



# Vasculitis and Acute CNS Vasculopathies

Dr Ferghal McVerry

RCP Update

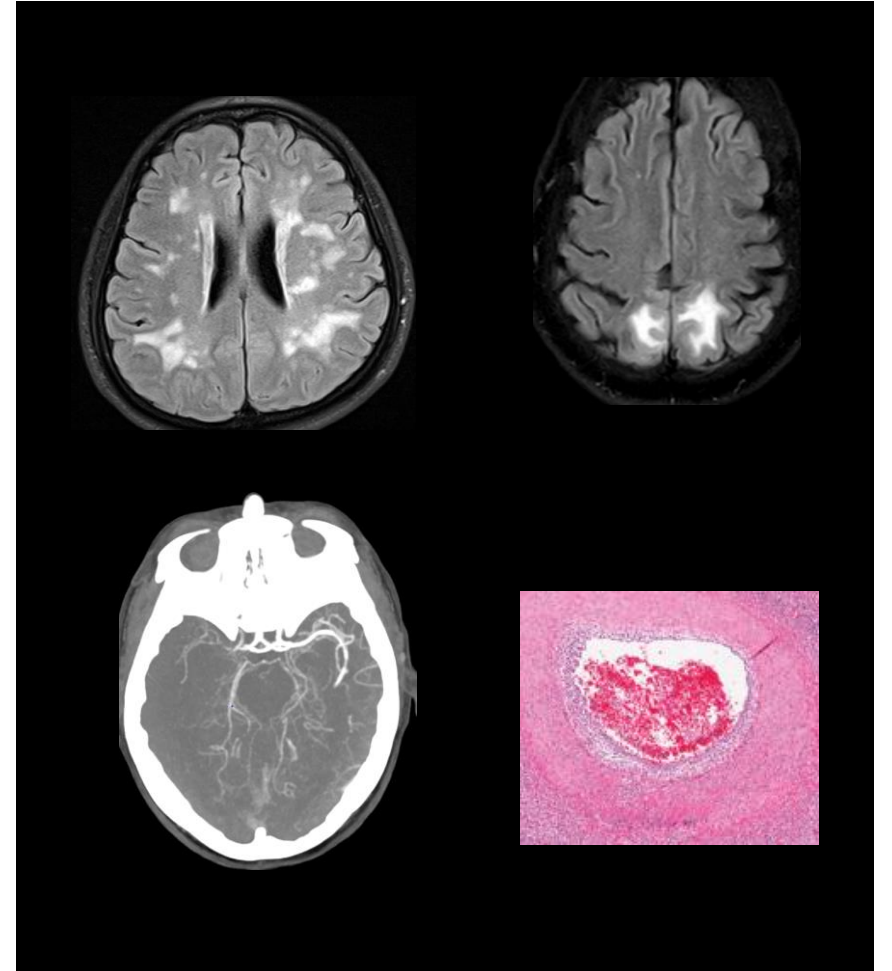
Nov 2024

# Declarations

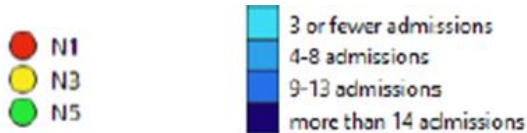
I have no financial interests or relationships to disclose regarding the subject matter of this presentation.

# Acute CNS Vasculopathy

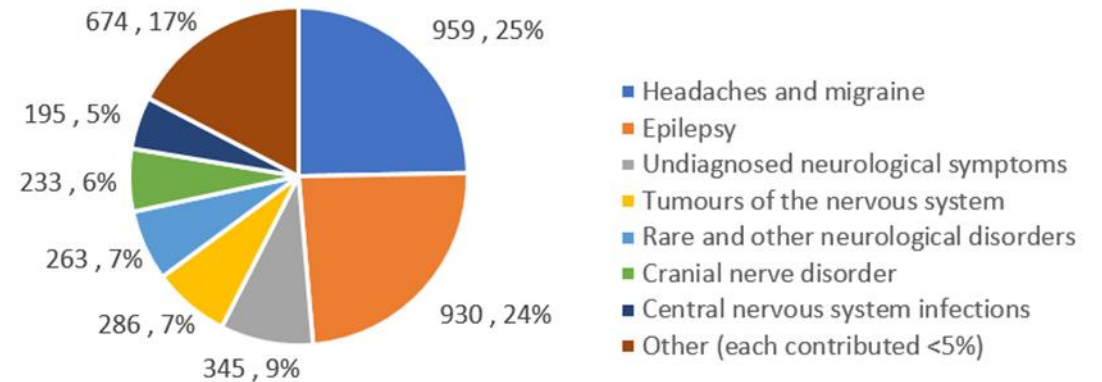
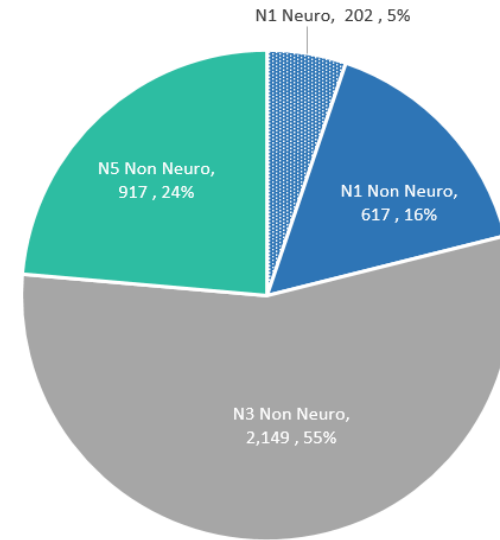
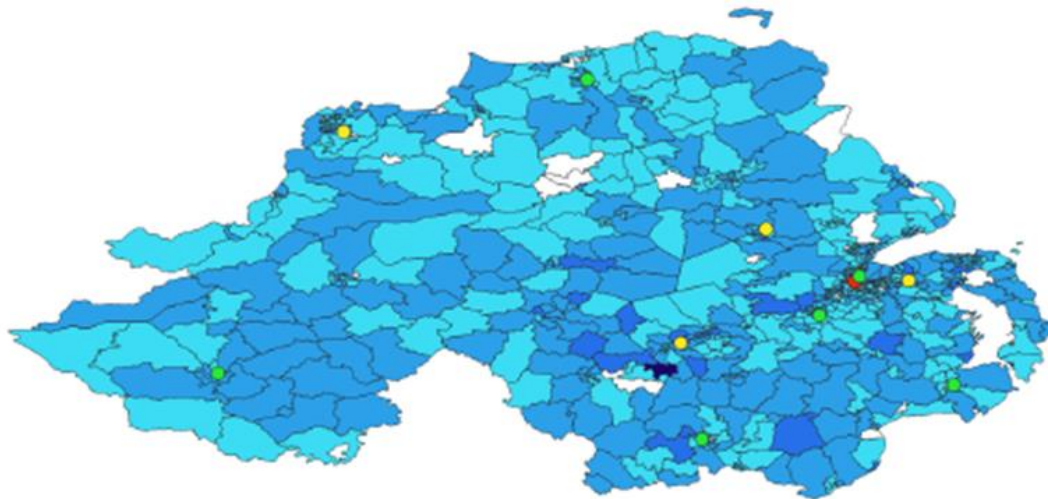
- Encountered frequently in Acute Neurology referrals
- Acute Medical Unit / Medical Ward/ Stroke Unit/ ICU
- Rare subgroups are common on differential diagnosis lists
- Myriad Clinical features
- Radiology Crucial, features overlap
- Benign to fatal outcomes



# Acute Neurological Admissions

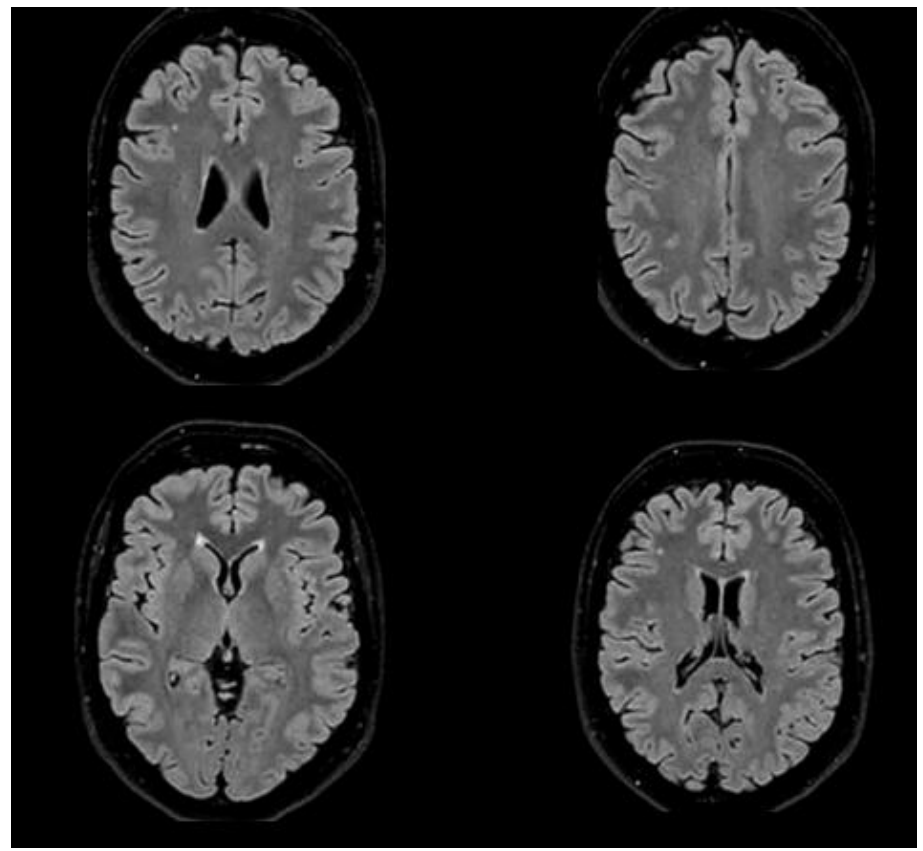


Individuals treated in N1-N5 sites.

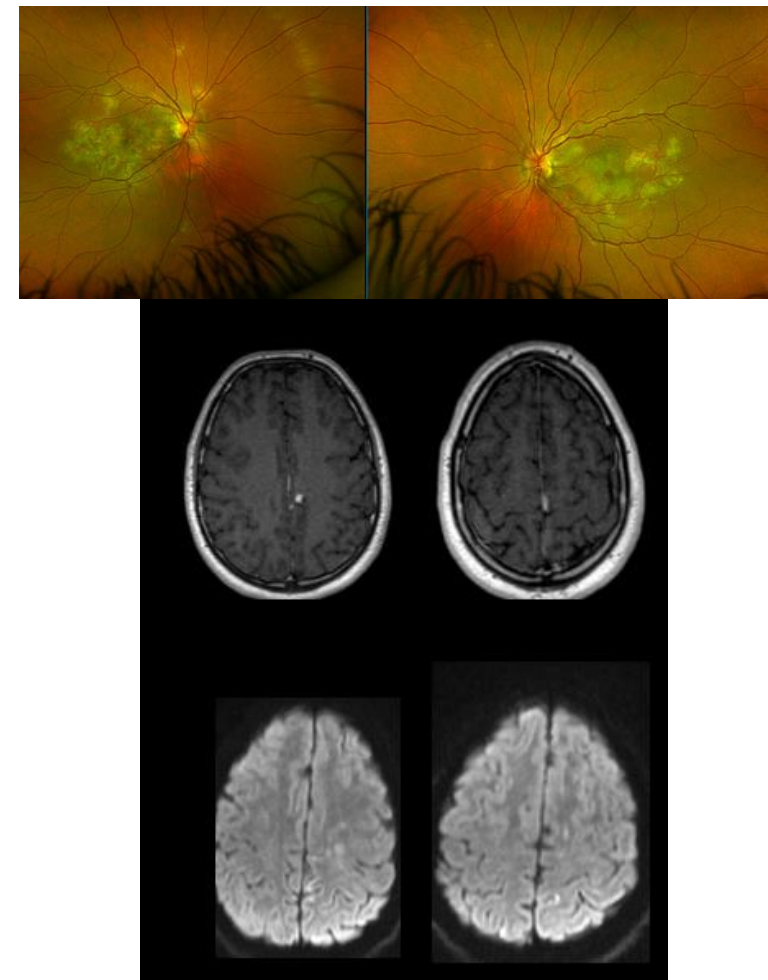


# Recent Referrals- CNS Vasculitis?

## Post-Covid Syndrome

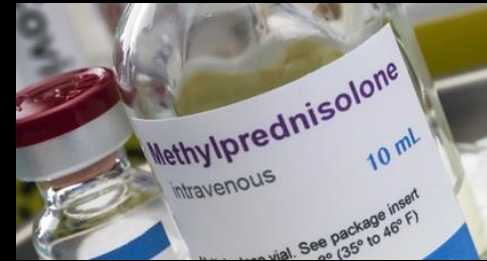


## Pigment Epithelopathy



# Primary CNS Vasculitis

- Uncommon
- Frequently considered- Imaging/ clinically
- Previously considered uniformly fatal
- No RCTs .
- Treatment well known



HSC Health and Social Care Board  
Infectious Diseases Specialist Medicines

### Cyclophosphamide

Dermatology / Immunology / Nephrology / Neurology / Respiratory / Rheumatology shared care guideline.

Specialist details	Patient identifier
Name: _____	_____
Location: _____	_____
Tel: _____	Date: _____

**Introduction**

This shared care guideline refers to the use of cyclophosphamide in the treatment of **NON-CANCER CONDITIONS ONLY**.

**Unlicensed indications:** severe vasculitis and arthritis, and organ complications of connective tissue disease, pemphigus, dermatomyositis, polymyositis, myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, inflammatory neuropathies.

**Adult dosage and administration**

Cyclophosphamide can be administered as pulse IV treatment (under which circumstance monitoring will be managed by secondary care) or as a daily oral dose, normally 2mg/kg/day. A typical dose may be 50 - 150mg orally daily as a single or divided dose. The dose is tailored according to the individual patient requirements with a maximum dosage of 200mg/day. Duration of treatment may be variable ranging from weeks to months depending on indication. Use with caution if evidence of renal or hepatic dysfunction as dosage reduction may be required.

**Available as:** cyclophosphamide 50mg tablets.  
In exceptional circumstances, a liquid preparation may be required. Cyclophosphamide 50mg/ml is the standard strength that must be used (available from special order manufacturers eg. Nova Laboratories).

**Hospital specialist responsibilities**

- Assess if the patient is suitable for treatment with cyclophosphamide.
- Agree shared care with the patient's GP.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of medication.
- Patients should be counselled regarding the recognised complication of infertility and cyclophosphamide treatment.
- If the liquid formulation is used, provide training on safe handling, storage, spillage and waste disposal (provide a cytotoxic spill kit and cytotoxic sharps box if necessary).
- Provide shared care monitoring record booklet if required.
- Undertake baseline tests as indicated in monitoring table.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.



## Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria

L H Calabrese<sup>1</sup>, J A Mallek

- Unexplained **neurological deficit**

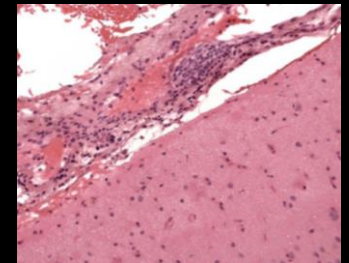
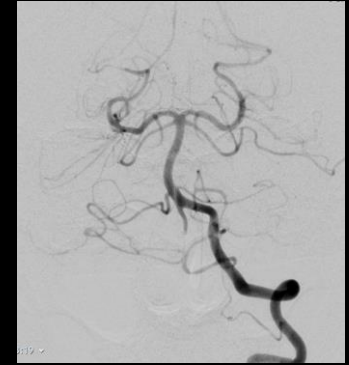
Either :

- Classic **angiographic evidence** of vasculitis

Or

**histopathologic evidence** of vasculitis

- No evidence of systemic vasculitis or any other condition to which the angiographic or pathologic evidence can be attributed



# CNS Vasculitis Case Series

**Table 2. Clinical Manifestations at Presentation**

Characteristics	All Patients (N = 101), n (%)	Patients Diagnosed by Biopsy (n = 31), n (%)	Patients Diagnosed by Angiography (n = 70), n (%)
Headache	64 (63)	16 (52)	48 (69)
Altered cognition	50 (50)	22 (71)	28 (40)
Hemiparesis	44 (44)	6 (19)	38 (54)
Persistent neurological deficit or stroke	40 (40)	8 (26)	32 (46)
Aphasia	28 (28)	11 (36)	17 (24)
Transient ischemic attack	28 (28)	5 (16)	23 (33)
Ataxia	19 (19)	5 (16)	14 (20)
Seizure	16 (16)	2 (7)	14 (20)
Visual symptom (any kind)	42 (42)	9 (29)	33 (47)
Visual field defect	21 (21)	5 (16)	16 (23)
Diplopia (persistent or transient)	16 (16)	5 (16)	11 (16)
Blurred vision or decreased visual acuity	11 (11)	0 (0)	11 (16)
Monocular visual symptoms or amaurosis fugax	1 (1)	0 (0)	1 (1)
Papilledema	5 (5)	2 (7)	3 (4)
Intracranial hemorrhage	8 (8)	2 (7)	6 (9)
Amnesic syndrome	9 (9)	4 (13)	5 (7)
Paraparesis or quadriparesis	7 (7)	4 (13)	3 (4)
Parkinsonism or extrapyramidal sign	1 (1)	0 (0)	1 (1)
Prominent constitutional symptom	9 (9)	4 (13)	5 (7)
Fever	9 (9)	4 (13)	5 (7)
Nausea or vomiting	25 (25)	6 (19)	19 (27)
Vertigo or dizziness	9 (9)	3 (10)	6 (9)
Dysarthria	15 (15)	2 (7)	13 (19)
Unilateral numbness	13 (13)	0 (0)	13 (19)

**Table 1. Diagnostic Test Findings (N = 101)**

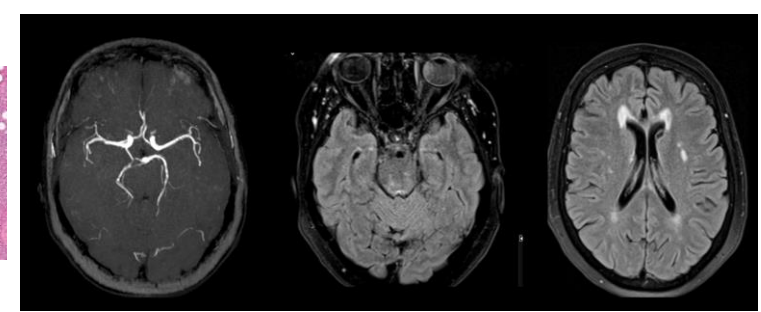
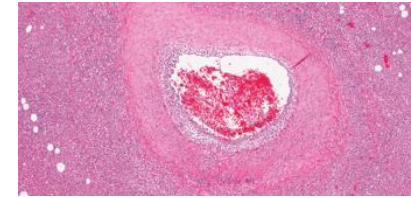
Finding	Patients, n
Angiogram, positive; CNS biopsy, positive	6
Angiogram, positive; CNS biopsy, negative	18
Angiogram, positive; CNS biopsy, not performed	52
Angiogram, negative; CNS biopsy, positive	8
Angiogram, not performed <sup>a</sup> ; CNS biopsy, positive <sup>b</sup>	17



# Diagnostic test results in primary CNS vasculitis

A systematic review of published cases

Ferghal McVerry, MD; Gavin McCluskey, MRCP; Peter McCarron, PhD; Keith W. Muir, MD; Mark O. McCarron, MD



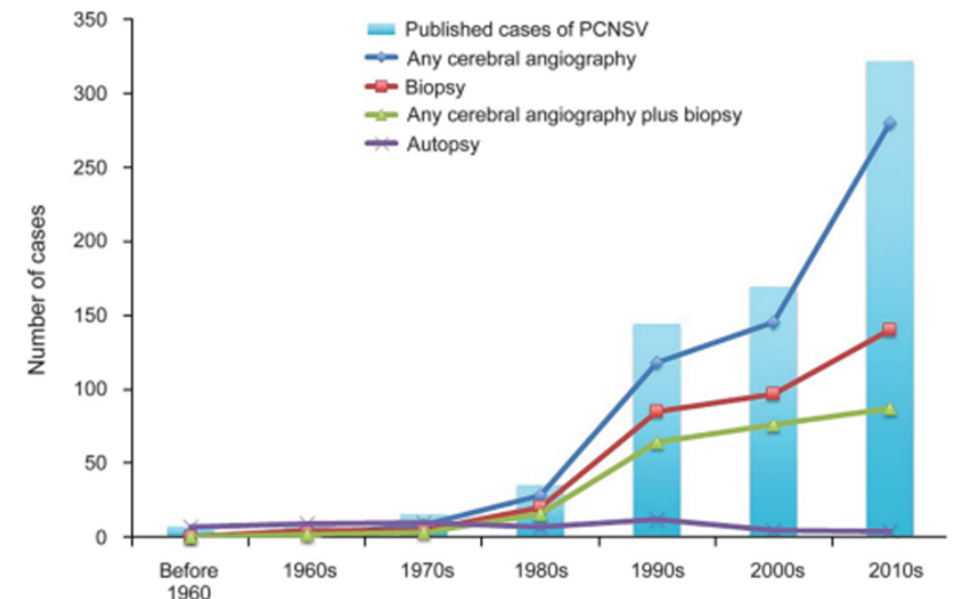
**Table 1** Frequency of angiography, biopsy, and postmortem in published cases of primary CNS vasculitis (PCNSV)

Test	No.	% of all PCNSV	% of total tested
No. of original PCNSV	701	100	
Any pathologic diagnosis made	301	42.9	74.1 <sup>a</sup>
Postmortem diagnosis	54	7.7	
Biopsy performed	352	50.2	
Biopsy positive	248	35.4	70.5
Biopsy negative	104	14.8	29.5
Postmortem PCNSV with previous normal biopsy	8	1.1	
Postmortem PCNSV with previous biopsy also showing PCNSV	1	0.2	8.3
Any angiogram performed	581	82.9	
Biopsy and any angiogram performed	248	35.4	
Biopsy and any angiogram both abnormal	71	10.1	28.6
Biopsy abnormal, angiogram normal	91	13.0	33.7
Biopsy normal, angiogram abnormal	74	10.6	29.8
Biopsy normal, angiogram normal	12	1.7	4.8
Biopsy abnormal with classic angiographic appearance <sup>b</sup>	26	3.7	11.2
Any pathologic diagnosis with classic angiographic appearances	32	4.6	11.9

<sup>a</sup>Percent of patients with any CNS pathological testing.

<sup>b</sup>Showing alternating areas of ectasia or stenosis in multiple areas within multiple cerebral vessels.

**Figure 2** Frequency of use of angiographic and tissue pathology testing in published cases of primary CNS vasculitis (PCNSV) per decade

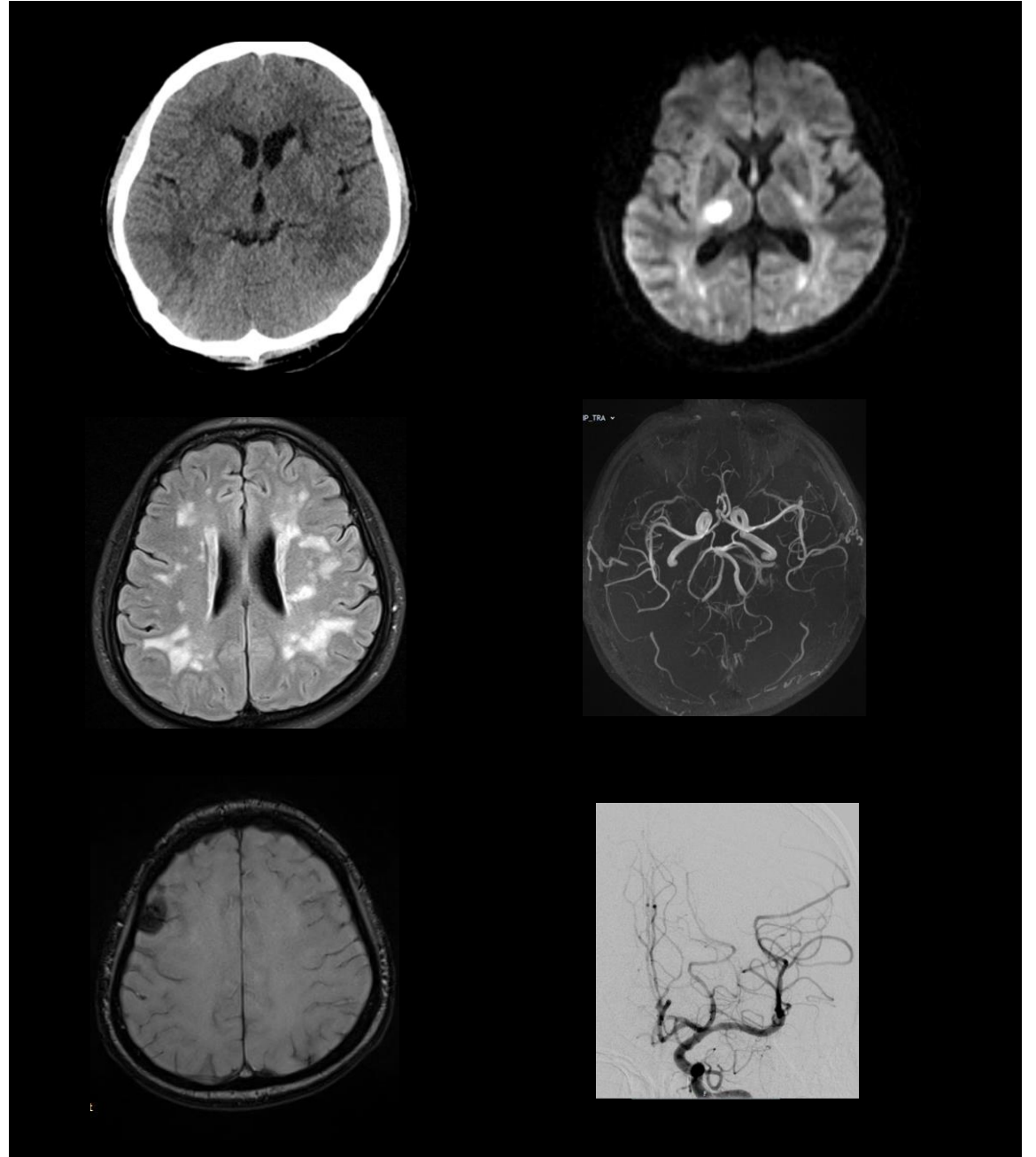


**Table 3** Proposed diagnostic criteria for primary CNS vasculitis (PCNSV) adapted from Birnbaum and Hellmann<sup>3</sup>

Classification of PCNSV	Description
<b>Definite</b>	Confirmation of vasculitis on analysis of a tissue biopsy specimen
<b>Probable</b>	In the absence of tissue confirmation, if there are high probability findings on an angiogram with abnormal findings on MRI and a CSF profile consistent with PCNSV

# Case

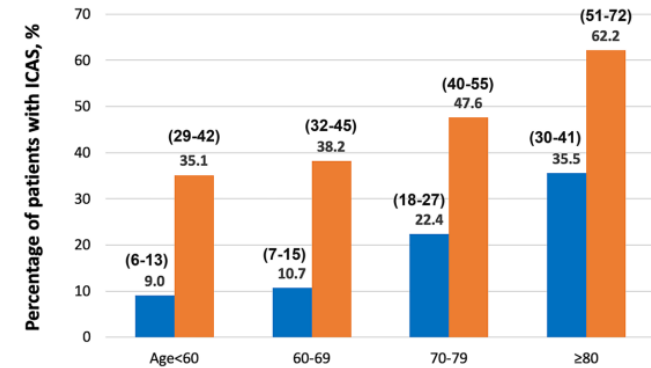
- 34. Headache. Hemiparesis
- Old & new ischemic lesions on imaging
- Narrowing on MRA/ DSA
- Brain biopsy - normal
- Rx: Steroid, cyclophosphamide
  
- Questions:
- Date of next Cyclophosphamide ?
- Duration of Steroid?
  
- Question:
- Diagnosis ?





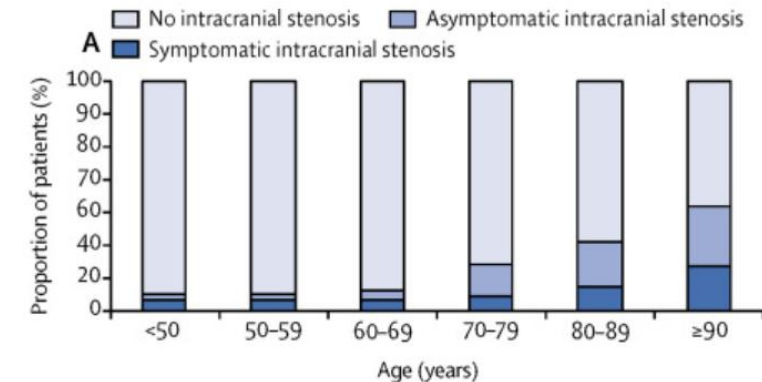
Original research

## Intracranial arterial stenosis in Caucasian versus Chinese patients with TIA and minor stroke: two contemporaneous cohorts and a systematic review



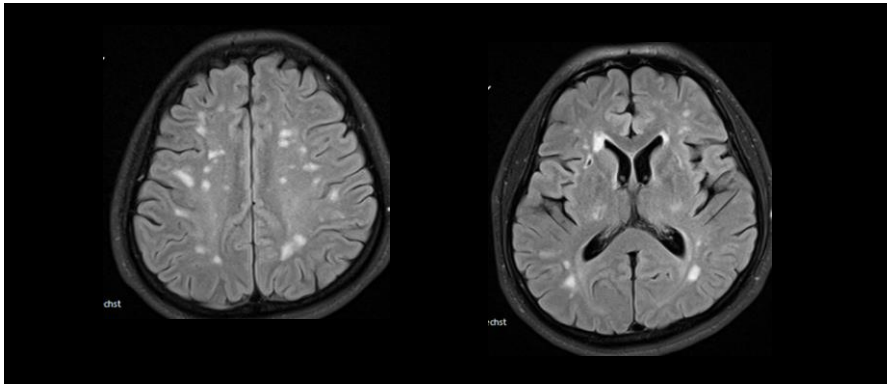
### THE LANCET Neurology

Prevalence, predictors, and prognosis of symptomatic intracranial stenosis in patients with transient ischaemic attack or minor stroke: a population-based cohort study



## History still matters

- Ex-Smoker
- Asian ethnicity
- Hyperlipidaemia
- Hypertension > 200mmHg



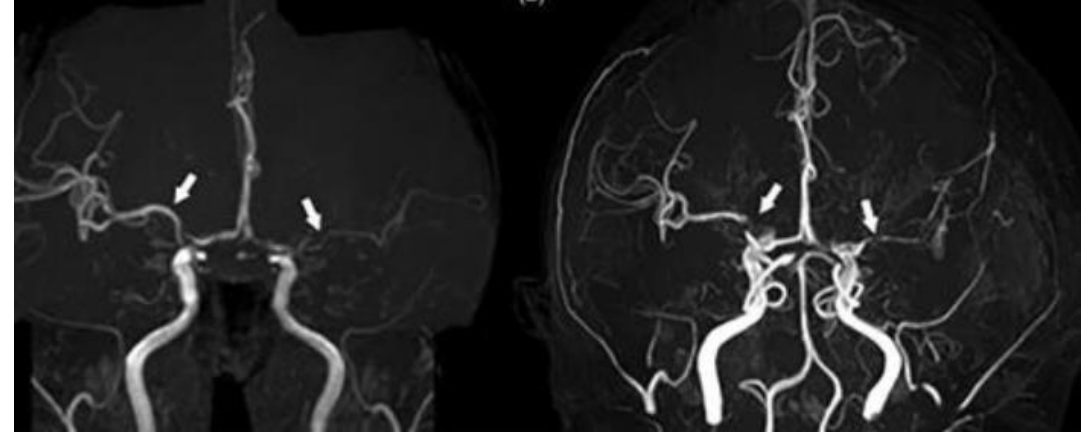
- Low pre-test probability for vasculitis
- No further immunosuppression
- Secondary prevention
- Remains well

# Can Vessel Wall Imaging Help ?

Cerebrovascular disease

REVIEW

High-resolution intracranial vessel wall imaging:  
imaging beyond the lumen



## Vessel Wall Contrast Enhancement: A Diagnostic Sign of Cerebral Vasculitis

Wilhelm Küker<sup>a,b</sup> Susanne Gaertner<sup>c</sup> Thomas Nägele<sup>d</sup> Christian Dopfer<sup>e</sup>  
Martin Schöning<sup>e</sup> Jens Fiehler<sup>a</sup> Peter M. Rothwell<sup>b</sup> Ulrich Herrlinger<sup>f</sup>

Review

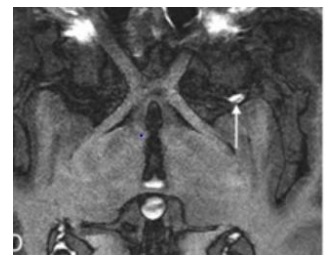
Black blood imaging of intracranial vessel walls

**Intracranial Vessel Wall MRI: Principles and Expert Consensus  
Recommendations of the American Society of Neuroradiology**

### Conditions that may show “ vasculitic” changes on angiography

Intracranial Atherosclerosis	Subarachnoid Haemorrhage
CADASIL	Intracerebral haematoma
Reversible Cerebral Vasoconstriction	Migraine
Antiphospholipid syndrome	Sickle Cell disease
Fibromuscular dysplasia	Alzheimer’s disease
Intravascular Lymphoma	Multiple Cerebral Emboli ( SBE)
Zoster vasculopathy	Marfan/ Ehlers Danlos
Vasospasm ( drug)	Severe Hypertension
Moya-Moya	Acute Trauma
Radiation Vasculopathy	

# Vessel Wall MRI + Comparison with Angiogram / Histopathology

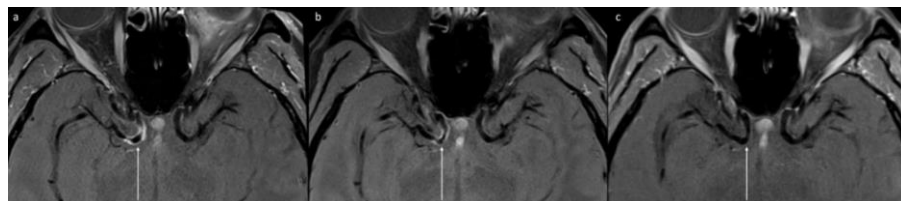


- Abnormal in most angiographic vasculitis
- Normal in most biopsy-proven vasculitis
- Also abnormal in multiple vasculitis mimics

	VWMRI abnormal	VWMRI normal
All PCNSV with VWMRI (n=73)*	55/73 (75%)	18/73(25%)
Angiographic PCNSV diagnosis with VWMRI (n=43)	39/43 (91%)	9/43(9%)
Histopathological PCSNV diagnosis with VWMRI (n=26)	12/26(46%)	14/26(54%)

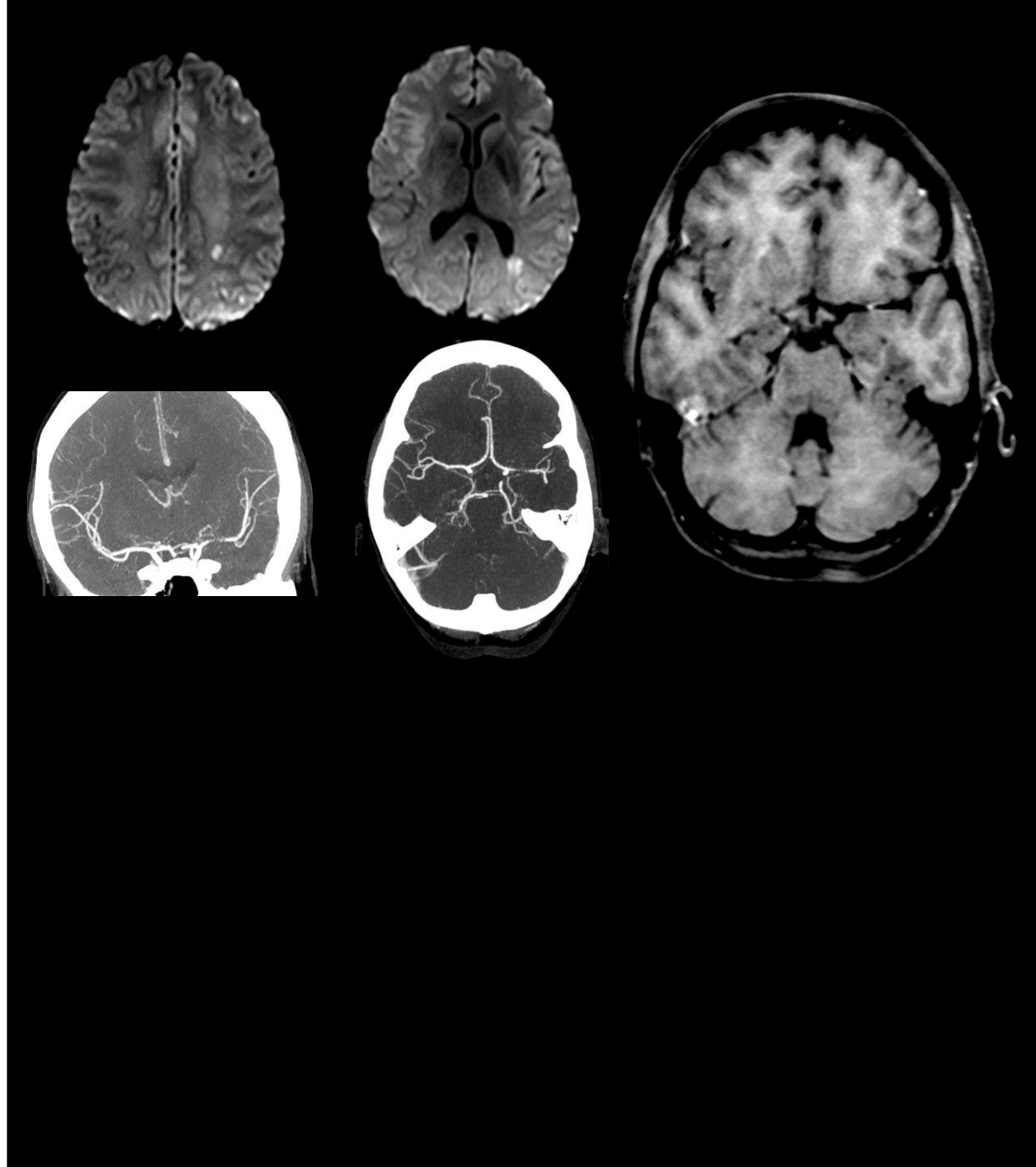
- Validation against biopsy-proven vasculitis lacking

	VWMRI abnormal	VWMRI normal
PCNSV mimics (n=65)	63/65 (97%)	2/65 (3%)
RCVS	3/4 (75%)	1/4(25%)
Intracranial Atheroma	4/5 (80%)	1/5 (20%)
Systemic / other autoimmune disorder	6/6 (100%)	-
Infectious vasculopathy	6/6(100%)	-
Moya-moya disease	1/1 (100%)	-
Arterial dissection	1/1 (100%)	-
Drug induced vasculopathy	1/1(100%)	-
Cerebral amyloid angiopathy	1/1(100%)	-
Unclear diagnosis	3/3 (100%)	-
Hypertension	37/37 (100%)	-



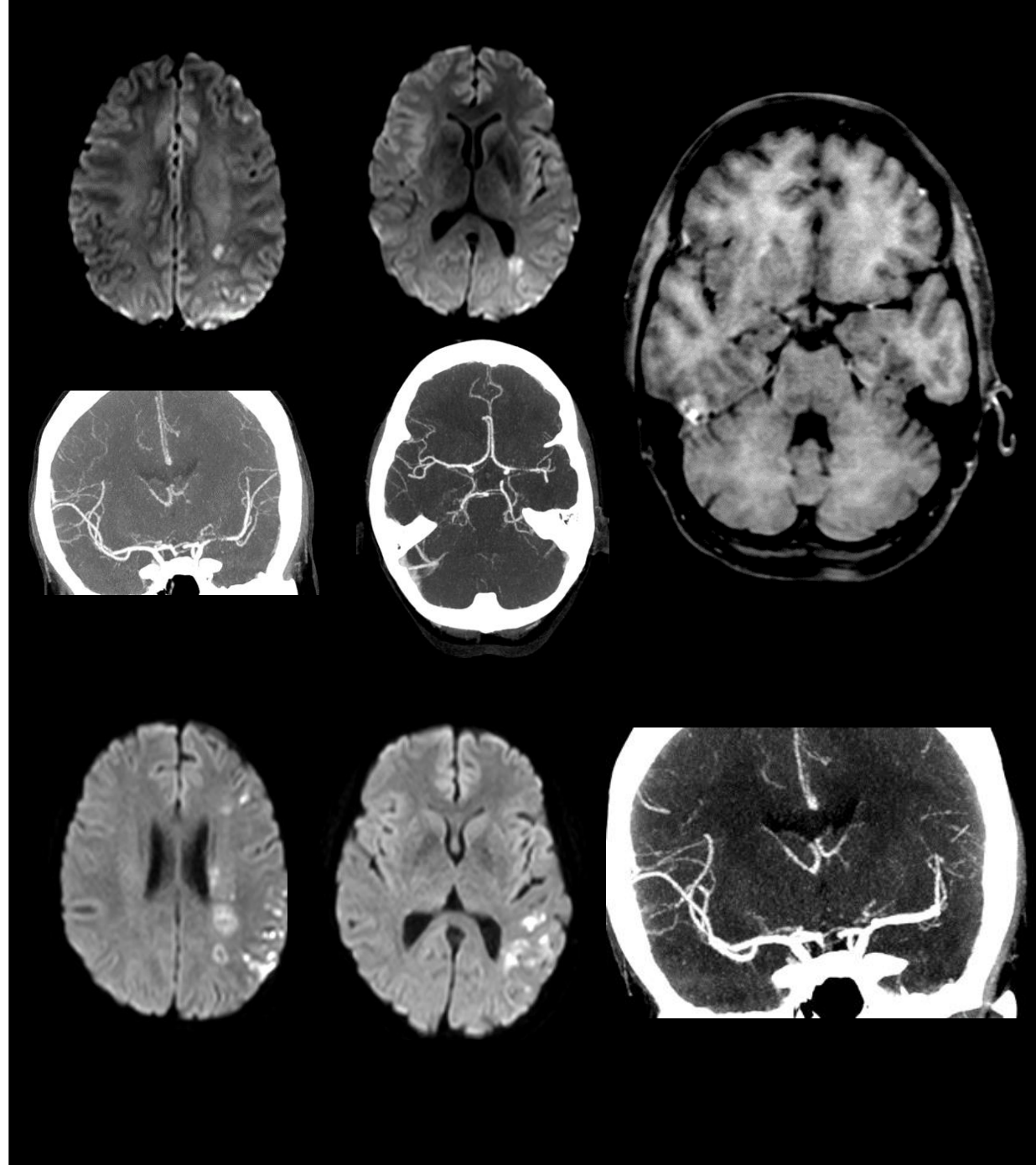
# Case

- Recurrent left hemisphere infarcts
- Vessel wall MRI= Vasculitis of left Middle cerebral artery
- Steroid, rituximab, cyclophosphamide
- Progressive infarction



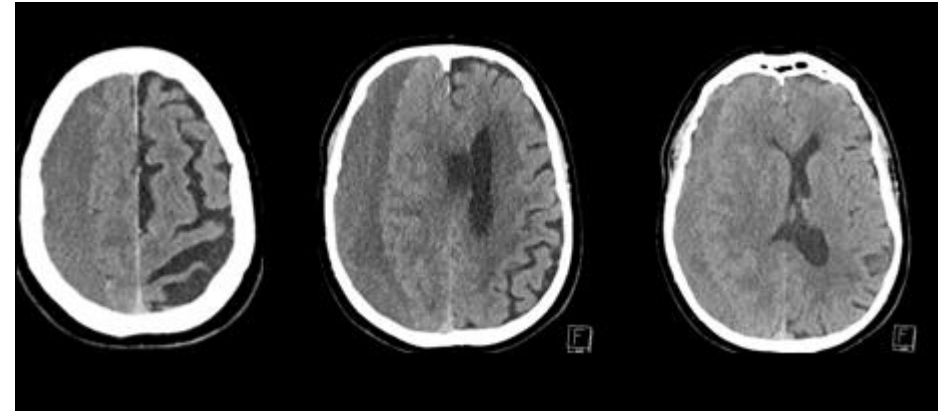
# Case

- Recurrent left hemisphere infarcts
- Vessel wall MRI= Vasculitis of left Middle cerebral artery
- Steroid, rituximab, cyclophosphamide
- Progressive infarction
- Stenting to left middle cerebral artery
- No further events, (yet)
- Vasculitis ? Focal atheroma?



# Other Vasculopathies

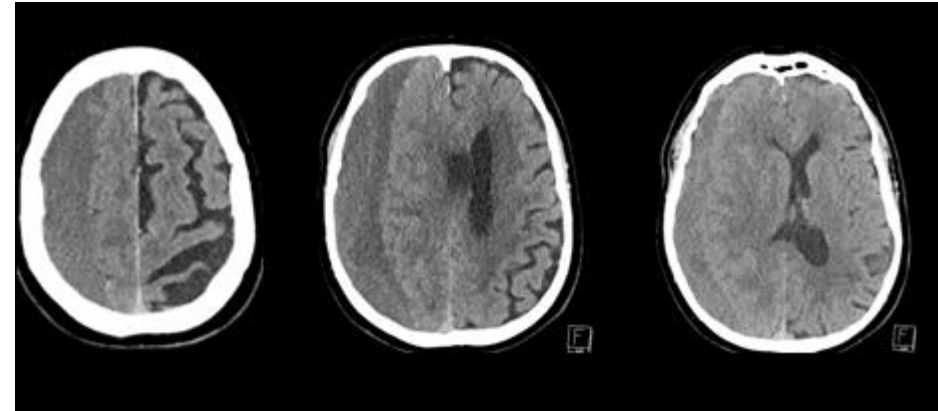
- 68
- Minor fall
- 3 Weeks later:
- Crashed car
- Shuffling on feet
- Struggling with gear change
- Poor coordination
- Surgical evacuation
- Discharge

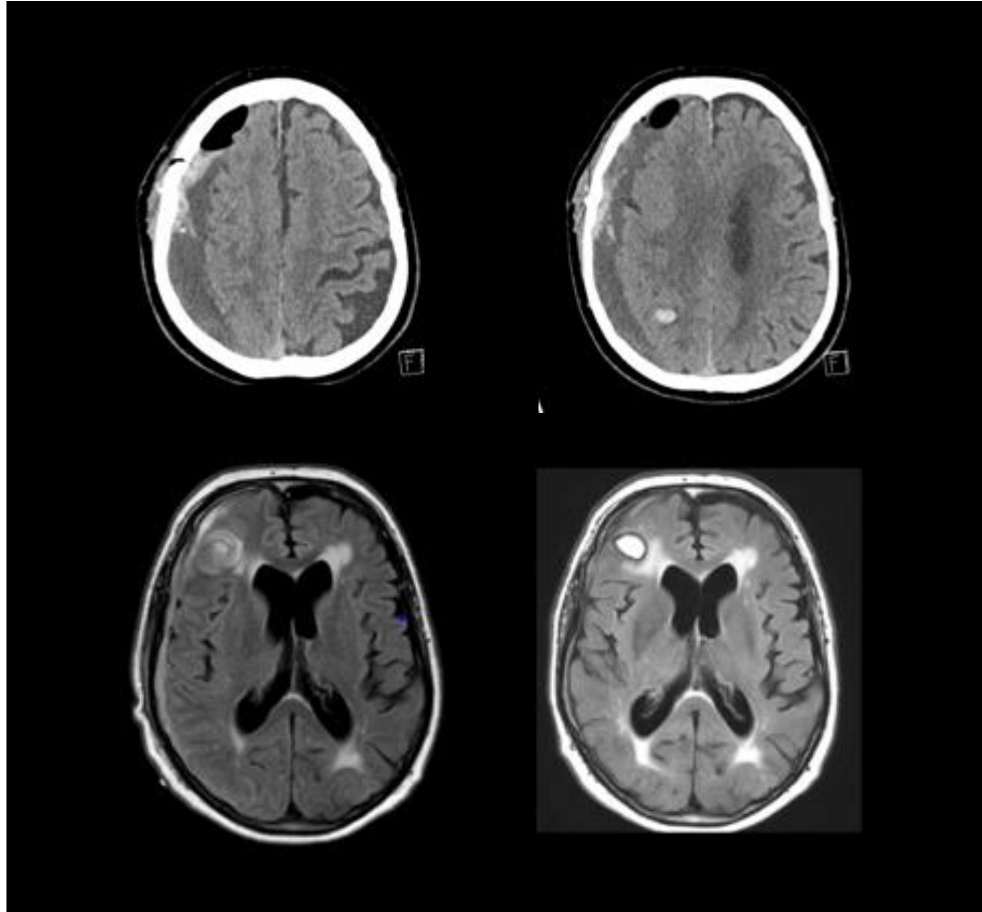




# Other Vasculopathies

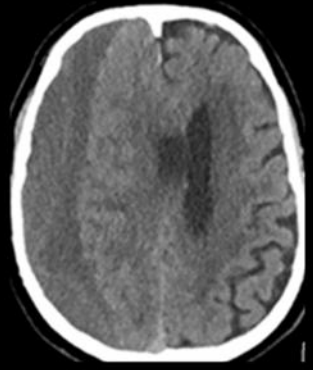
- 68
- Minor fall
- 3 Weeks later:
- Crashed car
- Shuffling on feet
- Struggling with gear change
- Poor coordination
- Surgical evacuation
- Discharge





- Surgical washout
- Antibiotics
  
- Began having falls
- Progressive left weakness
- Progressive cognitive impairment
- Bed bound

Video



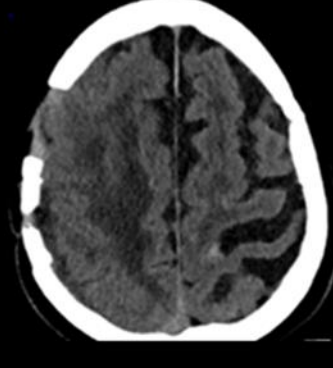
Feb 2023



Feb 2023



May 2023



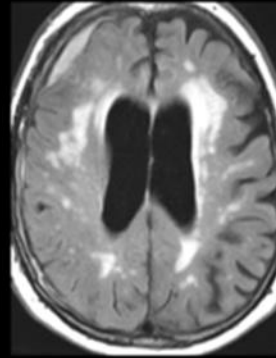
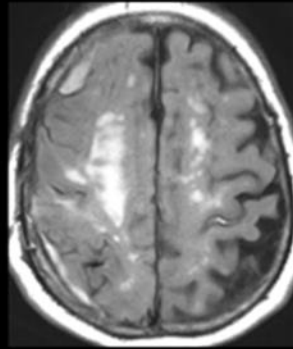
June 2023



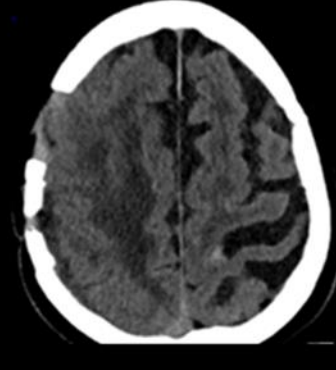
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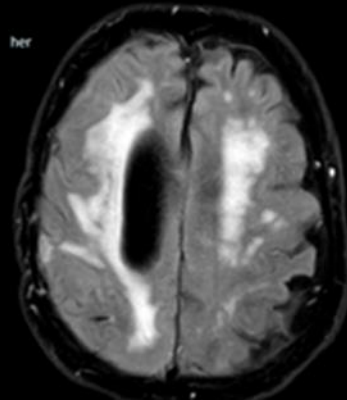
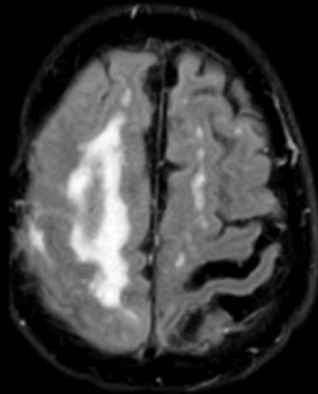
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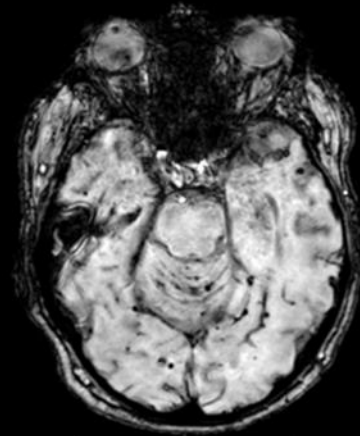
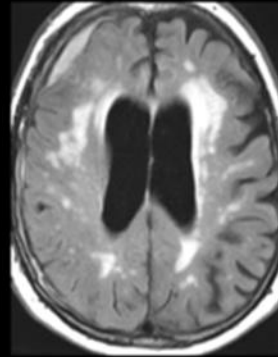
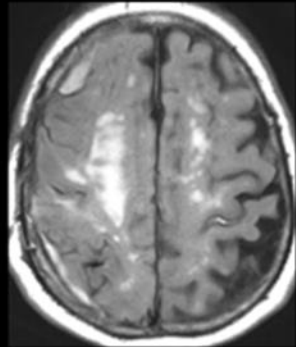




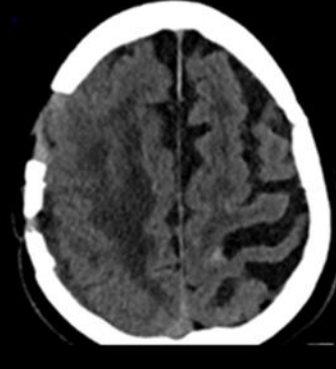
Feb 2023



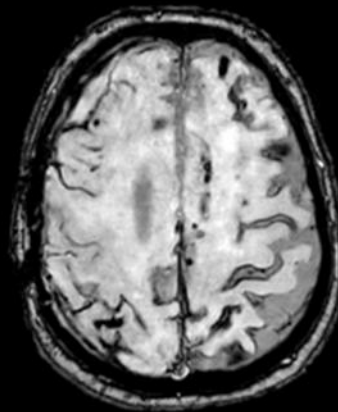
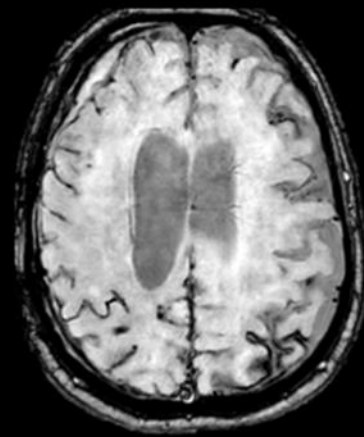
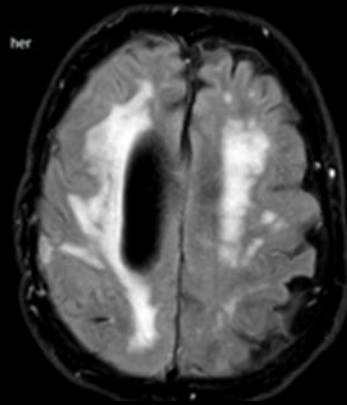
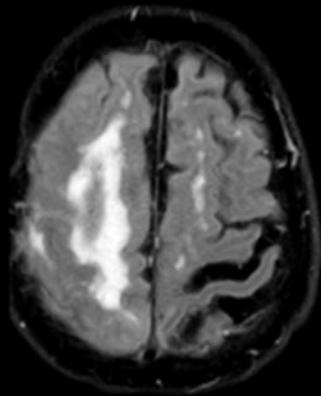
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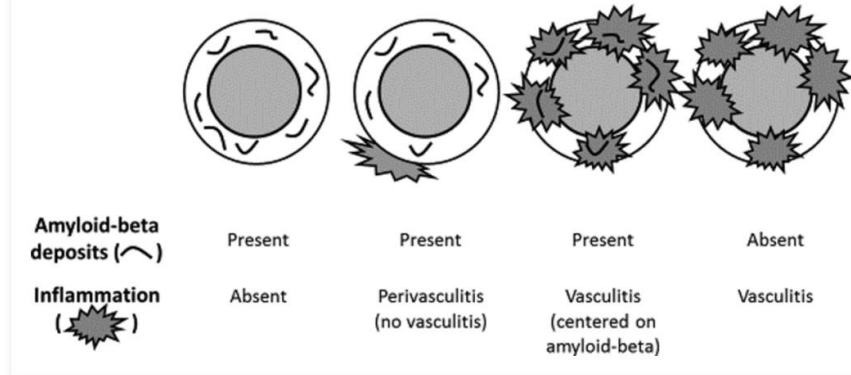
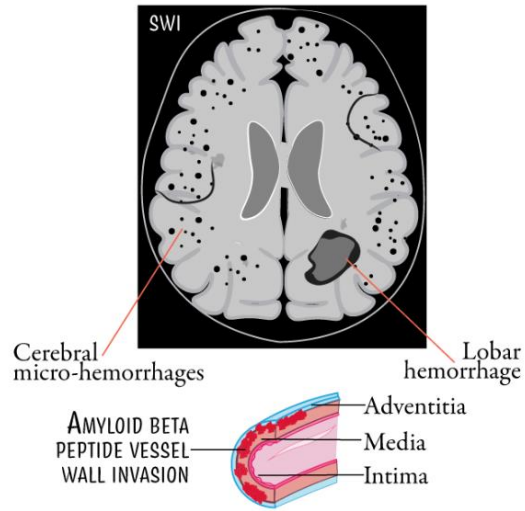
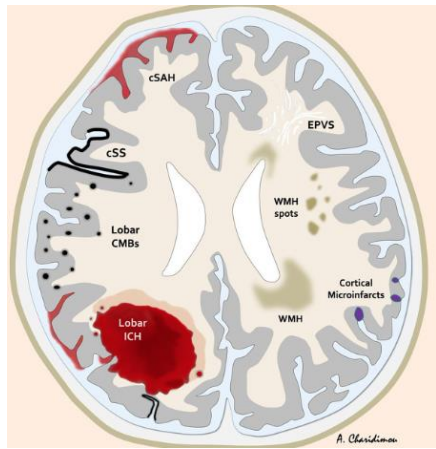


May 2023



June 2023





June 22, 2020

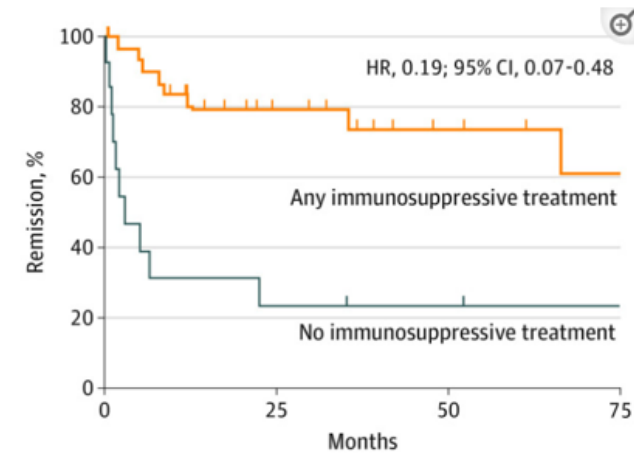
## Association Between Immunosuppressive Treatment and Outcomes of Cerebral Amyloid Angiopathy-Related Inflammation

February 2016

## Validation of Clinicoradiological Criteria for the Diagnosis of Cerebral Amyloid Angiopathy-Related Inflammation

Table 1. Criteria for the Diagnosis of CAA-ri

Diagnosis	Criteria
Probable CAA-ri	<ol style="list-style-type: none"> <li>Age <math>\geq 40</math> y</li> <li>Presence of <math>\geq 1</math> of the following clinical features: headache, decrease in consciousness, behavioral change, or focal neurological signs and seizures; the presentation is not directly attributable to an acute ICH</li> <li>MRI shows unifocal or multifocal WMH lesions (corticosubcortical or deep) that are asymmetric and extend to the immediately subcortical white matter; the asymmetry is not due to past ICH</li> <li>Presence of <math>\geq 1</math> of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis<sup>8</sup></li> <li>Absence of neoplastic, infectious, or other cause</li> </ol>
Possible CAA-ri	<ol style="list-style-type: none"> <li>Age <math>\geq 40</math> y</li> <li>Presence of <math>\geq 1</math> of the following clinical features: headache, decrease in consciousness, behavioral change, or focal neurological signs and seizures; the presentation is not directly attributable to an acute ICH</li> <li>MRI shows WMH lesions that extend to the immediately subcortical white matter</li> <li>Presence of <math>\geq 1</math> of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis<sup>8</sup></li> <li>Absence of neoplastic, infectious, or other cause</li> </ol>



No. at risk	0	25	50	75
Any immunosuppressive treatment	34	27	26	25
No immunosuppressive treatment	14	4	4	4

# Outcome Video

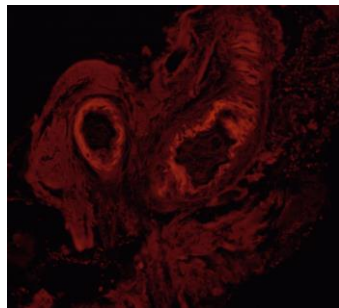
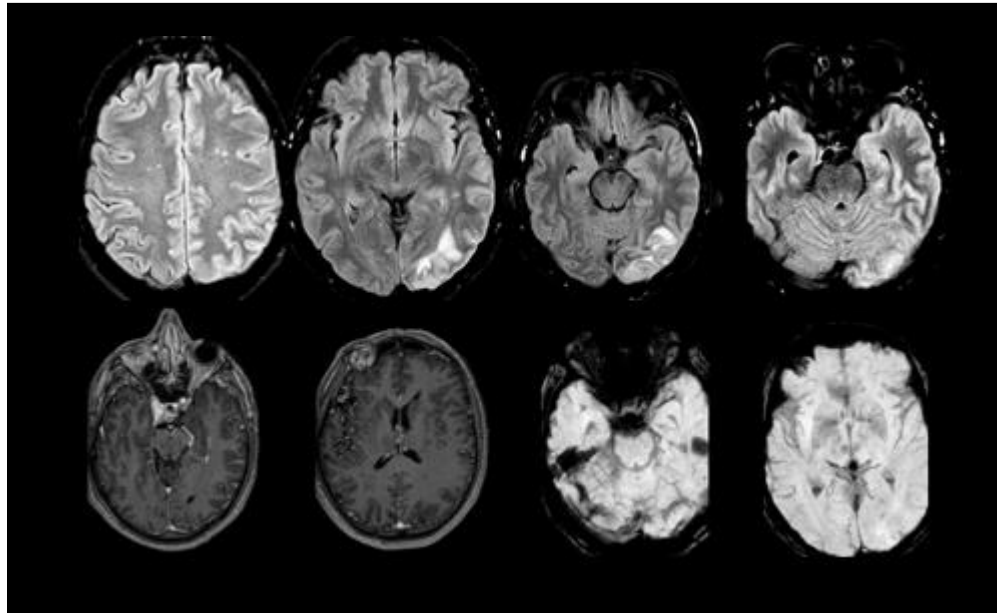


# Variation in Inflammatory Cerebral Angiopathy

**Headache**

**Mild encephalopathy. Visual disturbance**

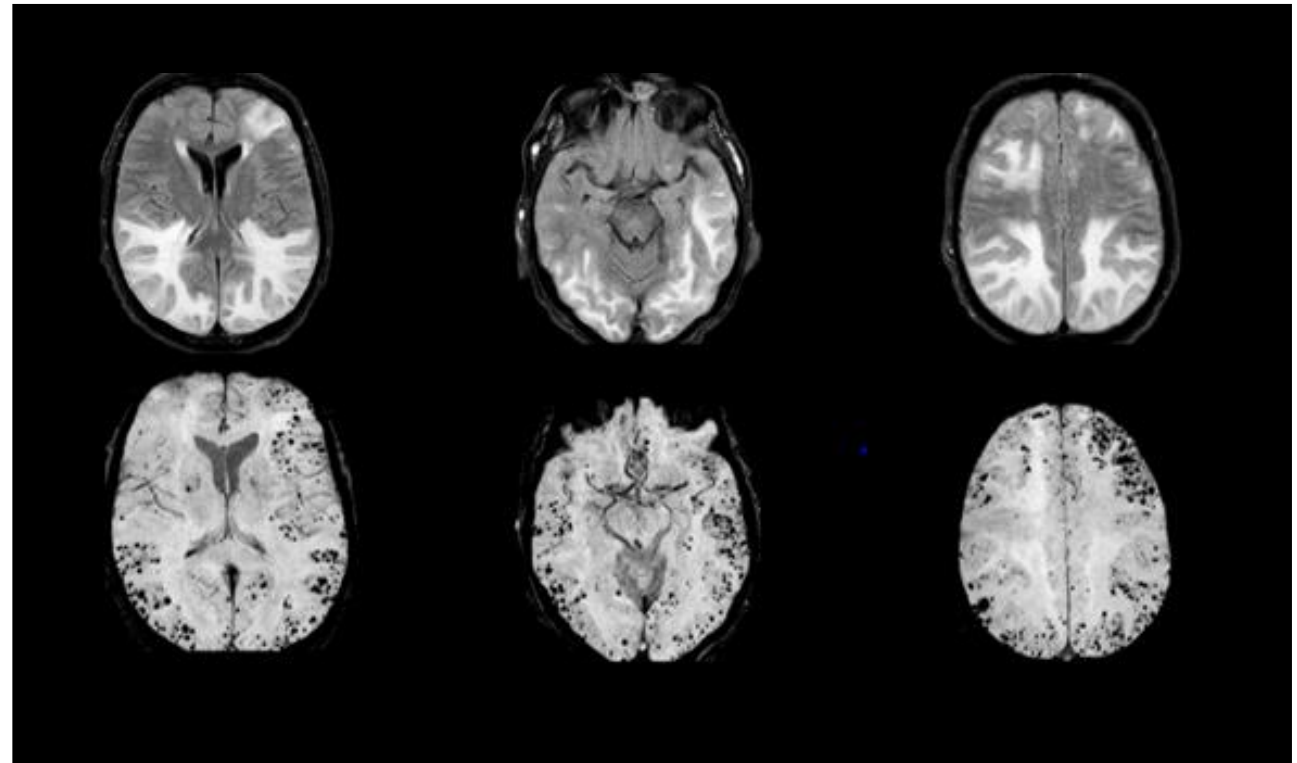
**No microhaemorrhage initially**



**Comatose.**

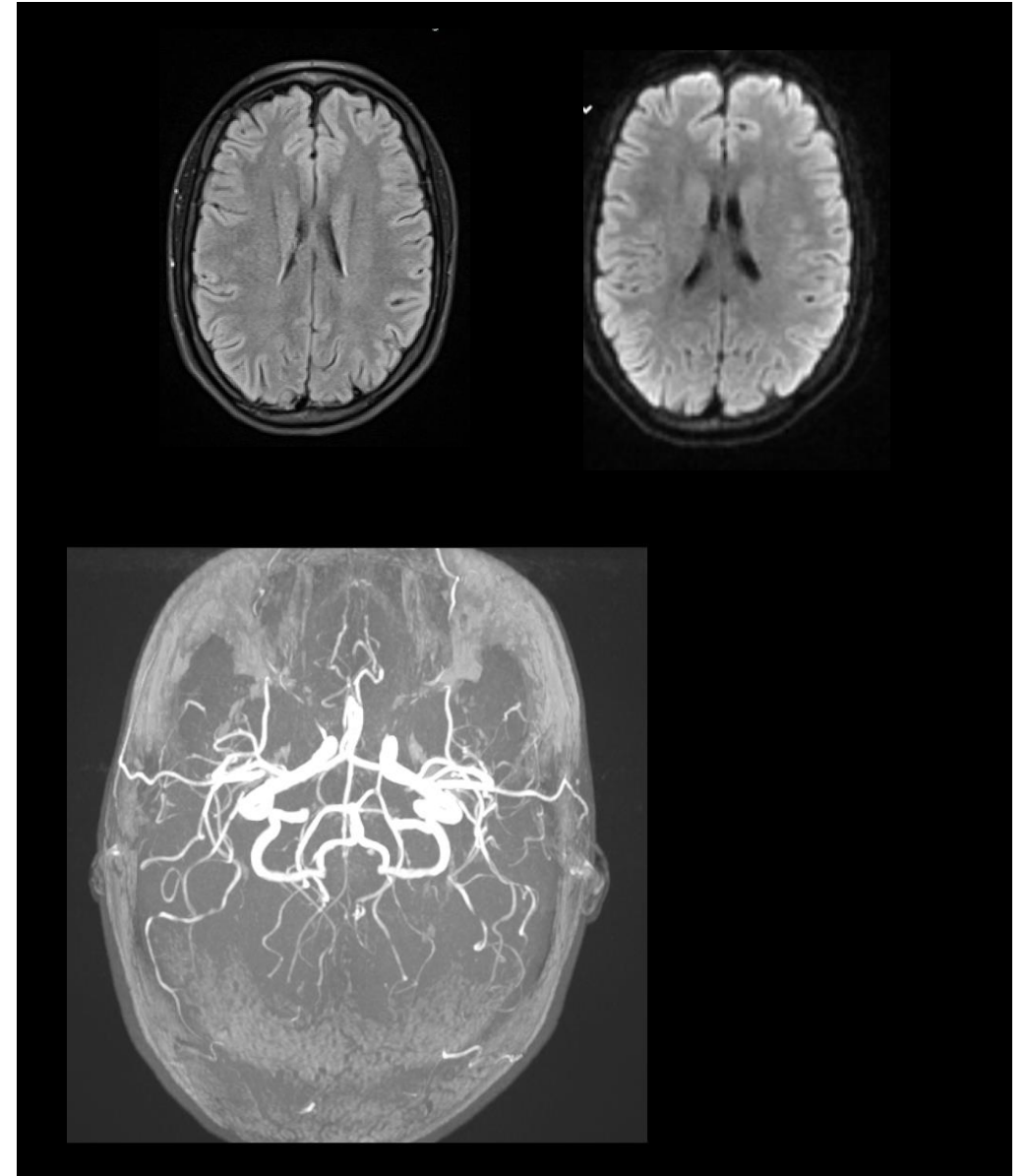
**Massive Brain oedema**

**Innumerable microhaemorrhages**



## Multifocal Arterial Narrowing

- 31
- Thunderclap headache during exercise
- Recurrent exertional headaches x1/52
- MRA: Multifocal beading -vasculitis ?
- CSF Normal



# Multifocal Arterial Narrowing

Calcium channel blocker

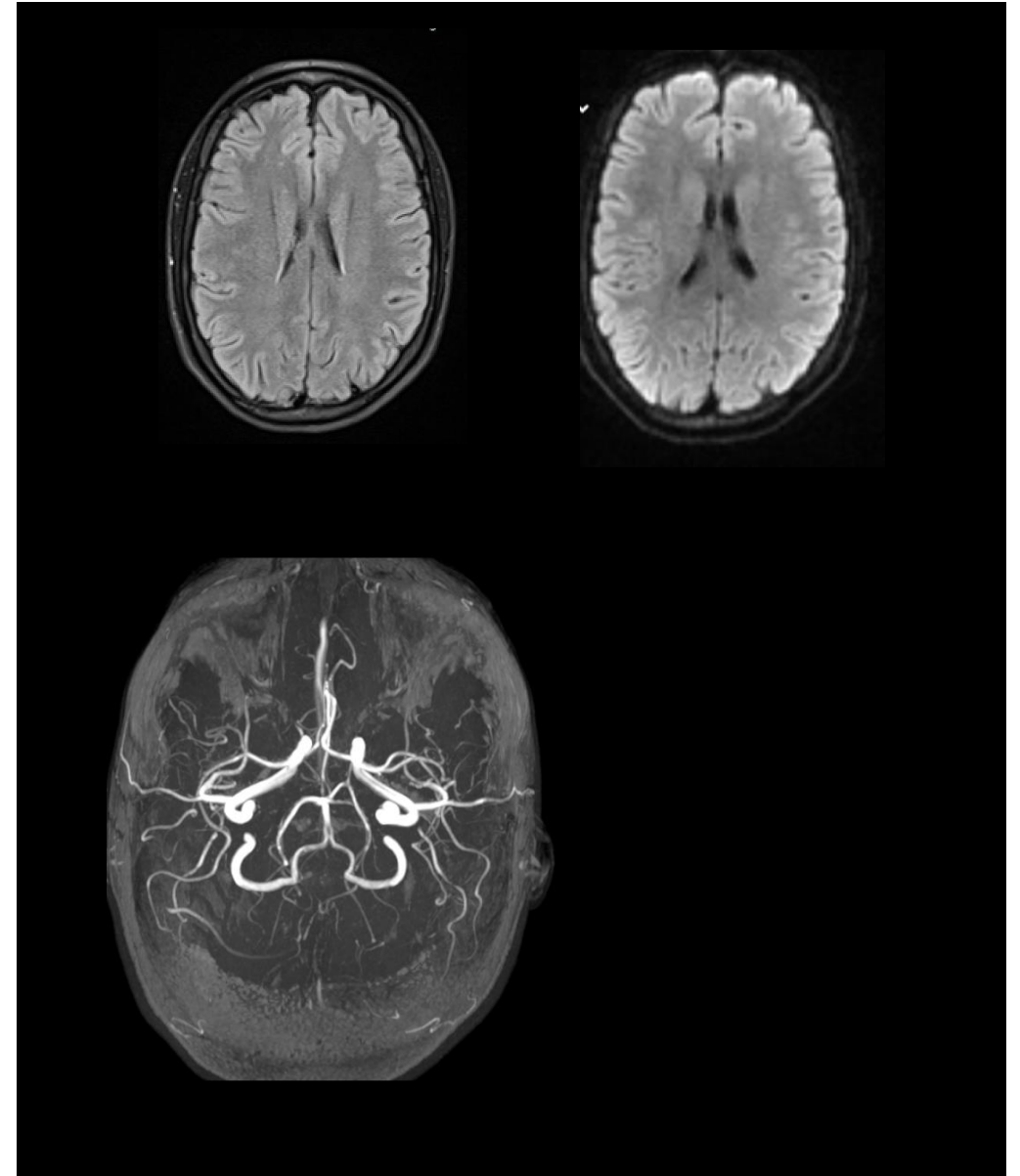
Headaches resolved

Resolution of changes on MRA

Consistent with RCVS

Unable to distinguish vasculitis & RCVS on initial angiogram

History suggests RCVS at outset



# Reversible Cerebral Vasoconstriction

## Clinical Characteristics

Thunderclap headache

Cerebral vasoconstriction at least 2 intracranial arteries

Resolution of vasoconstriction at 3 months

## Common Precipitants

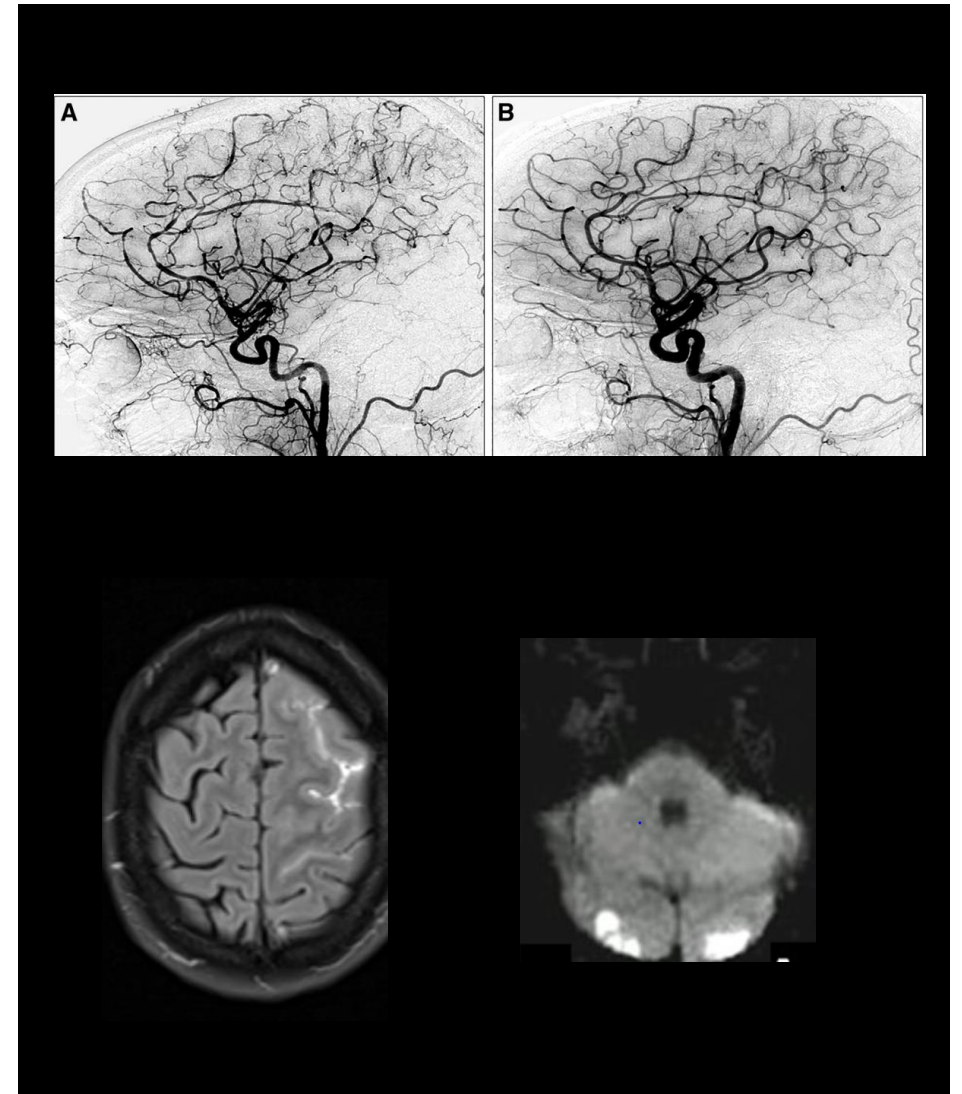
Post Partum

SSRI/ Decongestants/ cyclosporine/ triptans, interferon

## Complications/ Associated Findings

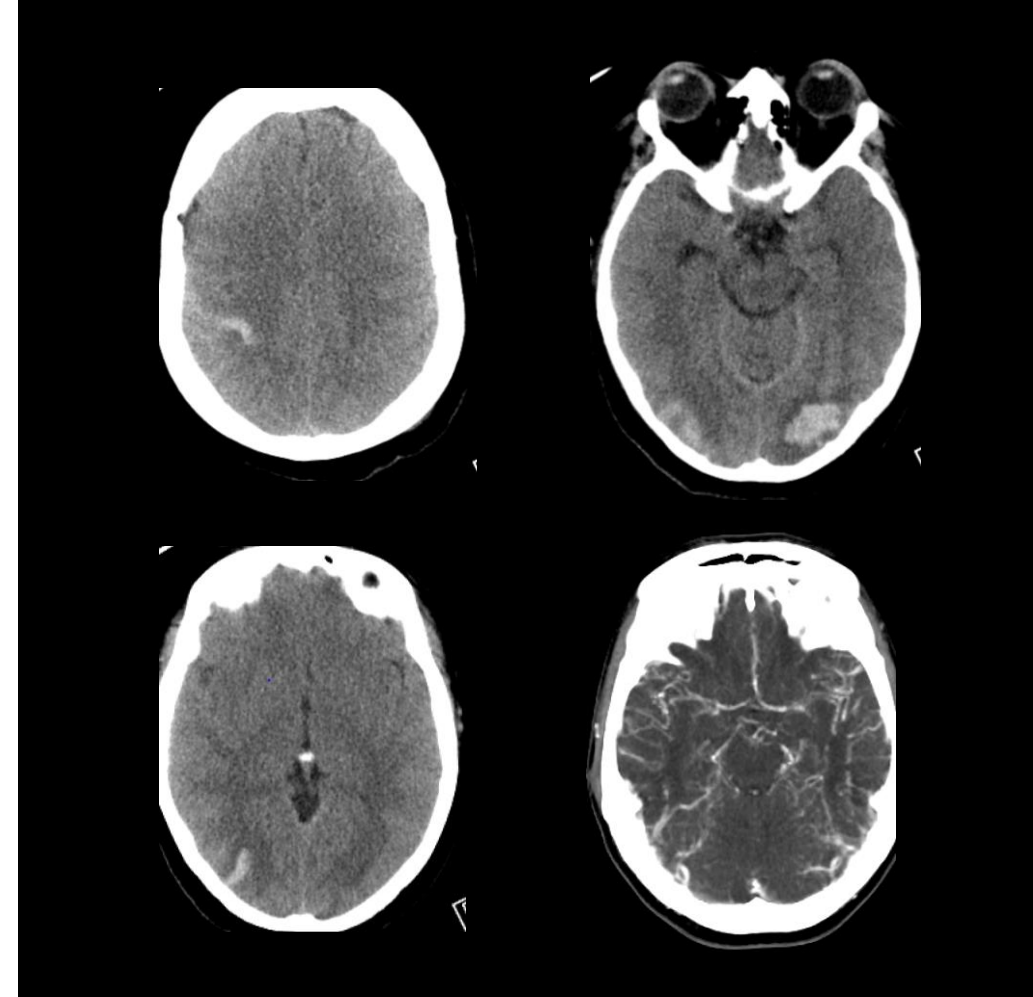
SAH/ infarction/ seizure/ ICH

PRES



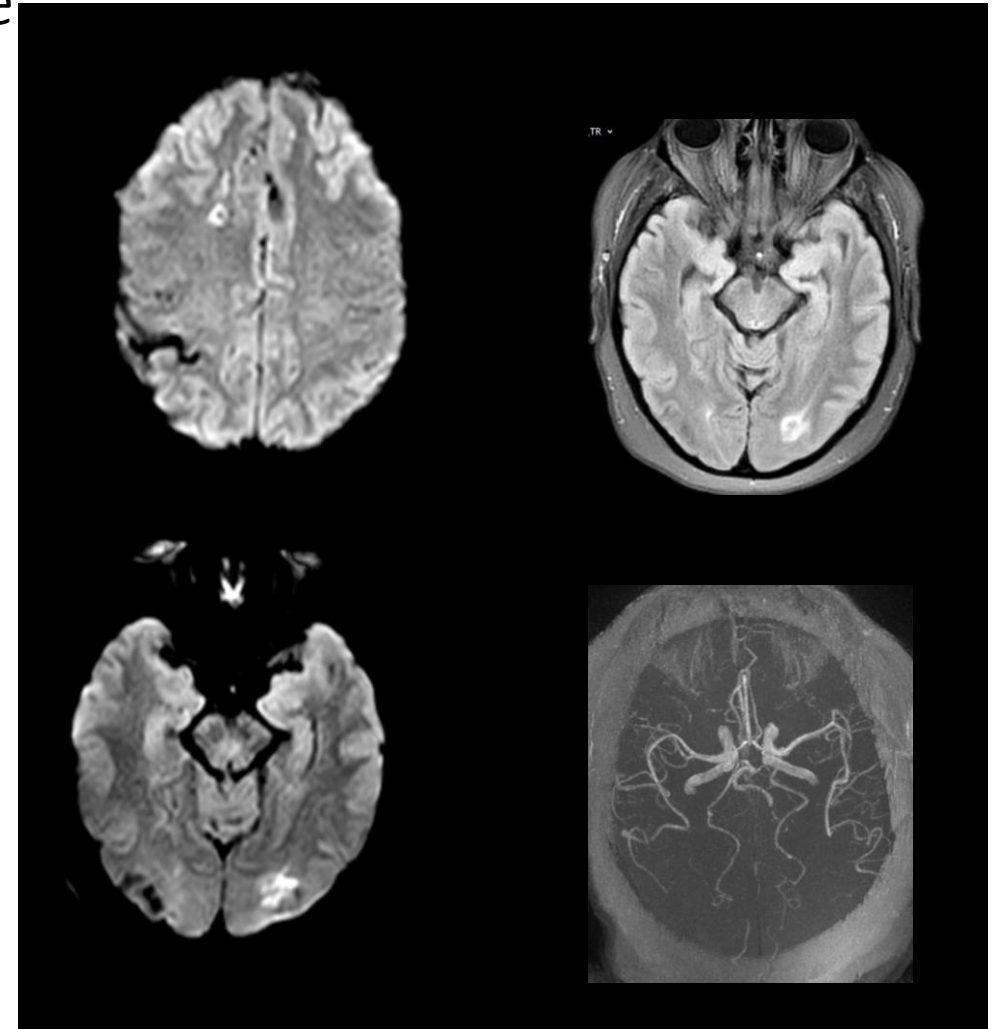
# Multifocal Vasculopathy with Haemorrhage

- Headache & Vomiting
- Found GCS 4
- Combative, confused
- ICU
- External Ventricular drain
- No Aneurysm
  
- Multifocal spasm in anterior & posterior circulation
- Calcium channel blocker



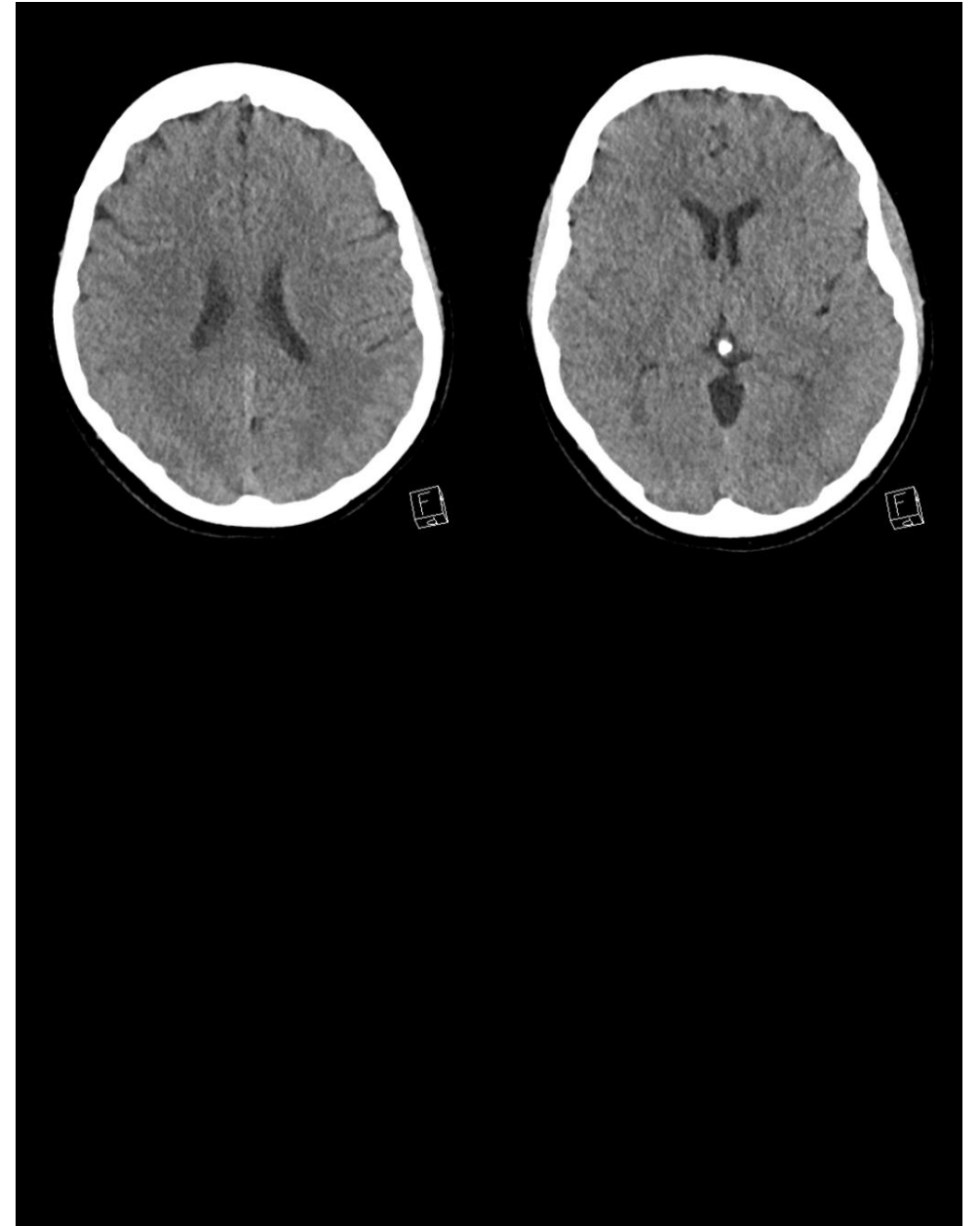
# Multifocal Vasculopathy with Haemorrhage

- Multifocal Gliosis MRI
- Gait/ Balance/ cognition affected
- Vasoconstriction reversed
- Disability persists



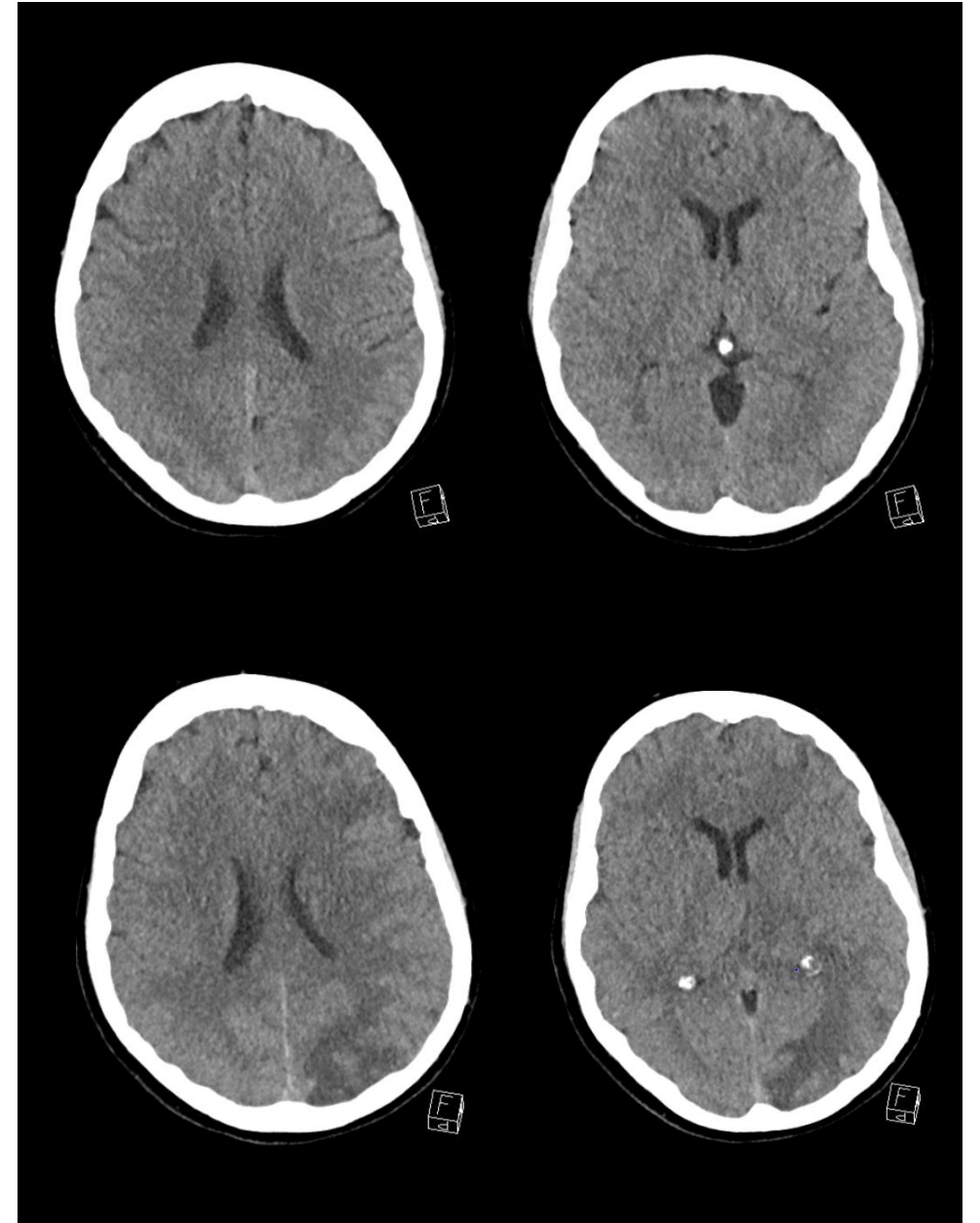
# Acute Encephalopathy

- 57. Goodpasture syndrome.
- Dialysis
- Cyclophosphamide + Prednisolone
  
- Sudden headache
- Right sided weakness
- GCS 9-3

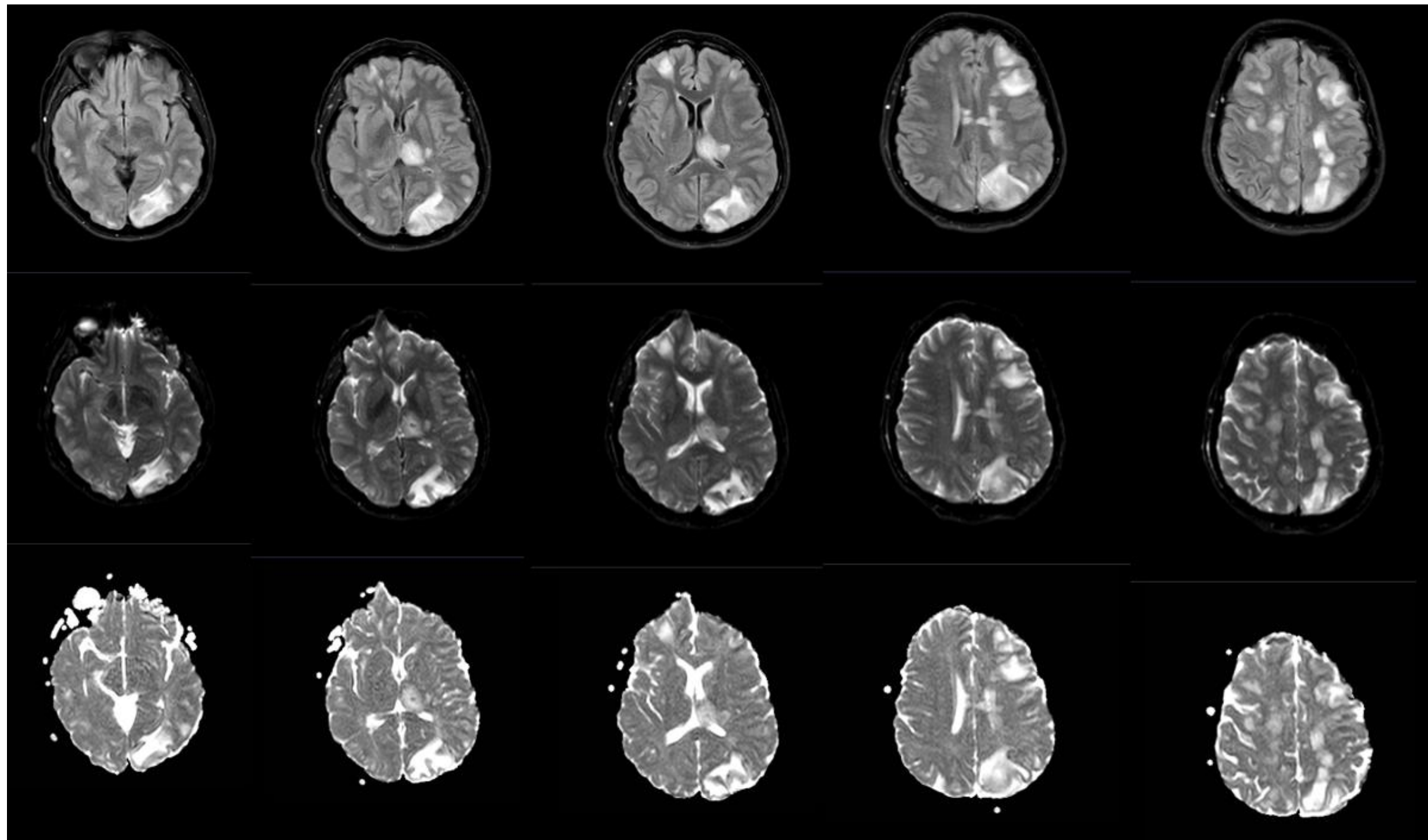


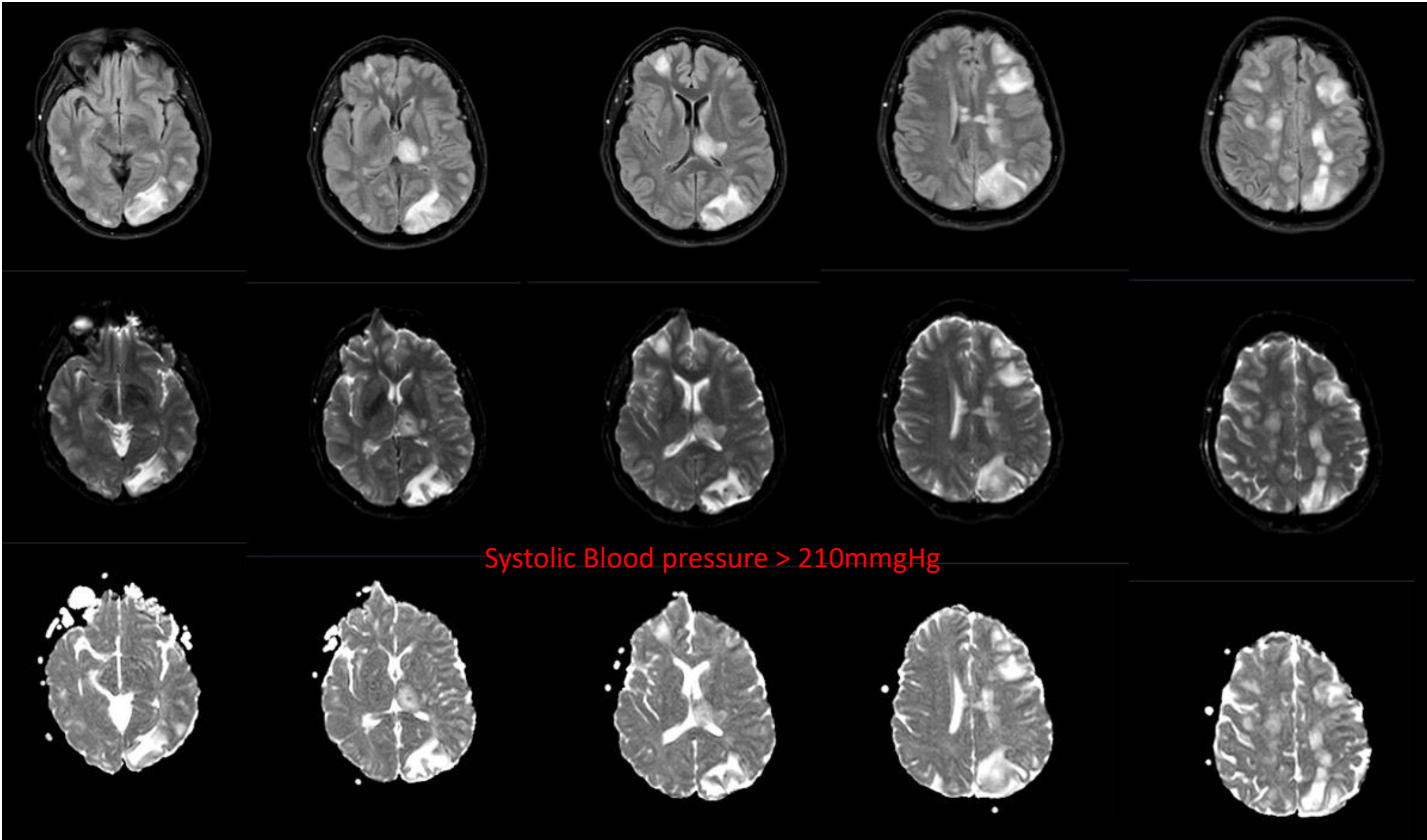
# Acute Encephalopathy

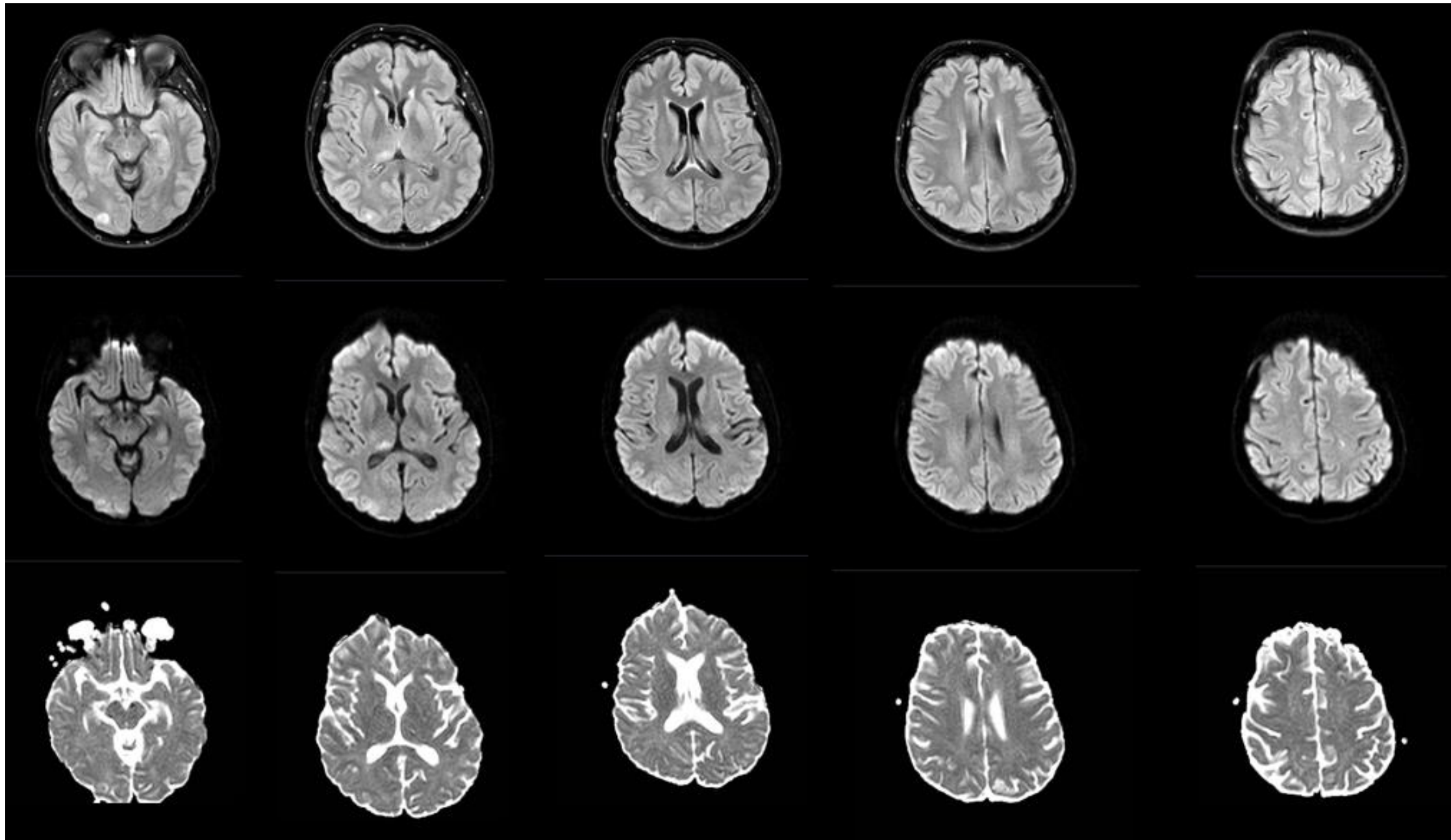
- 57. Goodpasture syndrome.
- Dialysis
- Cyclophosphamide + Prednisolone
  
- Sudden headache
- Right sided weakness
- GCS 9-3
  
- Repeat CT- multifocal brain oedema





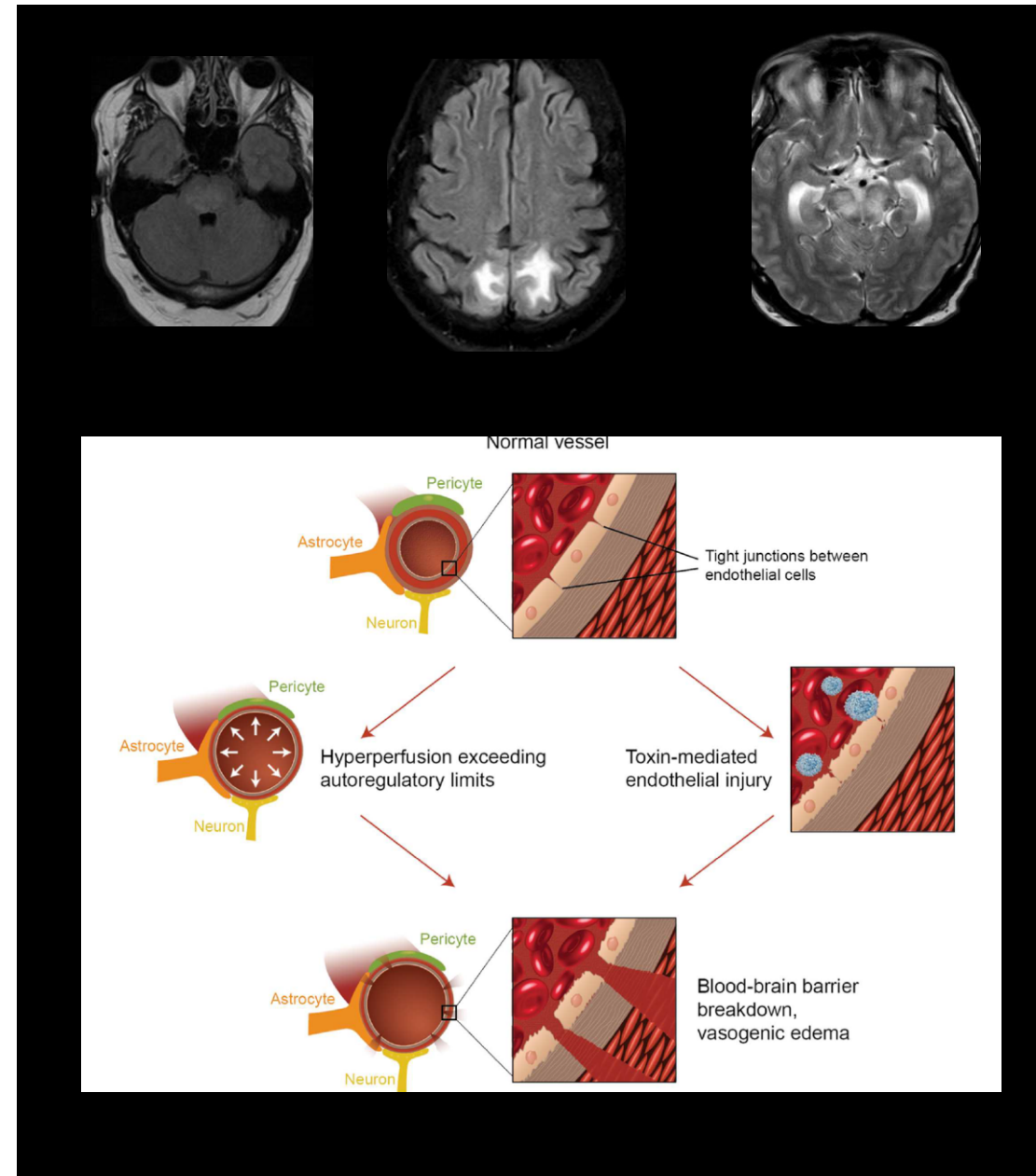






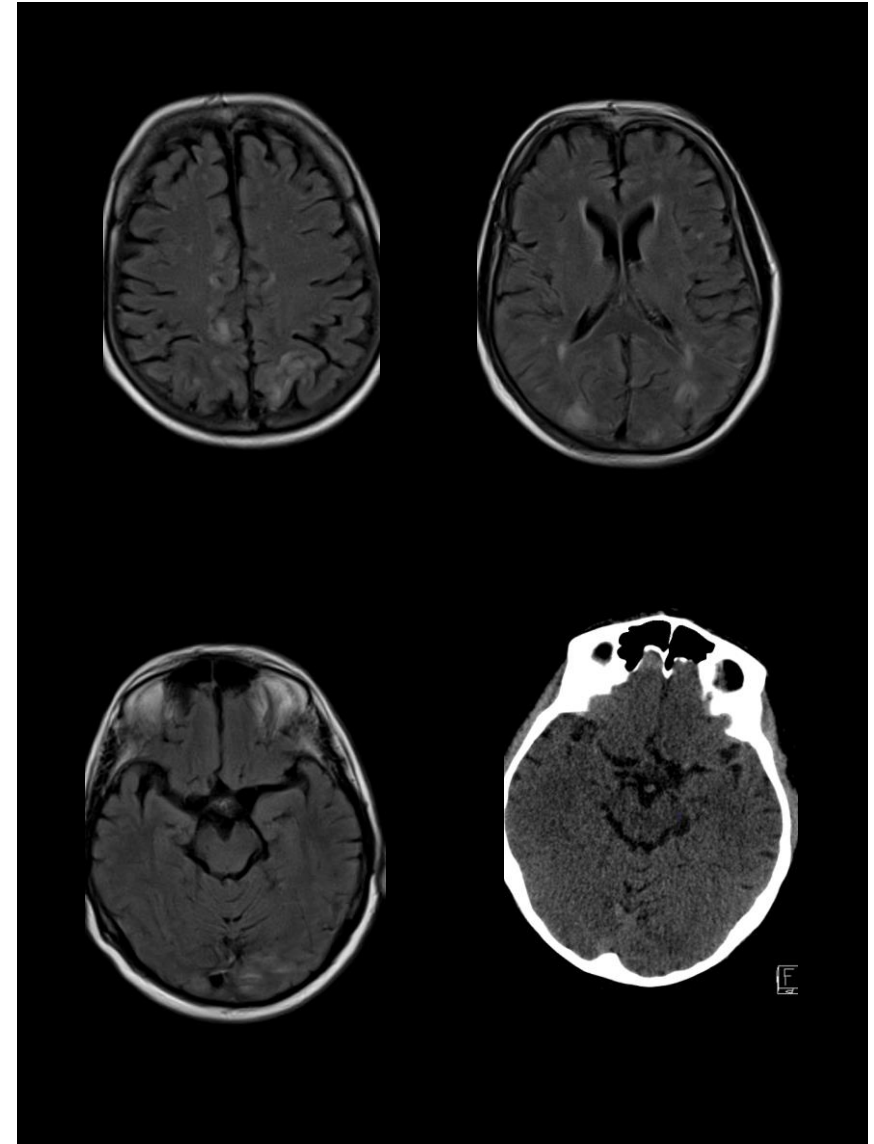
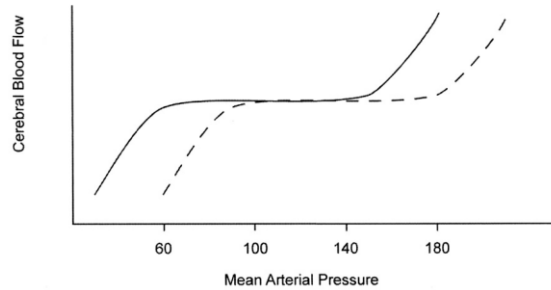
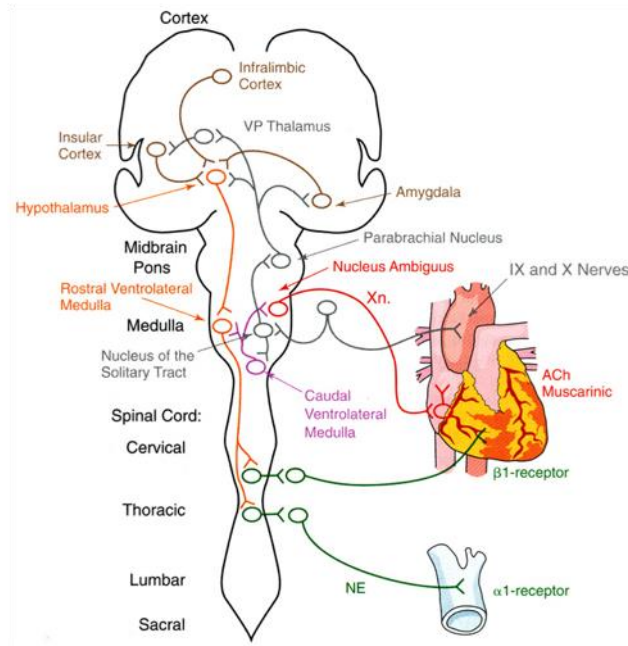
# Posterior Reversible Encephalopathy

- **Hyper-perfusion ?-**
- Elevated BP exceeds limit of cerebral Autoregulation= Blood Brain Barrier dysfunction , vascular leakage
- Plasma / macromolecule leak through tight Junctions resulting in vasogenic oedema
- Posterior Circulation Vulnerable due to impaired sympathetic innervation
- **Neuropeptide/ Cytotoxic ?**
- Vasoconstrictor, endothelin/ thromboxane A2 release , spasm / ischemia/ oedema
- Can occur with Normal BP
- Association with organ transplant/ renal disorders/ autoimmunity.



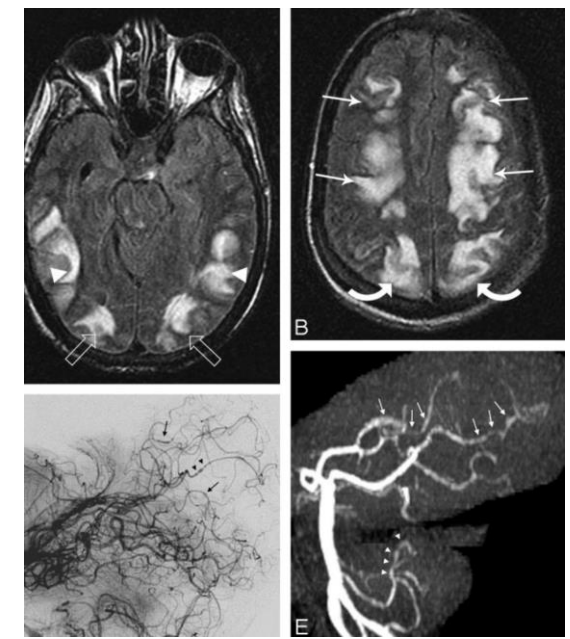
# PRES - Clinical

- Non-specific clinical presentation
- Encephalopathy
- Focal deficit/ Stroke-like
- Seizures
- Visual disturbance / Balint syndrome
- Headache
- Hypertension
- Triggering medications



# Reversible Vasoconstriction and PRES : Overlap

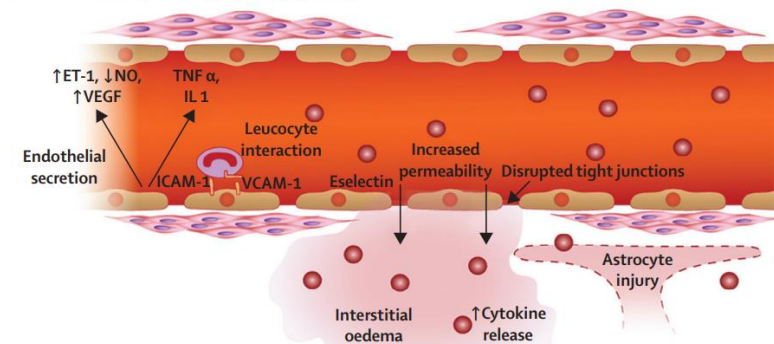
- Up to 30 % of PRES have vasoconstriction (not all have angiogram performed )
- Up to 40% % RCVS have reversible vasogenic oedema /PRES
- Debate- independent disorders vs a continuum
- Pathophysiology remains unclear, overlapping features
- Clinical presentation more distinct, but with overlap



## Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions

Jennifer E Fugate, Alejandro A Rabinstein

B Posterior reversible encephalopathy syndrome



# Acute CNS Vasculopathy: Conclusions

- Acute CNS Vasculopathy- Relevant for Acute Medicine/ Neurology/ Stroke/ ICU
- Parenchymal and vessel imaging critical
- Biopsy required for definite vasculitis.
- Caution required with angiographic vasculitis
- Inflammatory Cerebral Amyloid angiopathy- reversible encephalopathy , appears responsive to immunosuppression
- RCVS / PRES- not rare on medical wards
- “ Reversible” but not always benign
- Pathophysiology- More questions than answers

