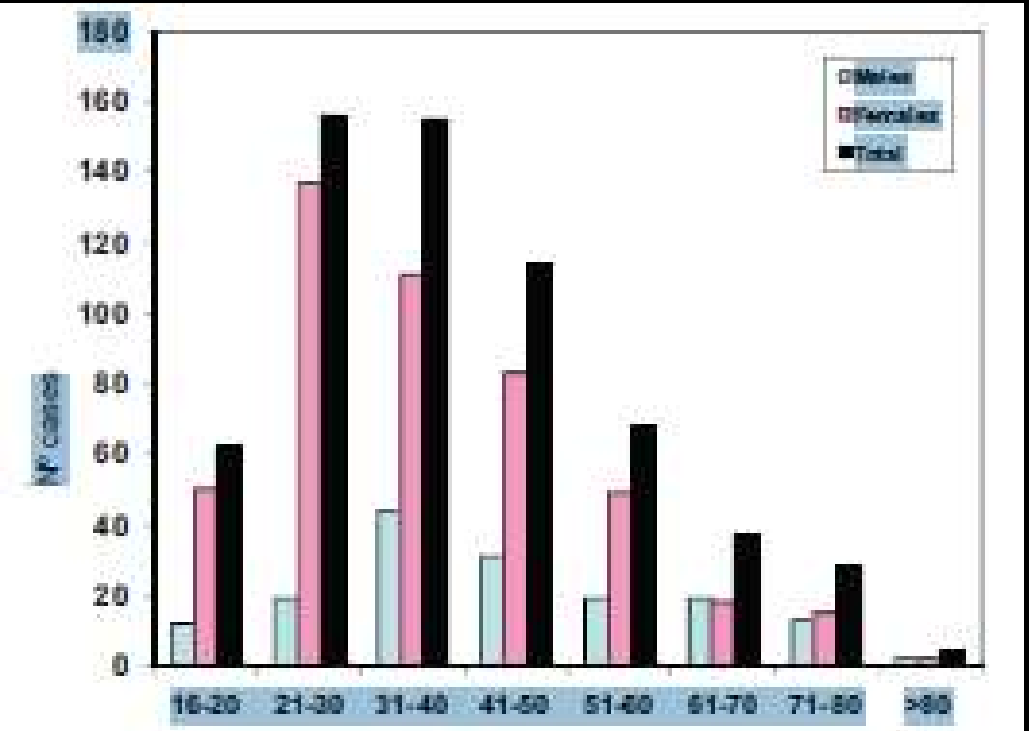
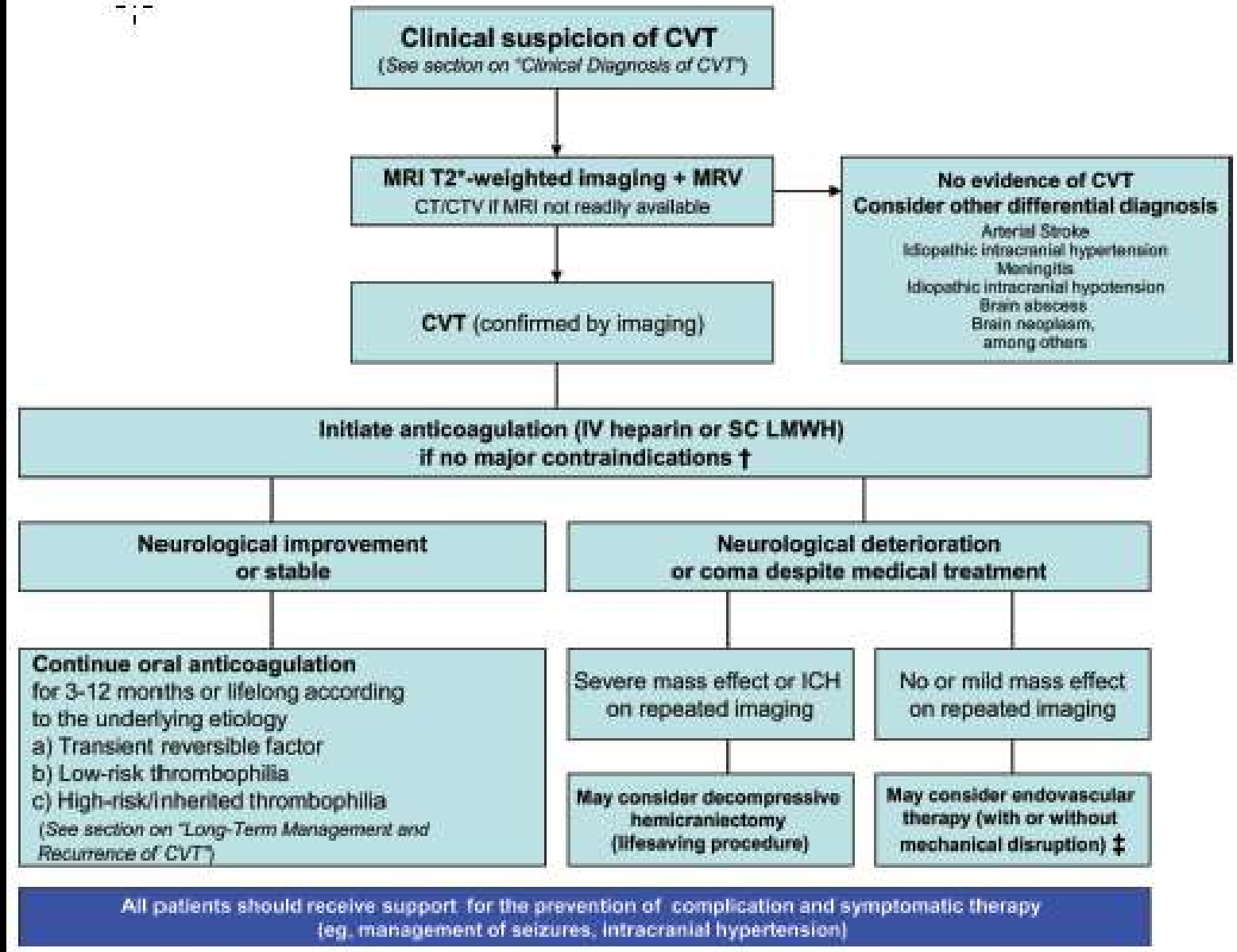


Figure 1. Age and sex distribution of cerebral venous and sinus thrombosis (CVT) in adults. Bars represent the number of patients with CVT for the specific age/sex category. Data provided by Dr Jose Ferro from the International Study on Cerebral Venous and Dural Sinuses Thrombosis.

Predisposing Conditions for Cerebral Venous Thrombosis

- Hypercoaguability (Factor V Leiden, prothrombin mutation, APS, Protein C/S deficiency, hyperhomocystemia)
- OCP and postpartum
- Severe dehydration
- Medications: androgen, danazol, lithium, Vitamin A , IVIG, ectacy, tamoxifen, L-asparaginase
- Cancer
- Perimeningeal infection (mastoidisis, otitis media, sinusitis)
- Intracranial hypotension
- PNH, iron deficiency anemia, nephrotic syndrome, polycythemia, thrombocythemia
- SLE, Behcet, Inflammatory bowel disease, thyroid disease, sarcoidosis

Proposed Algorithm for the Management of CVT

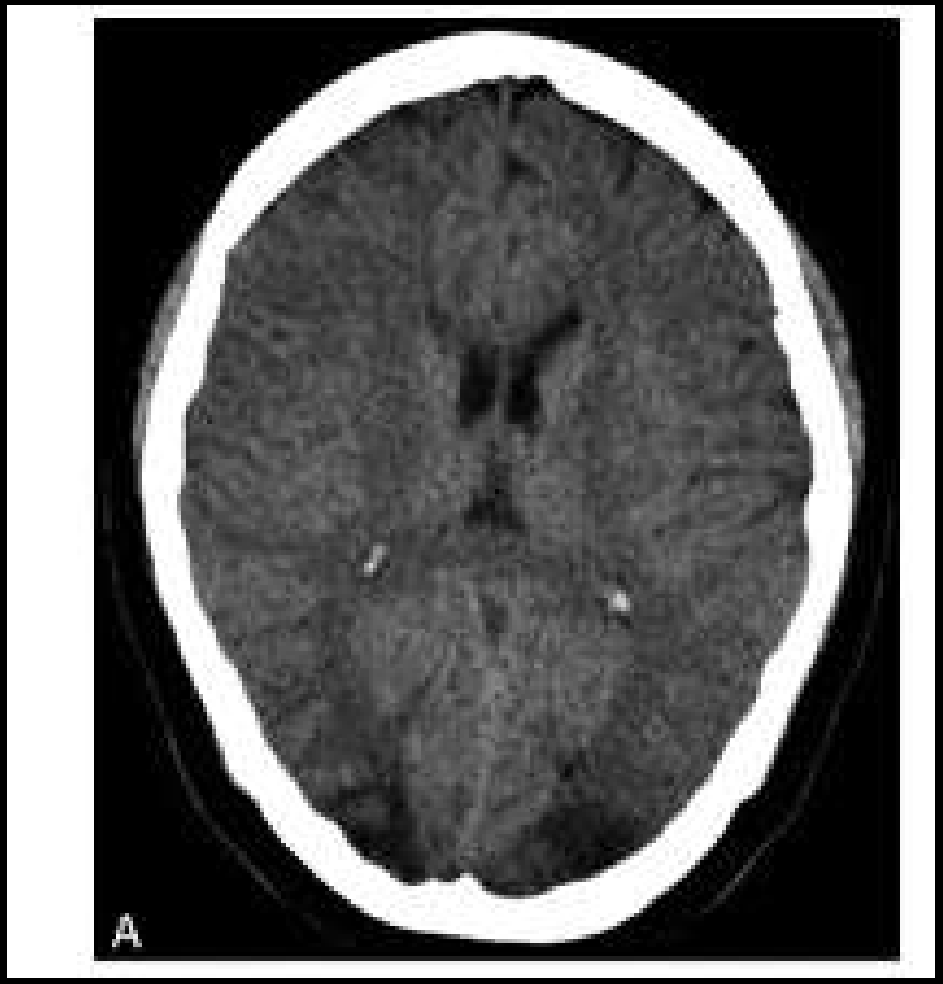


Case #3
Red Flags and Take home

- 52 yo woman with acute onset aphasia. According to her family she is has no vascular risk factors and is generally healthy but suffered from severe diarrhea 10 days ago that resolved except persistent headache. Exam shows fluent aphasia and questionable right visual field cut
- Imaging appearance (edema and hemorrhage) often looks much worse than clinical picture

Case # 4

- 64 yo man presents to ED with acute onset confusion. He is agitated can speak fluently but confabulates. His BP is 200/120
- Labs show new elevation of creatinine of 3.4
- Head CT read as bilateral subacute occipital lobe strokes



Posterior Reversible Encephalopathy Syndrome

Posterior Reversible Encephalopathy Syndrome

- **Posterior reversible encephalopathy syndrome** (PRES), also known as **reversible posterior leukoencephalopathy syndrome** (RPLS), is a syndrome characterised by headache, confusion, seizures and visual loss. It may occur due to a number of causes, predominantly malignant hypertension, eclampsia and some medical treatments. On magnetic resonance imaging (MRI) of the brain, areas of edema (swelling) are seen. The symptoms tend to resolve after a period of time, although visual changes sometimes remain

PRES

- PRES occurs due to the use of drugs like tacrolimus and cyclosporine, hence it may occur in people who have undergone an organ transplant, in which these drugs may be used to suppress transplant rejection. It also occurs due to eclampsia, severe high blood pressure and hypercalcemia. Low magnesium levels can augment PRES

PRES

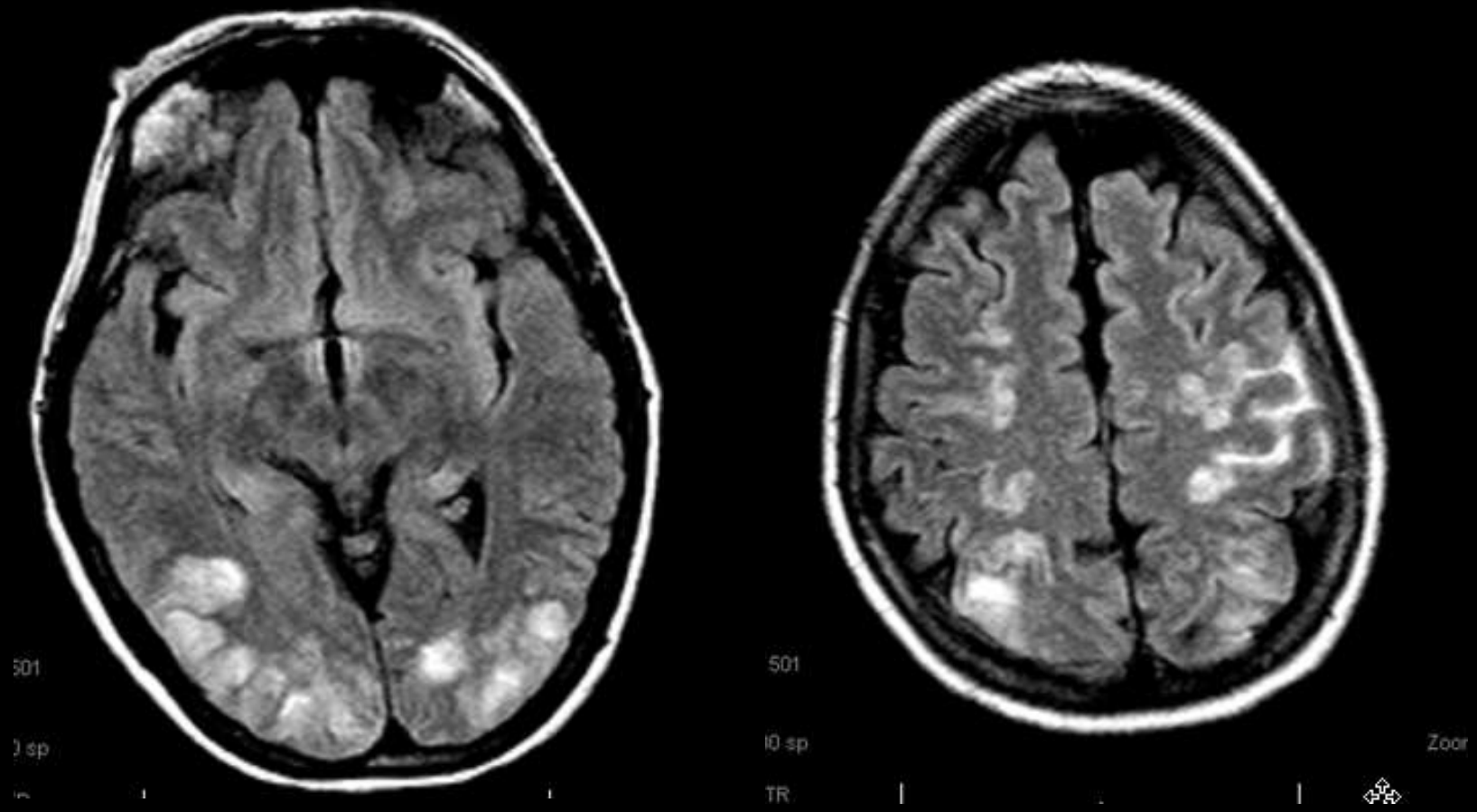
TABLE 1: Presenting Symptoms and Causes of Posterior Reversible Encephalopathy Syndrome (PRES) in 76 Patients

Presenting Symptoms	No. of Patients	Primary PRES Cause	No. of Patients
Seizures	58	CSA for transplant	34
Mental status changes[a]	10	Hypertension	17
Visual symptoms or loss	3	Eclampsia	5
Severe headache	3	Tacrolimus	4
Aphasia	1	Cocaine, methamphetamine use	3
Facial numbness	1	TTP/ITP	3
		Combined chemotherapy	2
		Systemic lupus erythematosus	2
		Chronic renal failure	1
		PEG L-asparaginase	1
		Hemolytic uremic syndrome	1
		NOS, anaphylaxis?	1
		NOS, alcohol withdrawal?	1
		NOS, steroids?	1

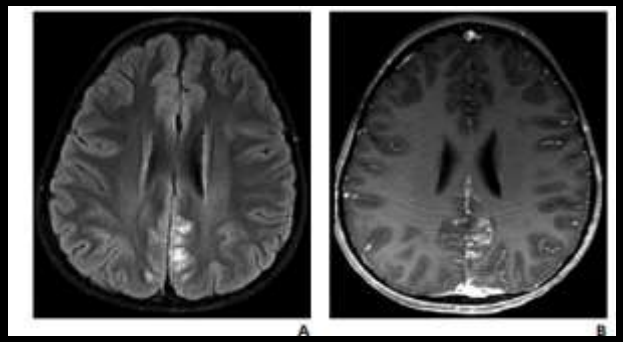
Note—CSA = cyclosporine A, TTP/ITP = thrombotic or idiopathic thrombocytopenic purpura, PEG = polyethylene glycol, NOS = not otherwise specified.

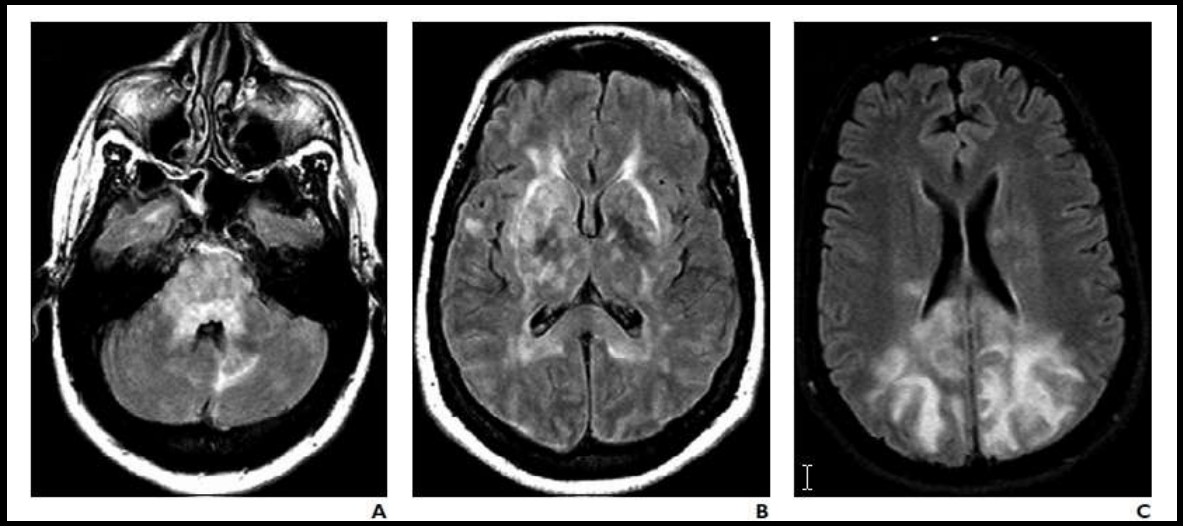
[a]Include acute decrease in consciousness or in responsiveness or acute confusion.

Classical MRI Appearance of PRES



PRES imaging variants





Regional Involvement of PRES

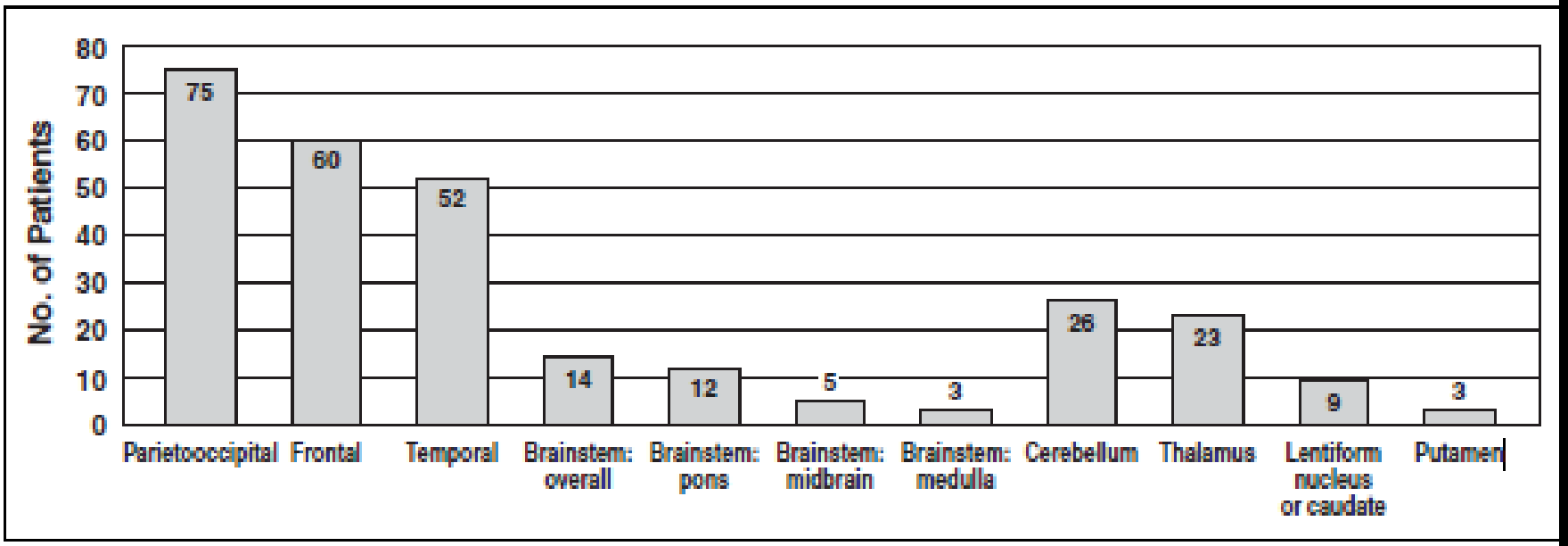
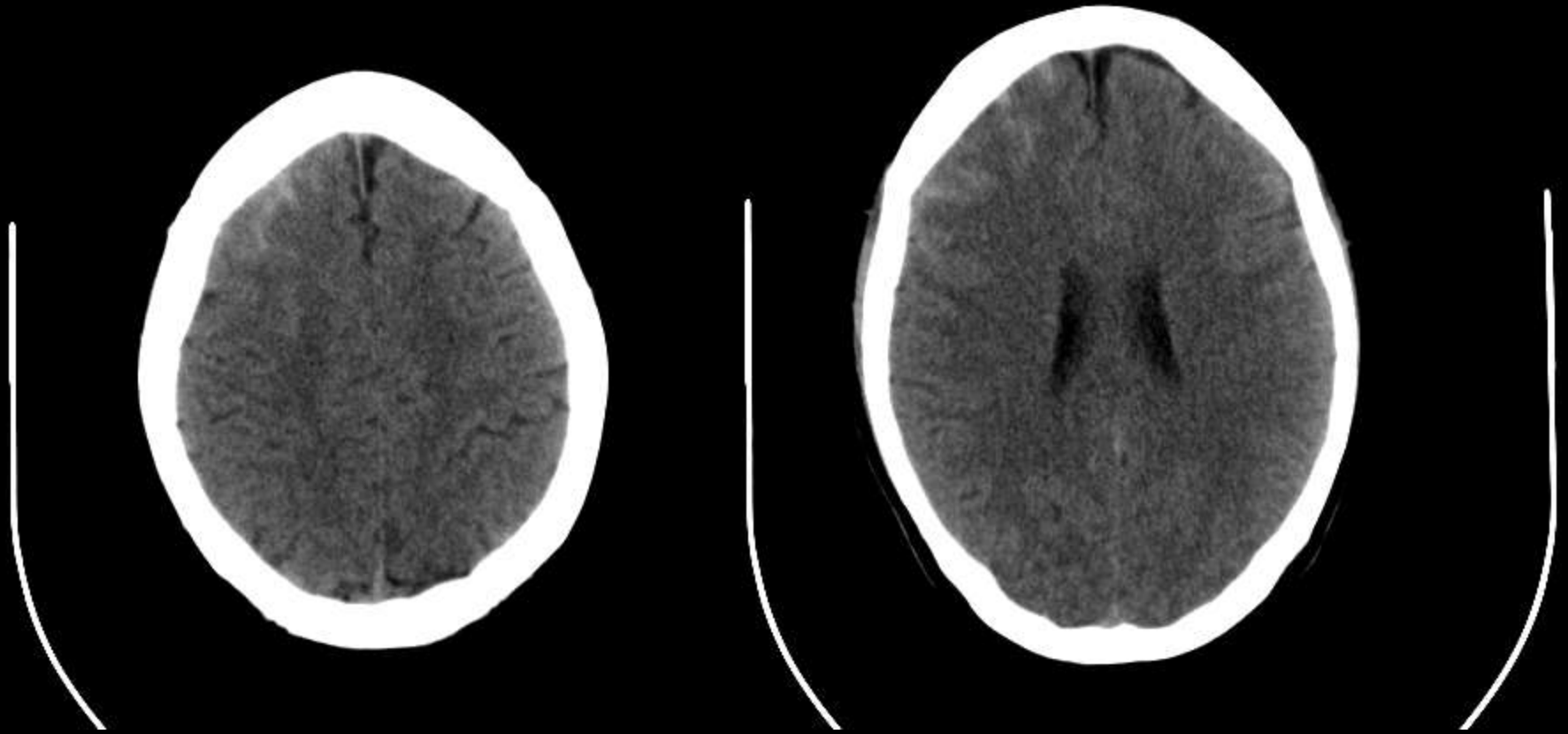


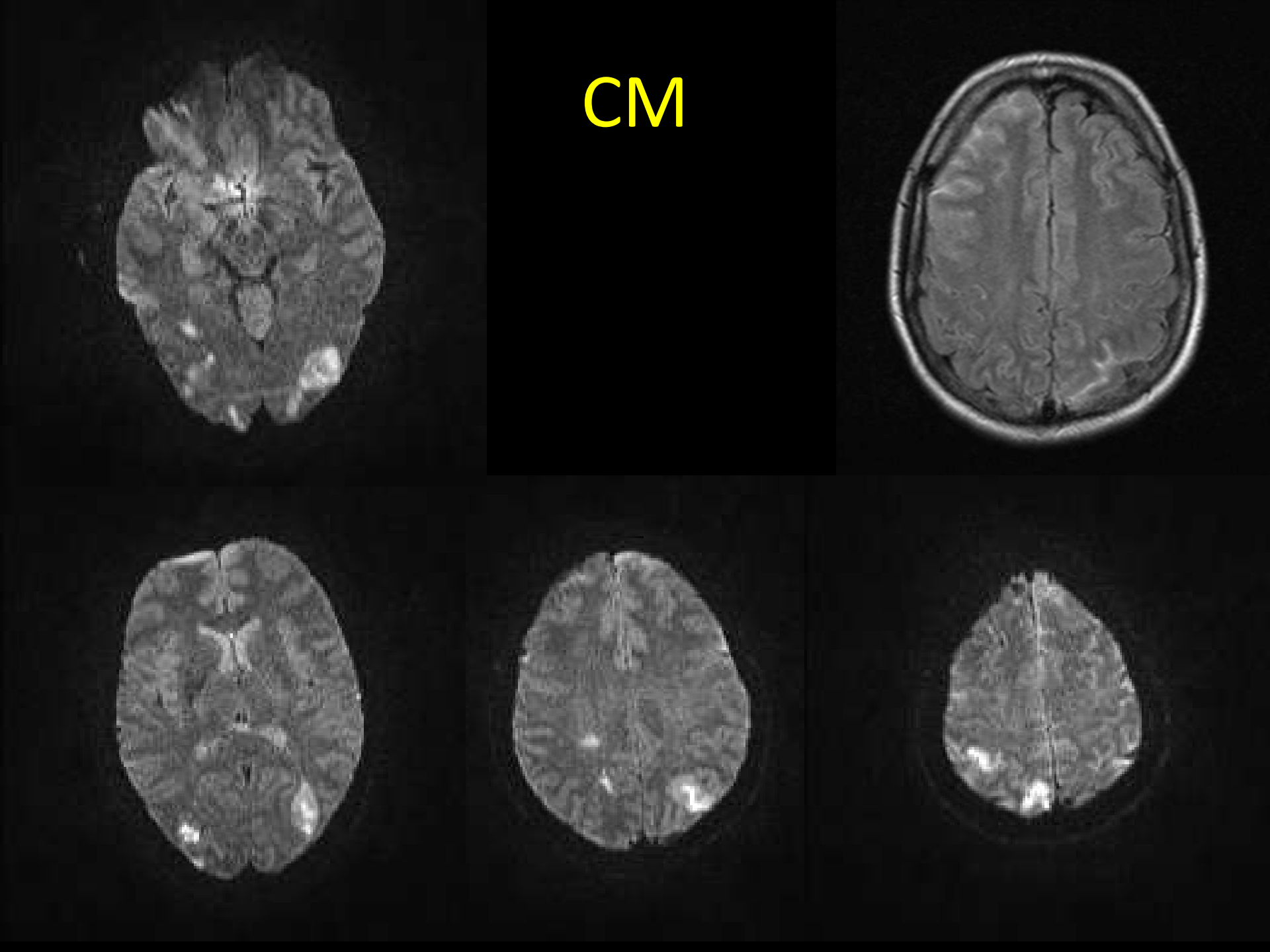
Fig. 4—Bar graph shows regional involvement by posterior reversible encephalopathy syndrome (PRES) in 76 patients. Number of patients in each region are listed in or above each bar.

Case # 5

- 49 yo female who presents with a sudden severe headache and progressive visual changes. PMH is negative. She denies drug use but consumes energy drinks daily and smokes marijuana. Exam shows mild word finding difficulties, right visual field cut
- Head CT is negative
- Tpa?

CM

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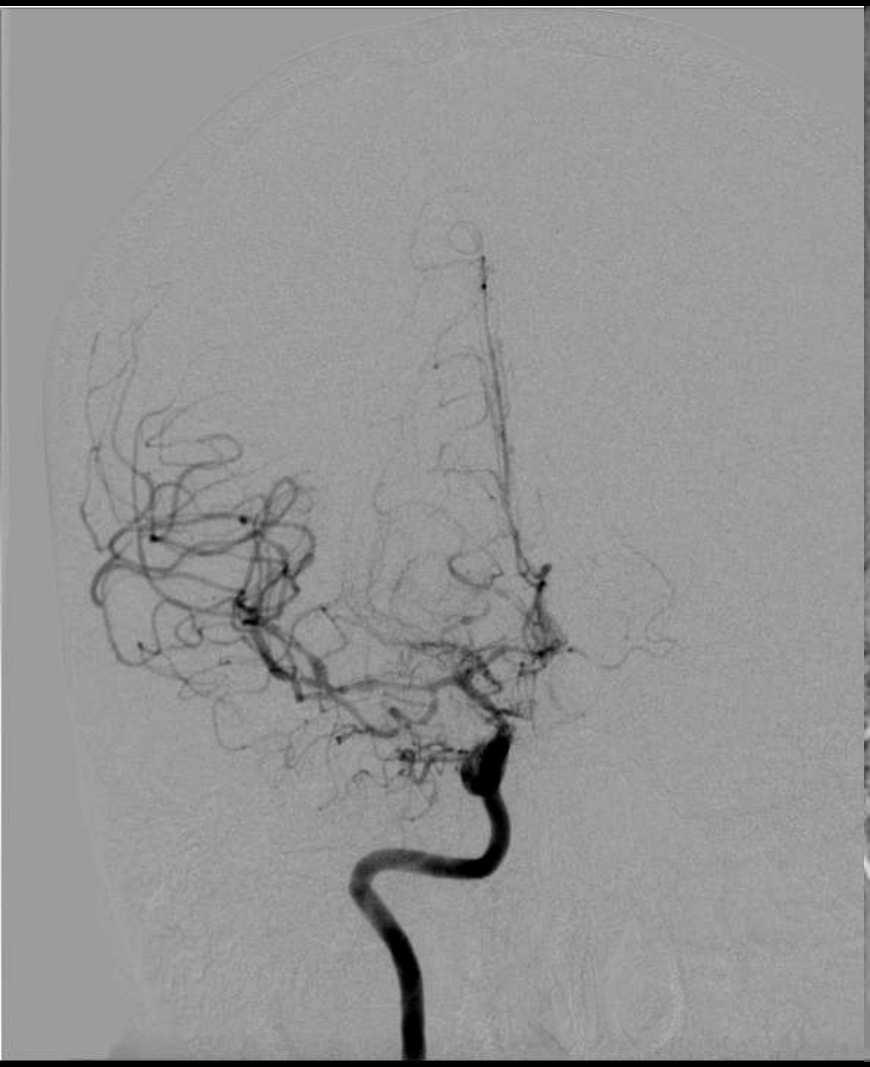
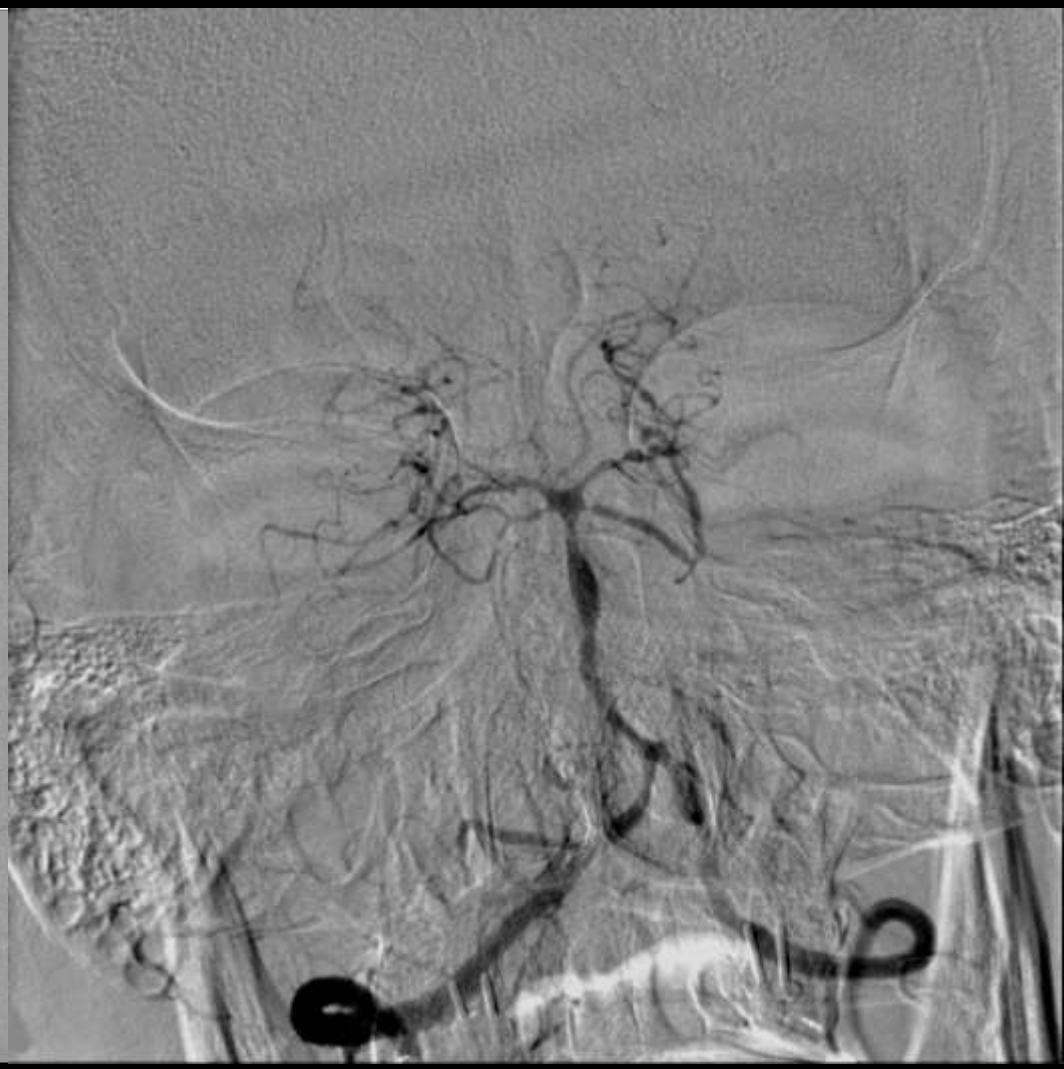




Reversible Cerebral Vasoconstriction Syndrome (RCVS)

- **Reversible cerebral vasoconstriction syndrome** (**RCVS**, sometimes called **Call-Fleming syndrome** or by a number of other names) is a poorly understood disease in which the arteries of the brain develop vasospasm without a clear cause (such as hemorrhage or trauma).
- Vasospasm narrows arteries and can trigger severe headaches that wax and wane. When the vasospasms subside the headaches are relieved.
- Symptoms result from vasospasms that narrow arteries, especially those around the circle of Willis, which can lead to a dramatic headaches that are often of the thunderclap headache (sudden-onset) character
- Ischemia damage in these patients which presents 3–4 days after headache onset as focal neurological symptoms

Table 1. Conditions Associated with Reversible Cerebral Vasoconstriction Syndromes*

Pregnancy and puerperium

Early puerperium, late pregnancy, eclampsia, preeclampsia, and delayed postpartum eclampsia

Exposure to drugs and blood products

Phenylpropanolamine, pseudoephedrine, ergotamine tartrate, methergine, bromocryptine, lisuride, selective serotonin reuptake inhibitors, sumatriptan, isometheptine, cocaine, ecstasy, amphetamine derivatives, marijuana, lysergic acid diethylamide, tacrolimus (FK-506), cyclophosphamide, erythropoetin, intravenous immune globulin, and red blood cell transfusions

Miscellaneous

Hypercalcemia, porphyria, pheochromocytoma, bronchial carcinoid tumor, unruptured saccular cerebral aneurysm, head trauma, spinal subdural hematoma, postcarotid endarterectomy, and neurosurgical procedures

Idiopathic

No identifiable precipitating factor

Associated with headache disorders, such as migraine, primary thunderclap headache, benign exertional headache, benign sexual headache, and primary cough headache

*Adapted from reference 1: Singhal AB, Bernstein RA. Postpartum angiopathy and other cerebral vasoconstriction syndromes. Neurocrit Care. 2005;3:91-7.

Table 2. Summary of Critical Elements for the Diagnosis of Reversible Cerebral Vasoconstriction Syndromes*

- Transfemoral angiography or indirect CTA or MRA documenting multifocal segmental cerebral artery vasoconstriction
- No evidence for aneurysmal subarachnoid hemorrhage
- Normal or near-normal cerebrospinal fluid analysis (protein level < 80 mg%, leukocytes <10 mm^3, normal glucose level)
- Severe, acute headaches, with or without additional neurologic signs or symptoms
- Reversibility of angiographic abnormalities within 12 weeks after onset. If death occurs before the follow-up studies are completed, autopsy rules out such conditions as vasculitis, intracranial atherosclerosis, and aneurysmal subarachnoid hemorrhage, which can also manifest with headache and stroke

*CTA = computed tomography angiography; MRA = magnetic resonance angiography.

Table 3. Differential Diagnosis of Disorders That May Mimic Reversible Cerebral Vasoconstriction Syndromes*

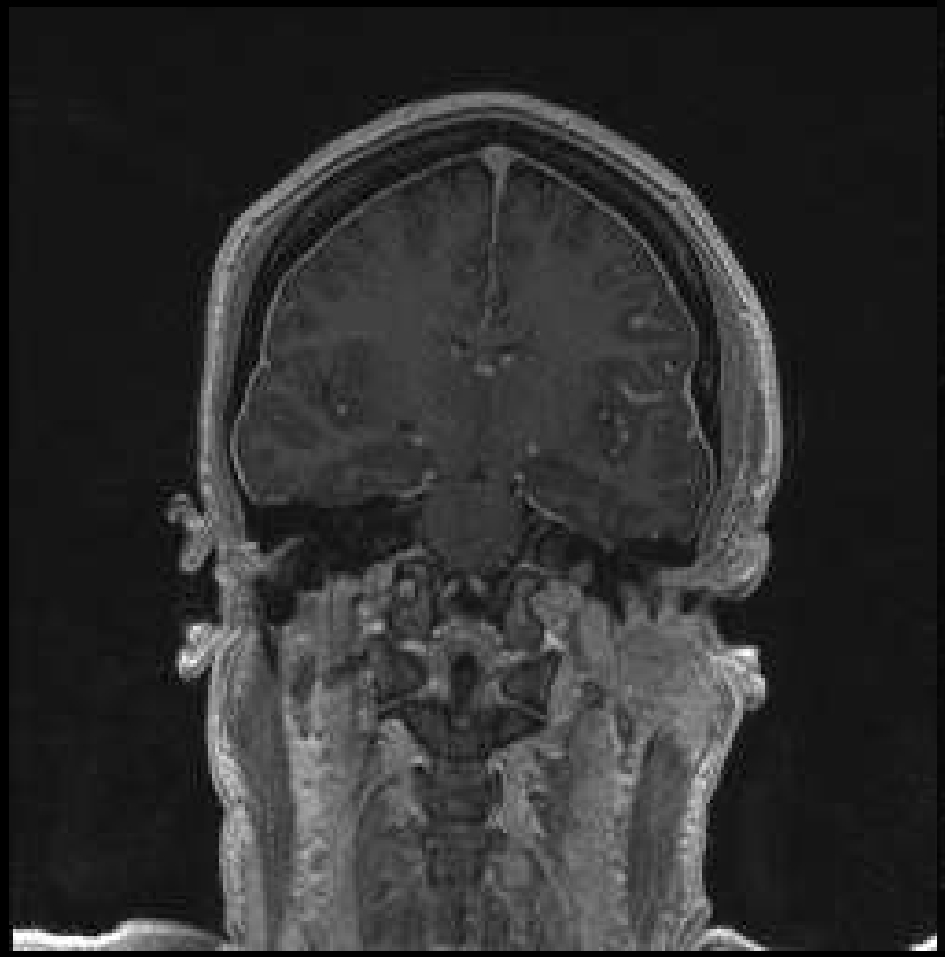
Variable	RCVS	PACNS	SAH	Arterial Dissection
Sex	Female predominant, ratio 2–3 to 1	No sex predilection	Female predominant, ratio 1.6 to 1	No sex predilection
Onset	Acute (seconds to minutes)	Typically subacute to chronic	Acute (seconds)	Acute or subacute
Headache	Acute and severe, throbbing, often thunderclap	Insidious and progressive, dull aching	Thunderclap	Thunderclap in about 13%
CSF examination	Normal or near-normal	Abnormal in >95% of PACNS; variably abnormal in non-PACNS variants	Abnormal (elevated erythrocyte count, xanthochromia)	Normal
CT/MRI of brain parenchyma	Normal in the majority of patients; or shows symmetric arterial "watershed" infarctions or parenchymal brain hemorrhage. In addition, small SAH overlying the cortical surface or reversible brain edema may occur.	Abnormal in 90% of cases of PACNS No characteristic findings but small infarctions in gray or white matter, varying ages, affects multiple vascular territories with or without diffuse white matter lesions	SAH, which usually correlates with the site and severity of arterial vasospasm. Ischemic stroke and brain edema can develop distal to the site of vasospasm. Rare patients can have "CT-negative" SAH.	Results of brain CT and MRI are normal in the absence of ischemic stroke. Axial MRI or CTA may show crescentic intramural hematoma involving the vertebral or internal carotid artery.
Neurovascular imaging	By definition, shows diffuse areas of multiple stenoses and dilatation involving intracranial cerebral arteries. These abnormalities are present in the acute stage and are reversible within days to weeks.	Variable sensitivity. Frequently normal in PACNS; otherwise, findings range from single or multiple arterial cut-off areas, to luminal irregularities in single or multiple arteries, to diffuse abnormalities that are occasionally indistinguishable from RCVS. These abnormalities are frequently irreversible.	Usually shows saccular aneurysm or alternate cause of the bleeding (e.g., arteriovenous malformation). Vasospasm typically is not multifocal, affects 1–2 medium arteries, and peaks between days 4 and 11. Acute vasospasm on the day of onset is extremely rare.	Long-segment stenosis, double-lumen, intimal flaps, and arterial pseudoaneurysms are characteristic angiographic signs. Stenosis resolves in 90% within 3 months. Unlike RCVS, stenosis is smooth, involves extracranial carotid extracranial and intracranial vertebral arteries, and involves a single vessel (except in rare cases of multivessel dissection).

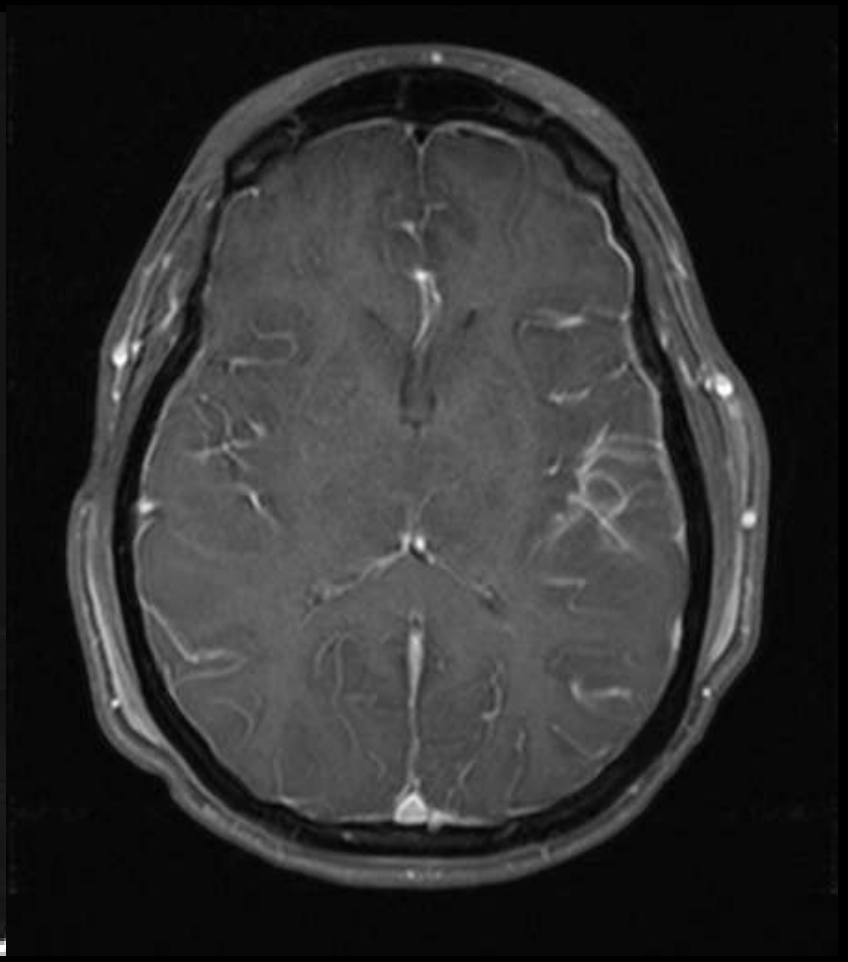
*CSF = cerebrospinal fluid; CT = computed tomography; MRI = magnetic resonance imaging; PACNS = primary angiitis of the central nervous system; RCVS = reversible cerebral vasoconstriction syndrome; SAH = subarachnoid hemorrhage

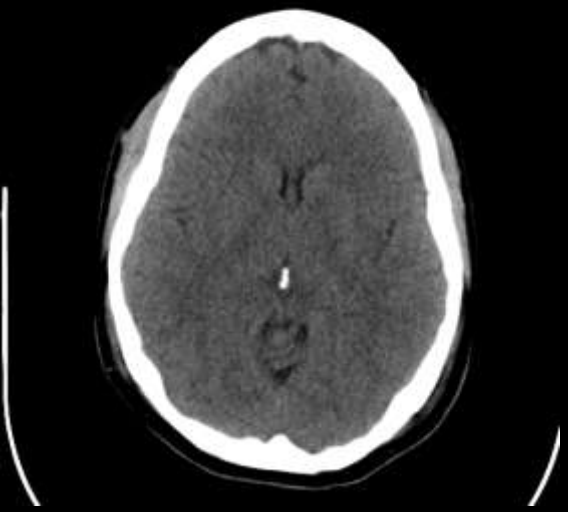
Case #6

- 18 year old female two weeks postpartum from normal vaginal delivery (epidural anesthetic) who presents with severe headache, fever and aphasia and right sided weakness.
- Non-contrast Head CT negative
- LP
  - WBC 4200 (89% PMNs) glucose low and protein normal, GS + cocci
- Lumbar MRI – epidural abscess

Meningitis—Stroke (KT)

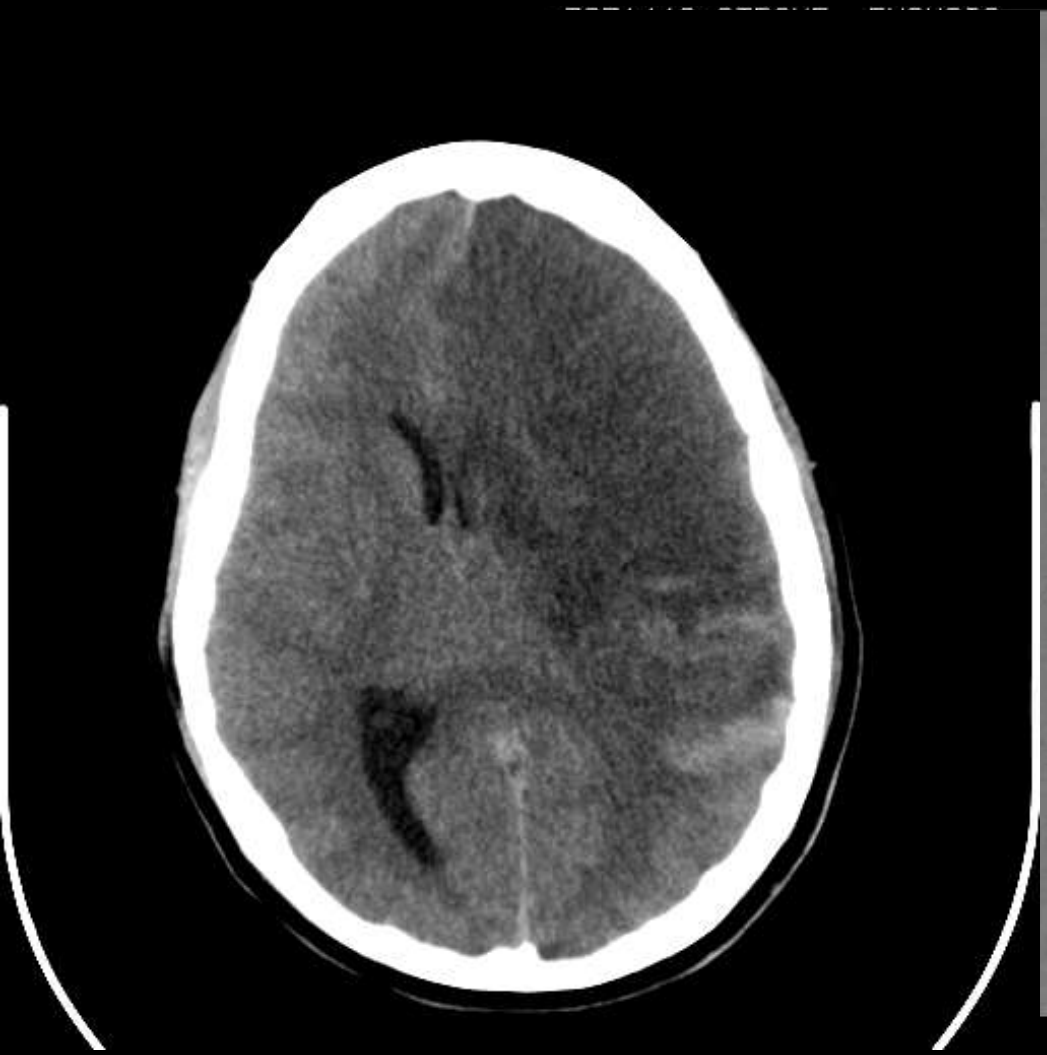


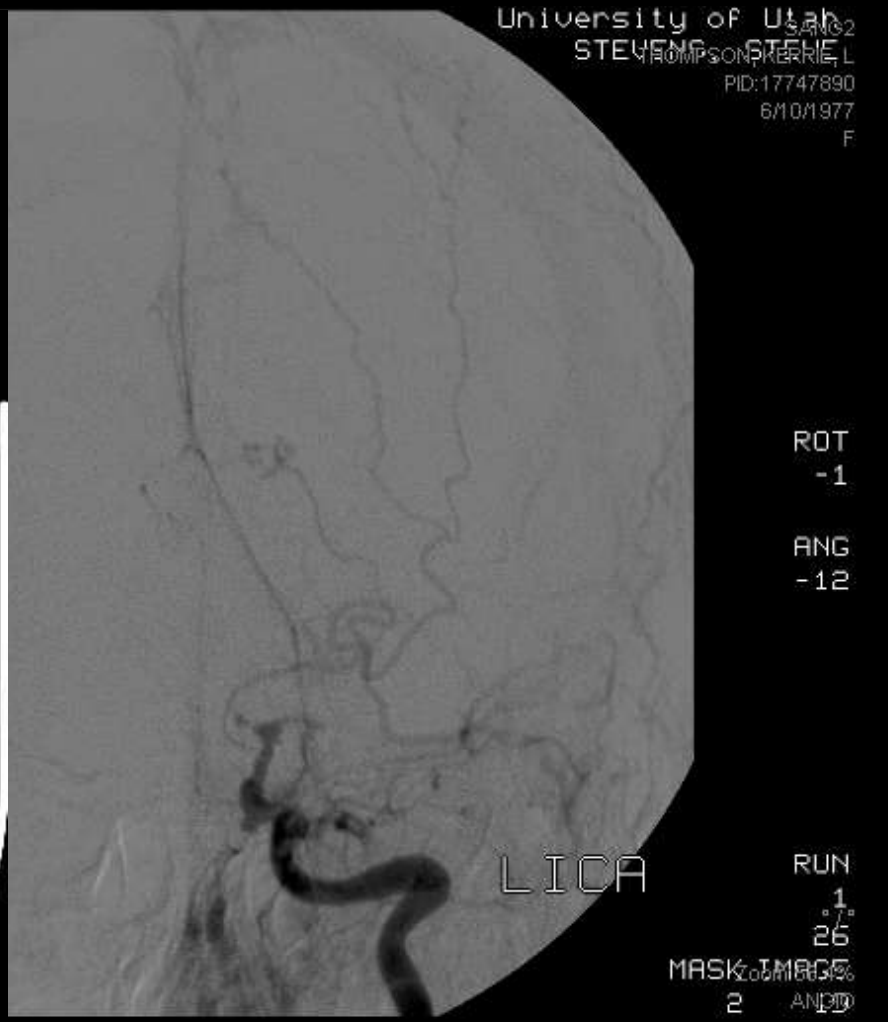




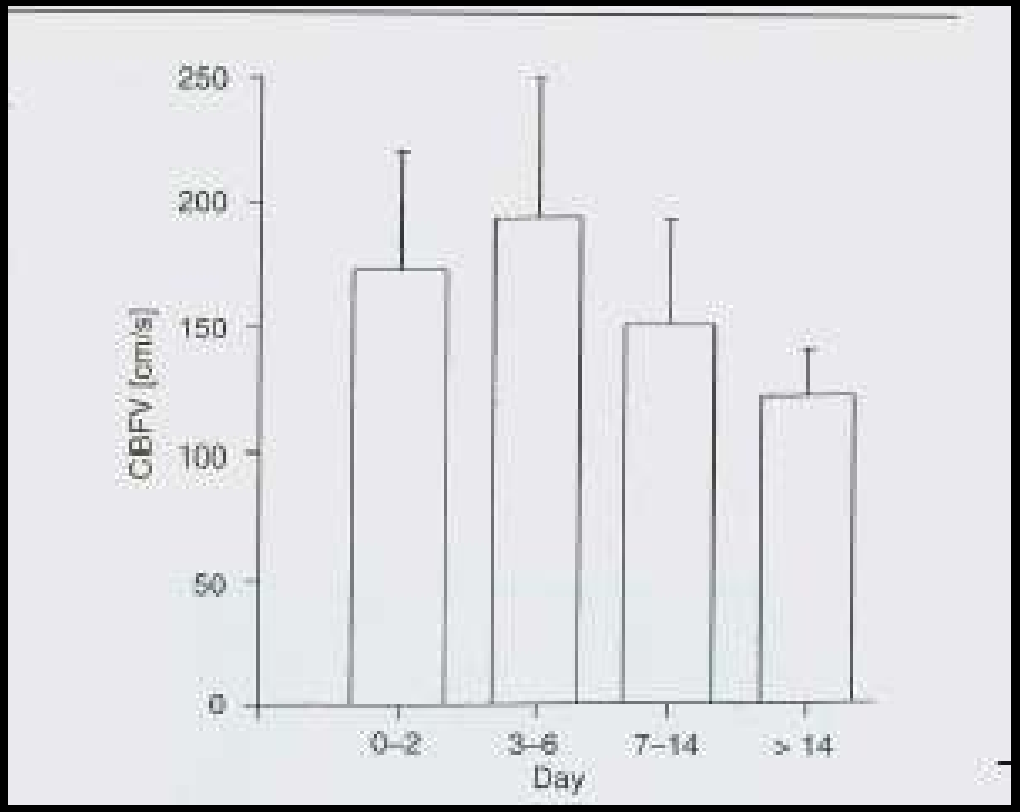
Meningitis—Stroke (KT)

Meningitis—Stroke (KT)





Transcranial Doppler in Bacterial Meningitis



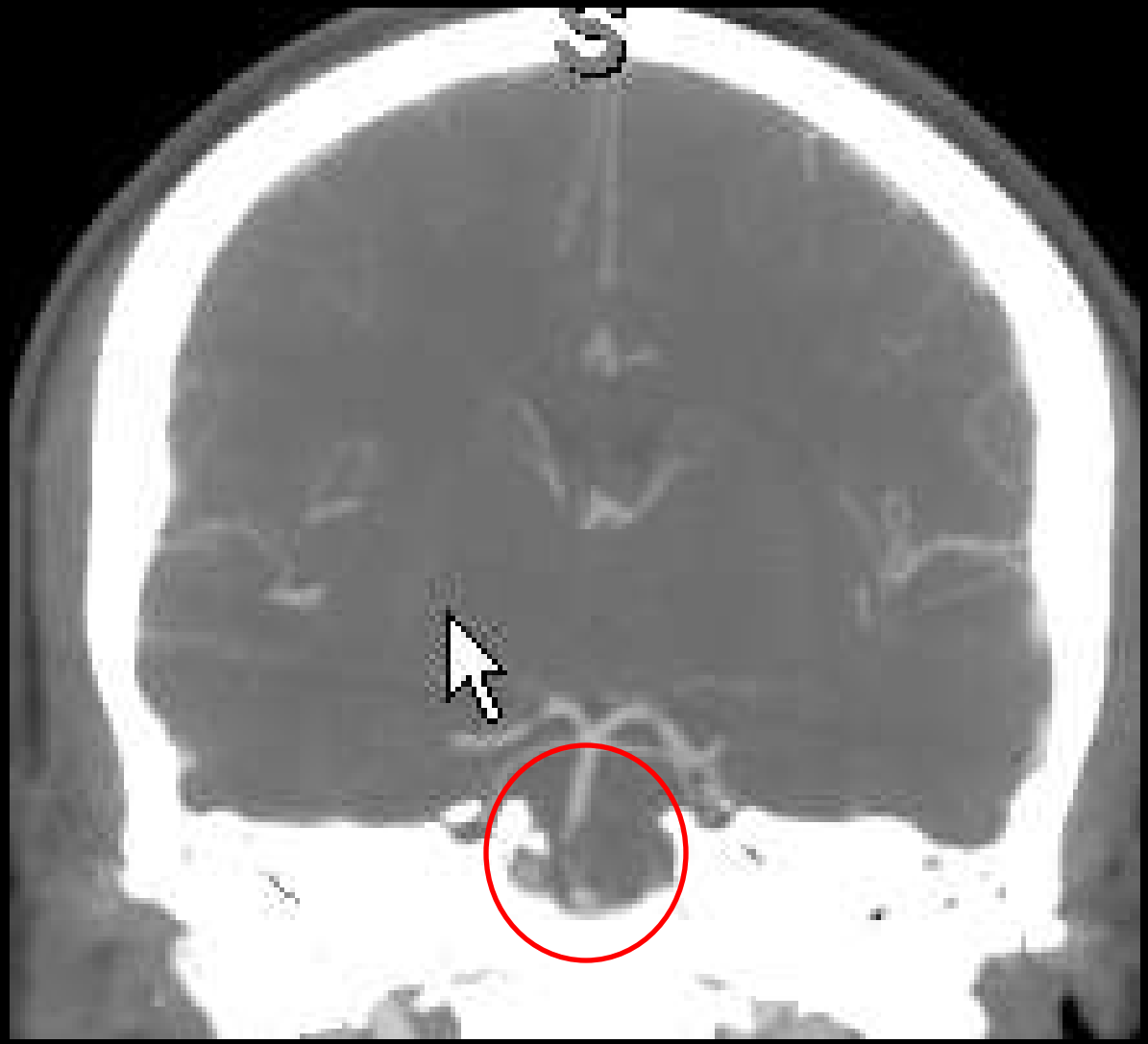
Red Flags

- Headache as a prominent feature
- FEVER
- No vascular risk factors
- Non-anatomic symptoms (mute and left sided weakness but not left handed)
- ANY CT findings
- Disconnect between imaging and clinical findings

Final case

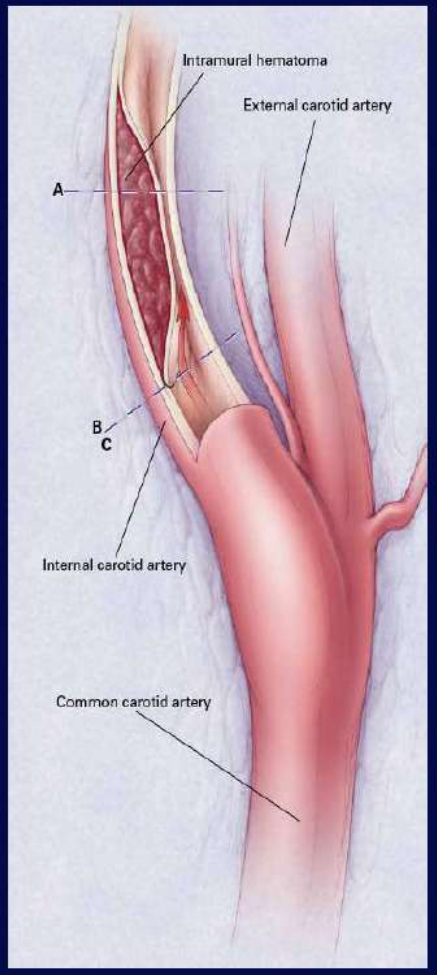
- 32 year old with history of migraine, who has had one week of atypical left sided headache then presents with ED with nausea, vomiting, diplopia, severe dysarthria and first left, than right-sided hemiparesis. Exam shows dysconguate gaze severe dysarthria but no facial droop, right sided moderate weakness
- Noncontrast head CT is negative, labs are normal.
- Tpa?
- Diagnosis?

Acute Basilar Thrombosis from Vertebral dissection



Cerebrovascular Dissection

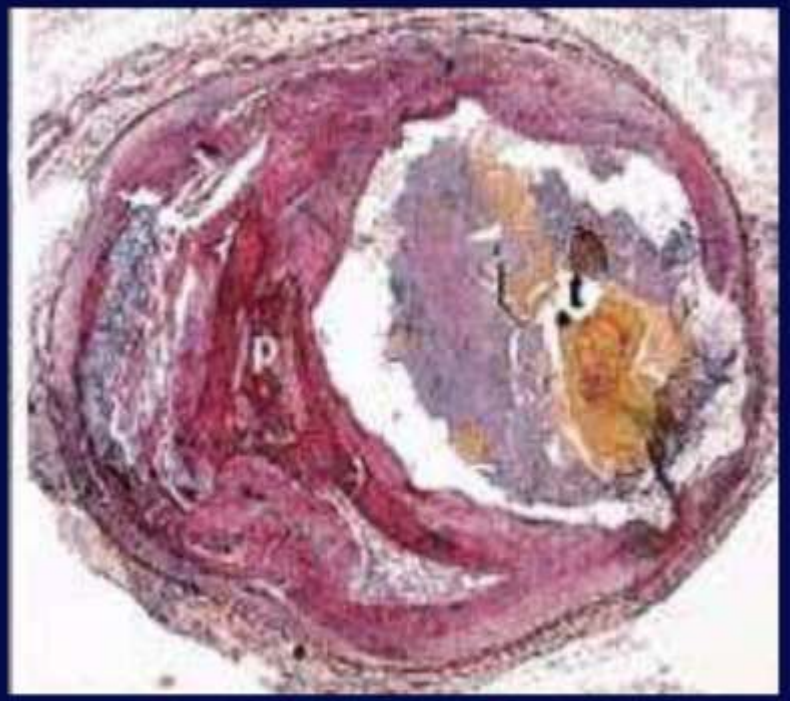
- Disruption of intima with infiltration of blood between mural layers
- Common cause of stroke in young and middle-aged adults
  - 5-20%
- Associated with trauma, neck manipulations, or can be spontaneous.
- More common in patients with collagen vascular diseases.



Schievink, NEJM 2001; 334:898

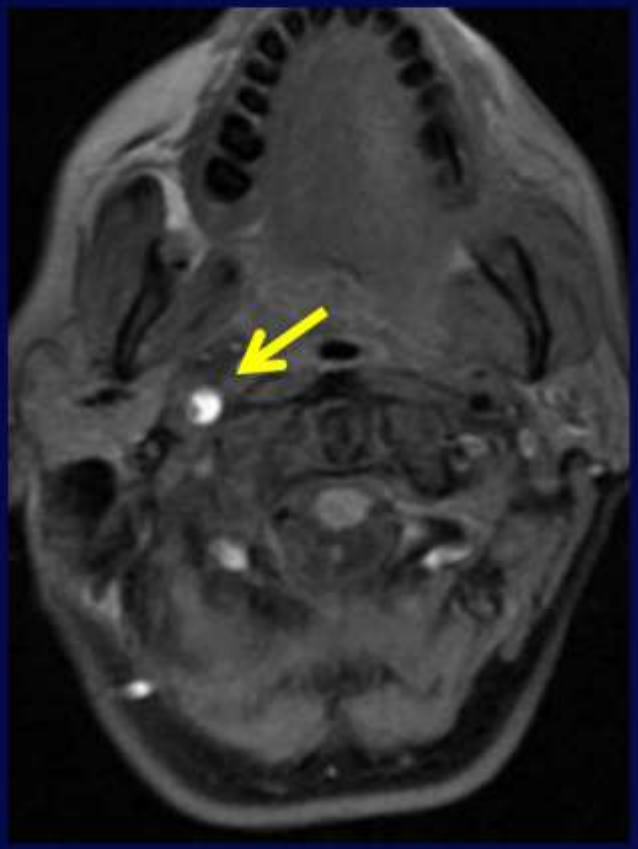
Cerebrovascular Dissection

- Features
  - Wall thickening
  - Stenosis & occlusion
  - Pseudoaneurysms
  - Intimal flaps
  - Thrombus & emboli
- Common Sites
  - Carotid: 1-2 cm beyond bifurcation to skull base
  - Vertebral: Below C6 (V1) or above C2 level (V3, V4)



MRI/MR Angiography

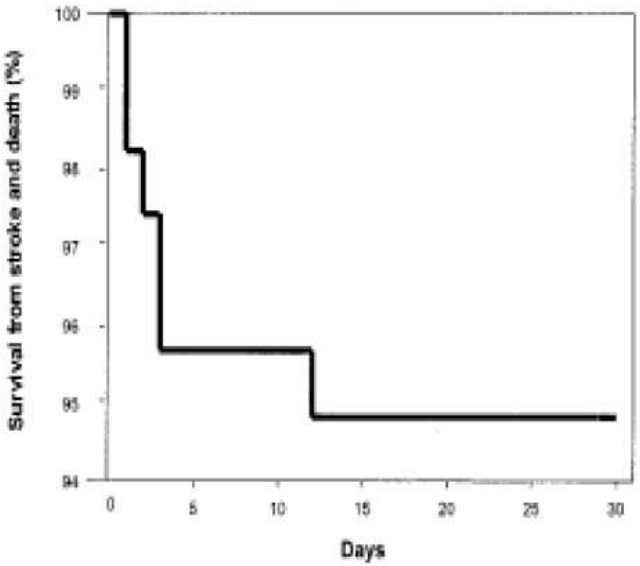
- MRI
  - Diffusion imaging for acute stroke
- MR Angiography
  - Flame-shaped occlusion
  - Long segment stenosis
  - Luminal irregularity
  - Pseudoaneurysm
- Intramural hematoma
  - T1 fat sat neck
  - Crescent shape or round rim
  - Methemoglobin



34 yo woman, right ICA dissection

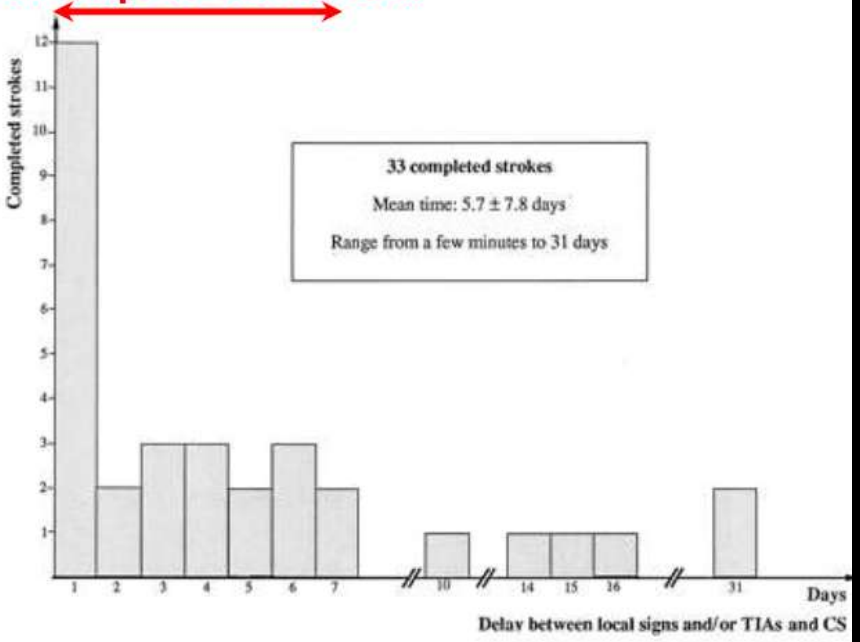
Early Recurrent Risk

2 weeks post-dissection



Beletsky *et al.*, 2003 Stroke

1 week post-dissection



Biousse *et al.*, 1995 Stroke

High risk period - 1st month

Final case
Take Home

- 32 year old with history of migraine, who has had one week of atypical left sided headache then presents with ED with nausea, vomiting, diplopia, severe dysarthria and first left, than right-sided hemiparesis. Exam shows dysconguate gaze, severe dysarthria but no facial droop, right sided moderate weakness

- Diagnosis: Migraine vs Conversion disorder----- but only after dissection is ruled out!

Conclusion

- TPA is a safe effective intervention in a select population
- Ischemic stroke is clinical diagnosis
- Explore the history and physical to exclude or include nonstroke or atypical syndromes
- Order the right test
- Look at the imaging!!!
- Limit Disability

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ENLS
Emergency Neurological Life Support