Uncommon Strokes

Ty Shang, MD, PhD

Associate Professor

Stroke and Cerebrovascular Disease Section

Department of Neurology

UT Southwestern Medical Center

UT Southwestern
Medical Center

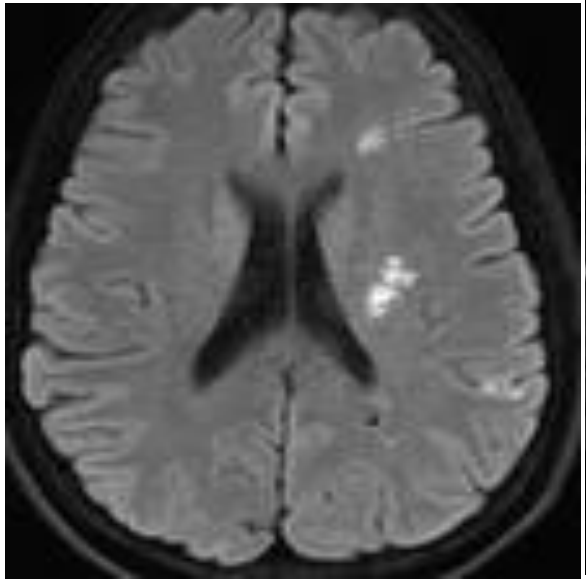
Outline

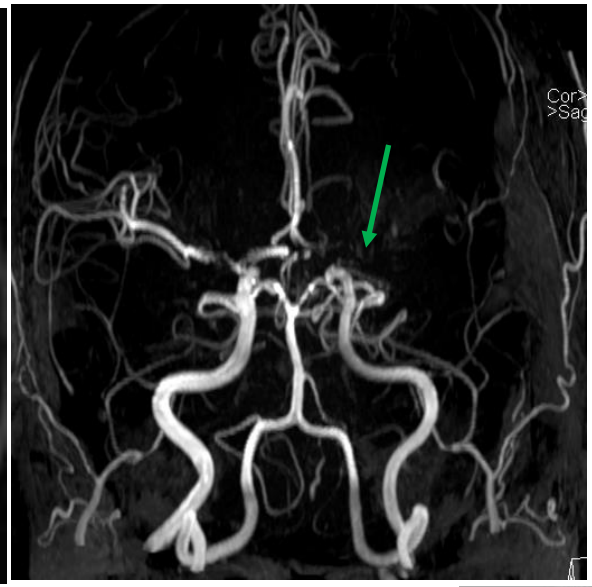
- Presentation of 9 cases
- Diagnosis
- Discussion

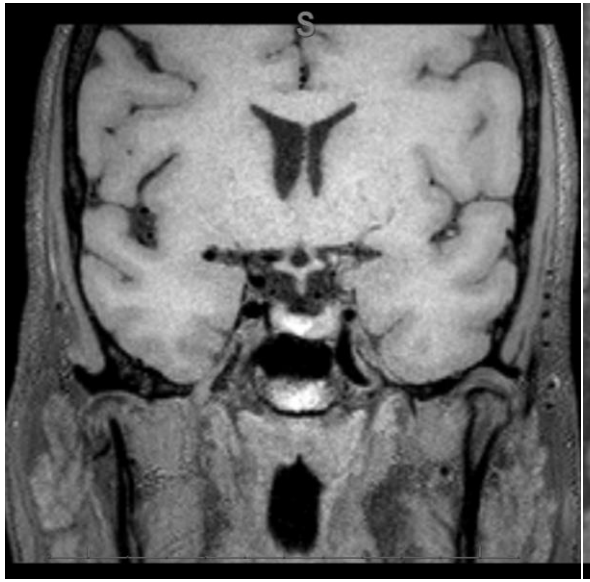
Case 1:

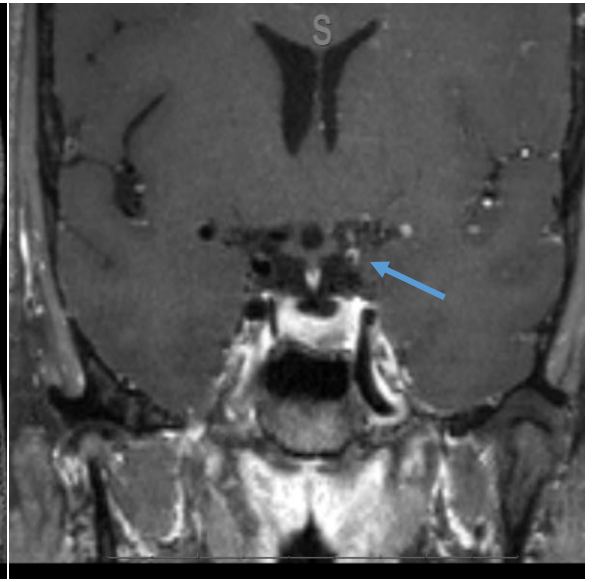
- A 51 F without risk factors, remote history of smoking but not on OCP, recent flu infection received antibiotics, presented with R side weakness, found to have L MCA ischemic stroke on 2/8.
- Exam: Awake, alert, follow commands, mild R drift, slow in communication.

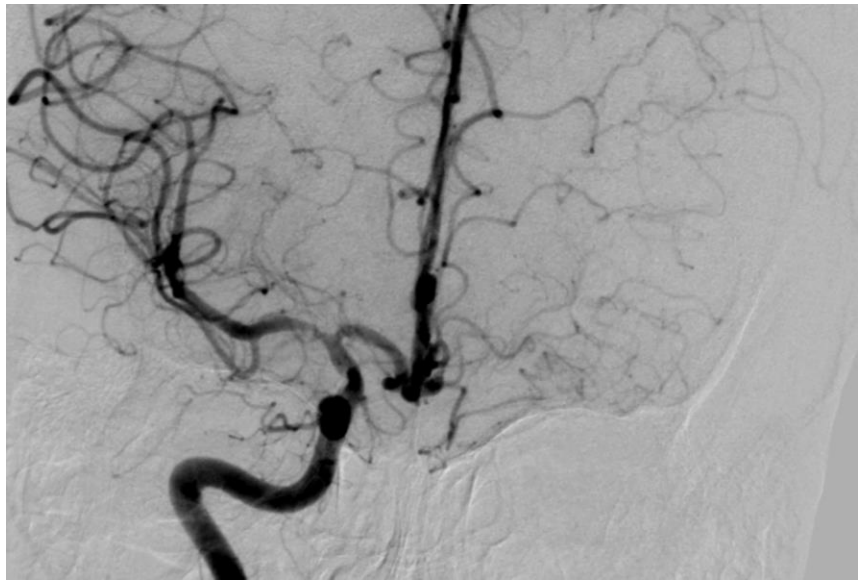
2/2019

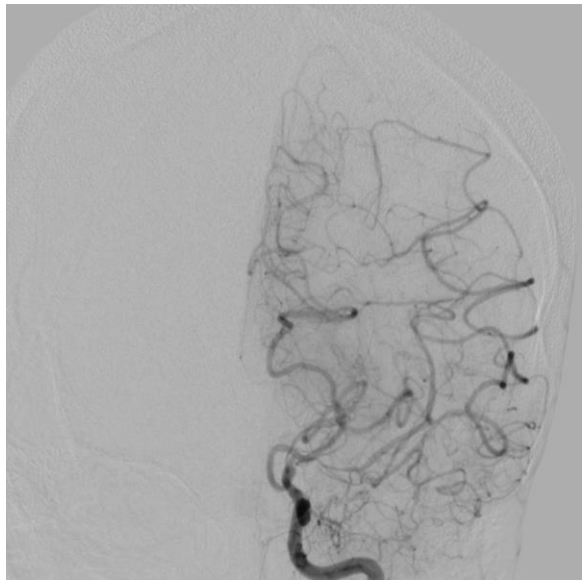


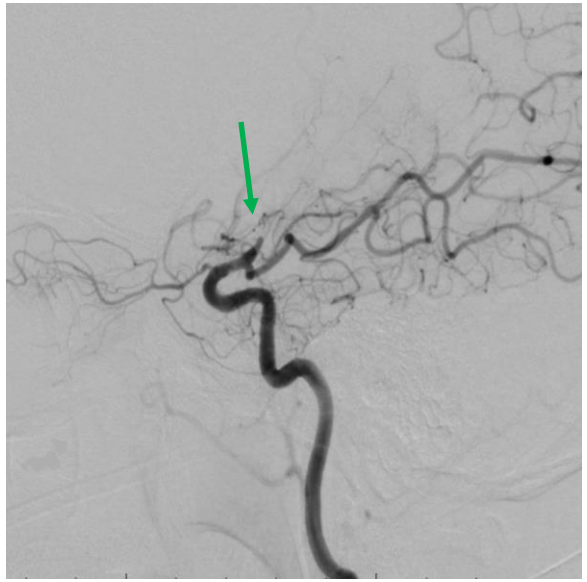


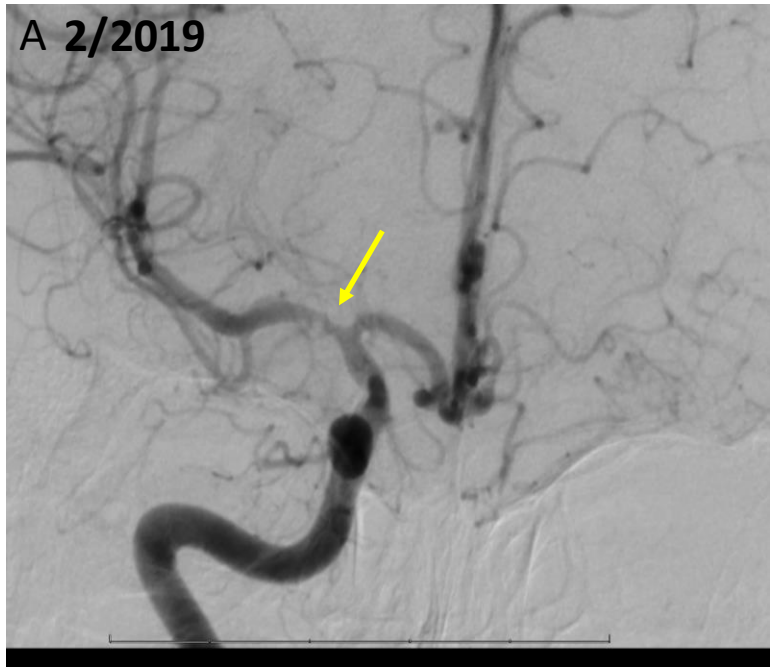


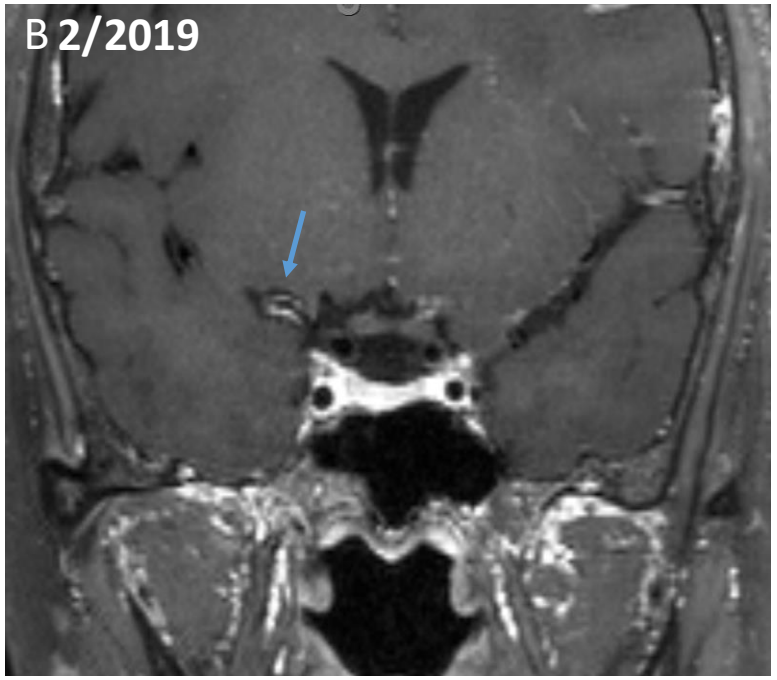


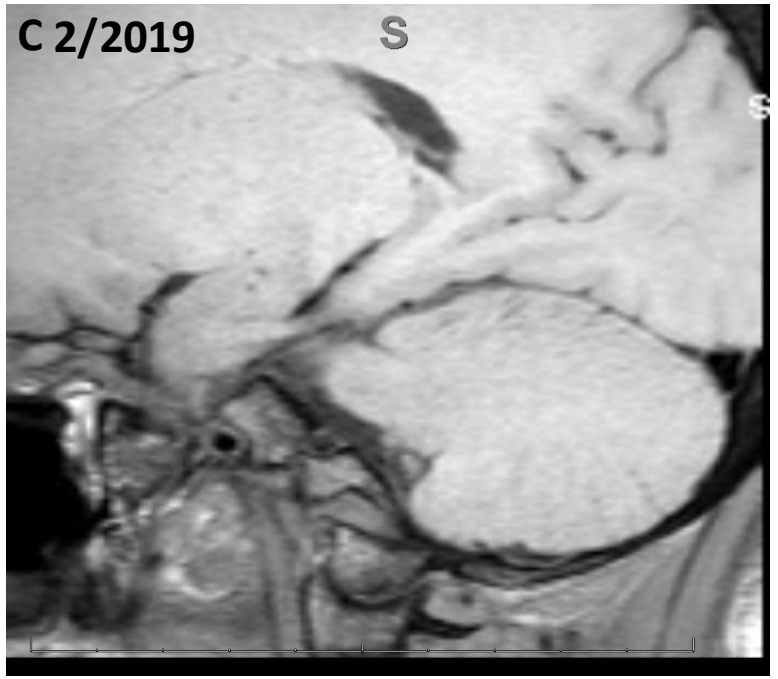


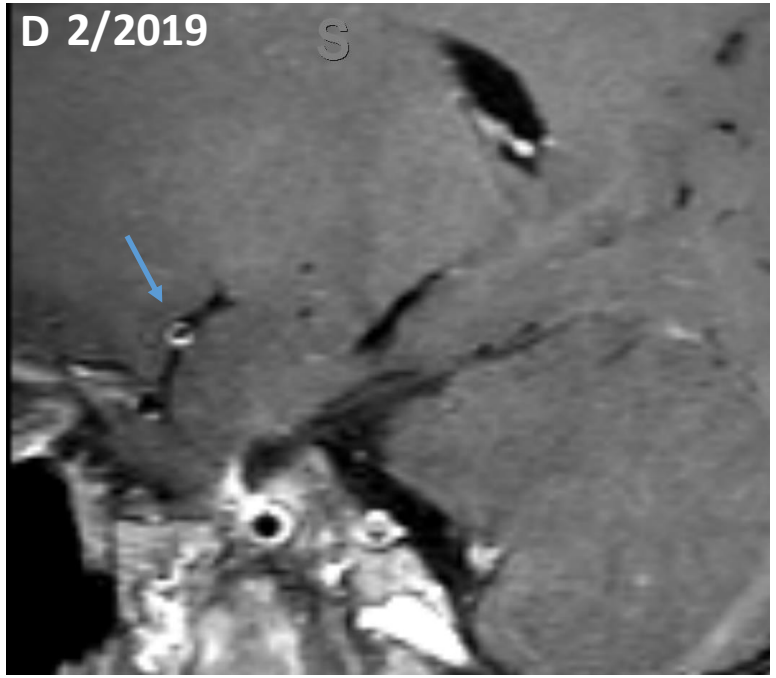


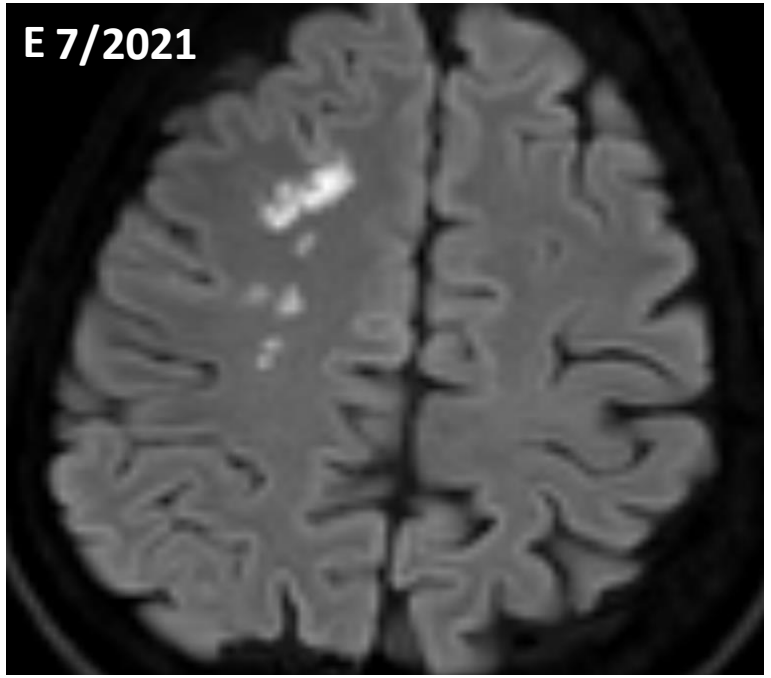


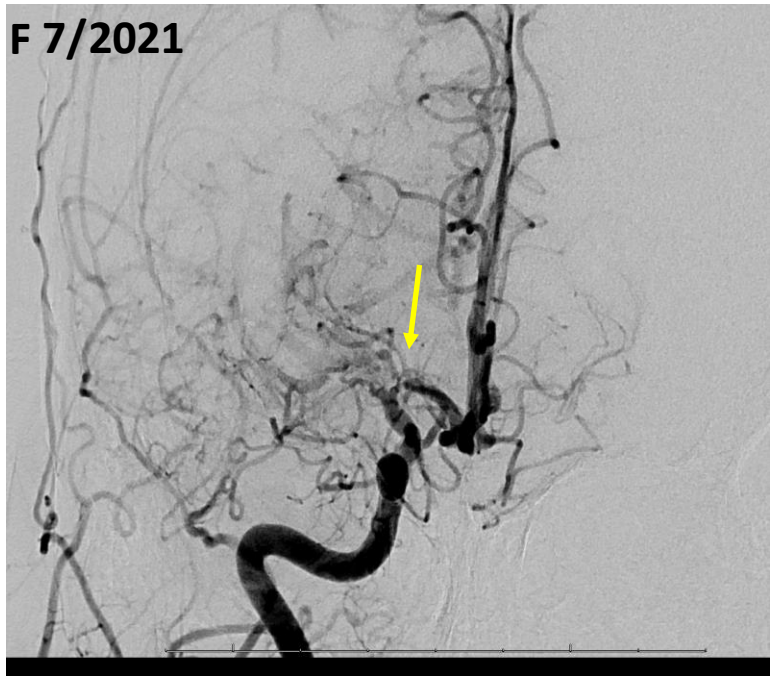

A 2/2019


B 2/2019


C 2/2019
S

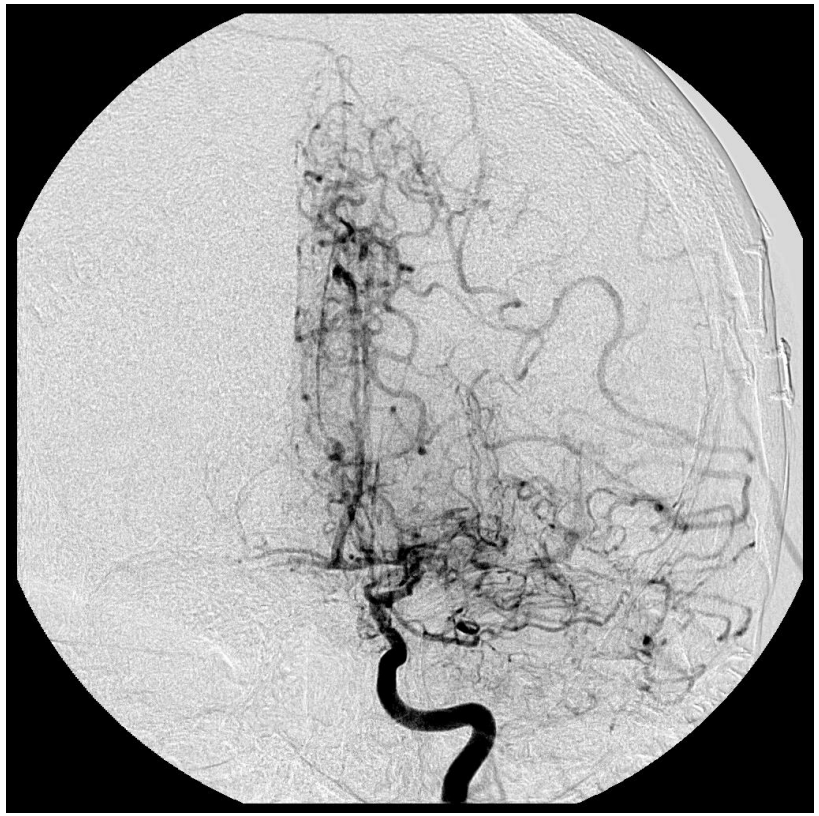

D 2/2019
S

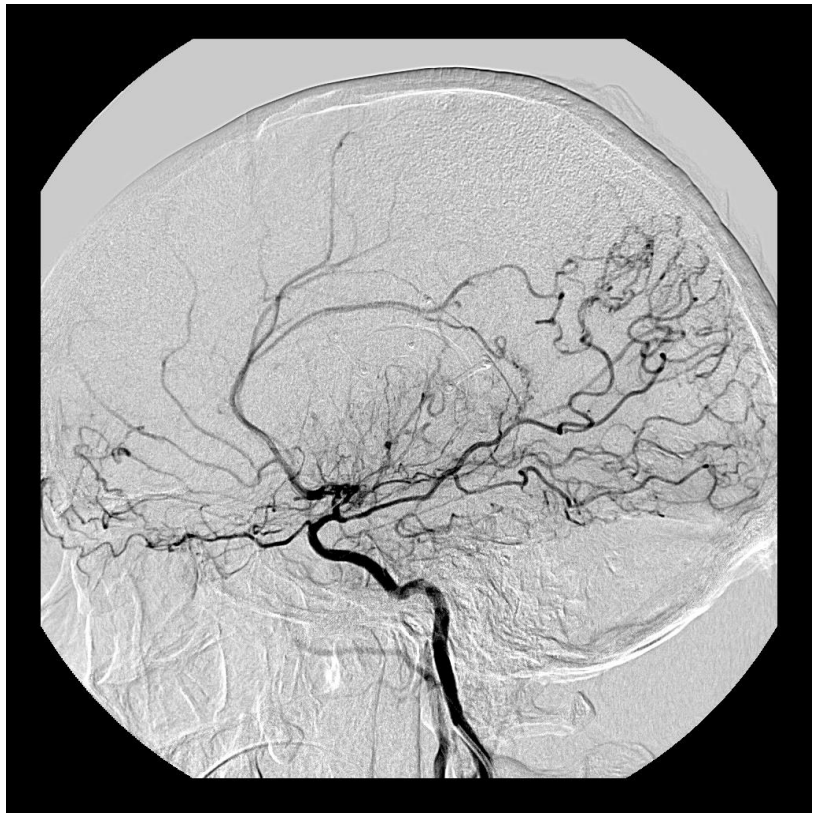

E 7/2021


F 7/2021

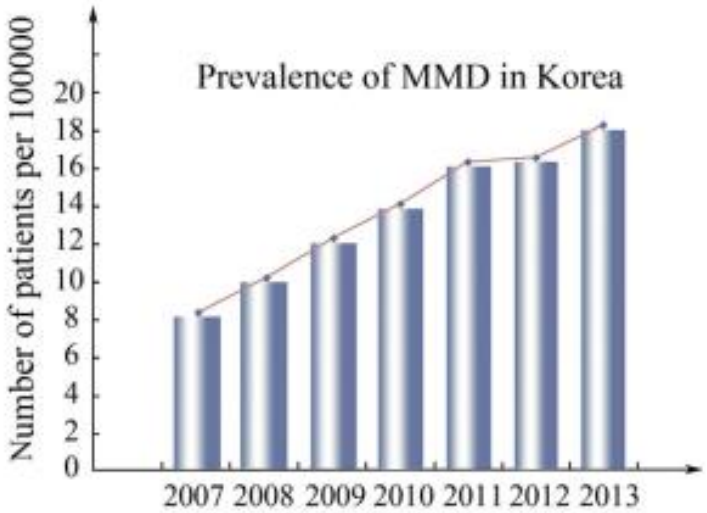
Moyamoya Disease

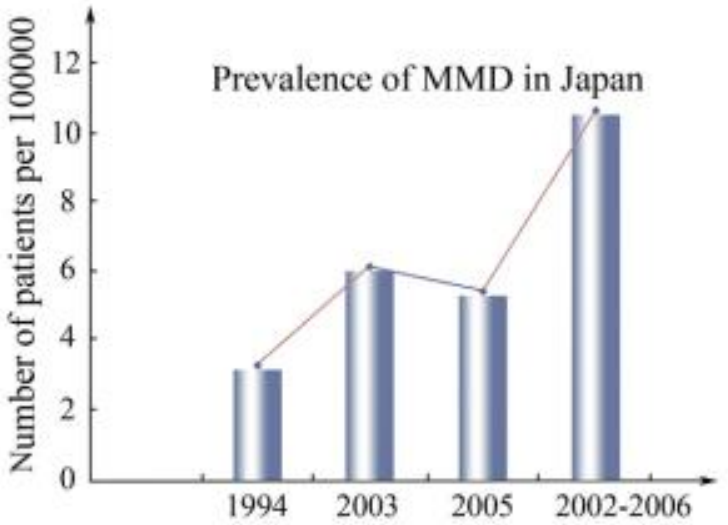
- Progressive **s**tenosis and occlusion of terminal ICA and proximal branches (MCA/ACA)
- Development of abnormal net-like blood vessel on angiogram, referred to as “Moyamoya”, over the stenotic or occluded arteries
- MMD
- MMS

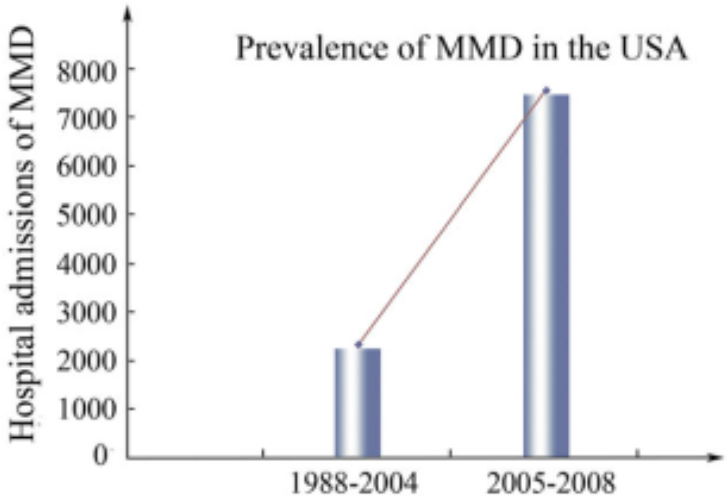




Rare Disease But Prevalence Increases Worldwide







Neurosurgical Review (2020) 43:371–382

Difference Between Asian and Non-Asian

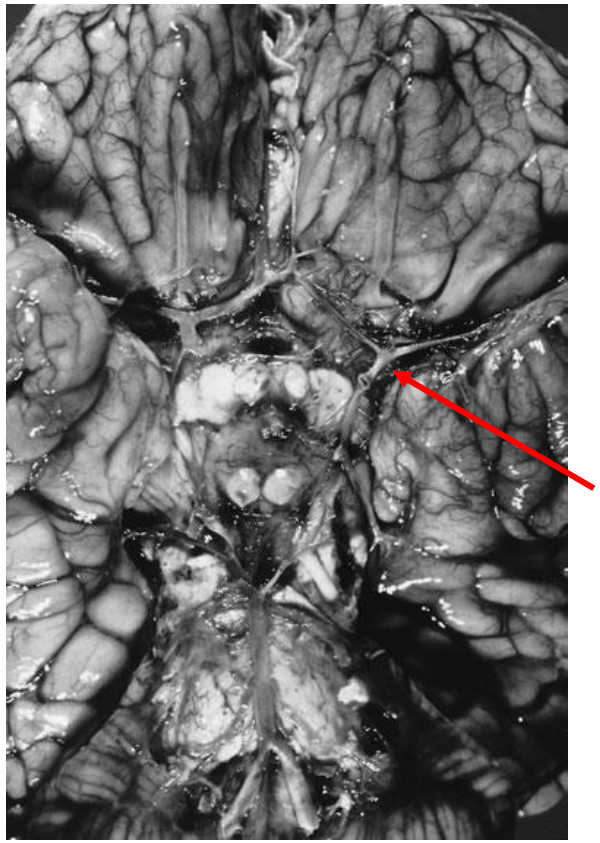
East

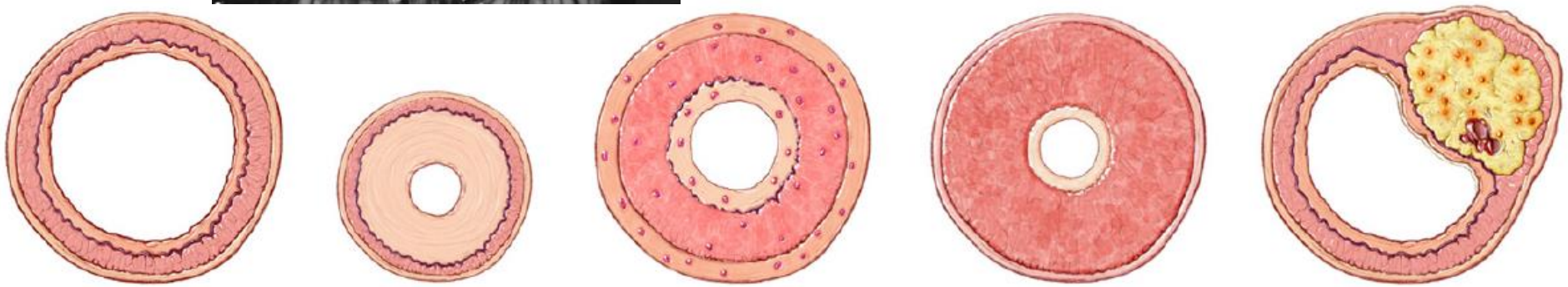
- **Incidence:** higher (0.5-1 per 100,000)
- **Phenotype**
  - More familiar occurrence (11%)
  - Apparent bimodal age distribution
  - Less female predominance: F to M: < 2:1
  - More progressive course
  - More cerebral microbleeds
  - More ICH in adults (21-50%)
- **Genotype**
  - RNF213 is a major susceptible gene

West

- **Incidence:** 1/10th of Asian
- **Phenotype**
  - Familiar MMD rare
  - Yong adult
  - More female predominance: F to M: 3:1
  - Less progressive course
  - Less cMB
  - ICH not common in adults (10%)
- **Genotype**
  - RNF213 not involved

Pathology: Artery Wall Changes in Different Vasculopathies





Pathogenesis Update and Management

- MMD is now recognized as a focal autoimmune or inflammatory vasculopathy
- No universal treatment halts progression or reverse the progression vasculopathy. But there has been case reports of successful treatment in MMS 2nd to inflammatory conditions
- Antiplatelet
- EC-IC bypass is recommended for selective patients
- As a Vascular Neurologist:
  - Workup to rule out infectious, systemic inflammatory or autoimmune conditions
  - Work with NSG for patient selection for bypass
    - Cerebral angiography
    - Evaluate impaired cerebrovascular reserve (VMR)
      - ❖ NM SPECT/MRP/CTP w/wo Diamox

(*Stroke*. 2014;45:1415-1421.)

Risk of Recurrent Stroke

Significant predictors	HR (95% CI)	*p* Value	Validation tests	Values
Asian	2.63 (1.00–6.94)	0.051	Somers D	0.640
TIA	4.18 (1.37–12.75)	0.012	R^2	0.340
Reduced CVR	4.40 (1.20–16.10)	0.026	60-month AUC	0.788

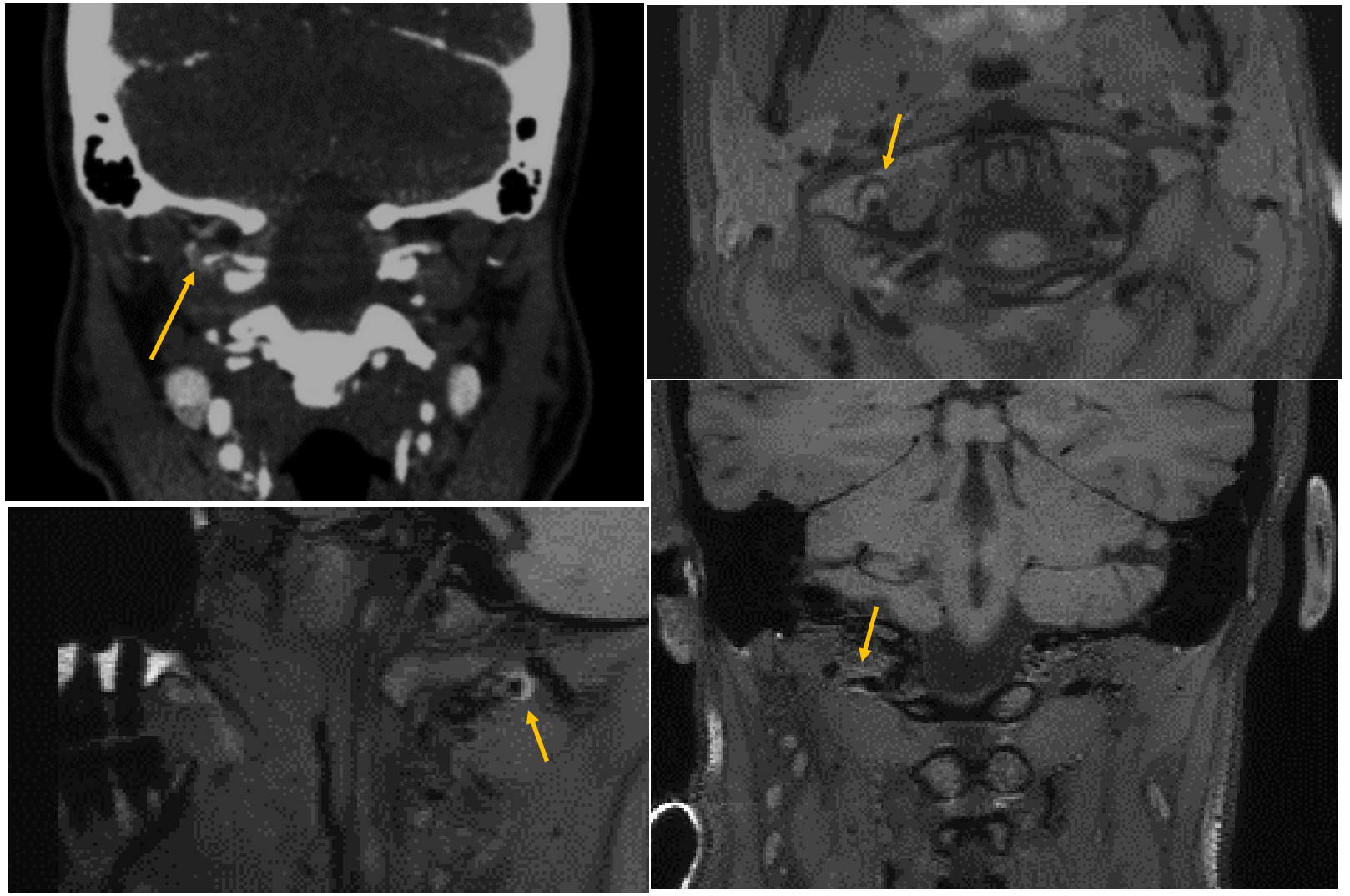
	Risk event at 3 years, %
No predictive factor	1.5
Previous TIAs	3.5
Asian origin	4.3
Asian origin and previous TIAs	10
Reduced CVR	15.6
Reduced CVR and previous TIAs	33.5
Asian origin and reduced CVR	39.2
All predictive factors	69.9

Neurology® 2019;93:e388-e397

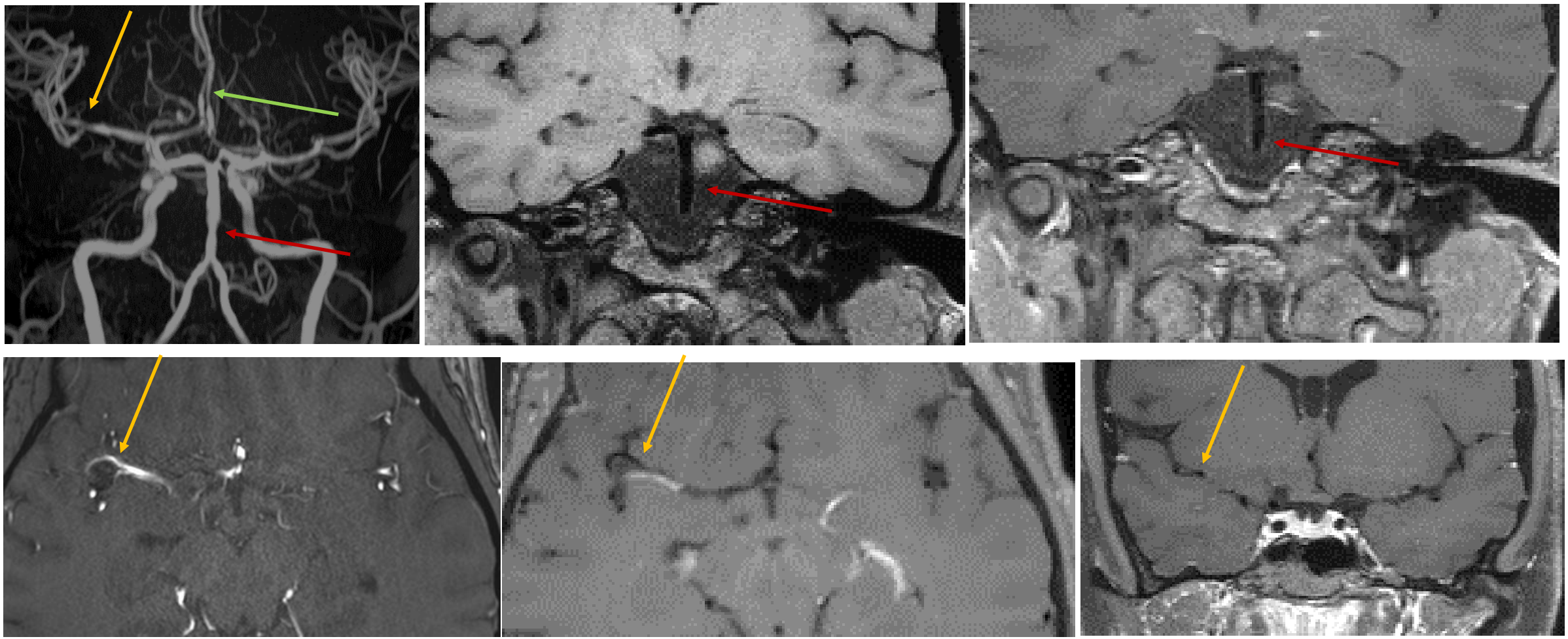
Case 2:

- A 40 F with Hx of PTSD had the worst headache of her life on 12/28. This resolved over the next few hours. She has had 2 other instances of this intense headache triggered by straining. In between instances she has had right neck tightness/pain. CTH, MRI and MRV on 1/5 were unremarkable.
- On 1/12 she developed new symptoms of flashing in both eyes accompanied by a headache. MRI brain 1/13 was again negative. CTA revealed scattered focal narrowing of intracranial vessels and severe stenosis of the right V3 at the level of C1.

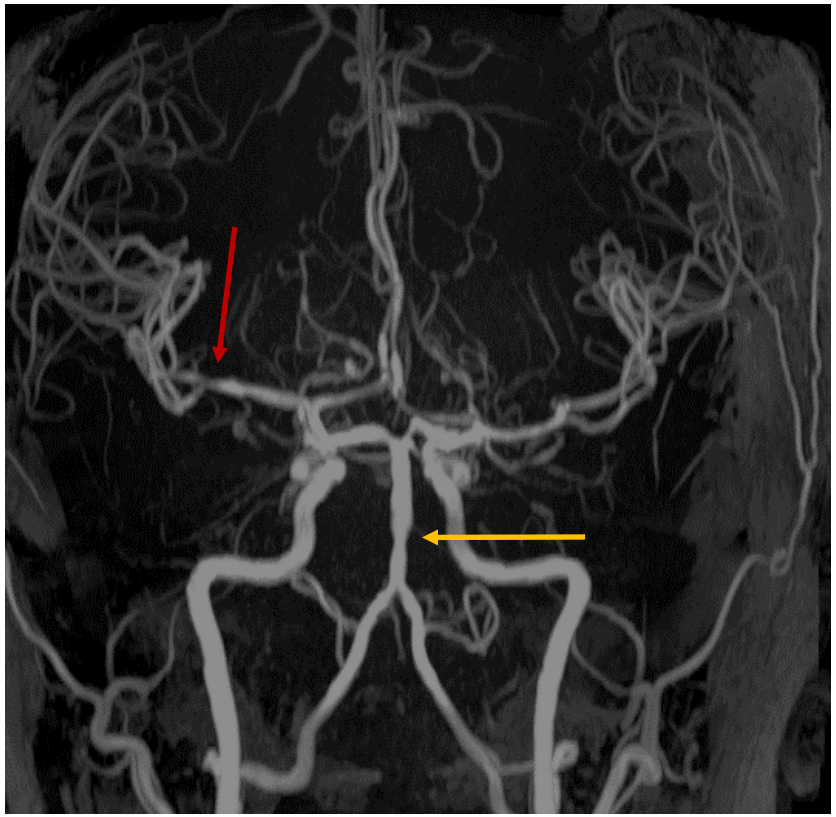
R V3 Dissection



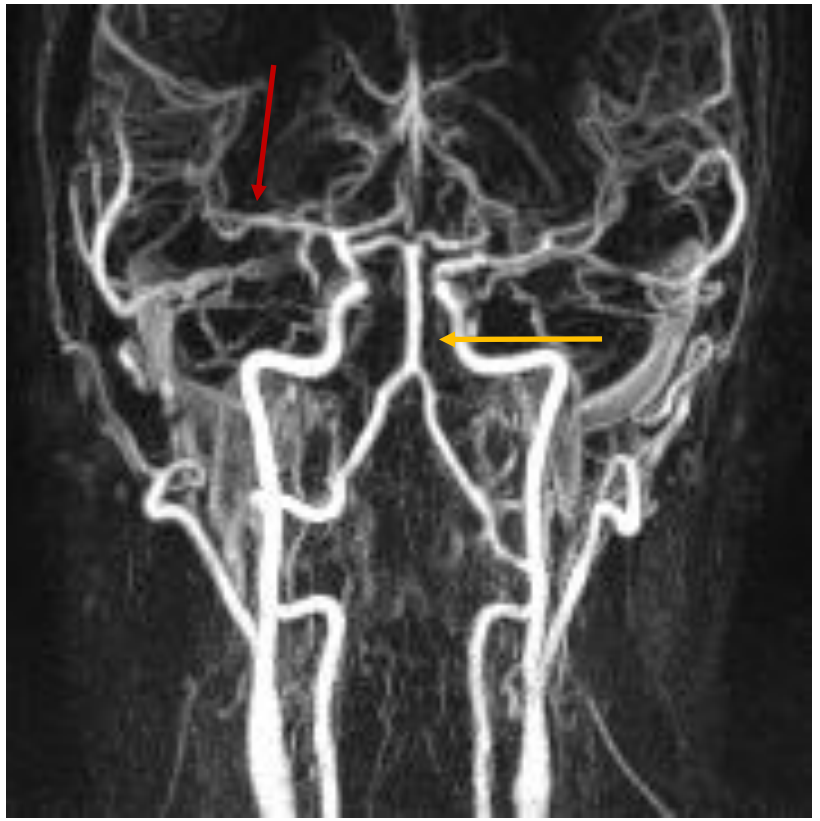
No Enhancement at Stenosis on MR VWI



Three Months Follow up MRA



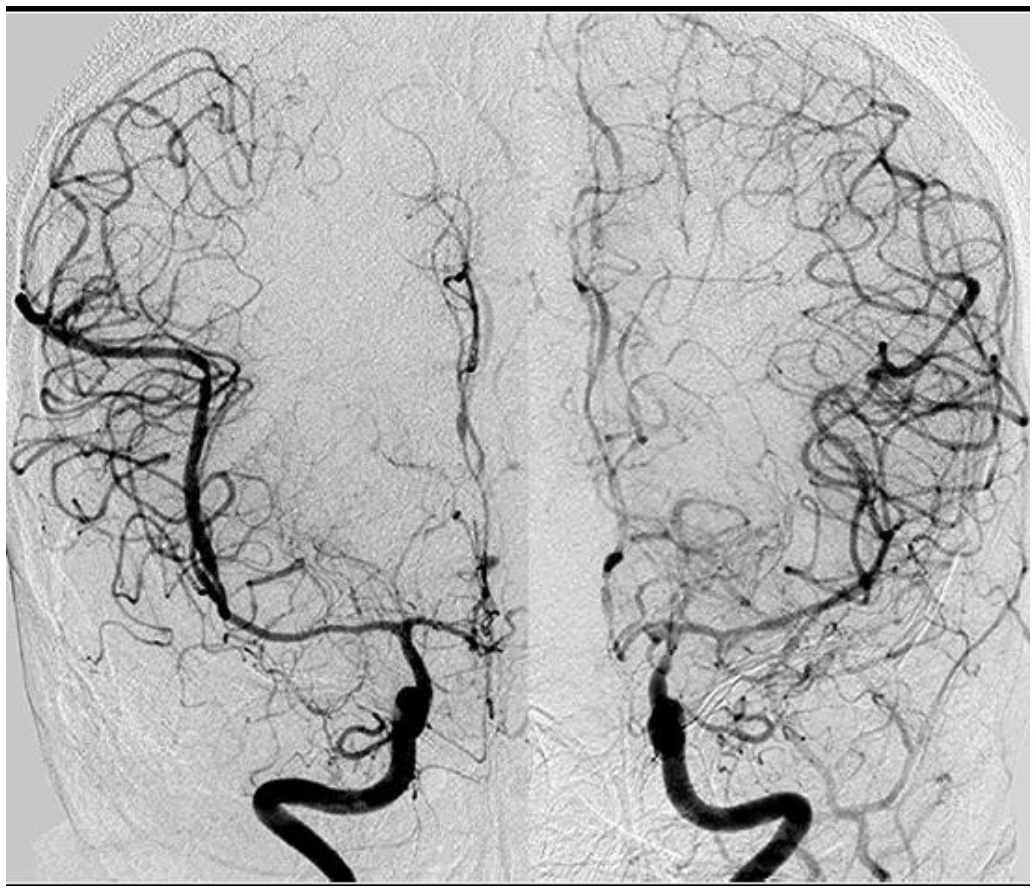
1/13



4/16

Narrative Review: Reversible Cerebral Vasoconstriction Syndromes

Leonard H. Calabrese, DO; David W. Dodick, MD; Todd J. Schwedt, MD; and Aneesh B. Singhal, MD



Ann Intern Med. 2007;146:34-44.

RCVS Epidemiology

- Young women
- Prevalence and incidence unknown
  - Reported incidence: 7% to 54%
- Infarct, hemorrhage, seizure, edema can occur
- Generally favorable outcome, most patients' symptoms resolved
- Long term prognosis depending on stroke
- < 5% severe form
- Mortality < 1%

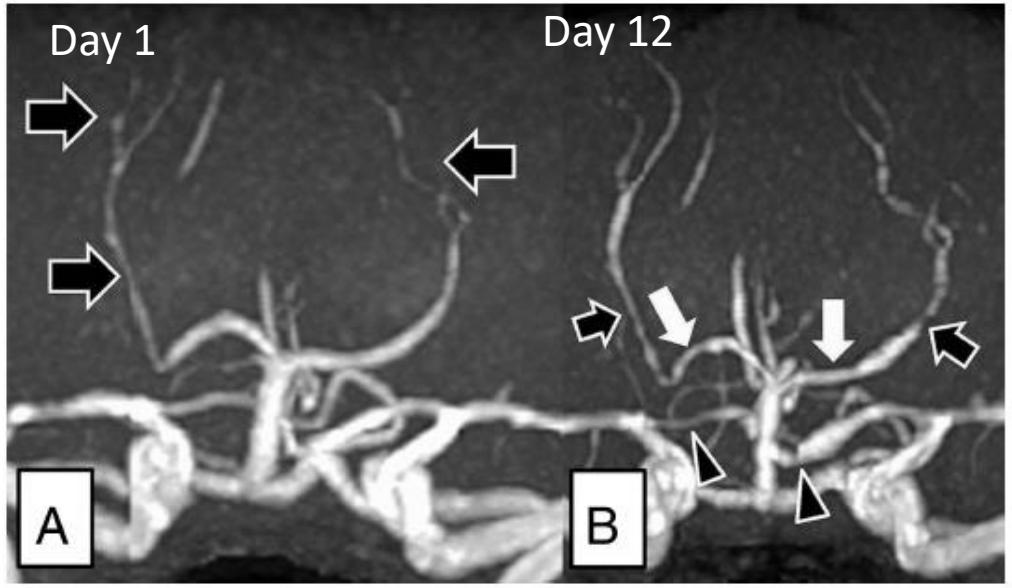
Key Elements for Diagnosis

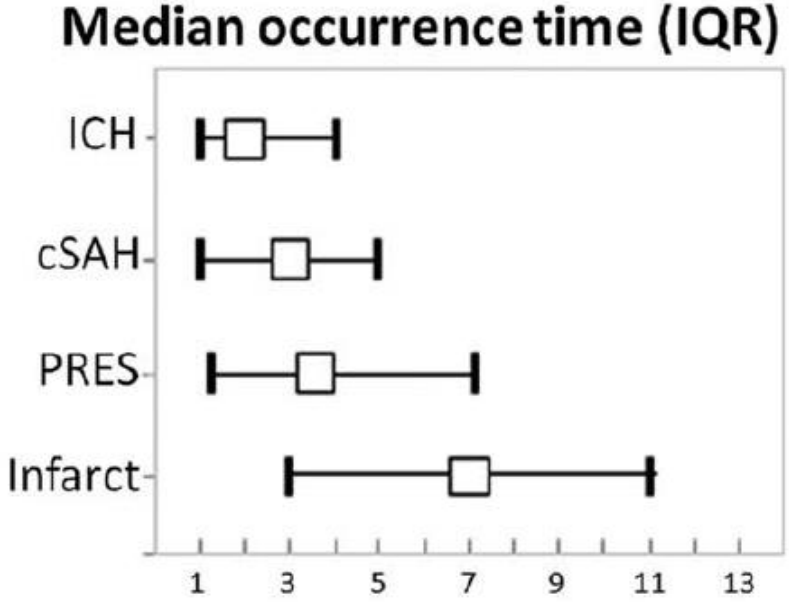
- Severe, acute, recurrent ‘thunderclap’ headache with or without additional neurologic signs or symptoms
- Normal brain scan despite diffuse vasoconstriction
- DSA / CTA/ MRA : multifocal vasoconstriction
- No evidence for aneurysmal SAH
- Normal CSF
- The diagnosis may be ‘confirmed’ if:
  a. Reversibility is documented (typically < 12 wks)
  b. Autopsy – no mimics (PACNS, Athero, aSAH)

Neurology® 2017;88:228-236

Treatment and Others

- RCVS could coexist with dissection, particularly vertebral artery dissection
- Centripetal propagation
- Consequently, hemorrhage usually occurs before infarct
- Treatment
  - Calcium channel blocker
    - ❖**Nicardipine**
  - Avoid Steroid





Neurology® 2017;88:228-236

JAMA Neurol. 2024;81(10):1060-1065.

Stroke. 2016;47:00-00

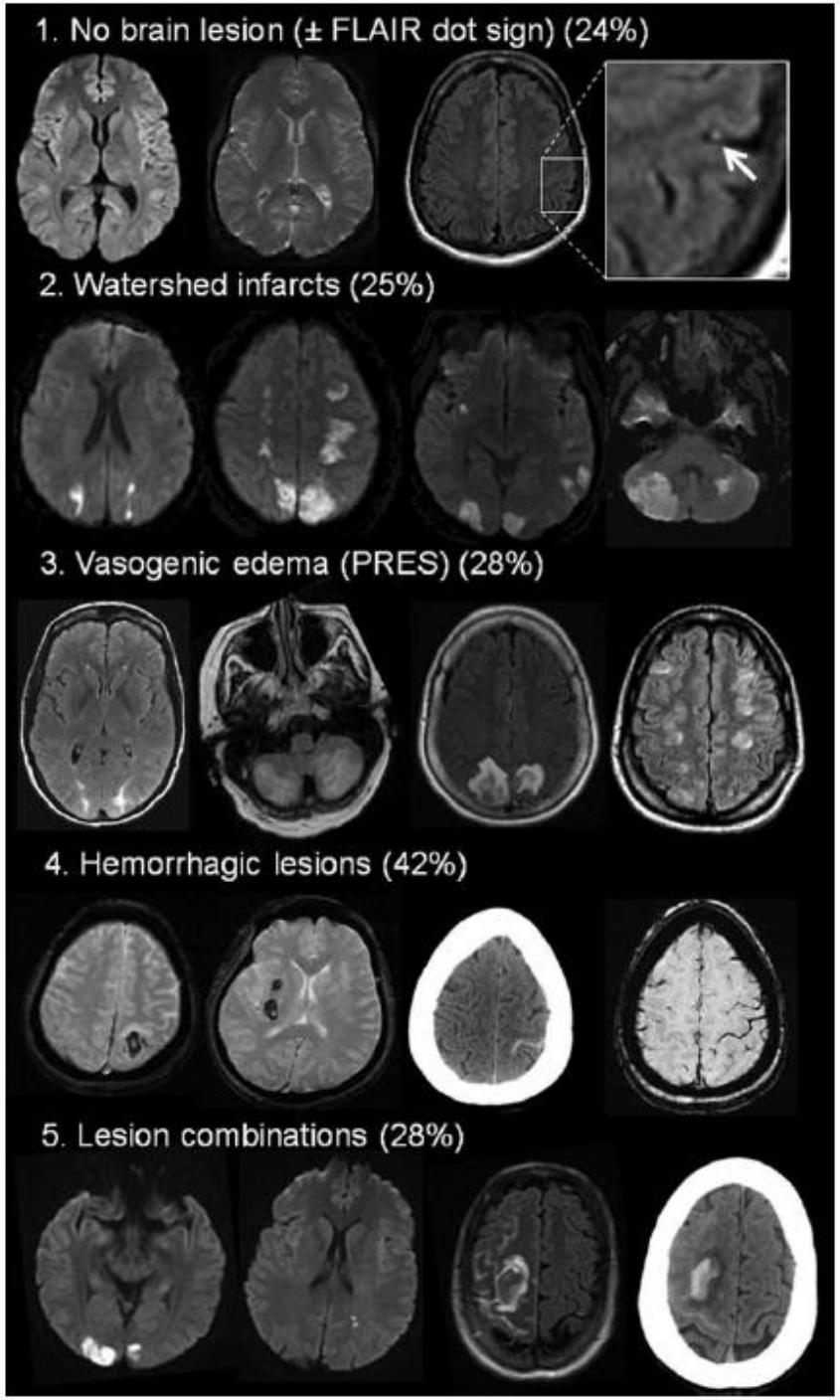
Neurology® 2013;81:821-824

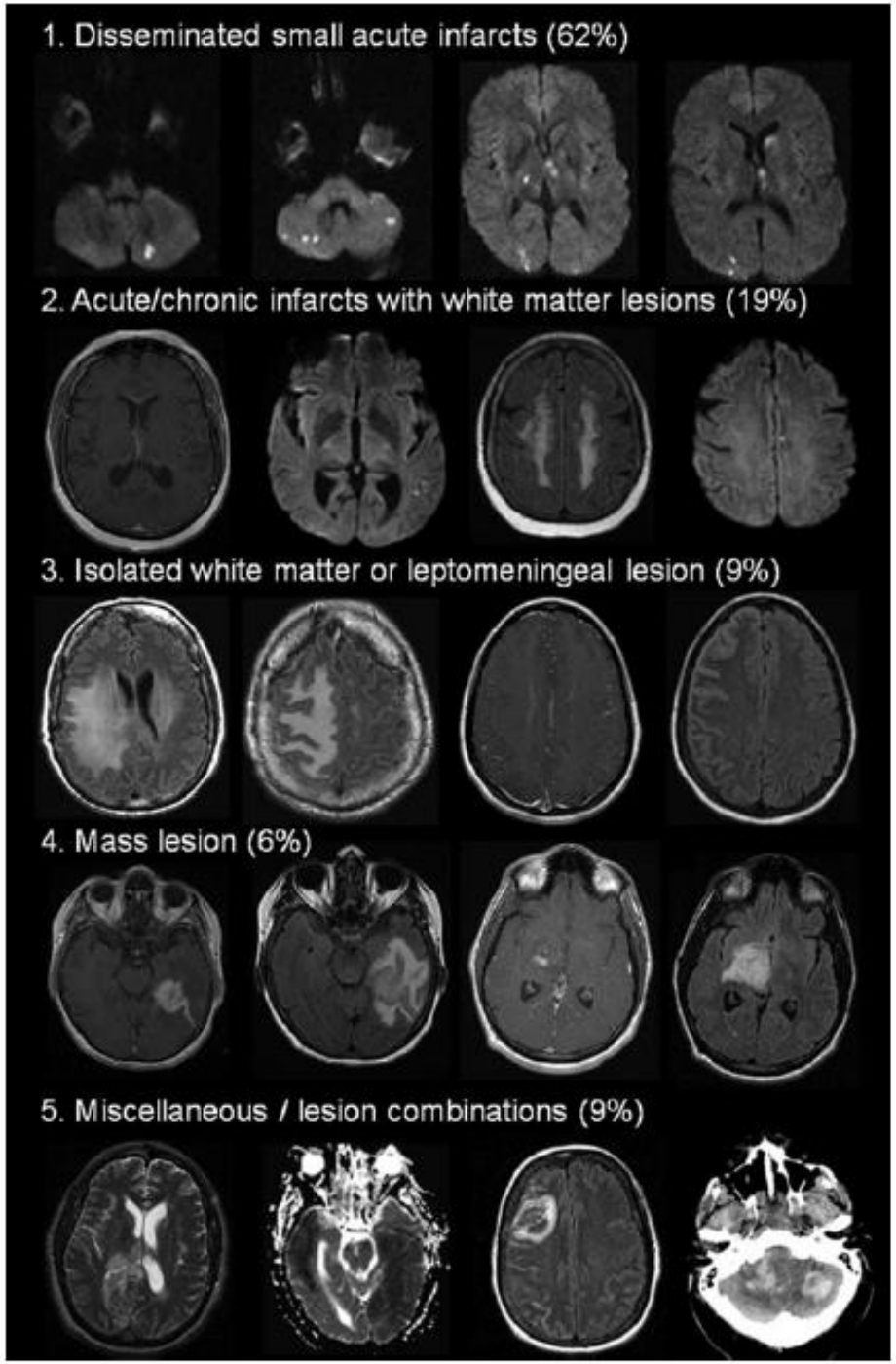
A Common Question: RCVS vs PCNSV

	RCVS	PCNSV
❑History	• Acute: thunderclap headache	• Subacute, chronic, insidious
❑Brain lesion patterns	• Could be normal or symmetrical, hemorrhage common	• Rarely normal, hemorrhage uncommon
❑Vessels	• Medium to large vessels	• Small to medium
❑Angiogram	• Smooth sausage	• Irregular, notched, ectasia
❑MR VWI	• No enhancement on MR VWI	• Enhancement of MR VWI if medium to large vessel involved

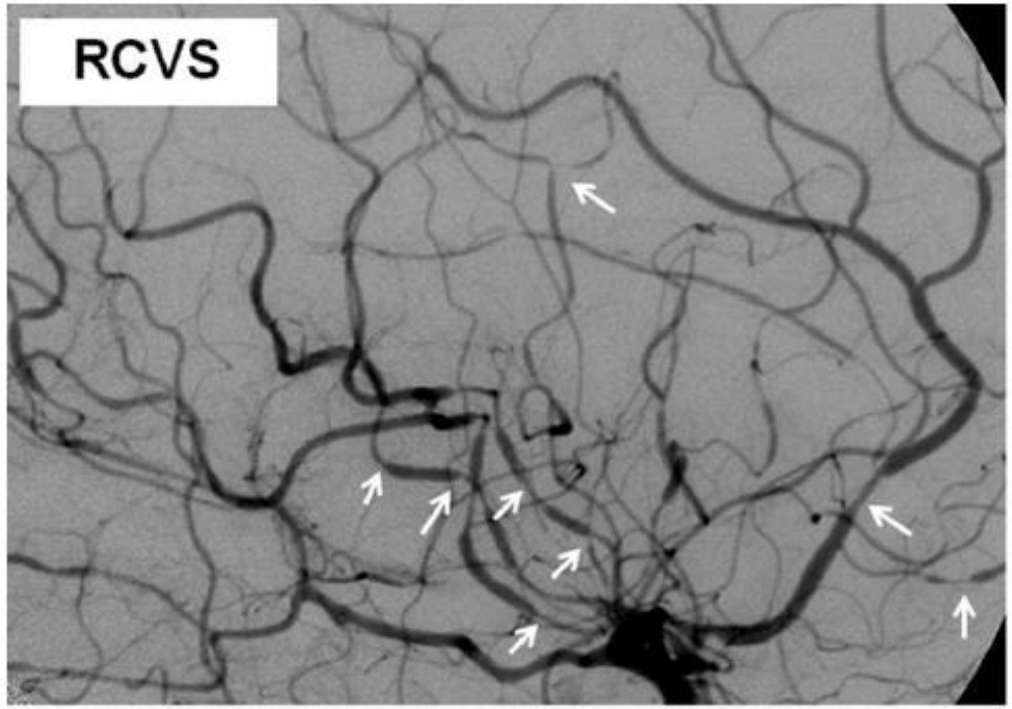
ANN NEUROL 2016;79:882–894
Neurology® 2018;91:e1468-e1478.

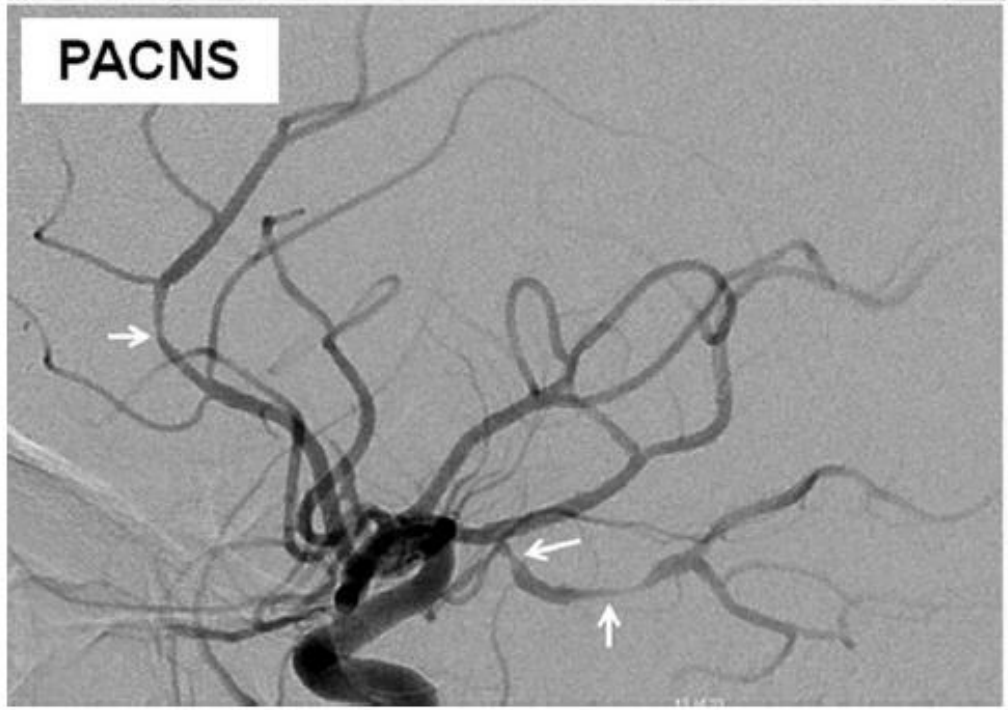
Brain Lesion Patterns

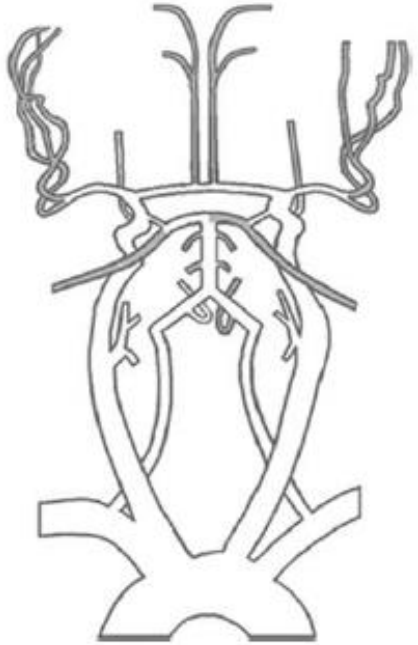




Angiogram Findings



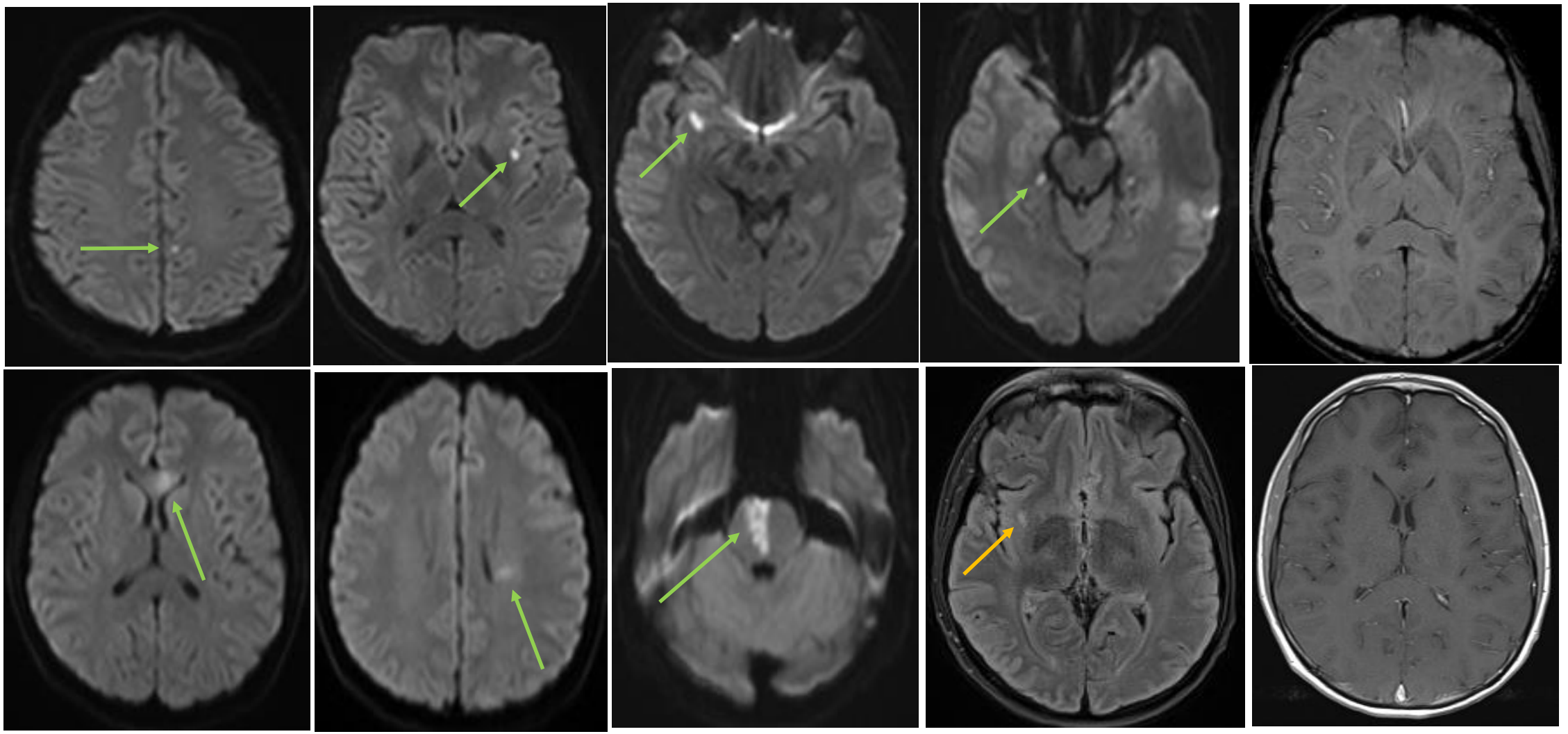




Case 3:

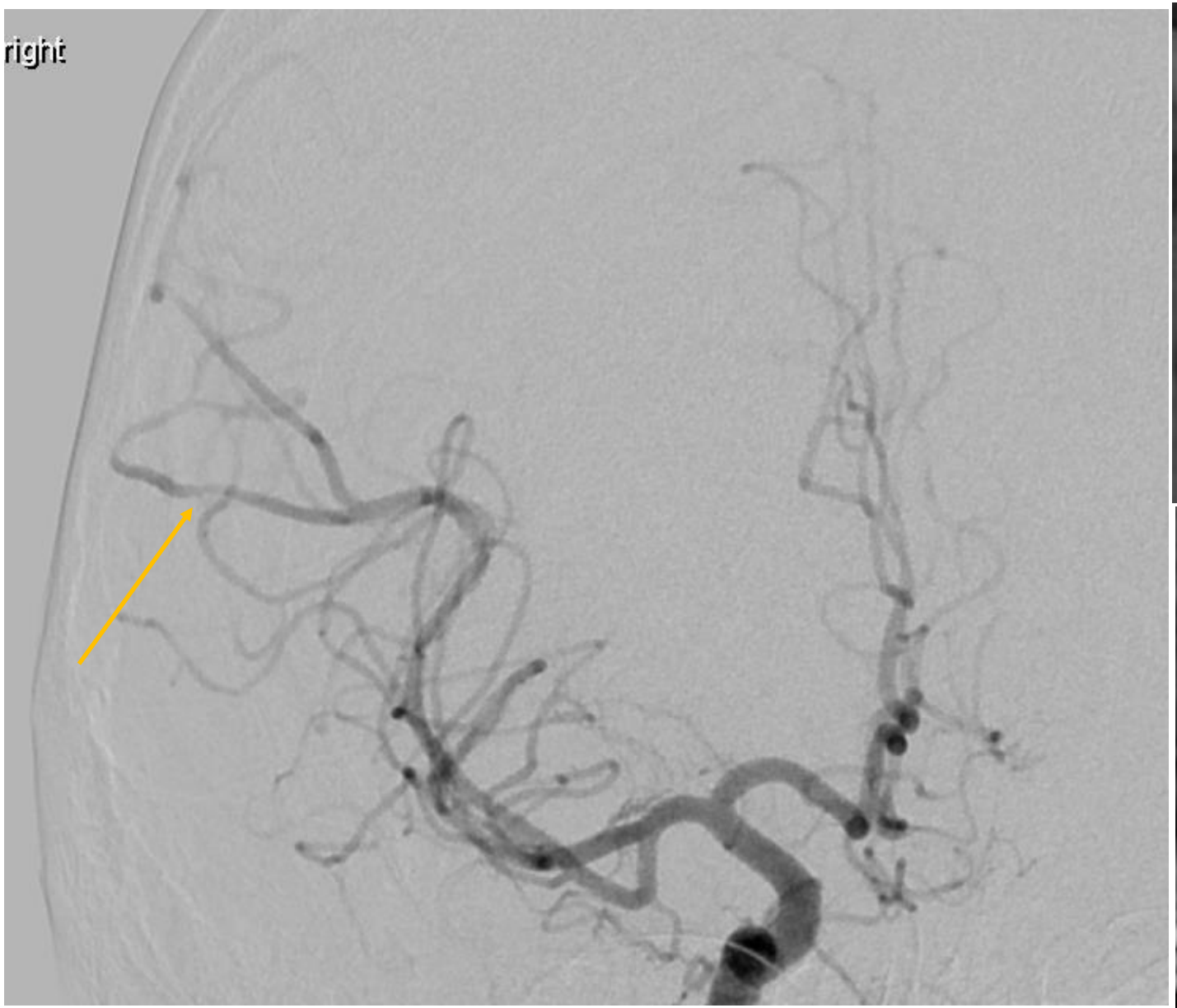
- A 29 M was in generally good health until mid February. He developed low-grade fevers myalgia and headache. He was given Medrol Dosepak at ED for a viral syndrome with resolution of some of his symptoms. However the symptoms recurred with some AMS on 3/22, which was described as uncharacteristically ignoring wife's concerns for his health. MRI brain showed multiple scattered small acute infarcts.
- LP: CSF protein of 77 (< 40 mg/dl) and mild pleocytosis (WBC 7). A comprehensive meningitis panel, CTA brain/neck/chest, and TTE/TEE were negative without shunt.
- For the next 3 weeks he felt more or less normal and even played soccer. At the end of 1 game, he felt mild weakness in R hand, mild dysphagia, and gait imbalance, and difficulty with depth perception. MRI on 4/15 showed new scattered subacute and acute infarcts.
- LP: evated CSF protein and mild pleocytosis (WBC 11). Autoimmune, hypercoagulation profile and cryoglobulins were all either negative or normal.

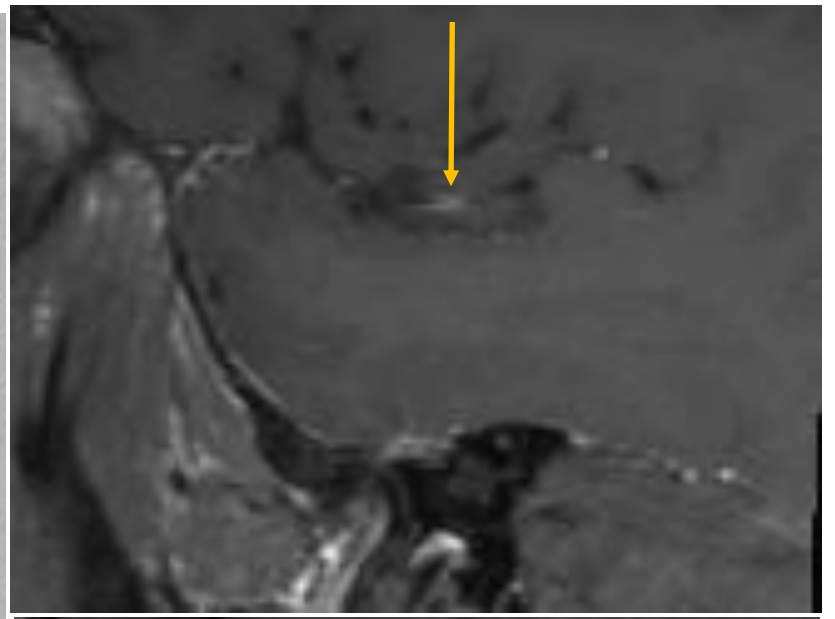
3/22

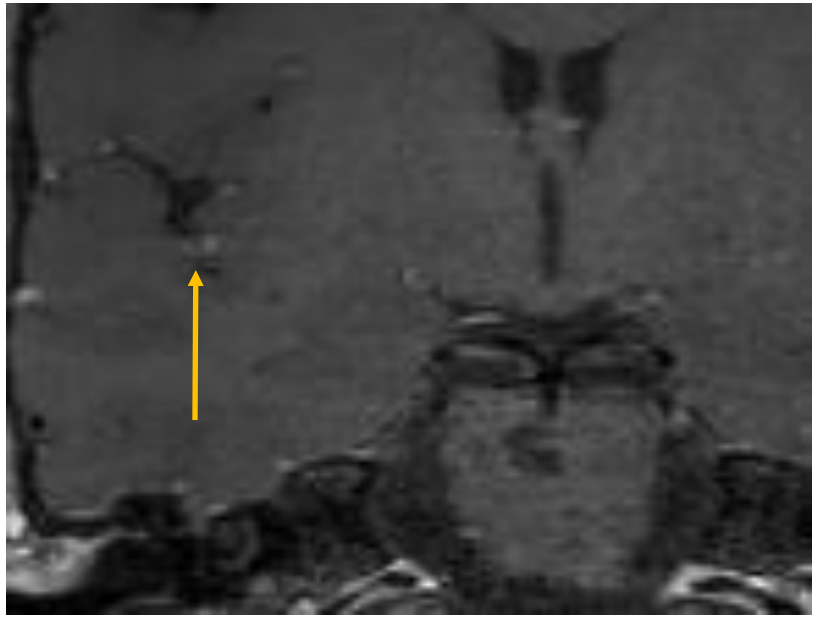


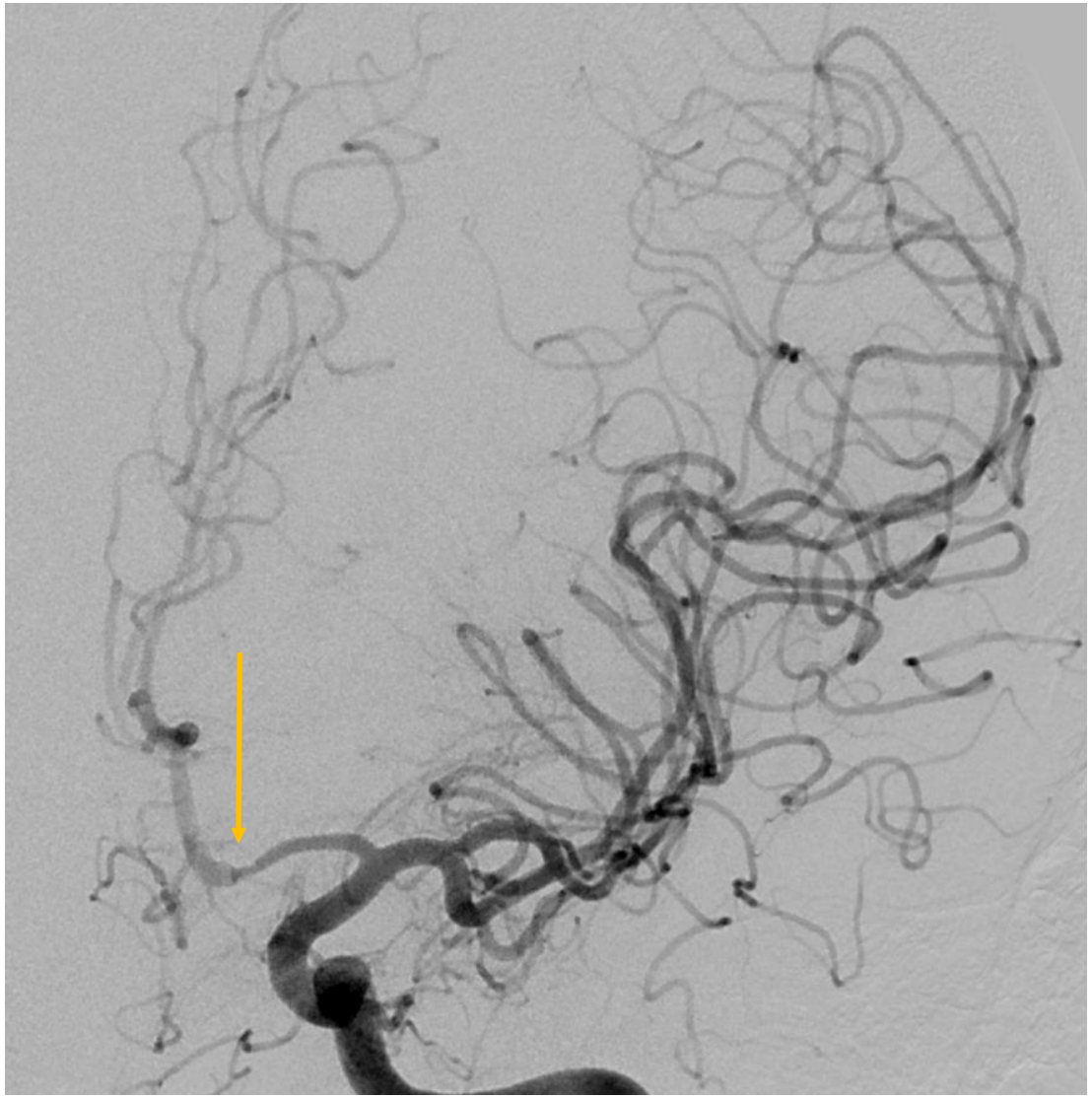
4/15

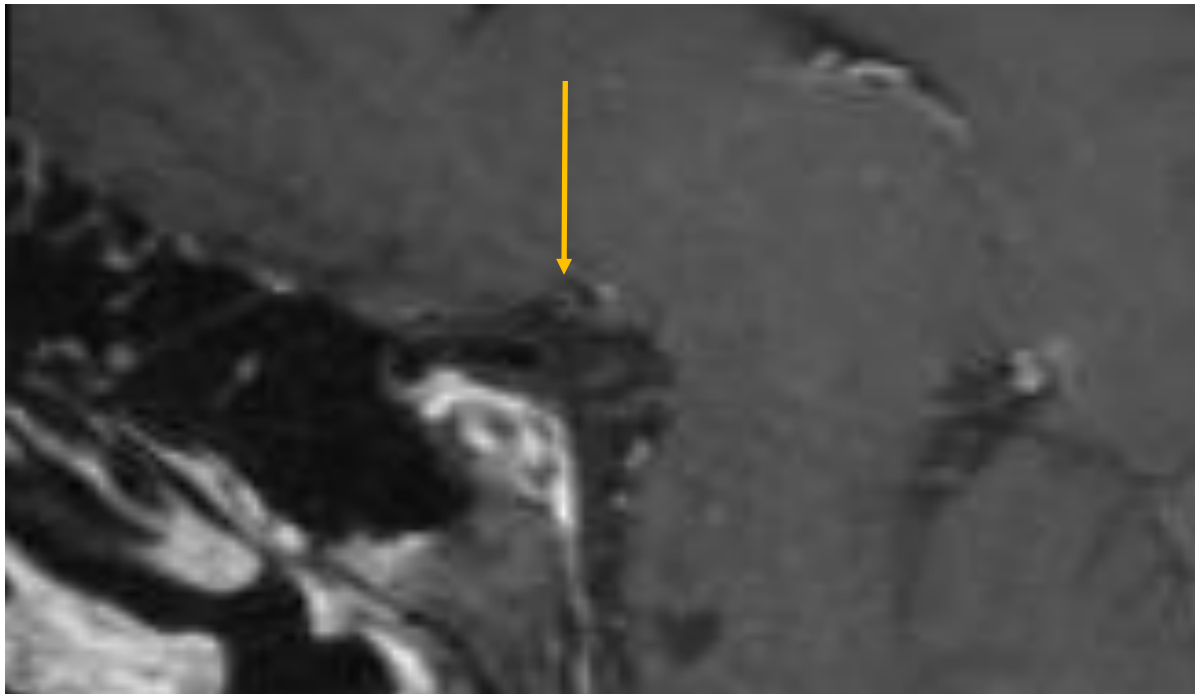
4/18

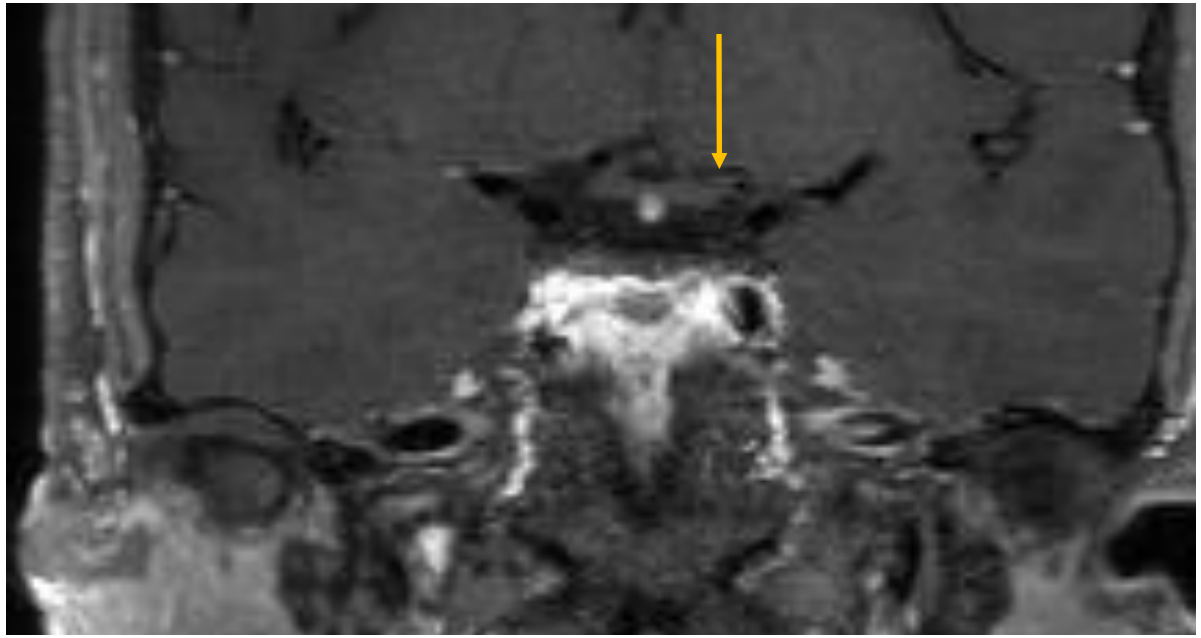


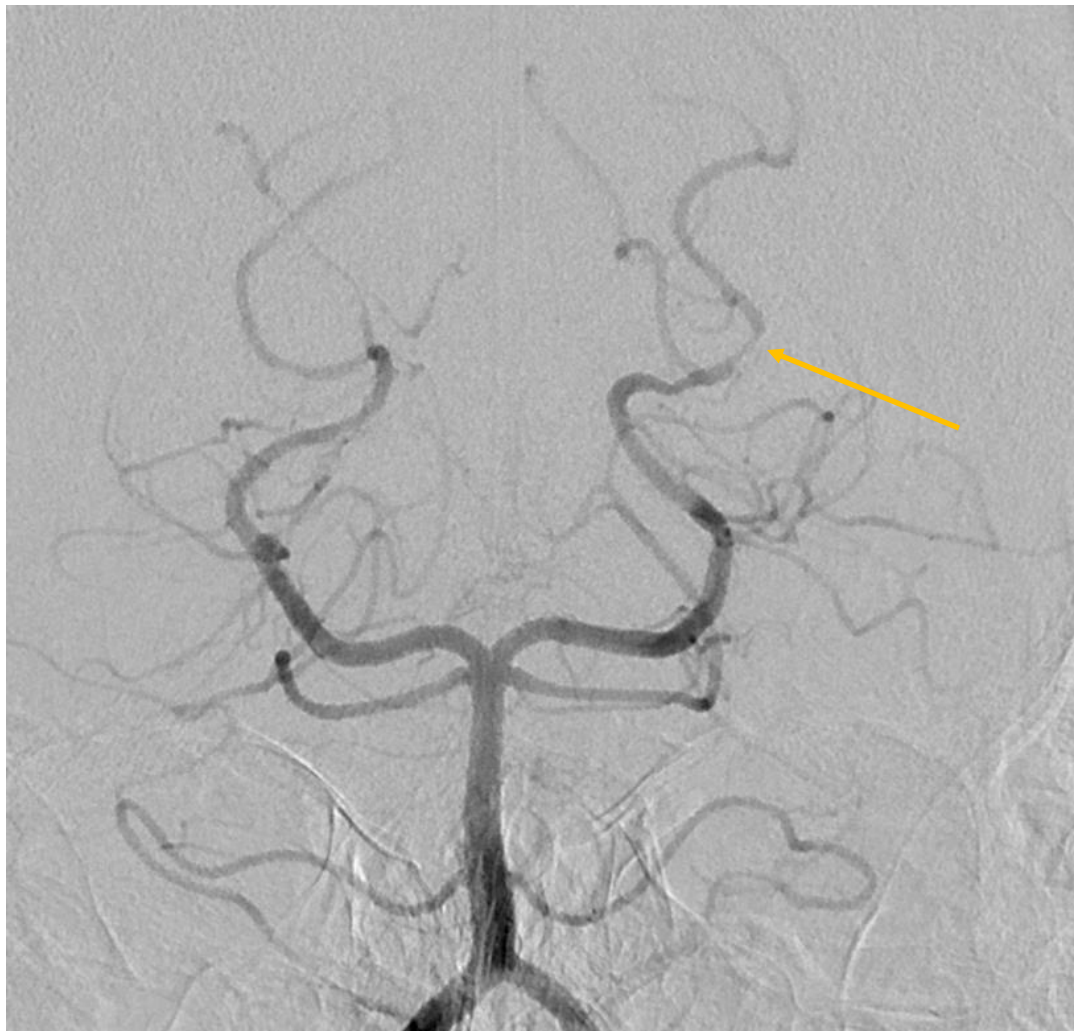


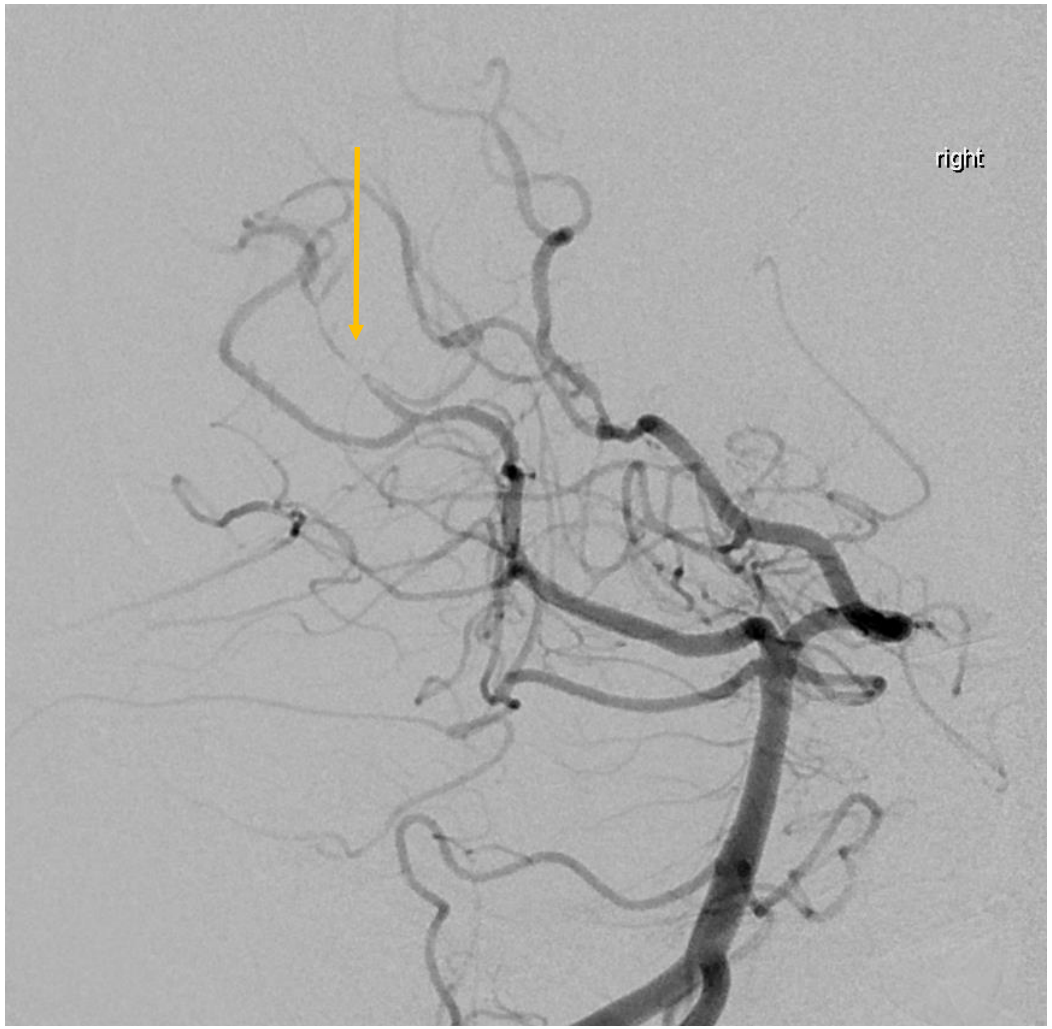











right

Primary CNS Vasculitis

- Epidemiology
  - 2.4 cases per 1 million person-years
  - 8-23% mortality
- Pathology
  - Granulomatous vasculitis
  - Lymphocytic
  - Necrotizing
- Diagnostic criteria
  - Calabrese and Mallek 1988
  - Definite, probable/possible

N Engl J Med 2024;391:1028-37.

Primary CNS Vasculitis

Small cerebral vessel

- Biopsy
- Meningeal/parenchymal enhancement on MRI
- Negative cerebral angiography
- Negative MR VWI
- R/o anti-MOG, intravascular lymphoma, et al

Medium to large cerebral vessel

- Cerebral angiography
- Biopsy could be negative
- Acute neurological deficits
- Multiple cerebral infarcts
- Enhancement on MR VWI
- R/o MMD, RCVS, VZV, et al

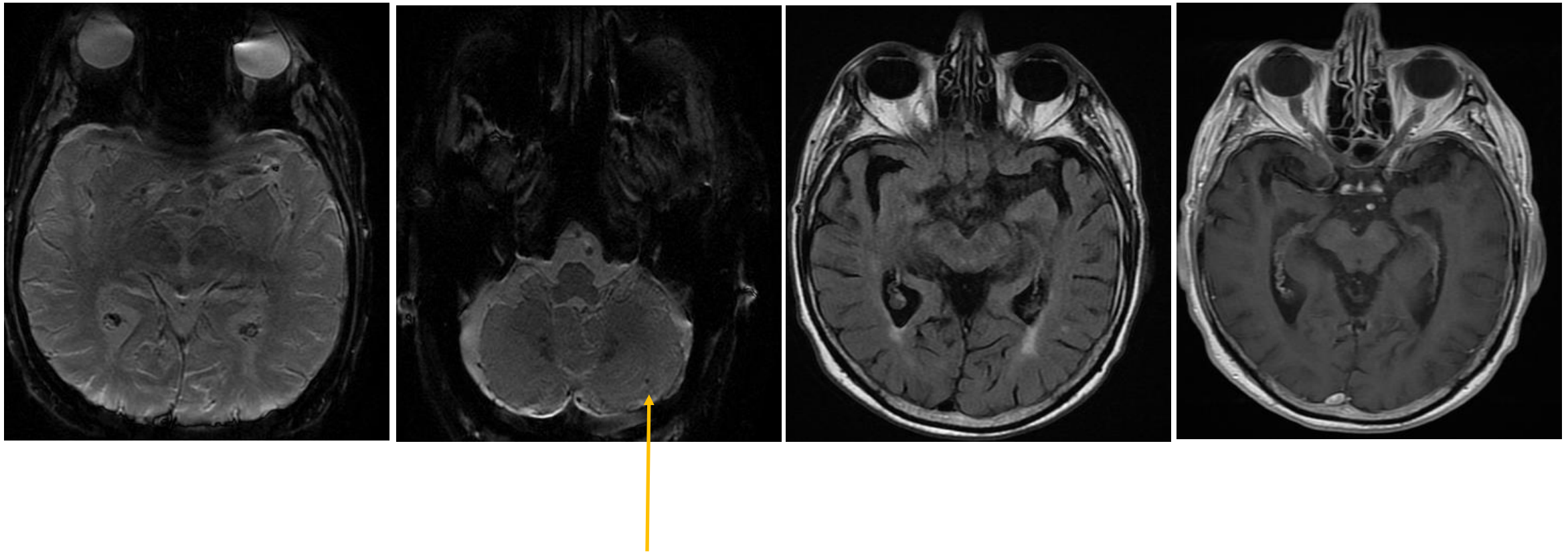
Treatment

- Induction therapy: glucocorticoids, cyclophosphamide, rituximab
- Maintenance therapy: mycophenolate mofetil, azathioprine, rituximab
- Duration: at lest 2 years in remission before cessation

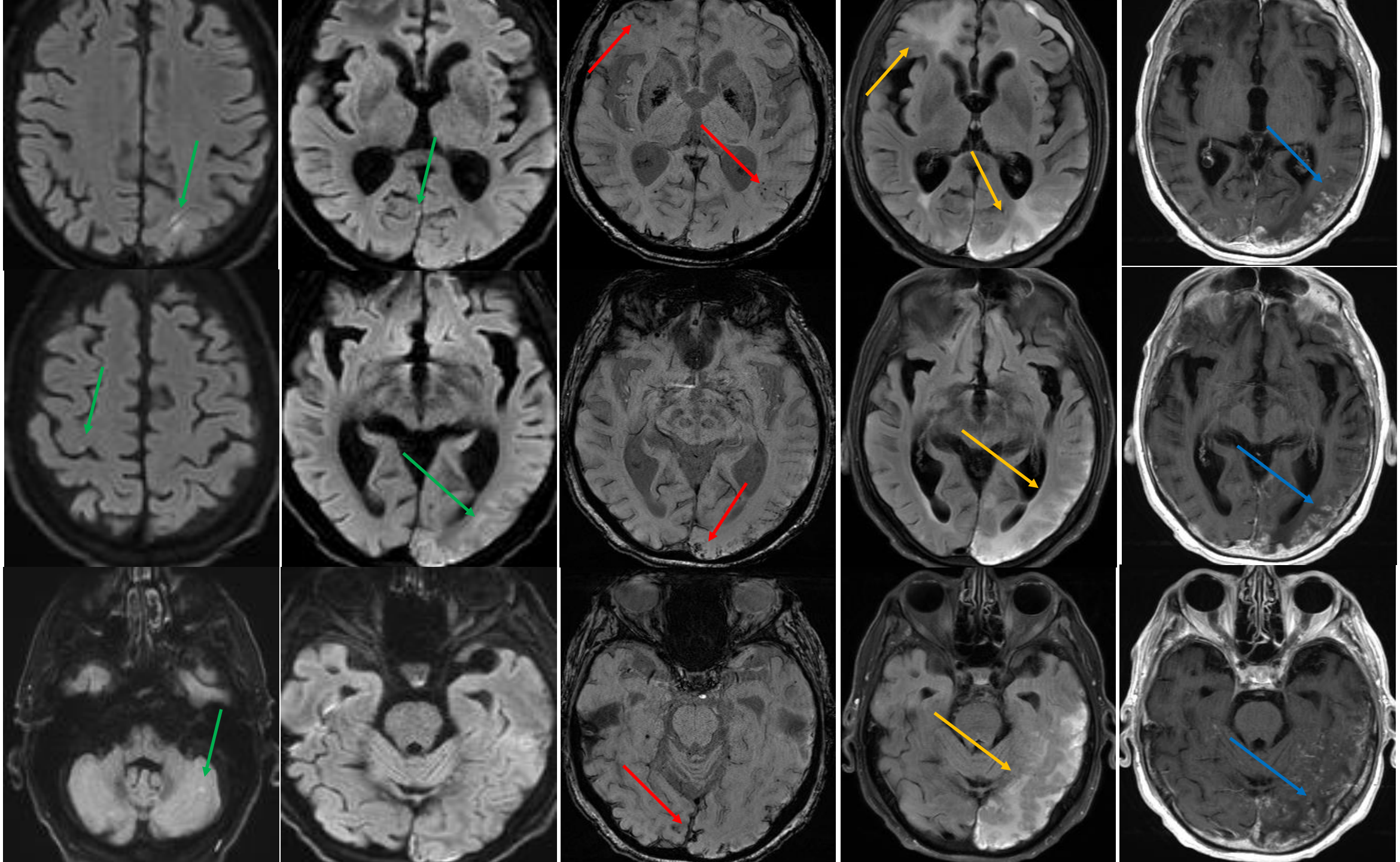
Case 4:

- A 81 M, high functional (retired financial counselor), Hx of HTN, BPH, and chronic, stable bilateral subdural hematomas 2nd to fall in Aug. 2017.
- Developed cognitive impairment in April 2018, first characterized by a bounced check, progressively worsened over 2 months to memory loss, disorientation, and poor command following. In June, he no longer remembered the password to the laptop he used everyday. He was more unsteady with frequent stumbling and one fall.
- CSF: elevated protein (157, <45 mg/dl) and pleocytosis (WBC 31/ml)
- ApoE ε3/3

MRI in 12/2017

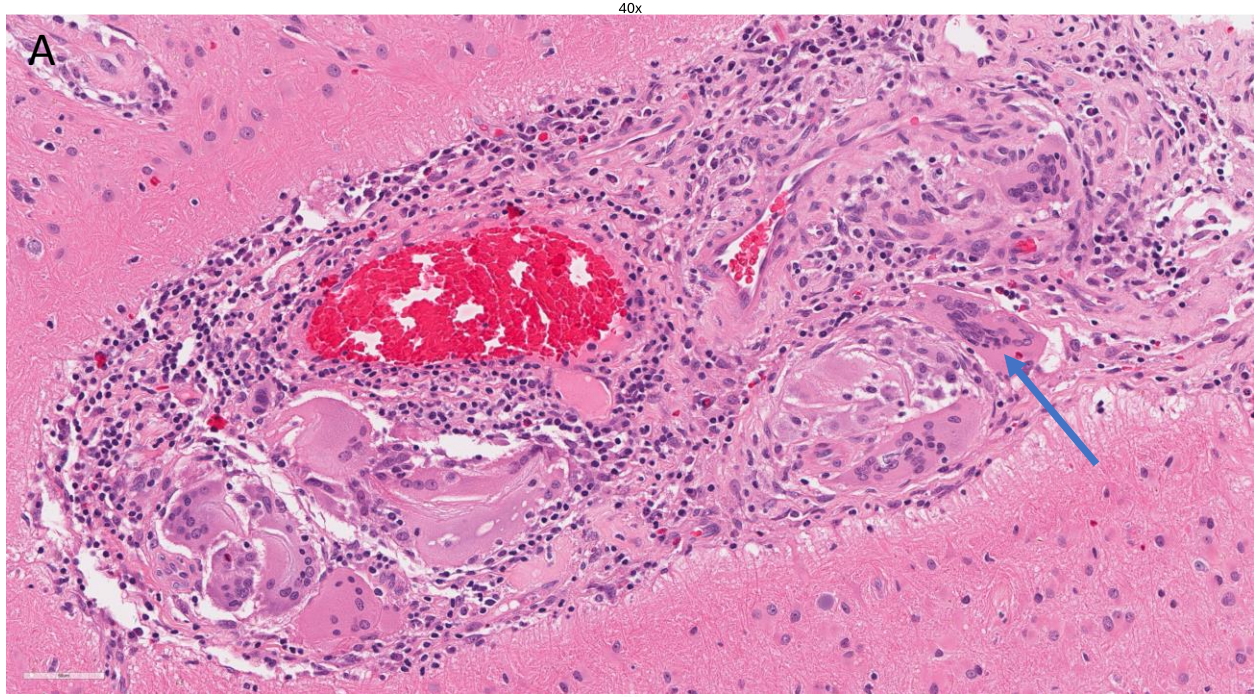


6/2018

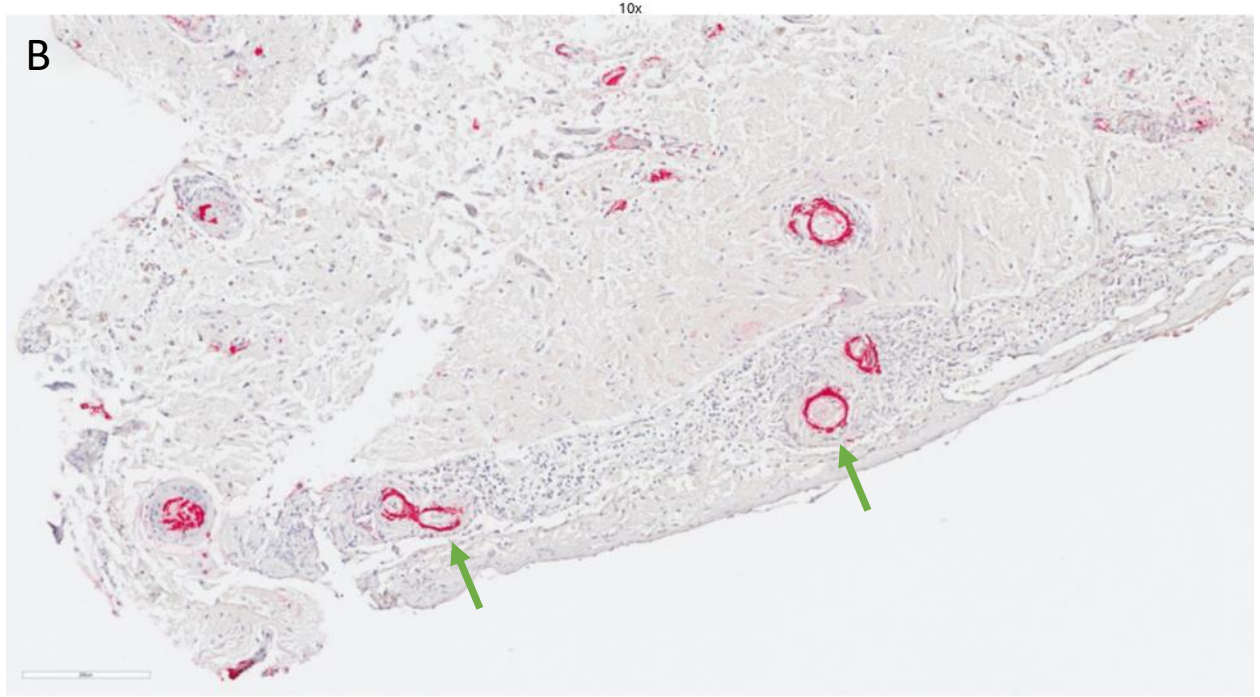


Amyloid Beta-Related Angiitis (ABRA)

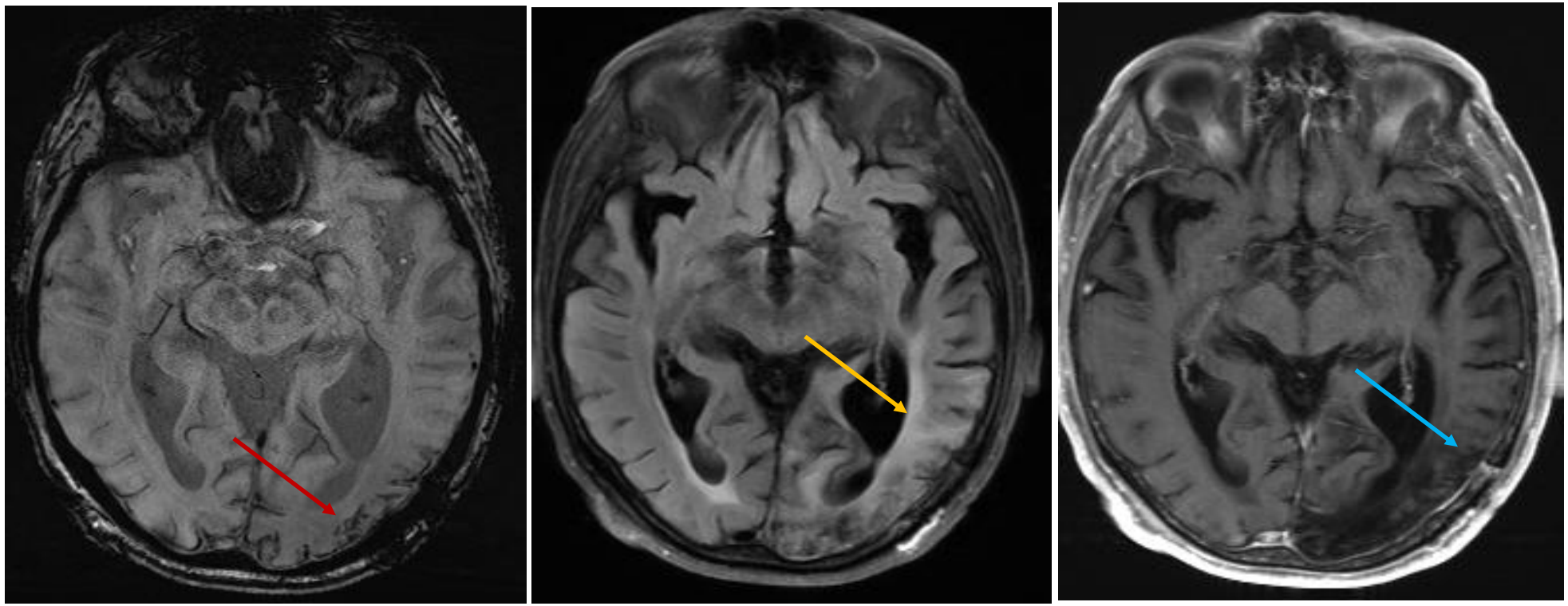
40x



10x



Six Years Later



1/2024

- Treated with glucocorticoids, cyclophosphamide X 1, and mycophenolate mofetil

Amyloid Beta-Related Angiitis (ABRA)

- Cerebral amyloid angiopathy (CAA) is marked by the deposition of Aβ peptides within the walls of small to medium-sized cerebral leptomeningeal and cortical arteries and arterioles.
- CAA-related inflammation (CAA-ri) and ABRA are infrequent inflammatory variants of CAA, characterized by an inflammatory response to Aβ deposits within vessels. CAA-ri is characterized by the presence of inflammatory cells encircling Aβ-laden blood vessels, while ABRA is distinguished by transmural inflammatory cell infiltration.
- WMH lesions (cerebral edema) present in 98% of CAA-ri cases and 79% of ARBA cases.
- cMBs present in 96% of CAA-ri cases and 83% of ABRA cases.
- Treatment same as PCNSV

Does ABRA Belong to CAA-ri Spectrum or PCNSV?

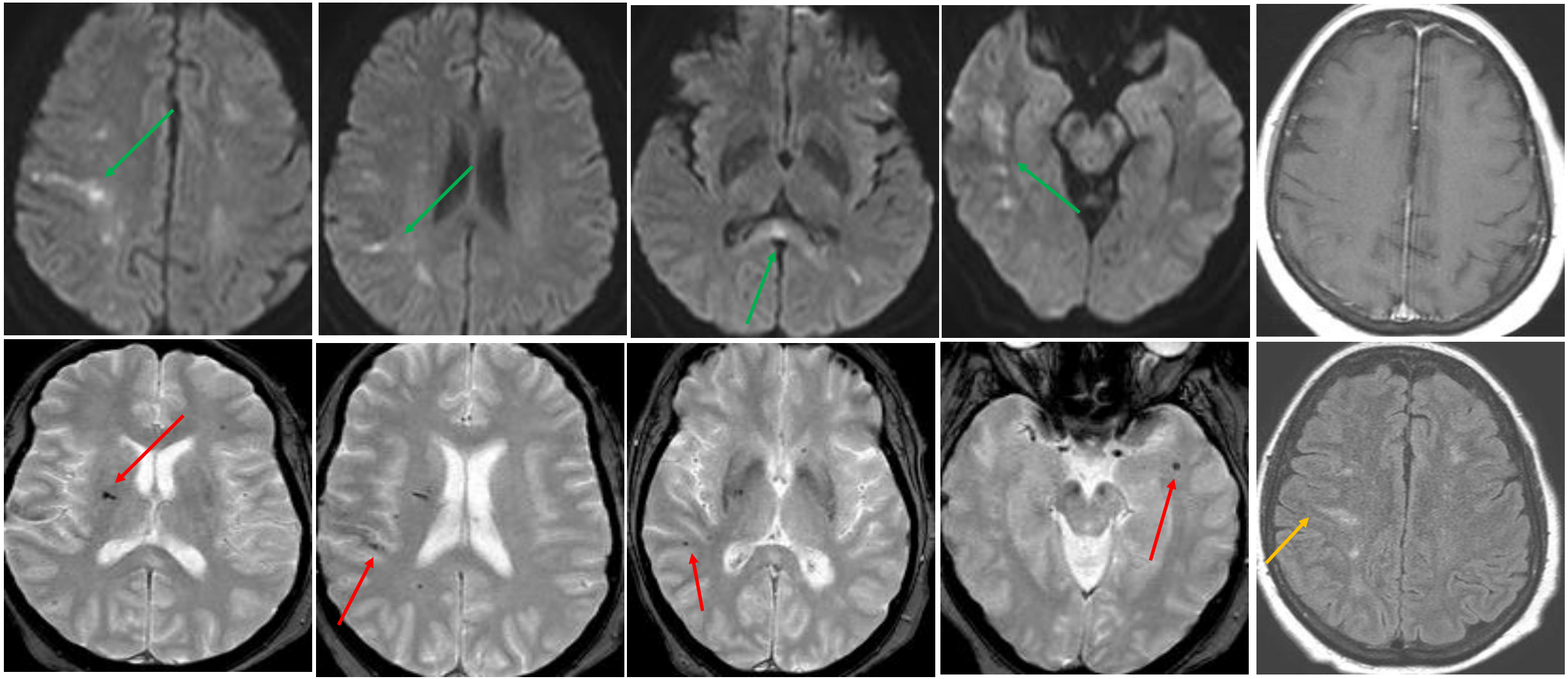
- Neurology: ABRA and CAA-ri are spectrum disorder. In one recent 104 case study, ABRA was under CAA-ri
  - ABRA is distinct from PCNSV
    a) Older
    b) More bleeding: SAH, ICH, cMB, cSS
    c) Leptomeningeal enhancement
    d) Less motor deficits
    e) Relapse rate is lower within first 2 year after remission
- Rheumatology: ABRA is still considered as PCNSV

Neurology® 2024;103:e209548.
Medicine • Volume 95, Number 20, May 2016
Neurology® 2013;81:1596-

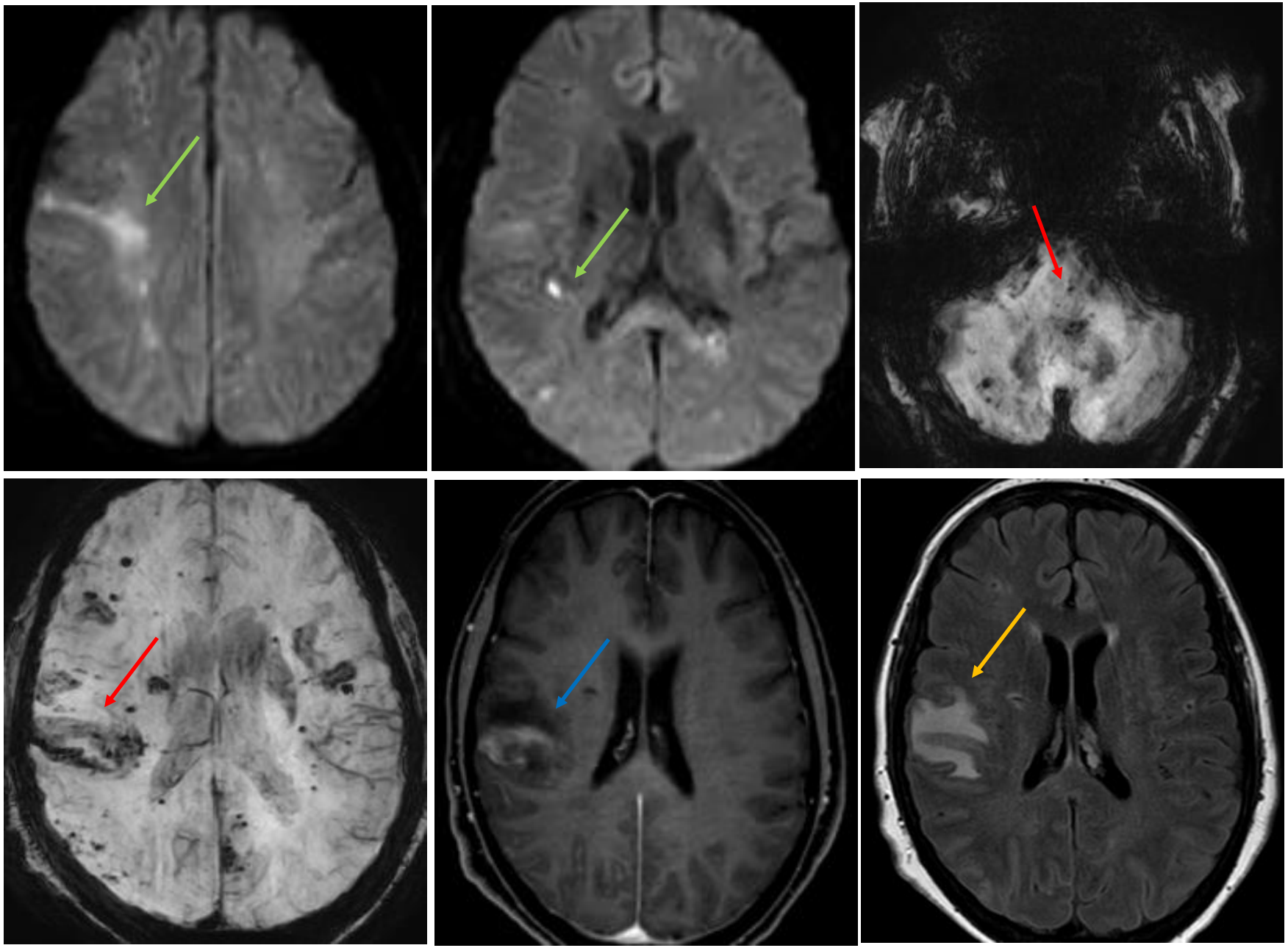
Case 5:

- A 66 F with Hx DM2, Afib on Rivaroxaban 20mg daily, hyperthyroidism had progressive cognitive decline for 6 weeks.
- In her usual health state until six weeks ago, when she started to forget time, forget to eat or go to work. She tended to lose things, was unable to use ipad or access email (was her routine habit). These symptoms wax and wane, lasted for hours, occurred several times a week. One week prior to admission, developed transient left side facial droop and numbness in left face and left arm. MRI at OSH was negative for acute infarct but WMH. She was told that she has TIA or MS.
- The night before admission, suddenly developed slurry speech, difficulty finding words, visual and olfactory hallucinations (seeing babies in the room and smelling stinky odor). She was suspicious that her daughter was trying to take away her business. These symptoms gradually resolved after 12 hours.

4/30



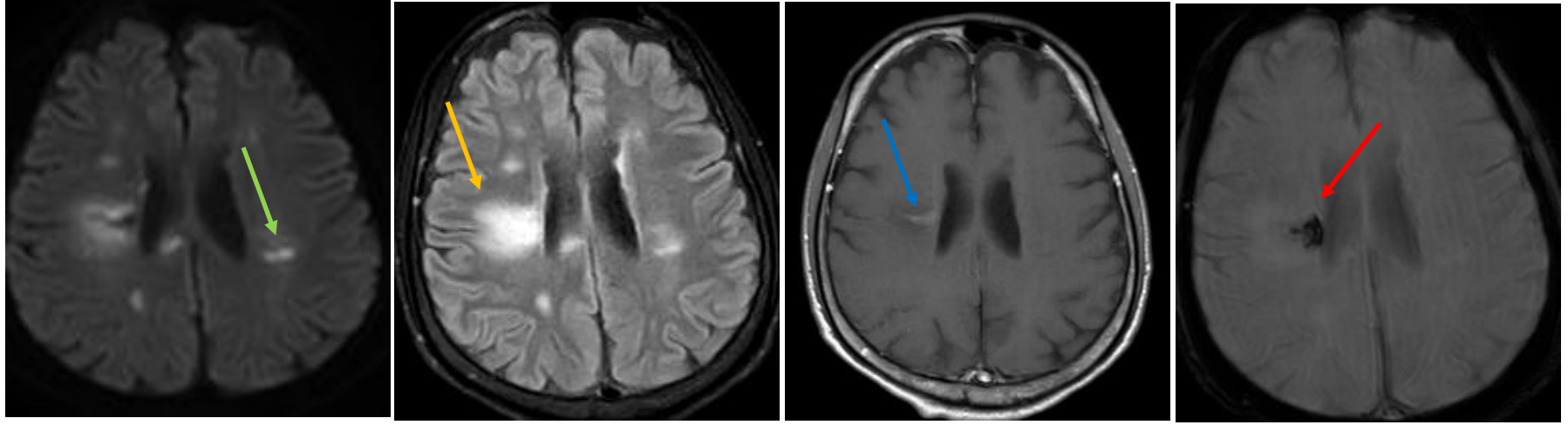
6/17



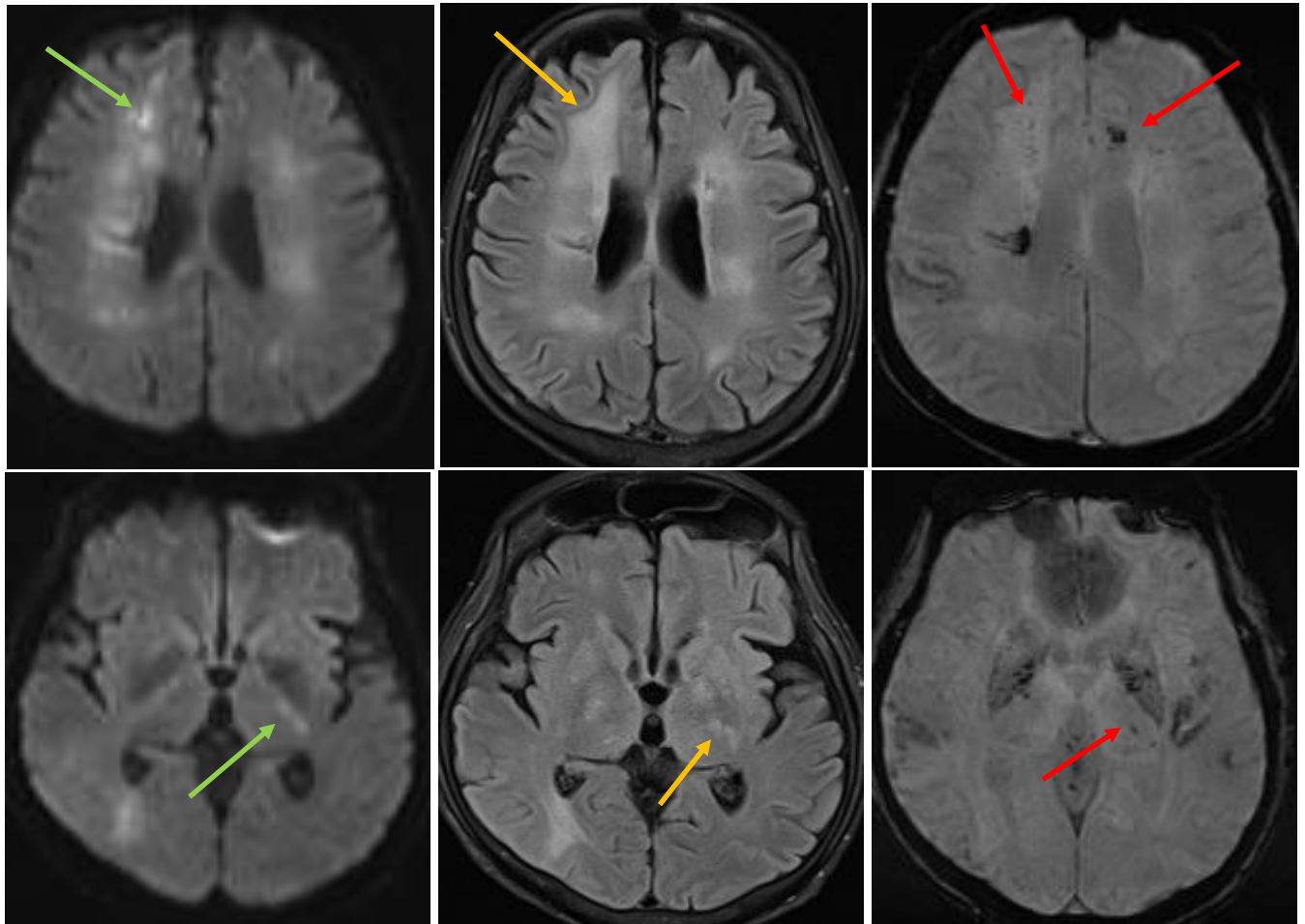
A Diagnostic Test Was Performed

- R temporal lobe open biopsy
  - Intravascular large B-cell lymphoma (IVL)

1/10/2023



4/10/2023



- A 64 M HTN, T2DM, HLD, ischemic strokes in 10/2022 and 12/2022.
- Skin biopsy X2: IVL

Intravascular lymphoma (LVL)

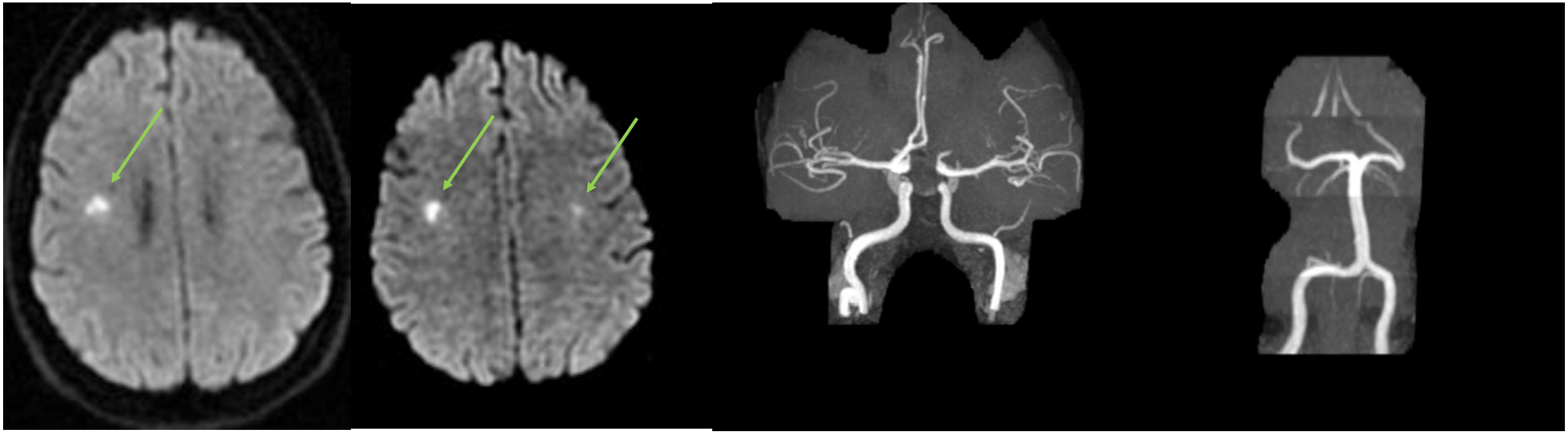
- Rare: one per million patient-years
- Characterized by infiltration and proliferation of malignant B cells within small blood vessel lumens.
- The CNS is the most common primary site, and heterogeneous presentation results in diagnostic delay such that 60% of CNS presentations are diagnosed post mortem.
- Microangiopathy pattern on MRI
  - Infarcts
  - WMH
  - Leptomeningeal/parenchymal enhancement
  - Mass/edema like lesions
  - **Cerebral microhemorrhage on SWI/GRE**
- Still a systemic disease

JAMA Neurology January 2022 Volume 79, Number 1

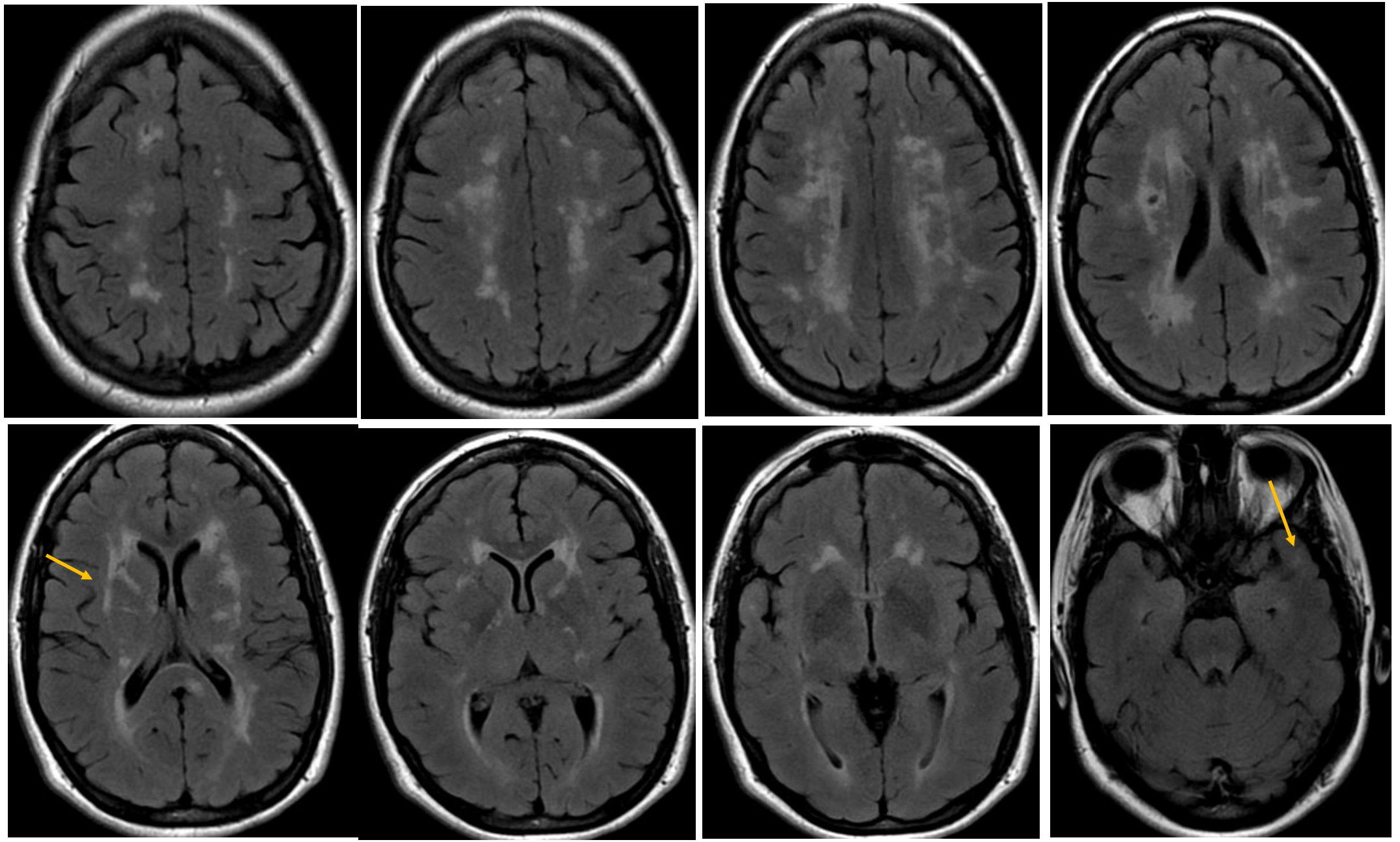
Case 6:

- A 40 F with Hx HTN on amlodipine 5mg, presented with left side weakness and sensory loss
- Exam: Mild L hemiparesis. MMSE is 24
- History of migraine with aura, reported neck pain, no alopecia.
- Her mother had memory loss at age of 50. She had two brothers and one sister. One brother had migraine and stroke. She has two children (one boy, one daughter, both in 20s), reported to have migraine.

2017



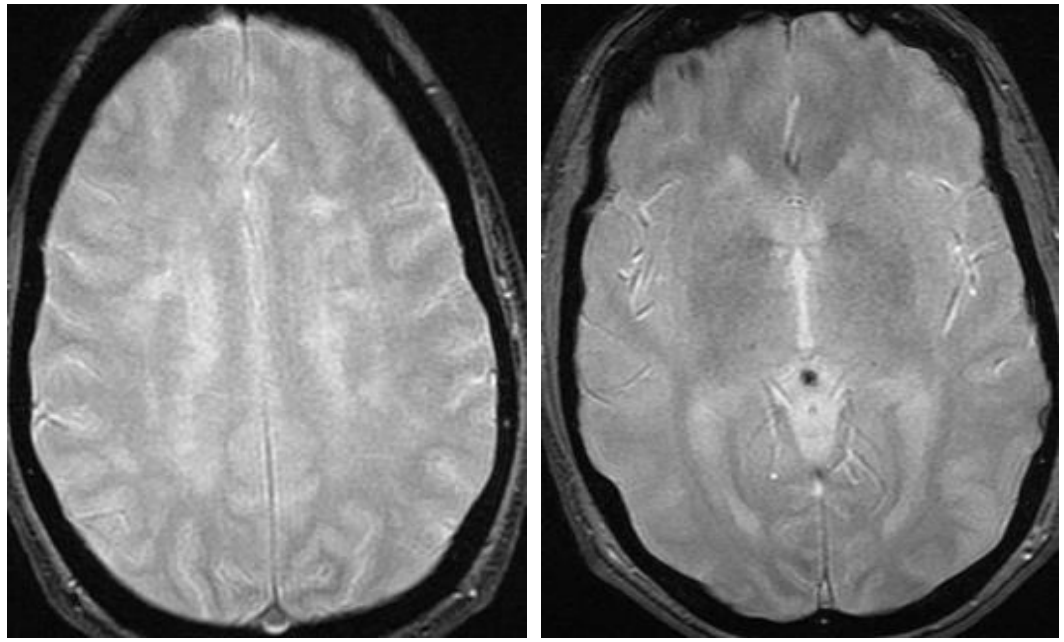
2017



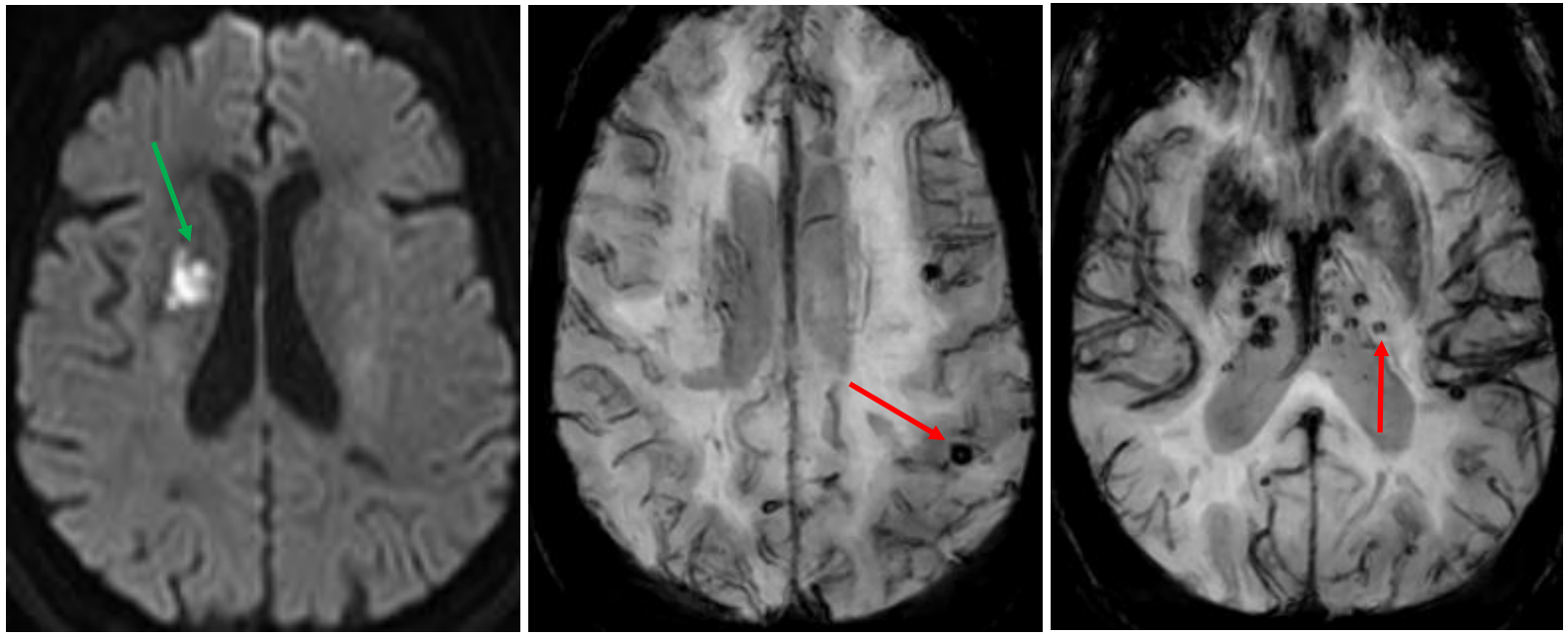
Diagnostic Tests Were Performed

- Left arm skin punch biopsy:
  - Periarteriolar extracellular granular electron dense deposit (granular osmiophilic material: GOM) surrounding smooth muscle cells present
- *NOTCH3* gene sequencing:
  - C.505C>T, p.Arg168Cys, heterozygous missense, autosomal dominant, pathogenic
  - Located in the EGFR number 4
- Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy (CADASIL)

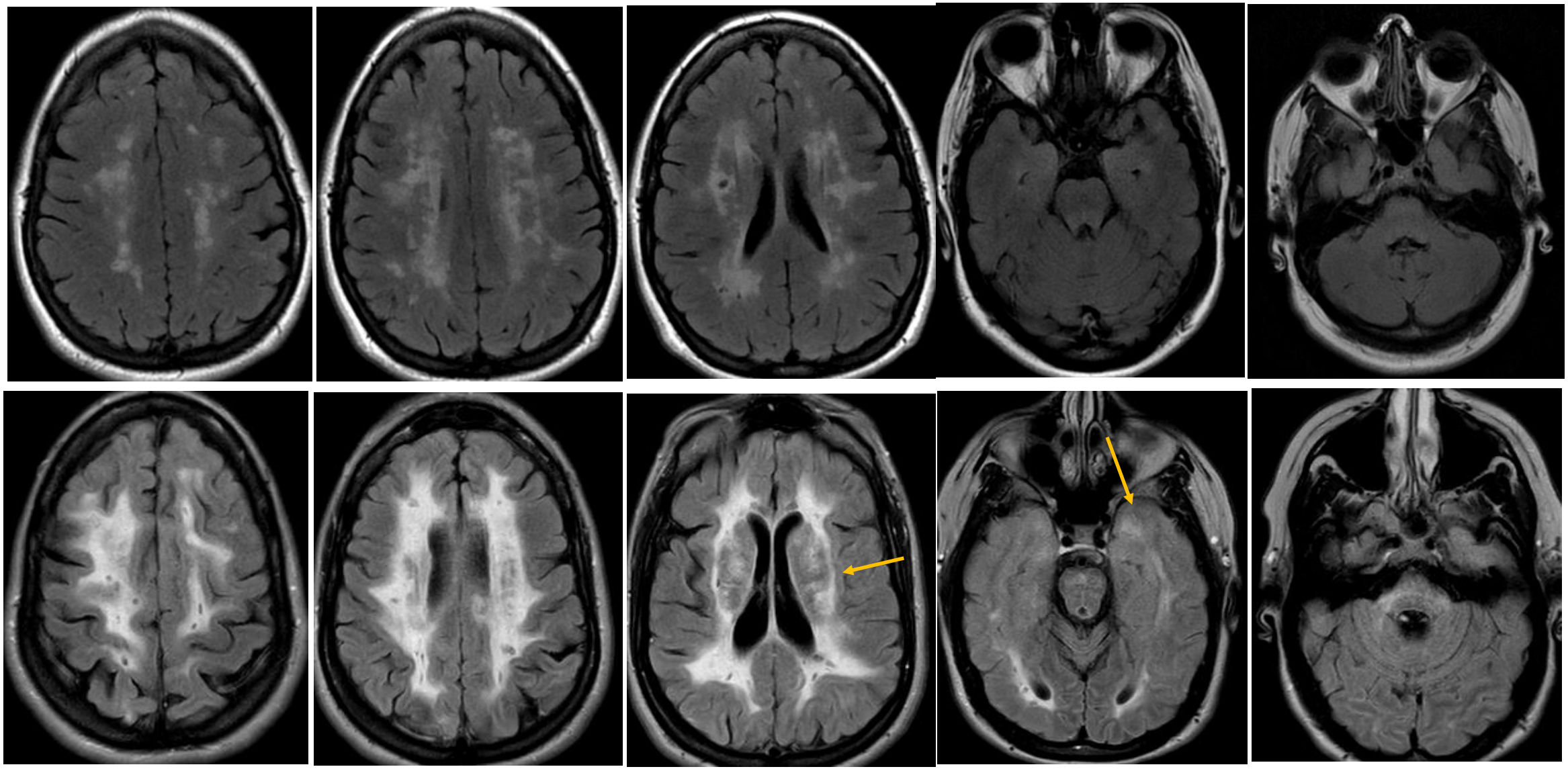
2017



2024 at age of 47



2017

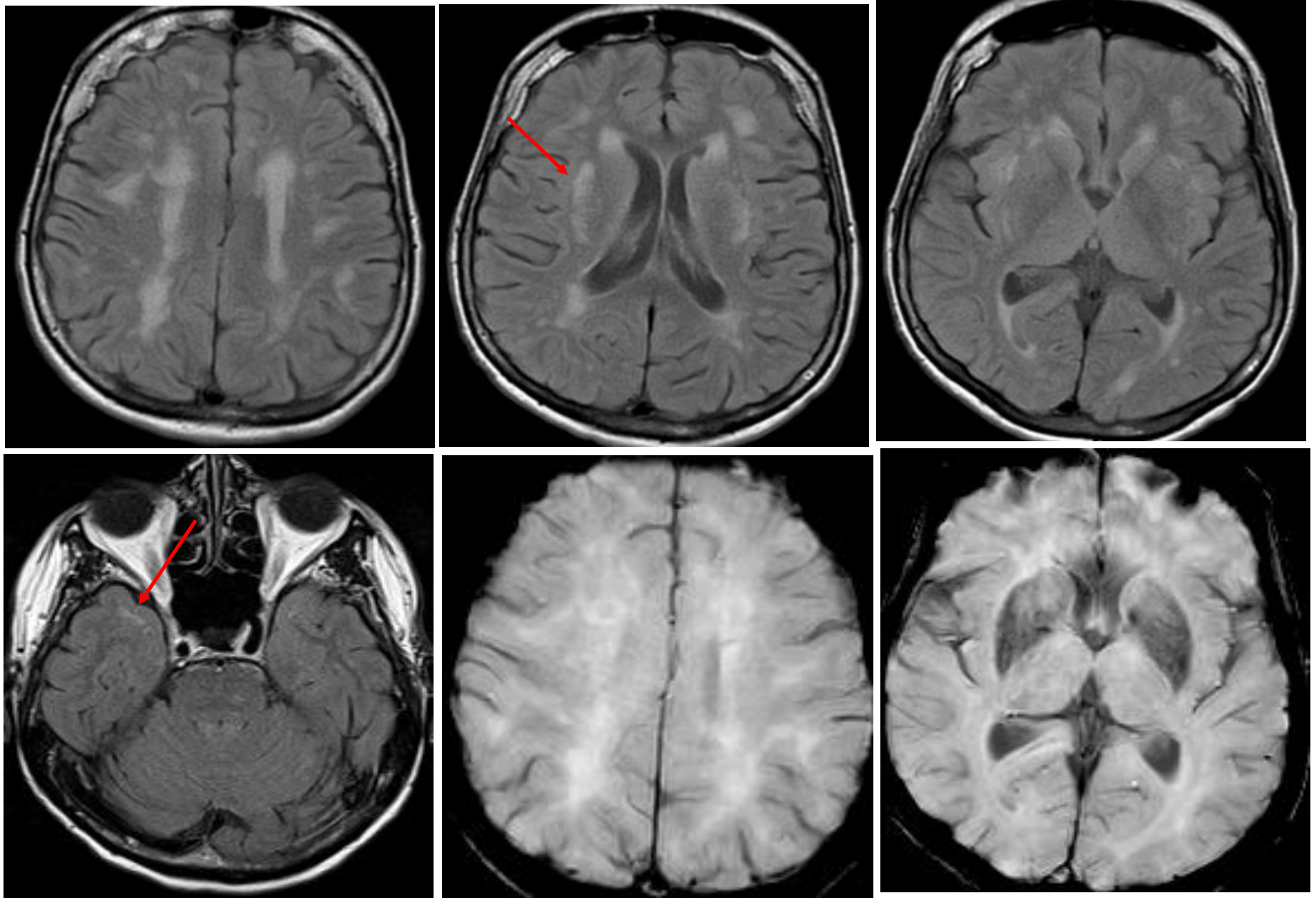


2024 at age of 47

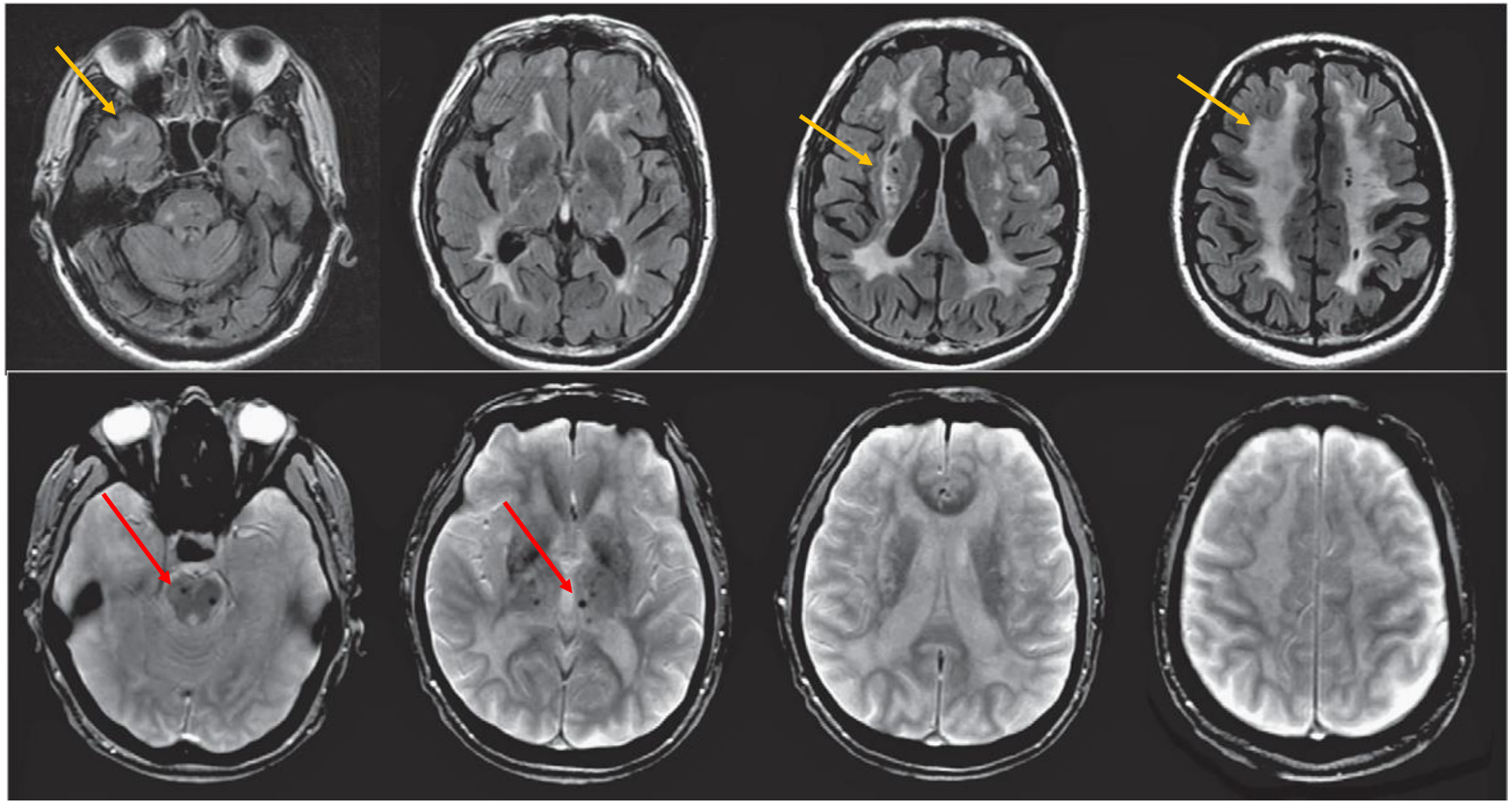
2020 at age of 70

- 70 healthy F with migraine with aura since age of 14

- *NOTCH3*:
  - c.1999G>T; p.Gly667Cys
  - Pathogenic
  - Located in EGFR 17

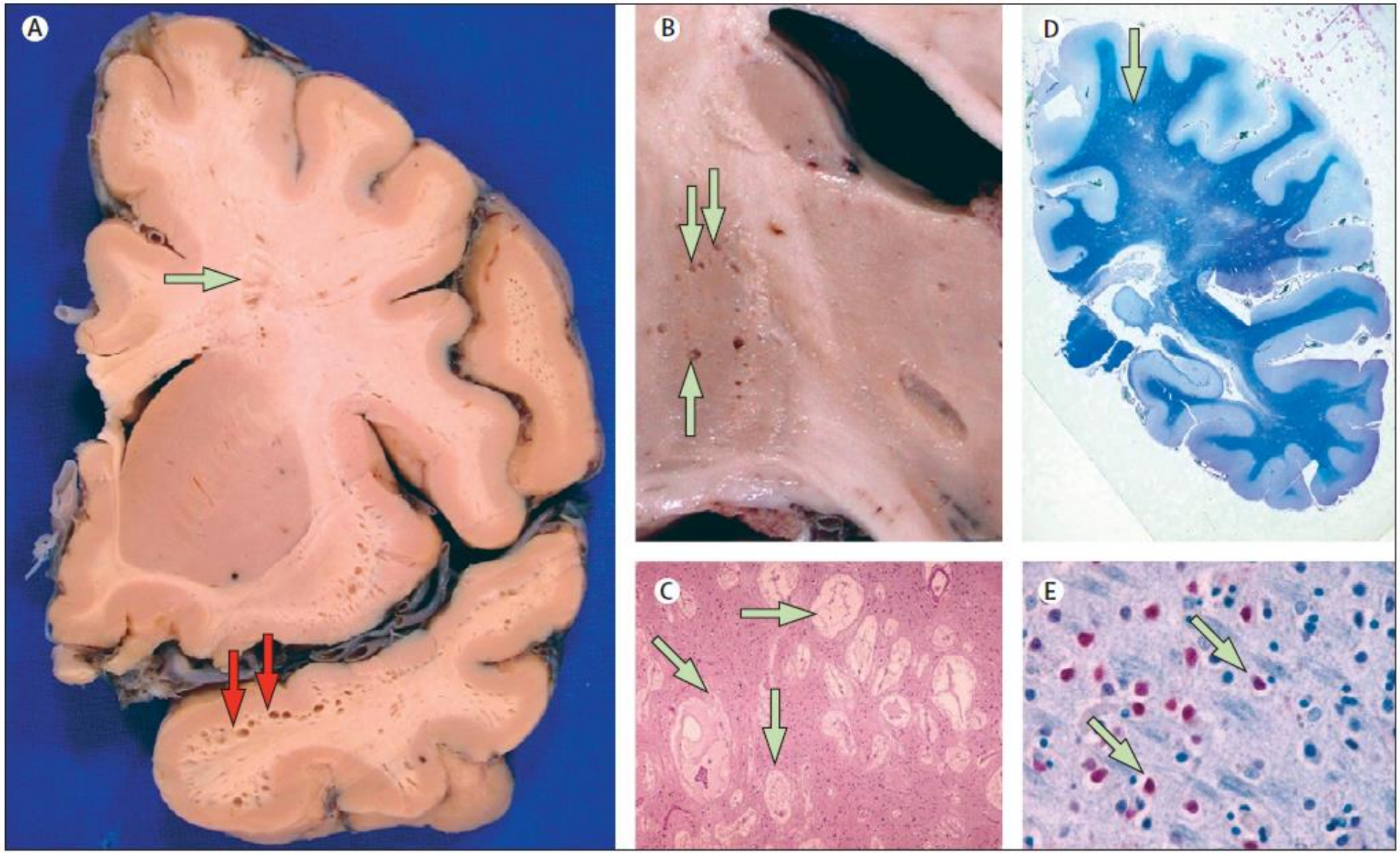


Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy (CADASIL)



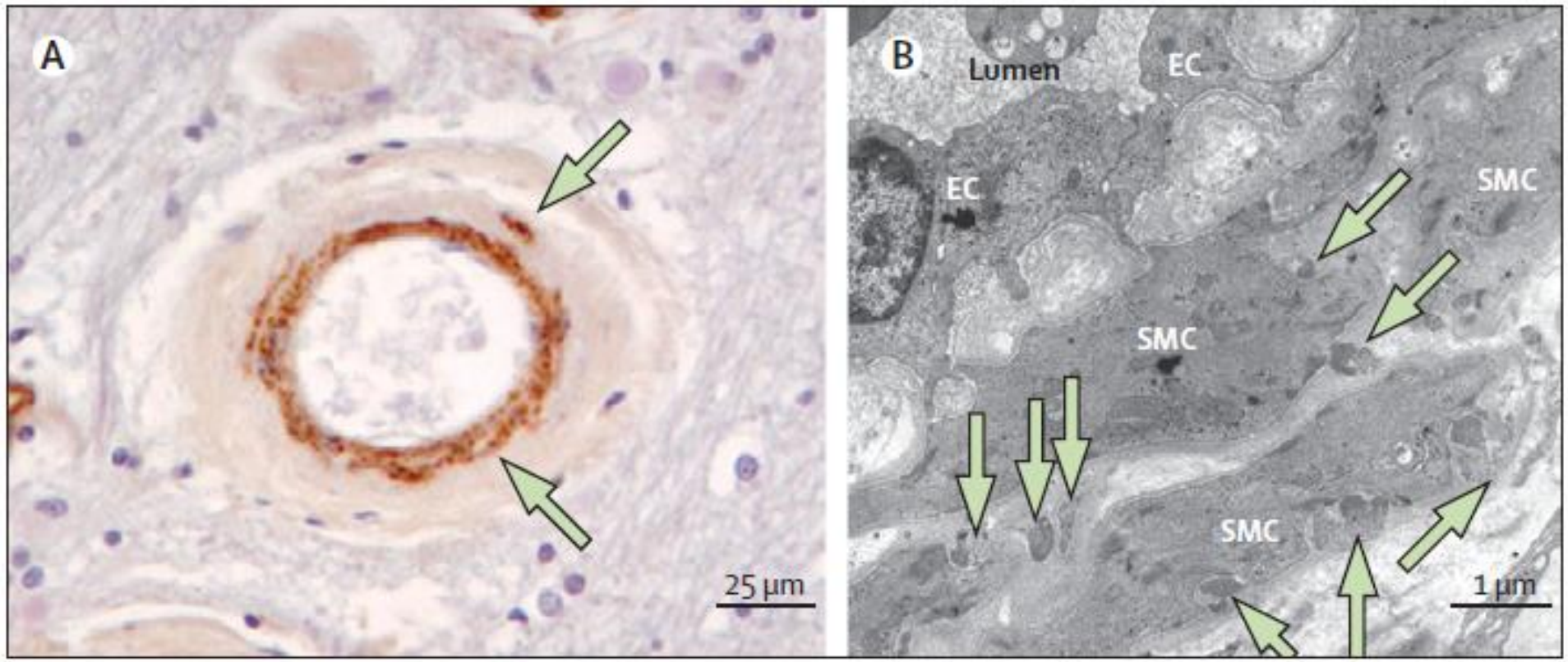
Lancet Neurol 2009; 8: 643-53

Pathology



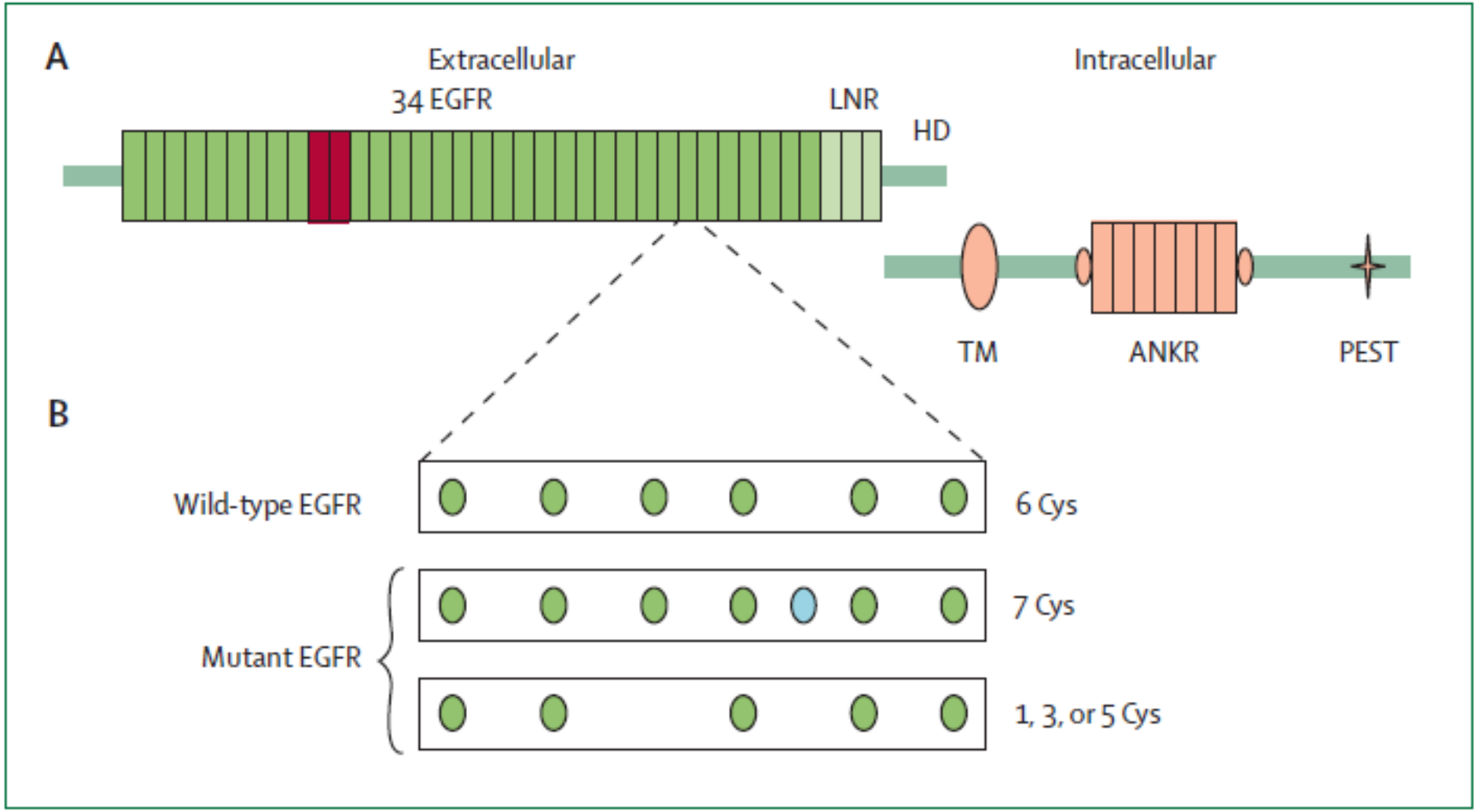
Lancet Neurol 2009; 8: 643–53

Extracellular NOTCH3 Protein Aggregates



Lancet Neurol 2009; 8: 643–53

Mutations in *NOTCH3* Gene



EGFR: epidermal growth factor repeats

Lancet Neurol 2009; 8: 643–53

Pathogenic Mechanism Unknown

- Loss of *NOTCH3* function does not cause CADASIL but vascular dysfunction in transgenic mice
  - Impaired mechanotransduction
    - Decrease flow induced dilation
    - Increase in pressure-induced contraction
  - Preserved agonist or receptor medicated contraction and dilation
    - Phenylephrine-induced contraction
    - Acetylcholine-induced dilation
- Gain of function mechanisms
- Extracellular matrix disease

Lancet Neurol 2009; 8: 643–53
(*Stroke*. 2005;36:113-117.)

CADASIL Epidemiology, Diagnosis and Treatment

- More common than expected
  - 443 in 200,632 subjects in UK Biobank (1 in 450): 0.2% was found to have cysteine alternating mutations in the 34 EFGR
- Mutation location matters
  - Phenotype from mutation in EGFR 1-6 is more sever than from EGFR 7-34
  - Genetic test recommended in addition to skin biopsy
- No pathognomonic imaging markers
  - Compared to sporadic cSVD, WMH extending to anterior temporal lobe (93% vs 45%) and external capsule (100% vs 50%) are just more frequent

Neurology® 2024;102:e209310.
Journal of Cerebral Blood Flow & Metabolism
2023, Vol. 43(1) 153–166
Neurology® 2010;74:57-63
Cho BPH, *et al. J Neurol Neurosurg Psychiatry* 2021;**92**:694–701.

CADASIL Scale

- Total 25 points
- A total ≥ 15 points is predictive of CADASIL diagnosis

Migraine	1
Migraine with aura	3
TIA or stroke	1
TIA/stroke onset ≤50 y	2
Psychiatric disturbances	1
Cognitive decline/dementia	3
Leukoencephalopathy	3
Leukoencephalopathy extended to temporal pole	1
Leukoencephalopathy extended to external capsule	5
Subcortical infarcts	2
Family history* in at least 1 generation	1
Family history* in at least 2 generations	2

(*Stroke*. 2012;43:2871-2876.)

CADASIL Treatment

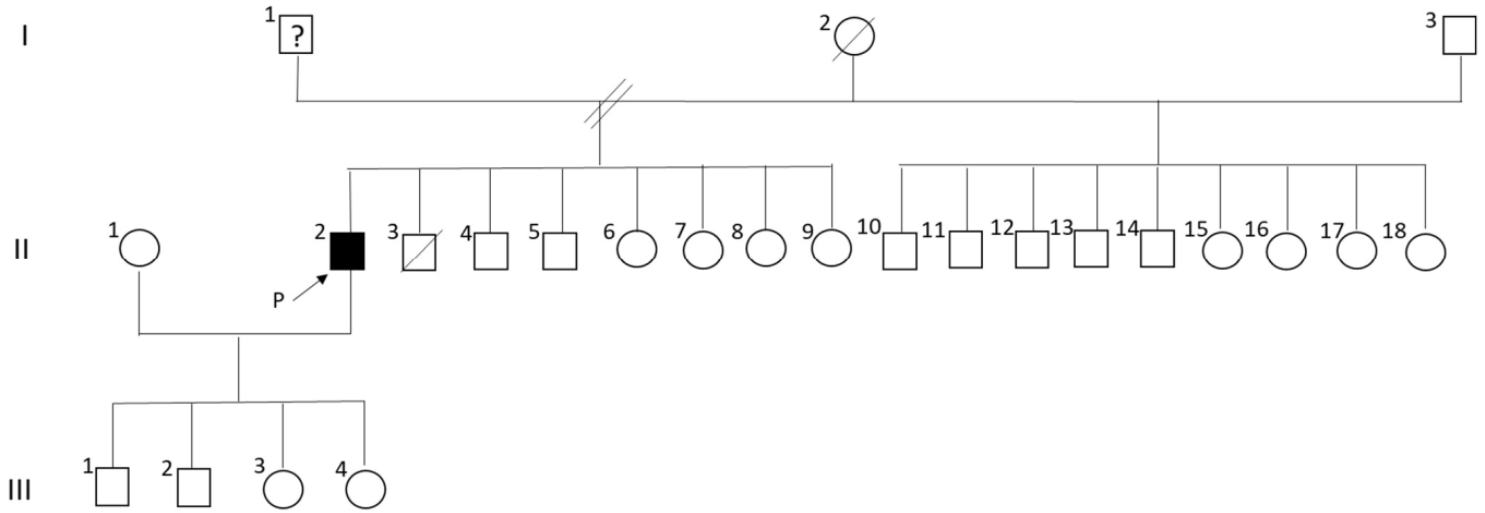
- No approved treatment
- One randomized controlled clinical trial
  - Effect of Sapropterin on Endothelium dependent vasodilation in CADASIL
  - Negative results
- The Lacunar Intervention Trial-3 (LACI-3)
  - Phase 3 clinical trial in sporadic cSVD, CADASIL is allowed
  - **Cilostazol and Isosorbide mononitrate**
  - January 2025 to April 2029

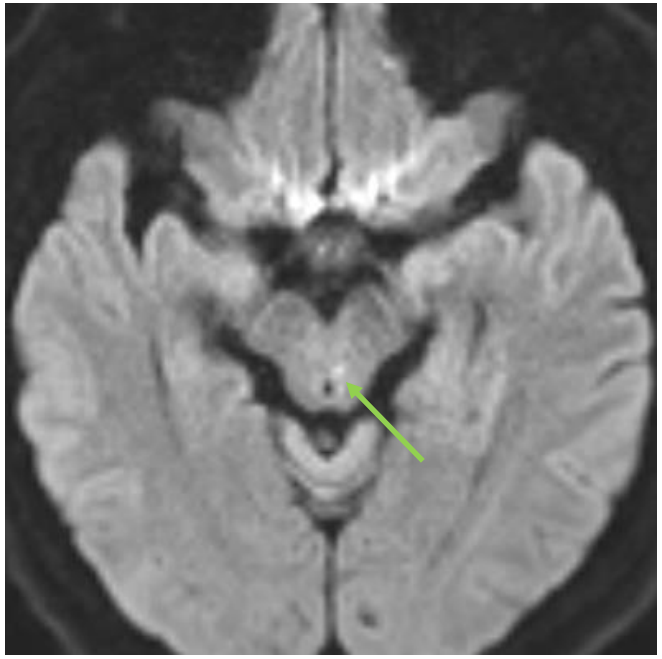
(*Stroke*. 2014;45:2959-2966.)

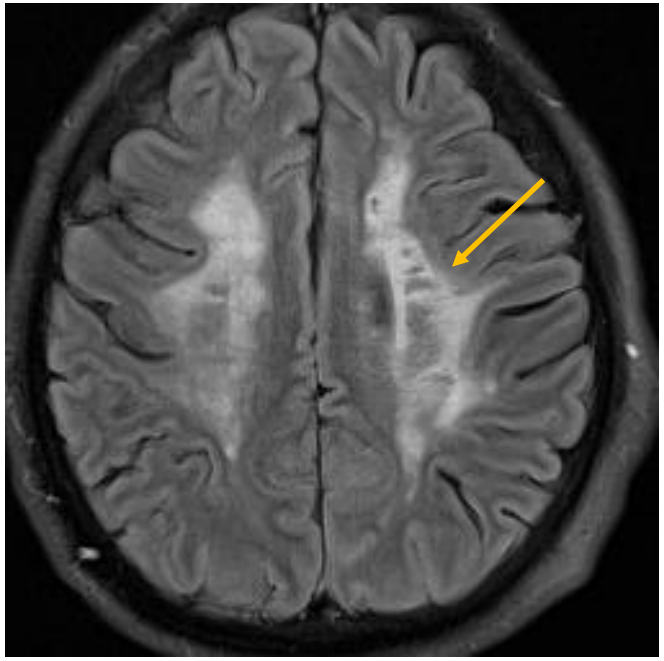
LACunar Intervention (LACI) Trial-3: Assessment of efficacy and safety of cilostazol and isosorbide mononitrate to prevent adverse outcomes in patients with cerebral small vessel disease (lacunar) ischaemic stroke - NIHR Funding and Awards

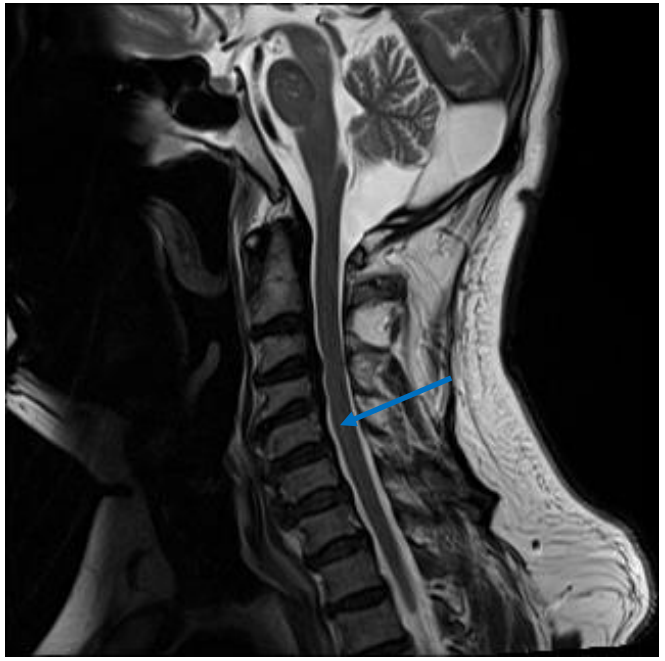
Case 7:

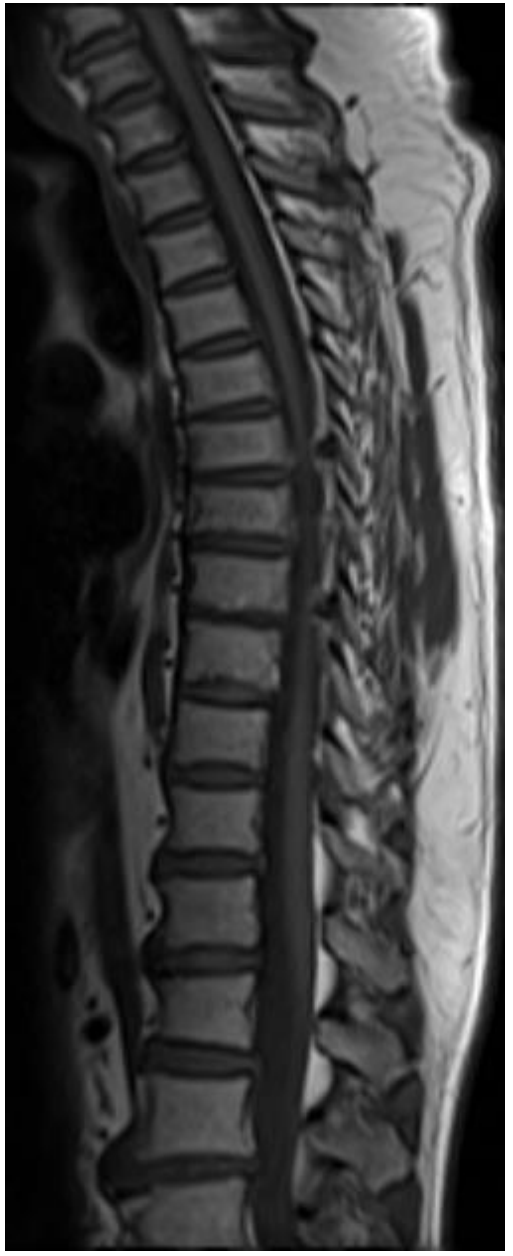
- A 49-year-old Mexican man without risk factors presented with L INO and cognitive impairment
- Neck pain
- No alopecia, no migraine
- Family history

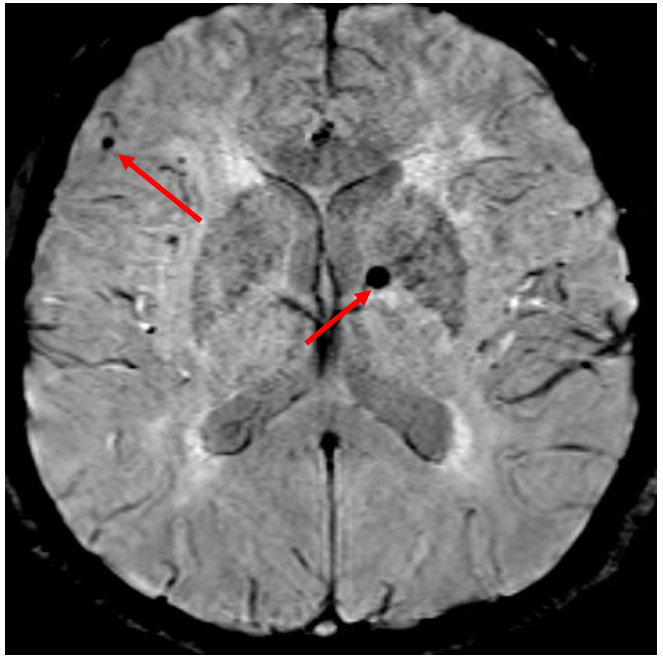


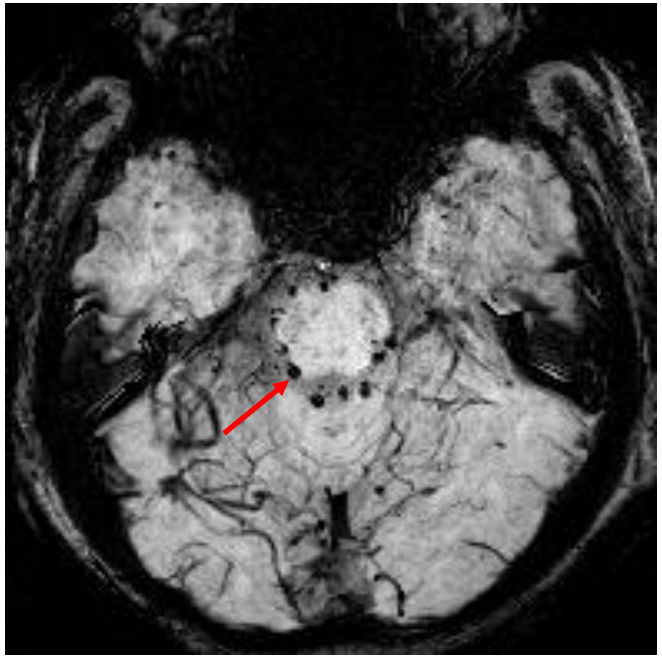


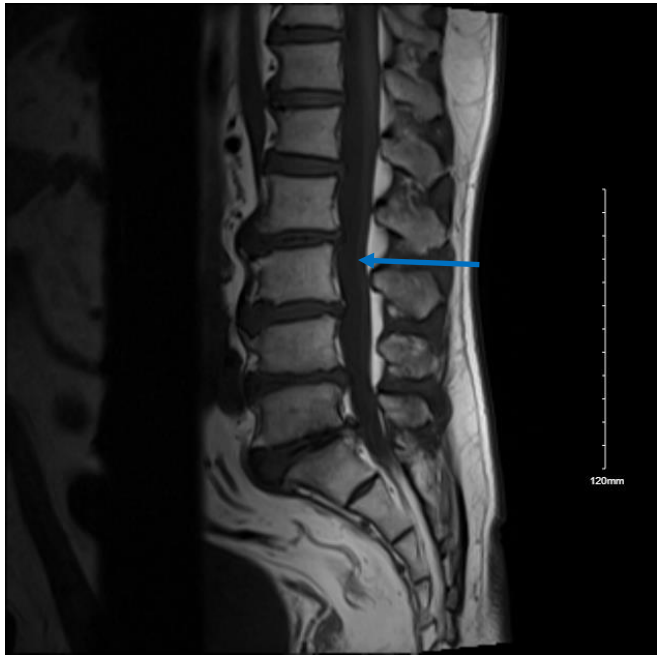






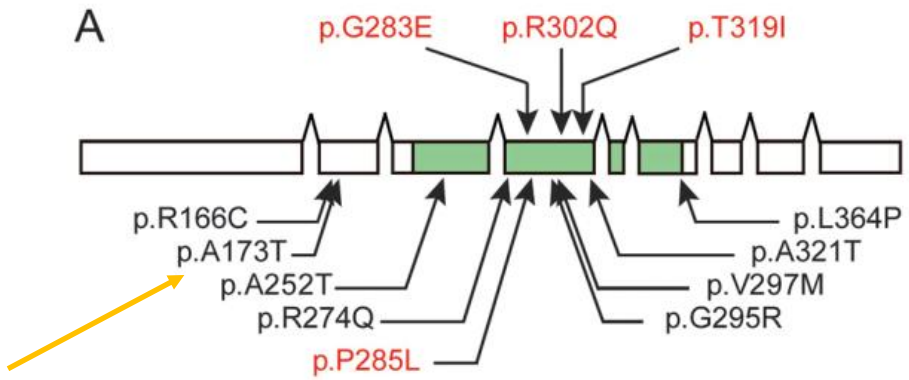





120mm

A Diagnostic Test Was Performed

- Genetic sequencing for *HTRA1* gene mutation:
  A. Homozygous missense mutation of p.Ala173Ser
  B. Undetermined significance
- Reported mutations in the same locus linked to *HTRA1*-CSVD
  A. Homozygous missense mutation of p.Ala173Thr in a Pakistani

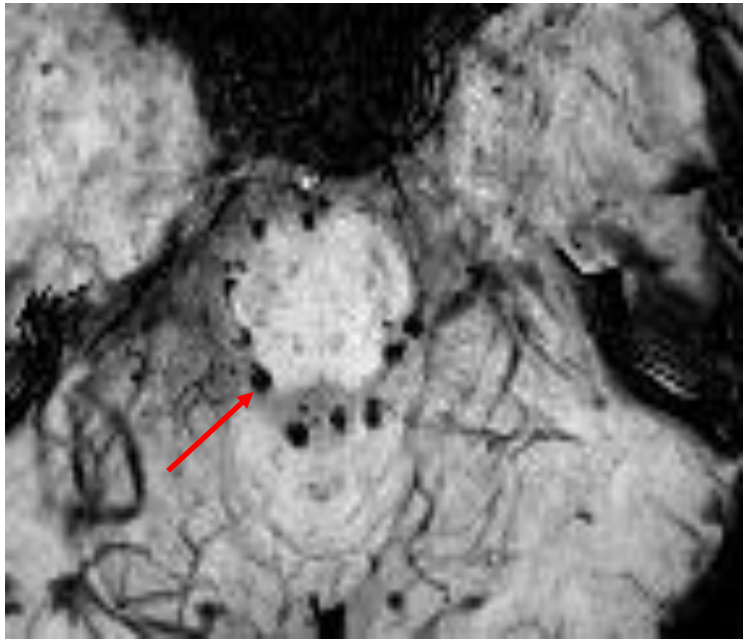


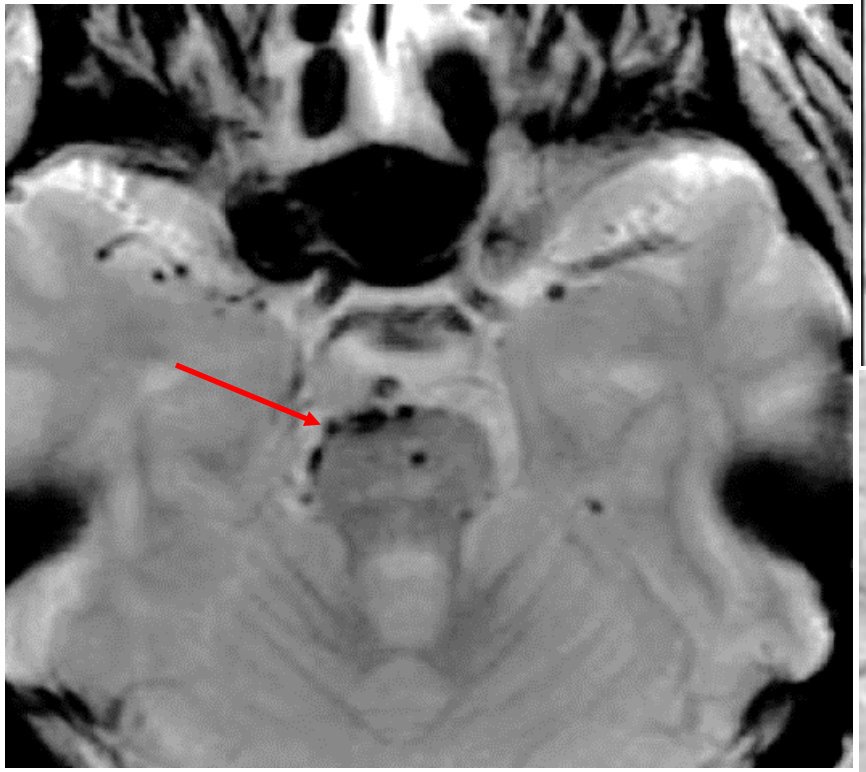
  B. Heterozygous missense mutation of p.Ala173Pro in a Caucasian
- p.Ala173Ser is a new and pathogenic mutation

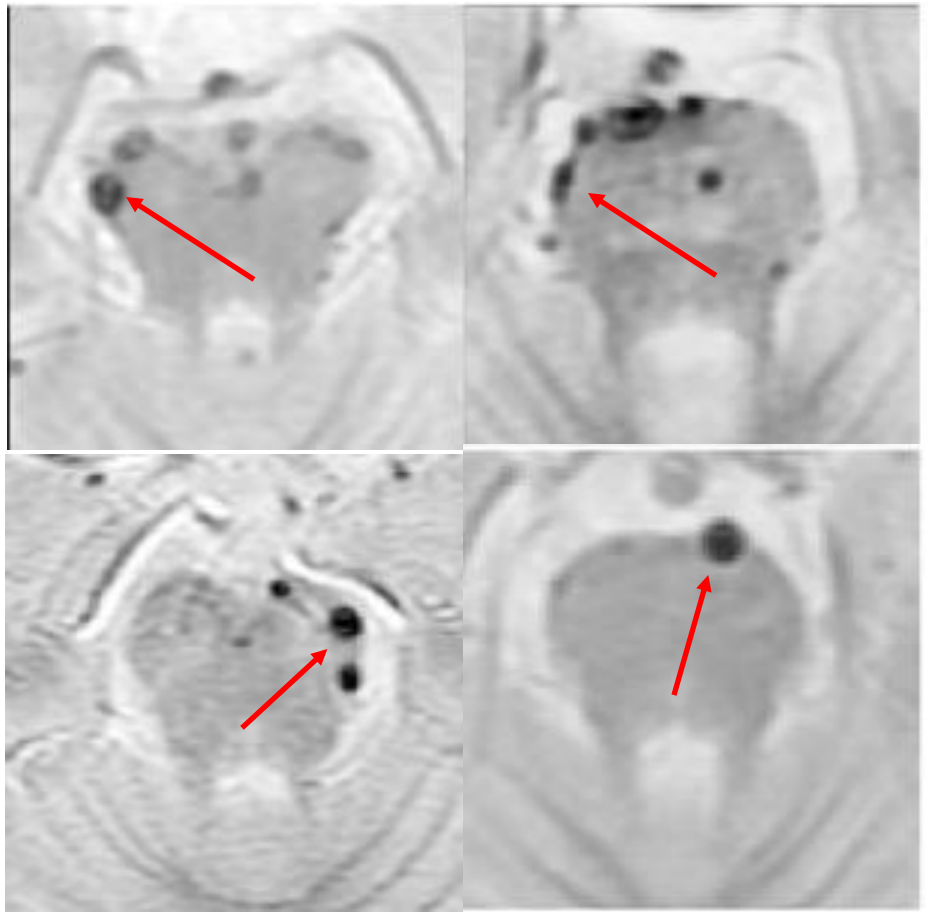
Cerebral Autosomal Recessive Arteriopathy With Subcortical Infarcts and Leukoencephalopathy (CARASIL)

- Rare: 30+ cases reported globally since 2009, most cases reported in Asian
- Caused by mutation in *high-temperature requirement A serine peptidase 1 (HTRA1)* gene
- Homozygous or compound heterozygous mutations
- Heterozygous mutation carries have a milder form
- Clinically characterized by dementia, lacunar stroke, spondylosis and alopecia
- Hallmarks of cSVD on MRI:
  - WMH involvement of external capsule and anterior temporal lobe
  - Atrophy
  - Microbleeds

An Imaging Biomarker: Subpial cMBs in Brainstem on SWI







Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 11 (November), 2021: 106029

Neurol Genet 2023;9:e200047.

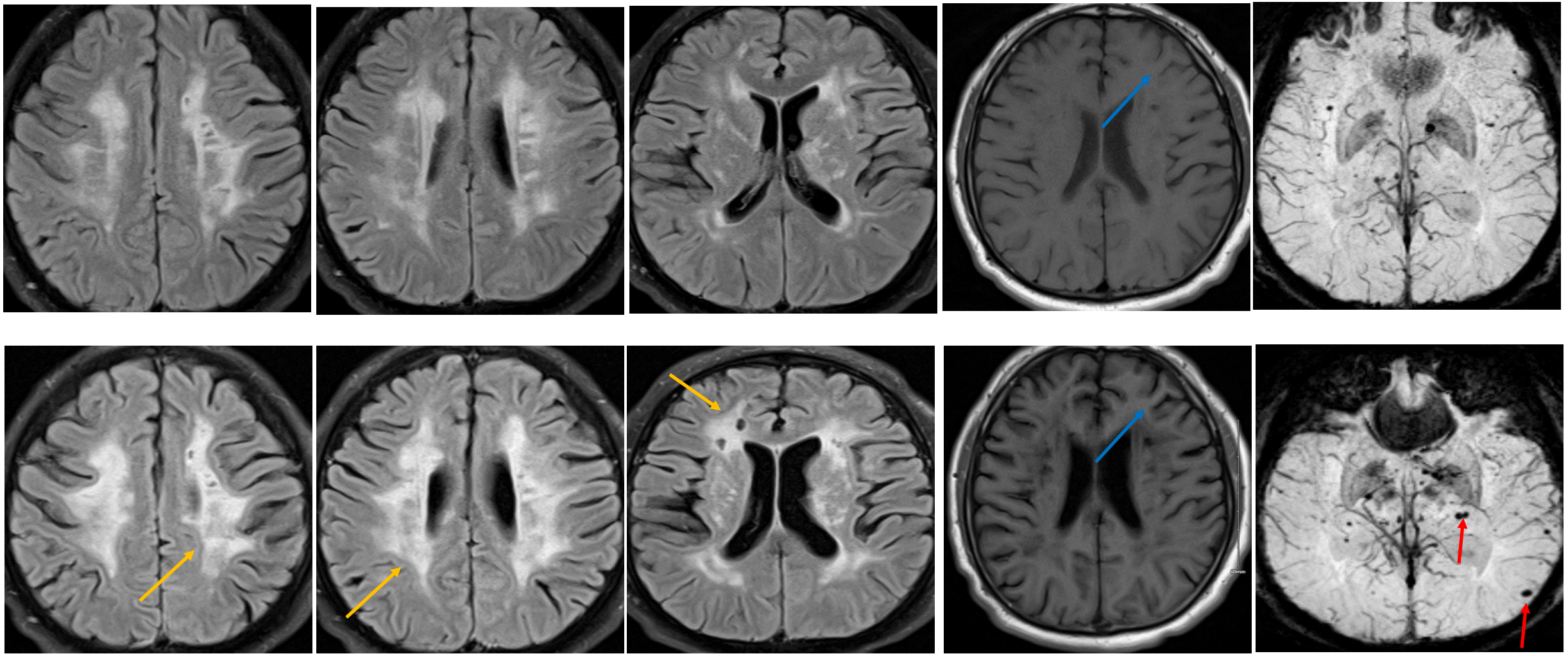
Journal of the Neurological Sciences 466 (2024) 123229

Treatment

- There is no treatment for CARASIL
- Elevated TGF-β activity was observed in pathological studies.
- Dugs known to suppress TGF-β activity and potentially could be used for therapeutic purposes
  a) Pioglitazone (Actos)
  b) Losartan
  c) Pirfenidone (Idiopathic pulmonary fibrosis)
- This subject was found to have insulin resistance. So he was prescribed with Pioglitazone according to the IRIS trial but with poor compliance.

N Engl J Med 2016;374:1321-31.

March 2018

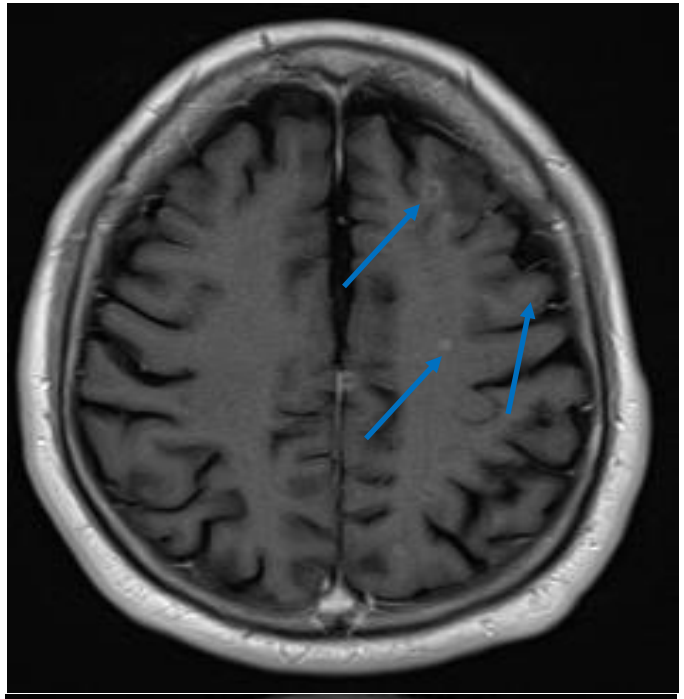


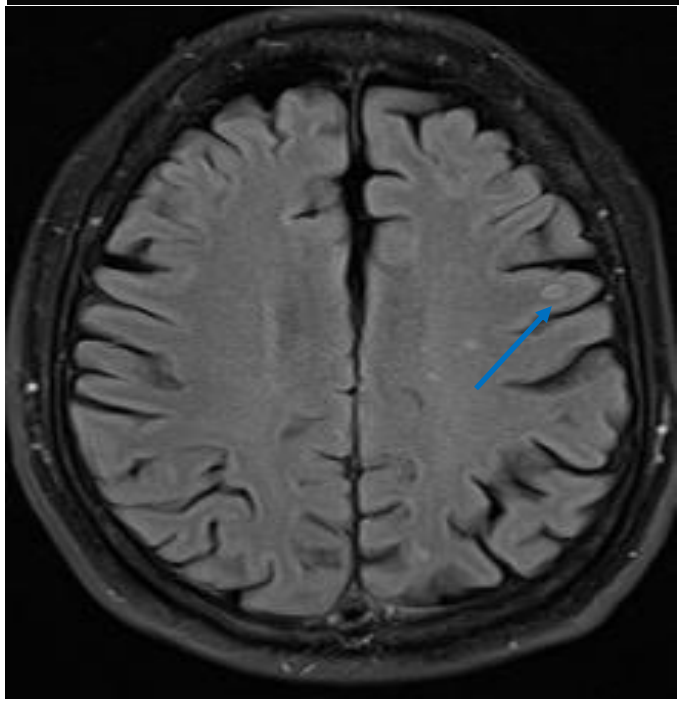
May 2022

Case 8:

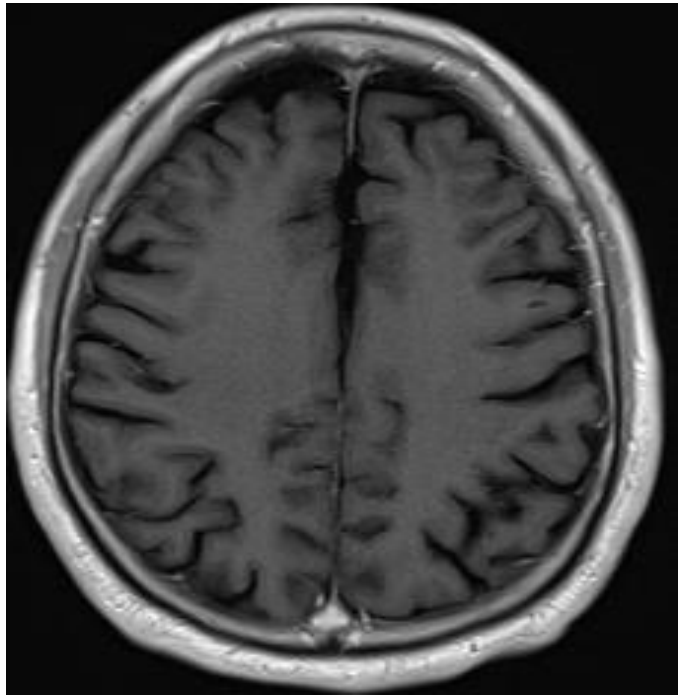
- 74 M w SCLC w brain mets s/p WBRT (many enhancing lesions on 9/2020 MRI, resolved after treatment by 1/2021) and HTN, HLD and DM II who presented with acute onset of confusion.
- Per wife, he was pretty sharp and able to do all his own ADLs. He went to bed in normal state of health on the night of 4/27/2024 and woke up in the morning of 4/28 altered. He was not able to answer any questions or answering inappropriately. Otherwise, he had unfocal neuro exam.
- CTA head and neck/TTE/EEG/infection workup: unremarkable
- Autoimmune encephalopathy panel and paraneoplastic panel were negative in CSF and serum

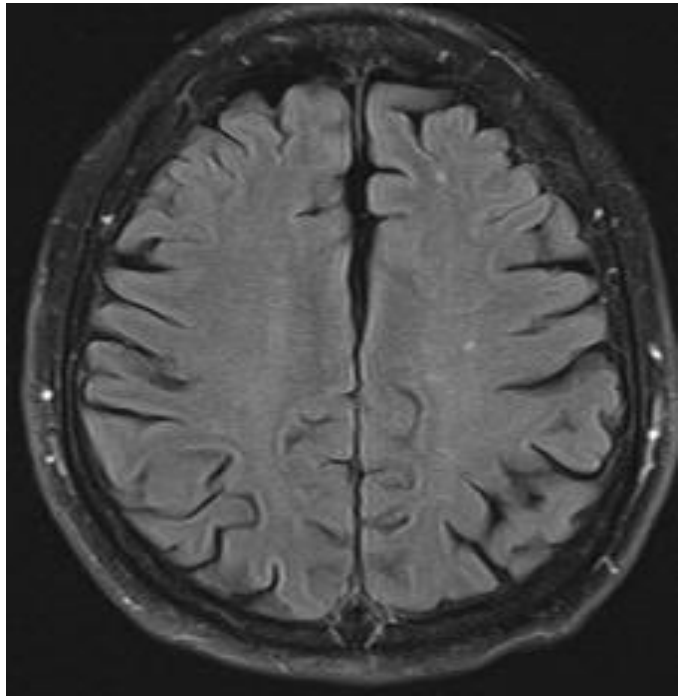
9/11/2020



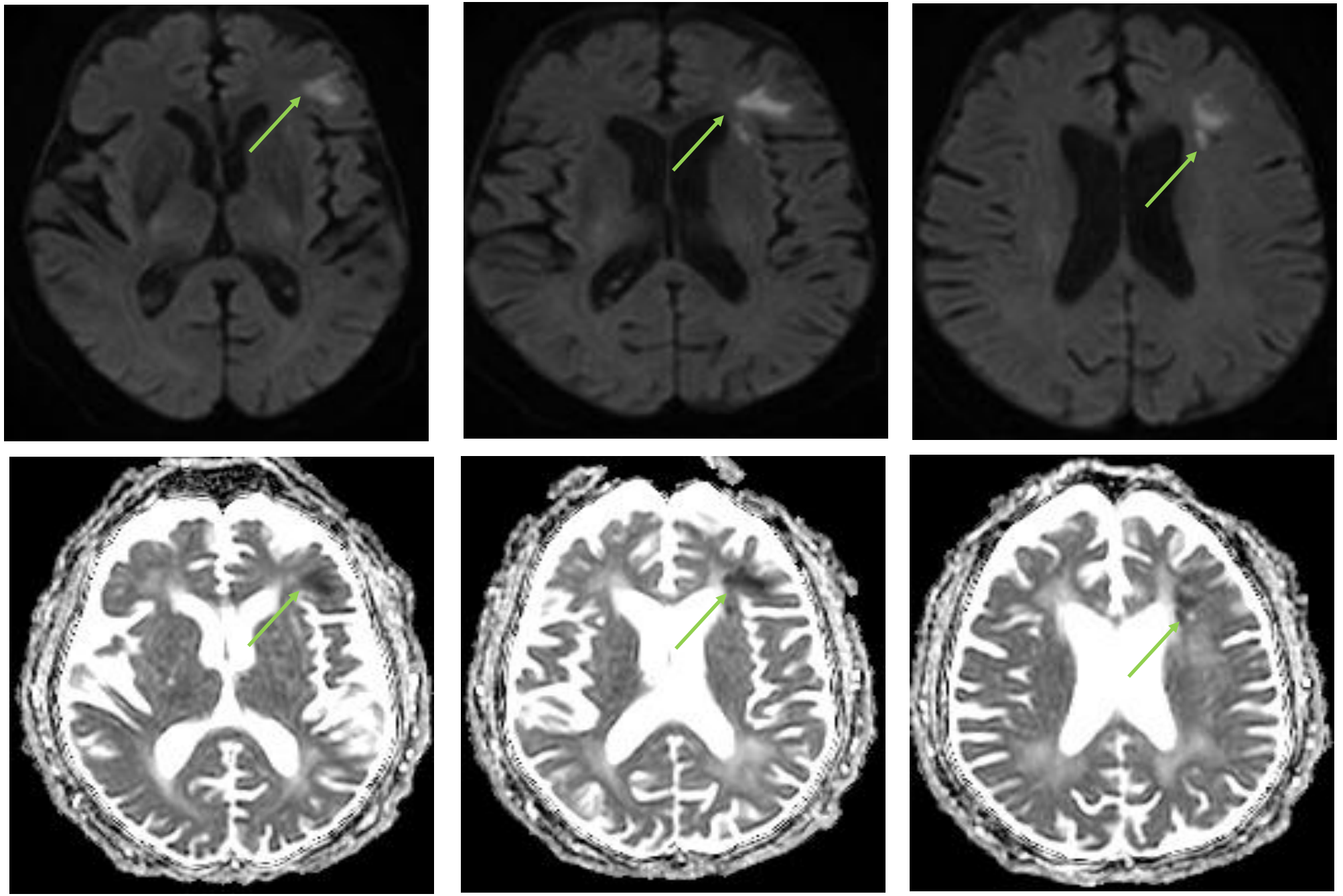


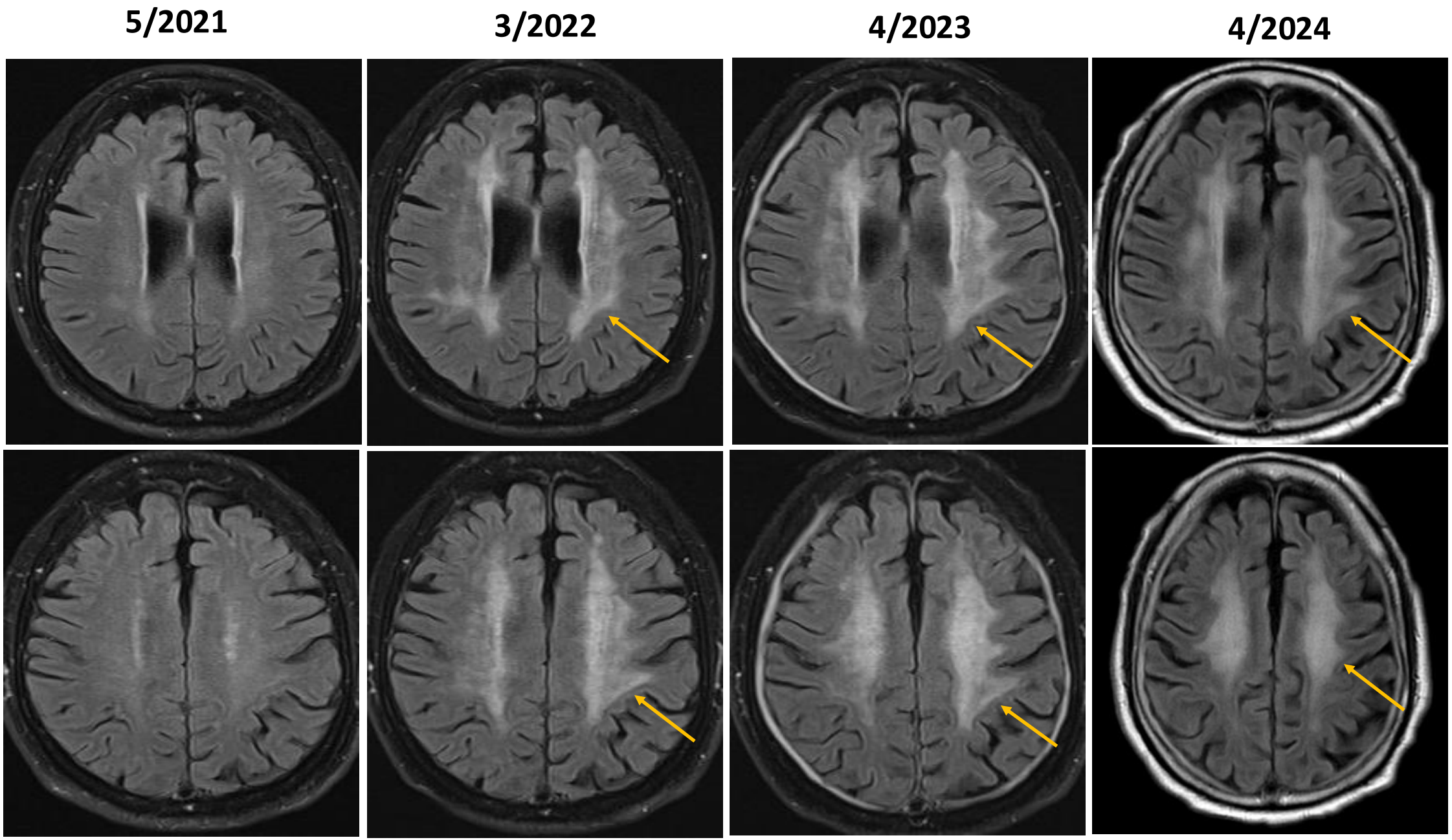
1/5/2021





4/29/2024




5/2021
3/2022
4/2023
4/2024

Inflammatory Profile in CSF

Date: 4/30

❑CSF

- RBC: 1 (≤ 1 /mm^3)
- WBC: 16 (≤ 5 /mm^3)
- Protein: 85 (< 45 mg/dl)
- Albumin: 55.4 (< 27 mg/dl)
- IL-2 Receptor Soluble: 97.2 (< 26.8 pg/ml)
- IL-5: 4.8 (< 2.1 pg/ml)
- IL-6: 698.2 (< 7.5 pg/ml)
- IL-8: 1094.3 (< 283.5 pg/ml)
- IL-10: 19.4 (< 12.7 pg/ml)

❑Serum

- IL-2 Receptor Soluble: 1175.7 (<858.2 pg/ml)
- IL-6: 10.8 (<2 pg/ml)
- IL-10: 14.5 (< 2.8 pg/ml)

Date: 5/3

❑CSF

- RBC: 2
- WBC: 7
- Protein: 61
- Albumin: 37.3
- IL-2 Receptor Soluble: 34.3
- IL-6: 23.2

❑Serum

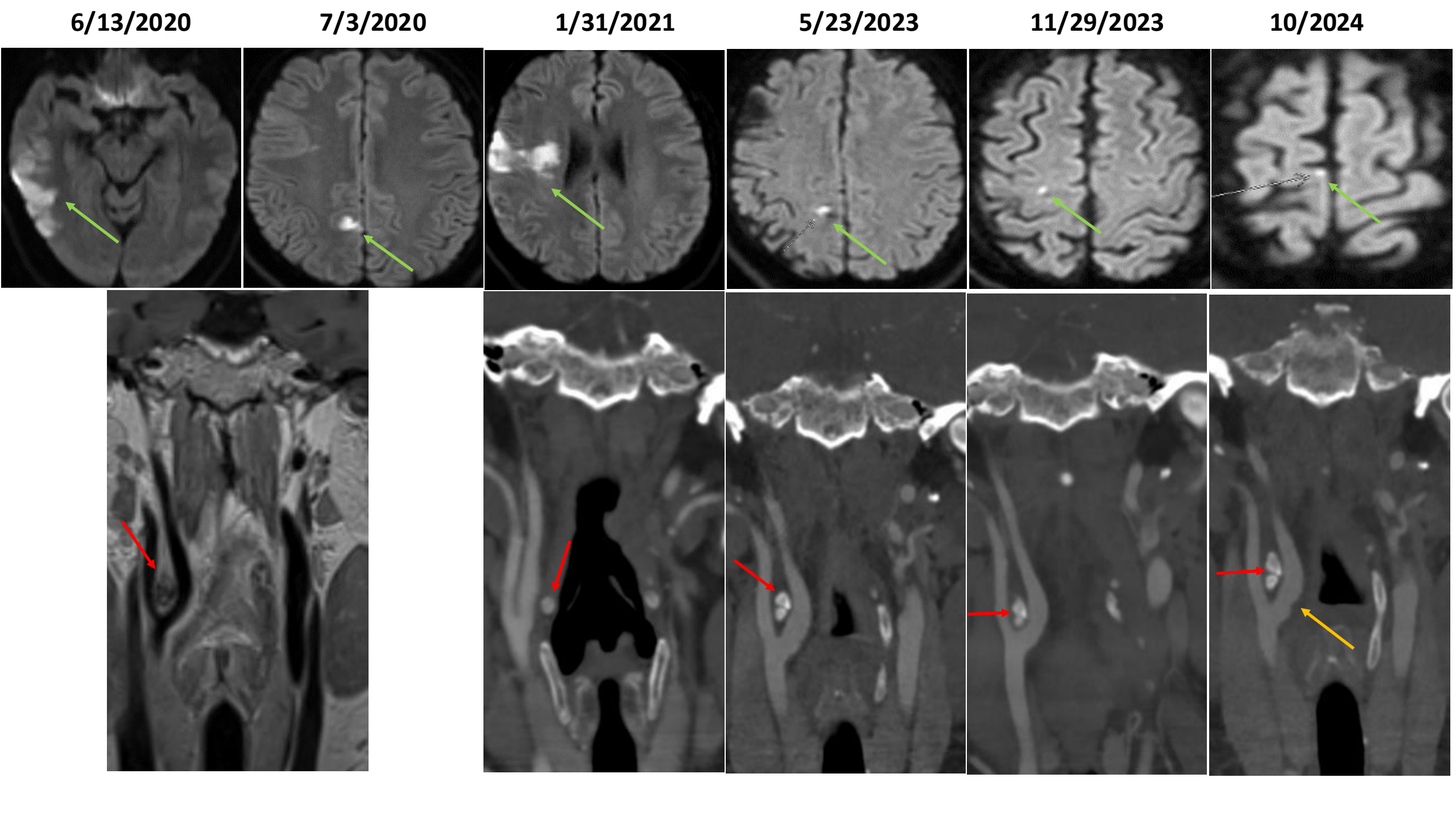
- IL-2 Receptor Soluble: 913.3
- IL-10: 8.4

Acute Late-onset Encephalopathy After Radiotherapy (ALERT) Syndrome

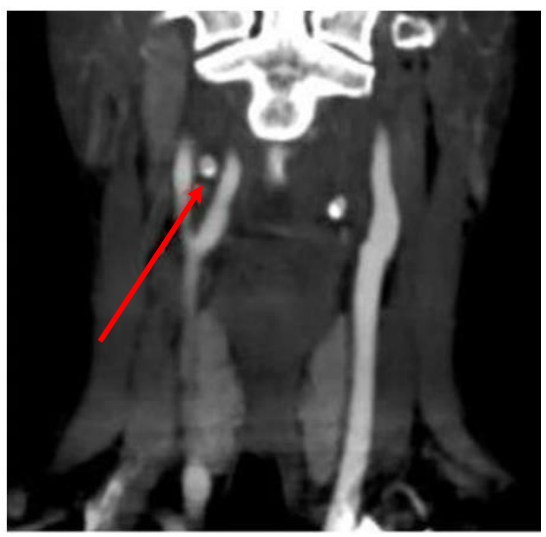
- Rare but significant complication observed in patients who have undergone WBRT
- Could happen years to decades after radiation completion
- MRI: WMH, infarct, edema, enhancement
- Continuous progression of WMH maybe a risk factor
- Acute flare from radiation induced inflammatory microangiopathy
- Cytokine storm
- Respond well to glucocorticoids

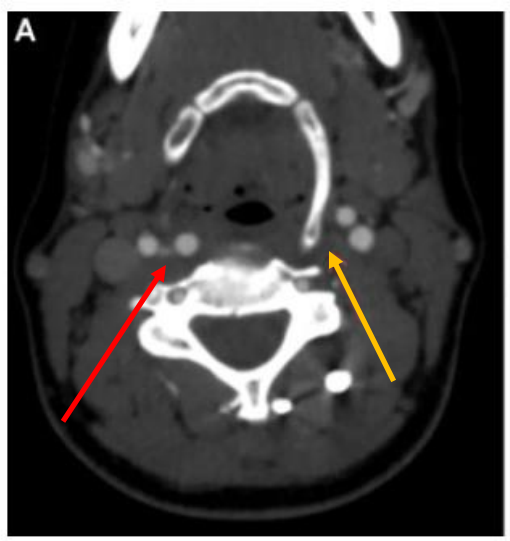
Case 9:

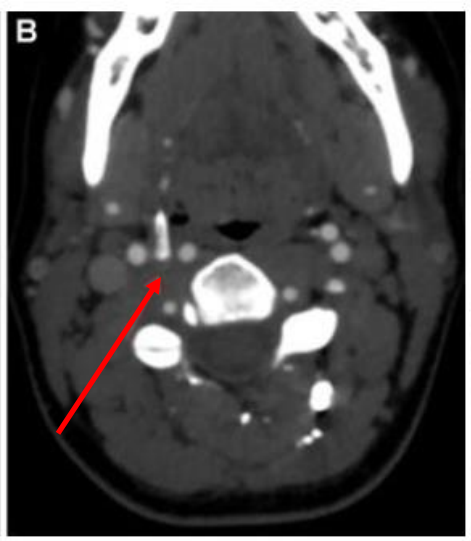
- 41 healthy F without risk factors, working in a car dealership, had 6 ischemic strokes since 2020. All infarcts localized in the R hemisphere.
- Extensive workup
  - PFO: closed
  - Prolonged cardiac monitor: negative for afib
  - Hypercoagulation profile: negative
  - Malignancy scans: negative
  - Catheter angiogram: negative
  - TTE/TEE/Cardiac CT: negative
- Tried different antithrombotics
  - ASA, Plavix, DOAC

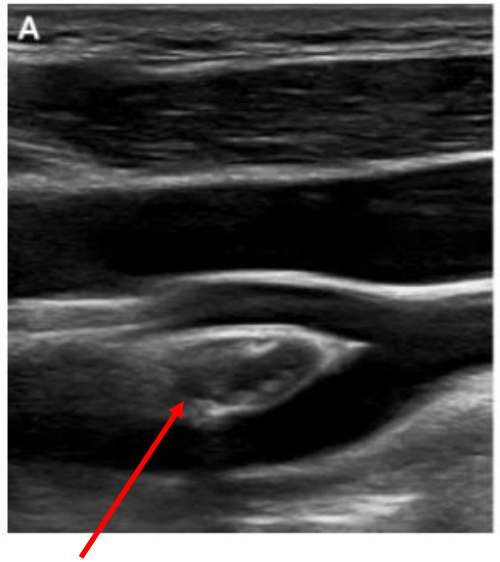

6/13/2020
7/3/2020
1/31/2021
5/23/2023
11/29/2023
10/2024

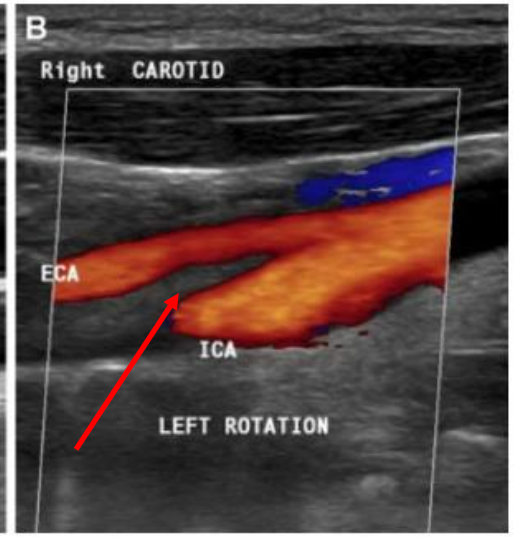
Multiple Strokes Related to Elongation of Hyoid Bone





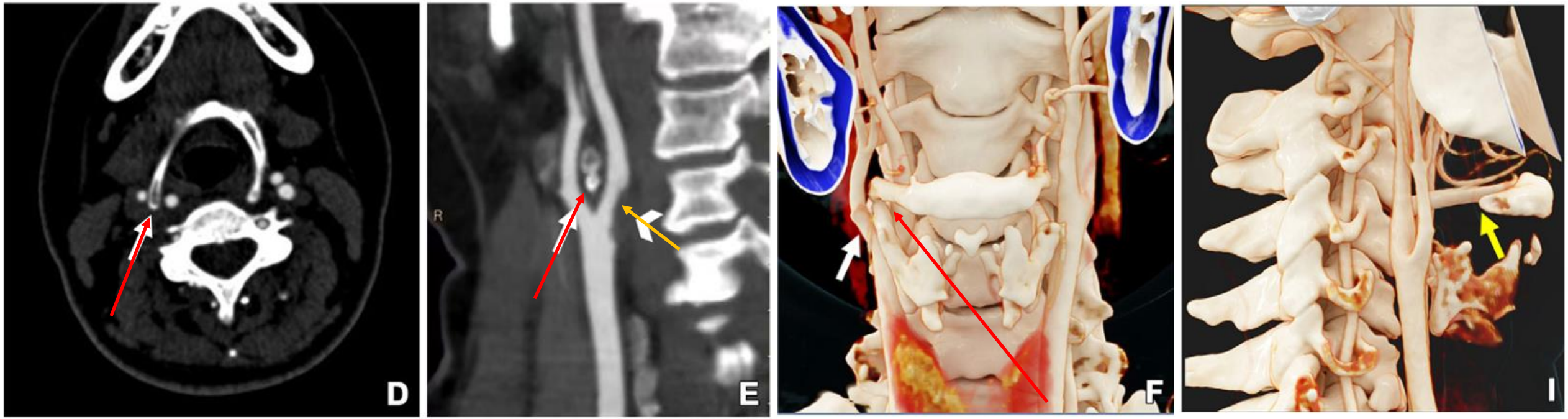






The Neurohospitalist 2018, Vol. 8(1) 35-37

Recurrent Ischemic Strokes Due to Anatomic Variation of the Hyoid Bone and Thyroid Cartilage



Radiology 2024; 313(1):e241186

Bony Stroke

- 6 patients among 4200 patients from 1/2017-3/2022 at one CSC
  - Eagle syndrome
  - Bow Hunter syndrome (N=2)
  - VA affection by a bony spur
  - VA compression by thyroid cartilage (n=2)
- Treatment: interdisciplinary approach
  - Conservative treatment n=1
  - Stenting n=2
  - Occlusion n=2
  - Surgical removal of bone/cartilage n=2
  - Sugiical bypass n=1
- Follow up 12 months wo new stroke
- Recurrent ischemic strokes in one vascular territory despite negative workup and sufficient medical therapy, look for bony stroke

Thank you!

There are many other uncommon strokes

ty.shang@utsouthwestern.edu

Cell: 786-449-4142

UT Southwestern
Medical Center