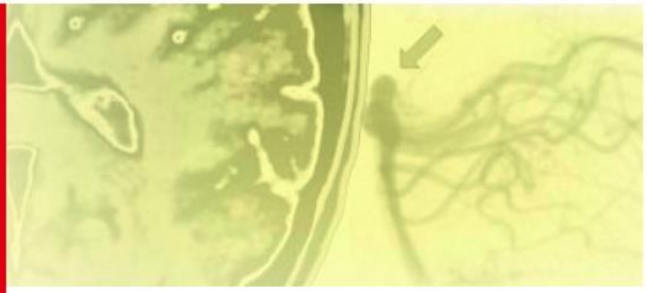
21st Annual Meeting
Swiss Stroke Society SSS
11.01.2018
Lausanne University Hospital

www.neurovasc.ch

Swiss Stroke Trialists' Meeting
12.01.2018
Lausanne University Hospital

Symposium of the Swiss Stroke Nursing Network
12.01.2018
Lausanne University Hospital

NEW!



SHG – SCS – SSS

Schweizerische Hirnschlaggesellschaft – neurovasc.ch
Société Cérébrovasculaire Suisse – neurovasc.ch
Società Cerebrovascolare Svizzera – neurovasc.ch
Swiss Stroke Society – neurovasc.ch

Centre hospitalier Sainte-Anne

Neuro-Sainte-Anne
Pôle Universitaire des Neurosciences - Paris Descartes

UNIVERSITÉ PARIS DESCARTES

Vasculitis and Stroke
Causes and Imaging

Dr G. Boulouis, MD-MSc and colleagues from
Centre Hospitalier Sainte Anne, Paris, France

Disclosures

- None

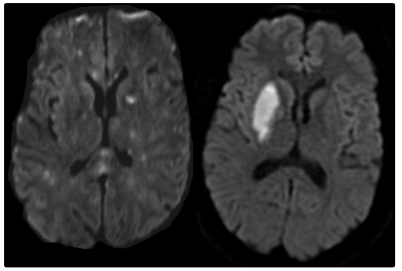
Cerebral Vasculitis

- **Non-atheromatous mural inflammation / necrosis**
  - **Cerebal** Arteries – Arterioles – Capillaries – Veinules – Veins

- Rare but **often severe w/o treatment**
- **Heterogeneous** nosologic corpus of diseases
  - Varied clinical-imaging presentation
  - Varied pathophysiology / pathology
  - Wide range of aetiologies
- **Adult-** and **childhood**

Challenging diagnosis

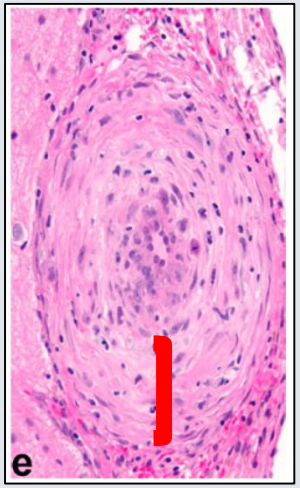
When a stroke...



Could it be a Vasculitis ?

What are the key imaging clues ?

Imaging cerebral vasculitis

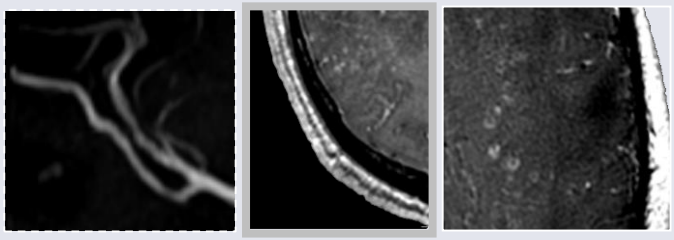


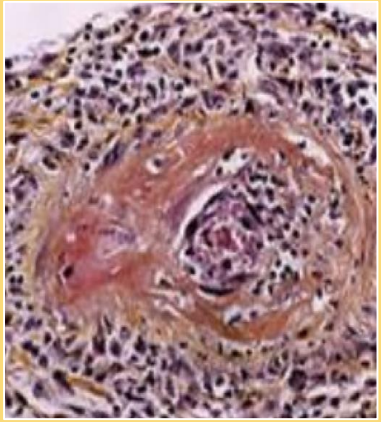
Transmural inflammation

Stenoses / Fusifom dilatations

Parenchymal Gadolinium uptake

Meningeal Gadolinium uptake





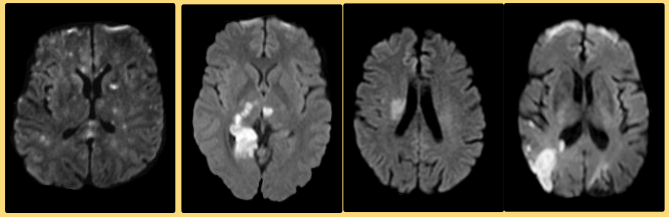
Intraluminal thrombosis

Ischemic Stroke

Distal / Non territorial

Leukoencephalopathy (medium / small vessels)

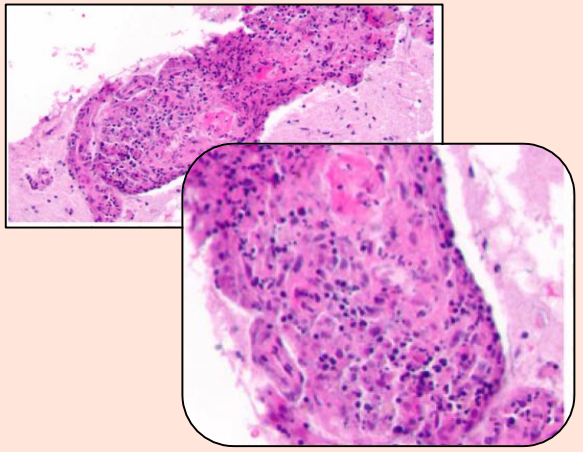
Progressive cerebral atrophy (smaller vessels)

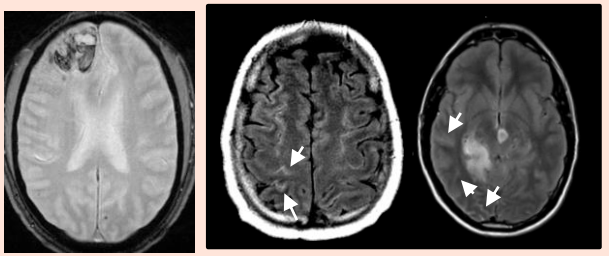


Vessel wall necrosis

Hemorrhages

- Parenchymal
- Subarachnoid

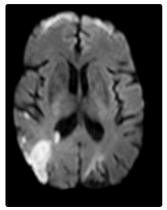




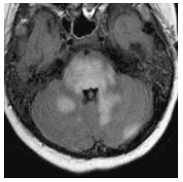
Acta Neuropathol. 2012 Jun;123(6):759-72. doi: 10.1007/s00401-012-0973-9. Epub 2012 Mar 16. Primary central nervous system vasculitis: pathology and mechanisms

Boulouis G, et al. Primary Angiitis of the Central Nervous System: Magnetic Resonance Imaging Spectrum of Parenchymal, Meningeal, and Vascular Lesions at Baseline. Stroke. 2017;48(5):1248–1255.

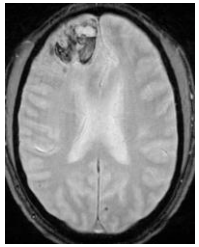
Imaging cerebral vasculitis



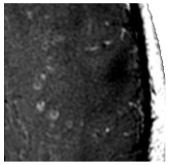
Ischemic Stroke



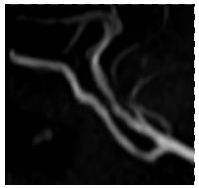
WM FLAIR anomalies



Parenchymal / Meningeal Hemorrhages



Parenchymal / Meningeal Enhancement



Vessels' Stenoses / Irregularities

And…

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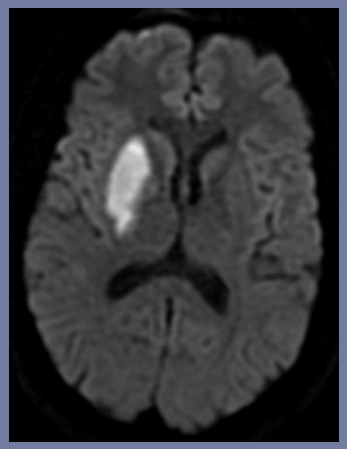
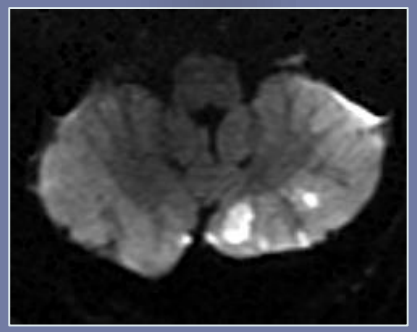
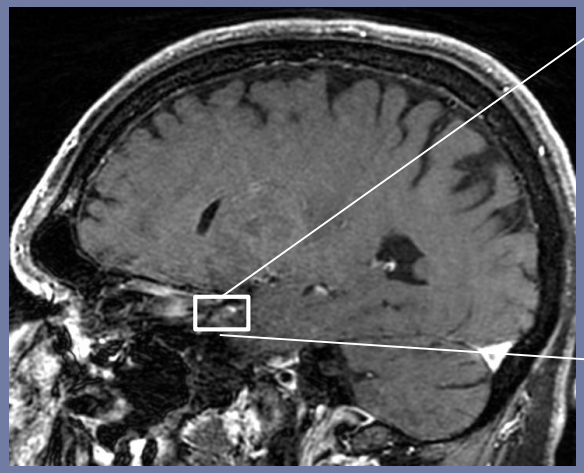
Imaging cerebral vasculitis

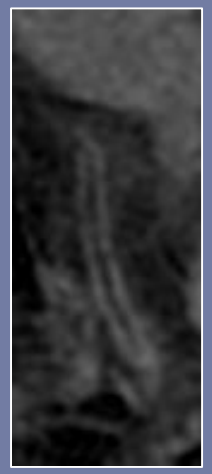
Vessel Wall Inflammation : VW Contrast uptake +++

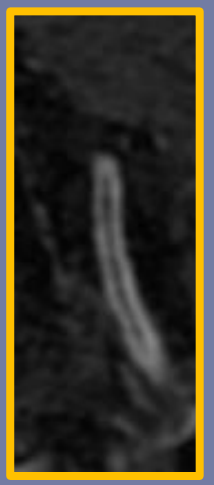






PACNS





Systemic Vasculitis

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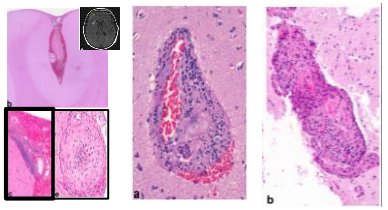
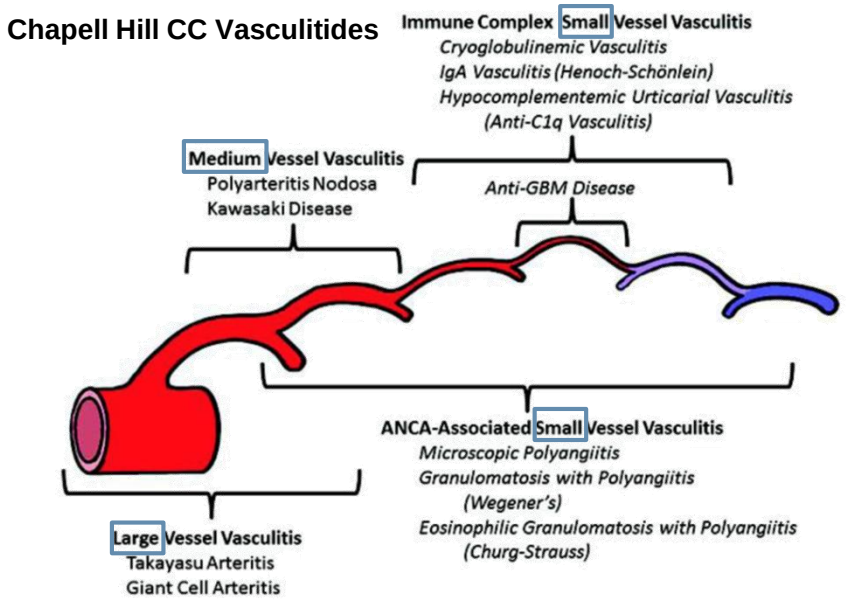
Vasculitis etiologic spectrum

INFECTIOUS VASCULITIDES

Virus, Bacteria, Parasites and Fungi



NON INFECTIOUS VASCULITIDES



Vasculitis associated with <u>systemic disease</u> or <u>probable etiology</u>

Lupus / Rheumatoid / Sarcoid vasculitis
Drug-associated (DA) immune complex / DA
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Variable vessel vasculitis (VVV)

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Vasculitis etiologic spectrum

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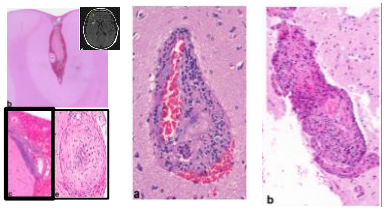
Virus, Bacteria, Parasites and Fungi



Vasculitis etiologic spectrum

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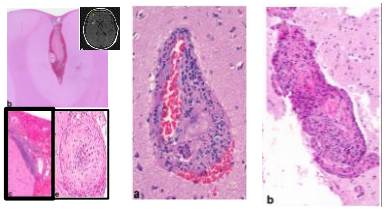


VIRUS:
- **HIV, CMV**
- **VZV, Herpes Simplex**
- **VHC, VHB**

Fungi :
- **Aspergillus, Coccidiode**
- **Histoplasma Capsulatum**
- **Actinomyces**

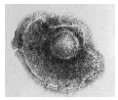
Intracranial Vessels

BACTERIA:
- Mycobaceria: Mycobacterium Tuberculosis
- Haemophilus Influenzae, …
- Spirochetes: Syphilis, Lyme

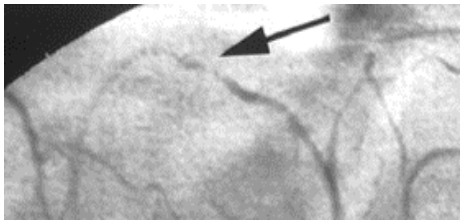
PARASITES
- Malaria
- Toxoplasmosis

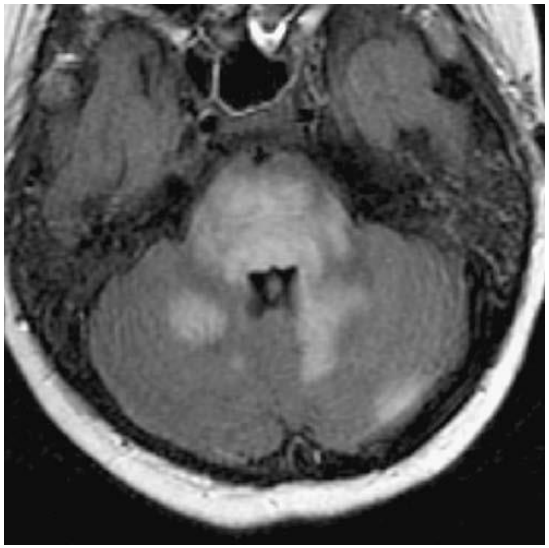
- ***Mutliple potential mechanisms and pitfalls.***
  - *Angio-invasive / Contiguous insult / Immune mediated*
  - ***RCVS under anti-infectious treatment***
  - ***Infectious complications under systemic vasculiitis treatment***

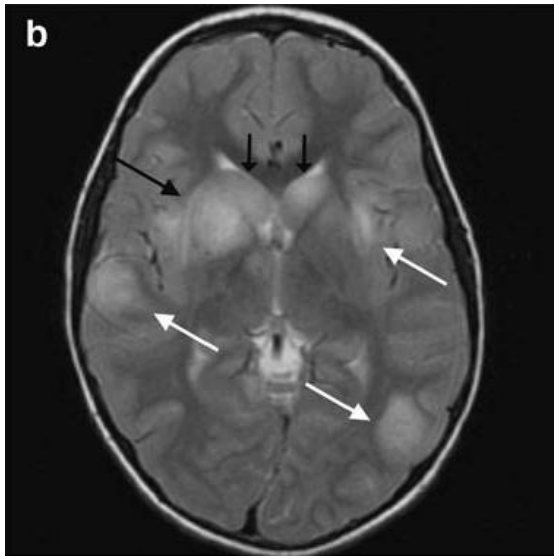
Viruses

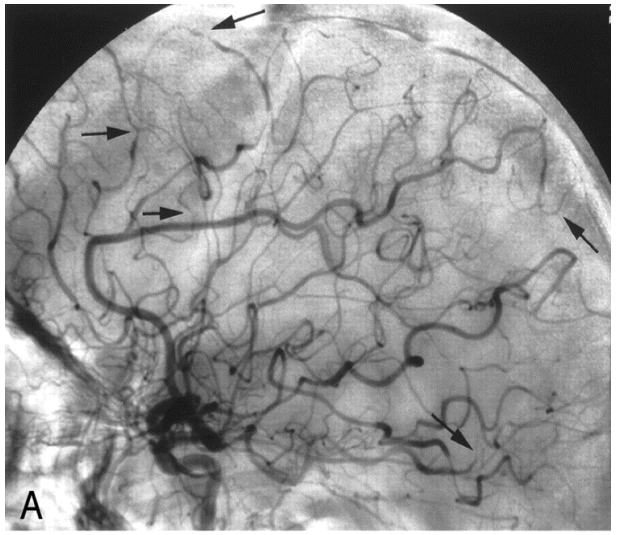
- VZV 
  - **Even if no skin/mucosal symptoms**
  - **Also in immuno-competent individuals**
  - Multifocal Leuko-encephalopathy
    - Smaller to medium vessels, Cerebellar vessels.
  - Ischemia / Hemorrhage – **Necrotizing vasculitis**

Children +++

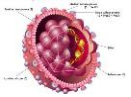


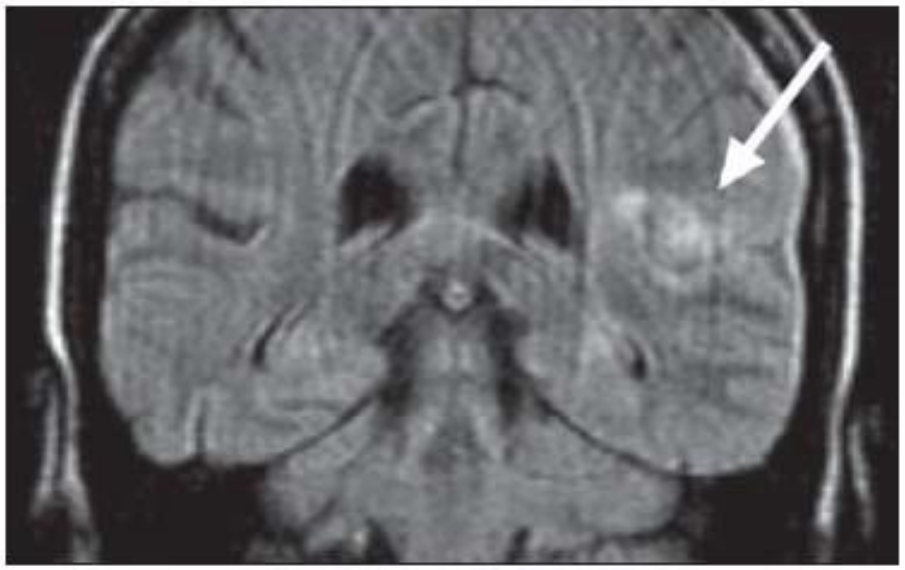


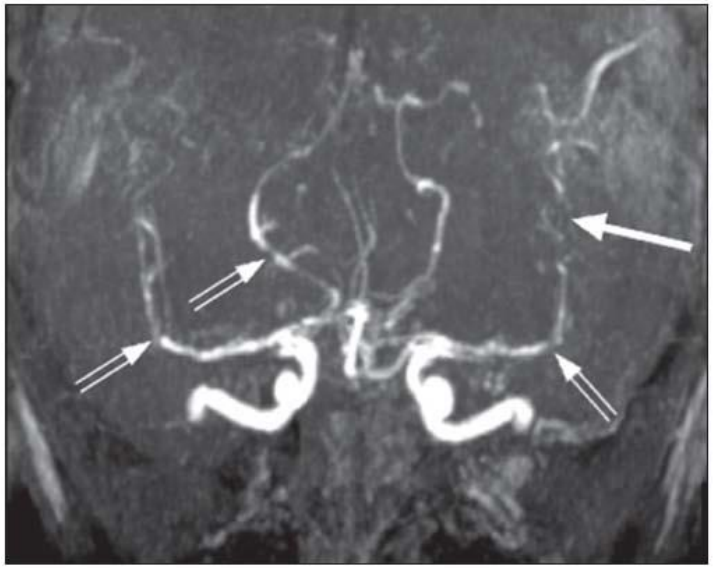




Viruses

- B and C Viral Hepatites 
  - PAN and cryoglobulinemia
- HIV
  - After ruling out opportunistic infections and treatment complications.

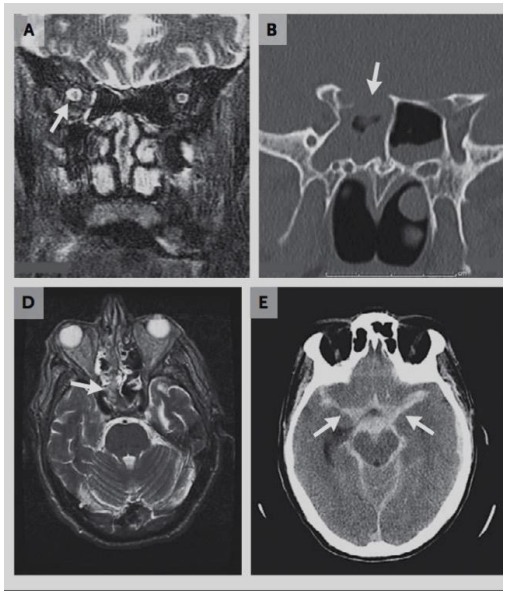




CNS Vasculitis: A Protean Manifestation of HIV/AIDS - Rheumatology Network – 2011
J Neurol Sci. 2014. Central nervous system vasculitis associated with hepatitis C virus infection: a brain MRI-supported diagnosis.

Fungi

- Aspergillosis
  - **Highly Angio-invasive**
    - Parasinusal angiitis ++
    - Embolic angiitis
  - Major Rupture risk : INR needs to be considered



Case 18-2008 — A 68-Year-Old Man with Headache and Visual Changes after Liver Transplantation - NEJM

Id for Candida, Coccidioides* et *Mucorale

Brain Nerve. 2015. [Central nervous system Vasculitis due to infectious diseases].
Neurol India. 2007 . Cerebral Aspergillus arteritis with bland infarcts: a report of two patients with poor outcome.

Infection vasculitis

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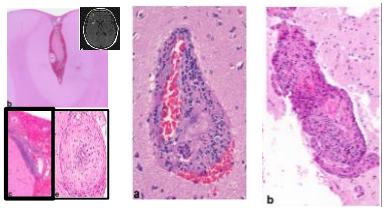

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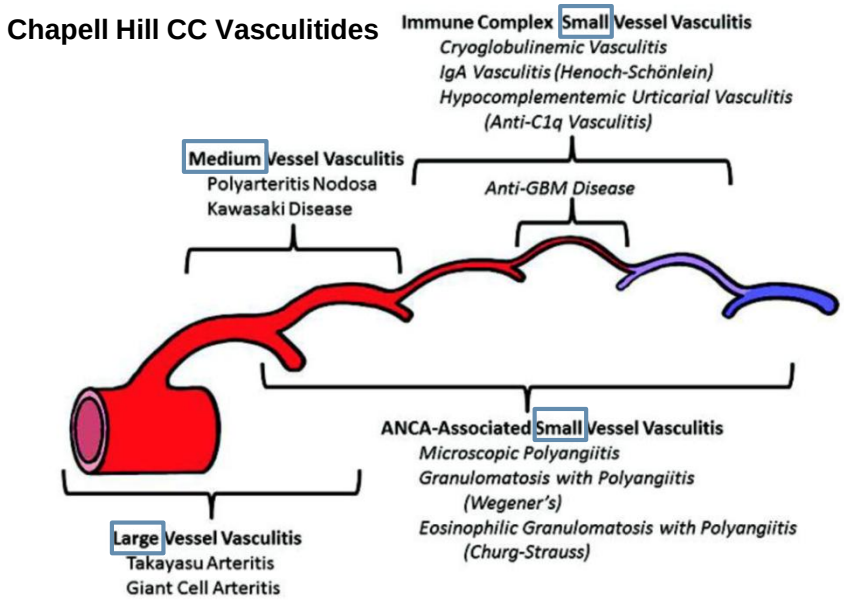

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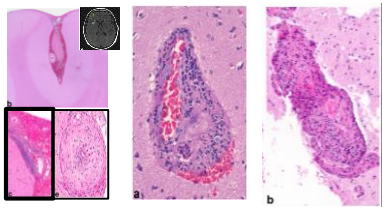

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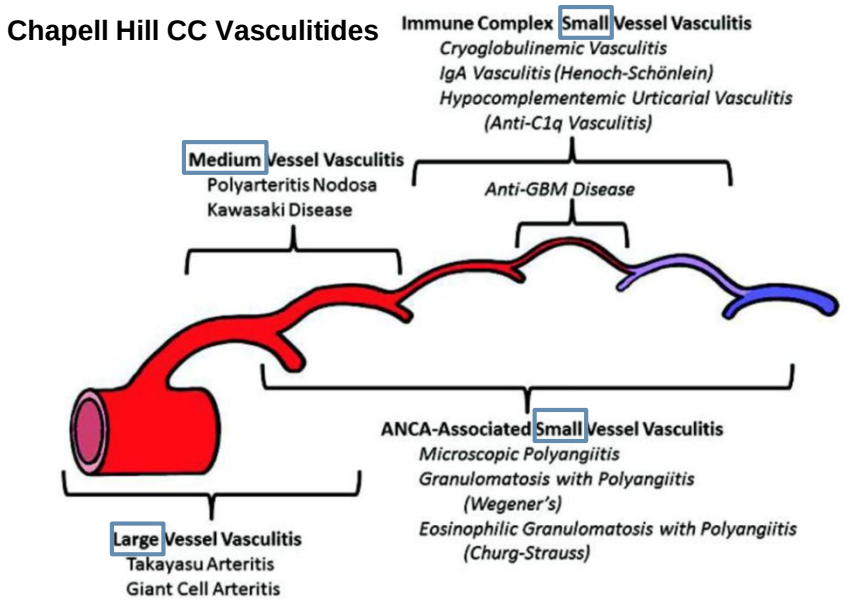

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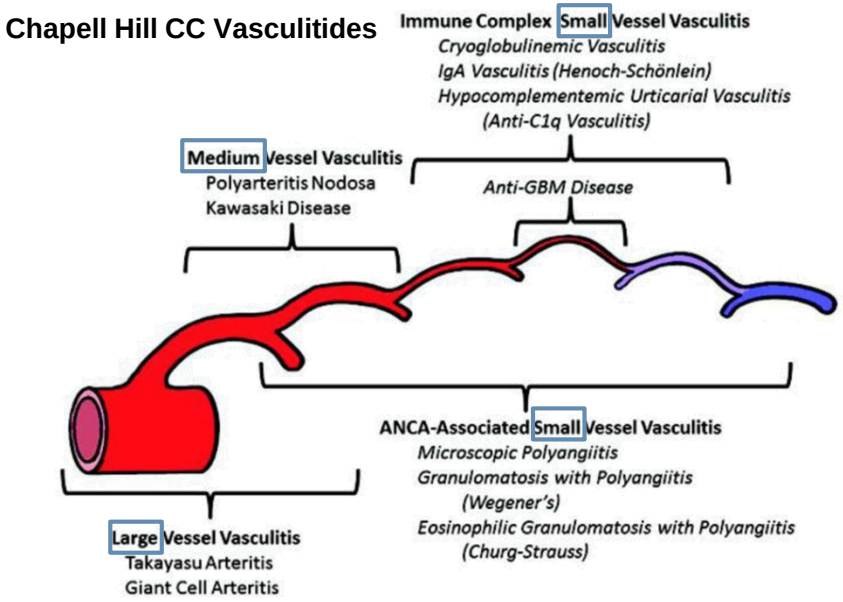
Non-infectious vasculiitis

By vessel size



Nosologic spectum

Vasculitis associated with <u>systemic disease</u> or <u>probable etiology</u>

Temporal GCA. Takayashu.
Drug-associated (DA) immune complex / DA
ANCA-associated / Cancer-associated

And stroke…

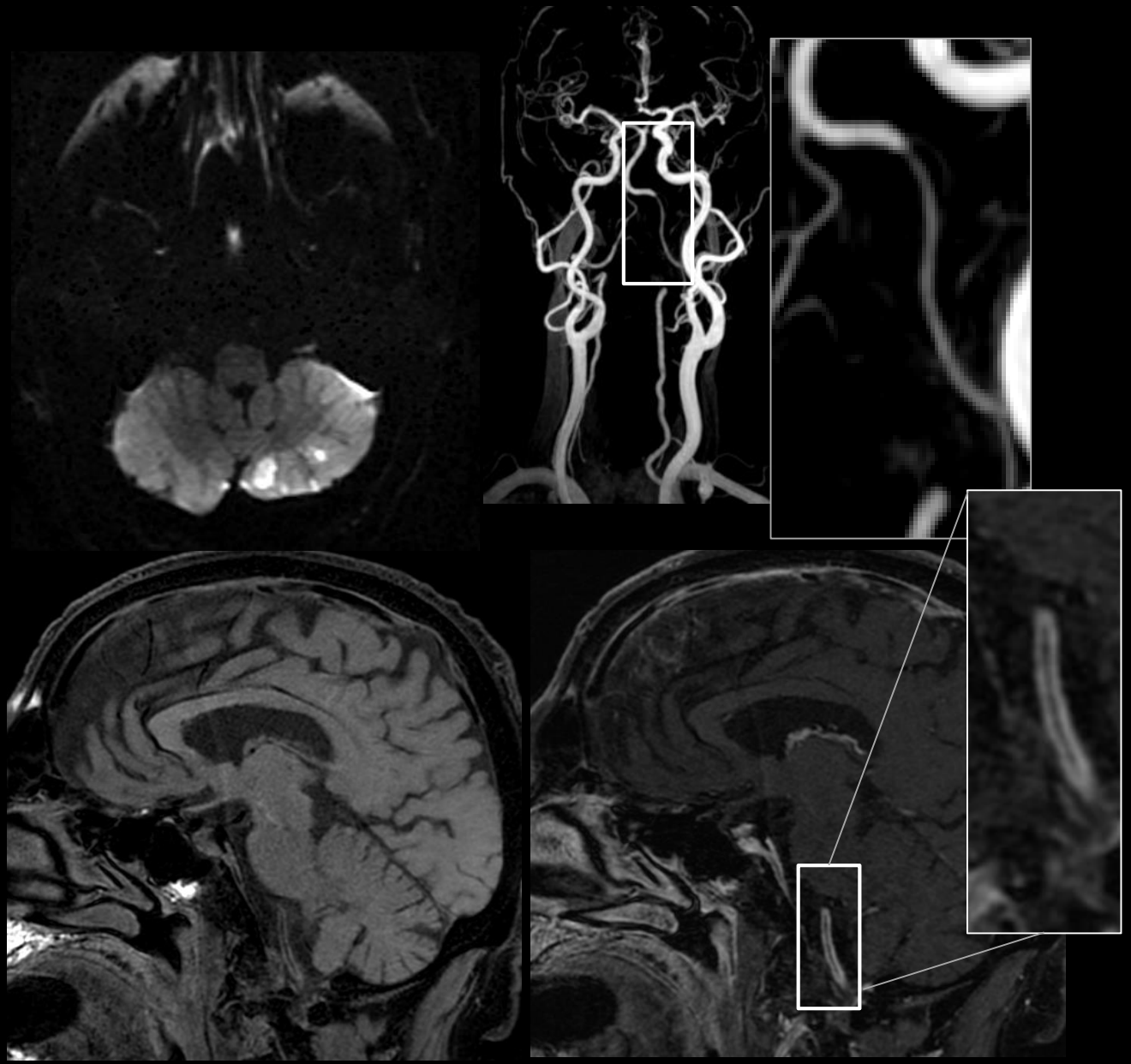
Variable vessel vasculitis (VVV)

Behcet's disease (BD)
Cogan's syndrome (CS)

Single-organ vasculitis (SOV)

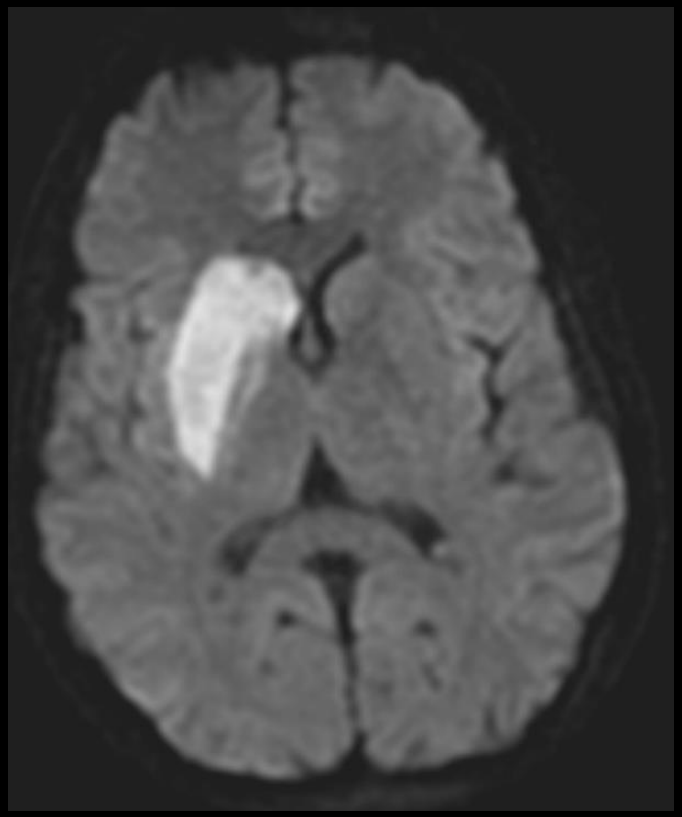
Cutaneous leukocytoclastic angiitis
Cutaneous arteritis
Primary central nervous system vasculitis
Isolated aortitis / Others

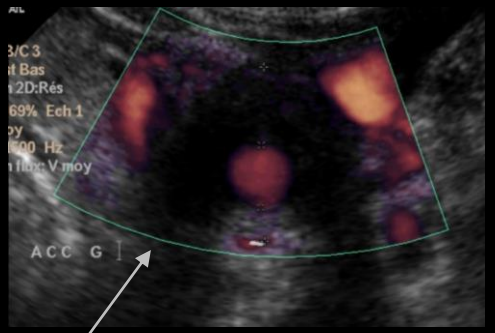
75 yo female.

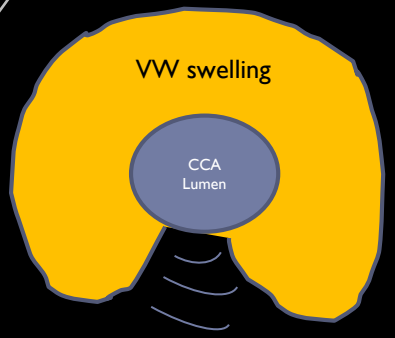


GCA

30 yo female.

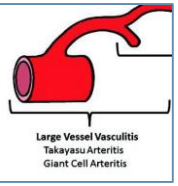






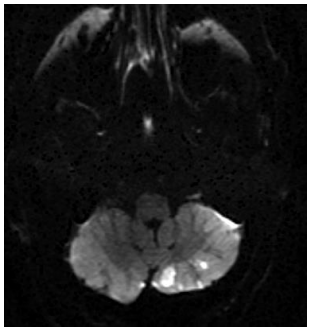
TAK

Primary Systemic Vasculitis and Stroke



Horton

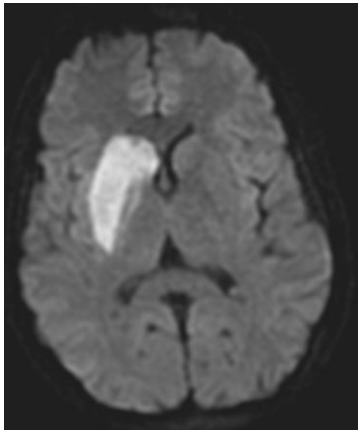
(Temporal) Giant cell arteritis
Headaches +increase in SR, > 50 ans
Blindness
Posterior circulation TIA and I. Stroke

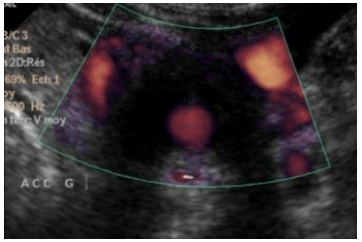


Centre hospitalier Sainte-Anne

Takayashu

Large vessel angeitis
Younger patients. Ischemic Stroke 10-20%





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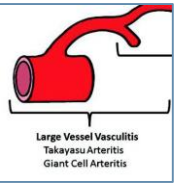
Bley TA, Arthritis & Rheumatism, 2005
Bley TA, AJNR, 2006

Non infectious svasculitis

Vasculitis associated w/ syst. dis



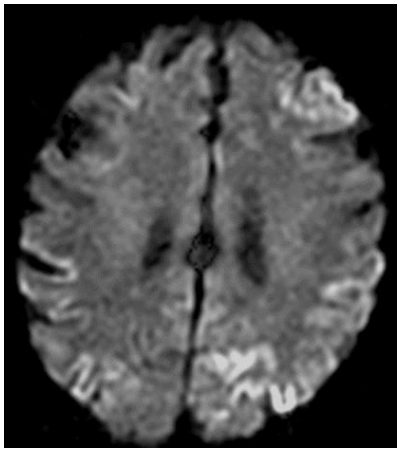
Disseminated Lupus Erythematosus

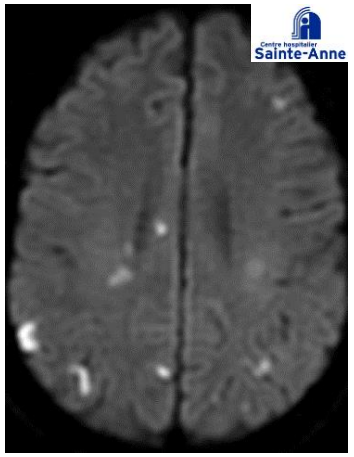
Lupic angiitis / Immunomediated (APLS)

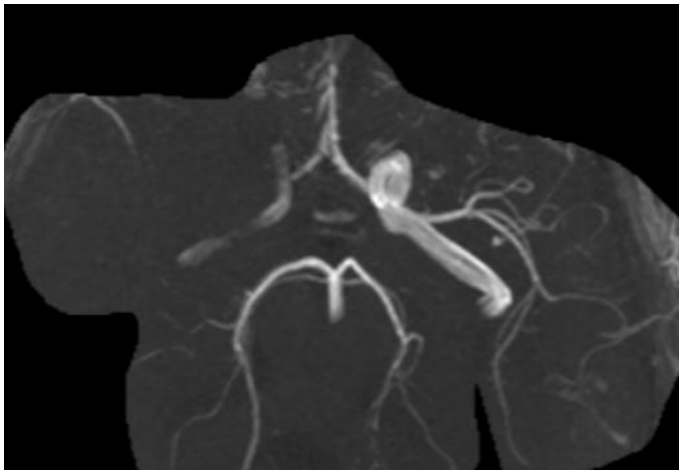
Larger and middle sized vessels
Territorial stroke in the youth

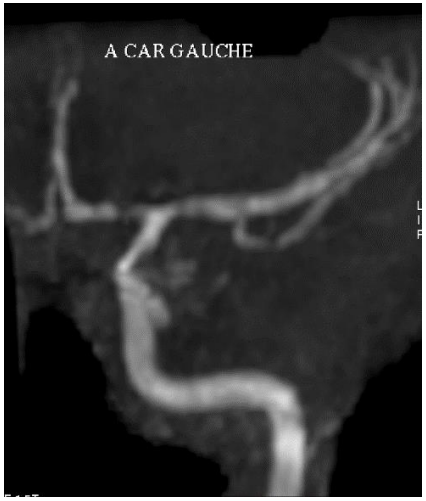
Smaller sized vessels
Lacunes, cortical infarcts

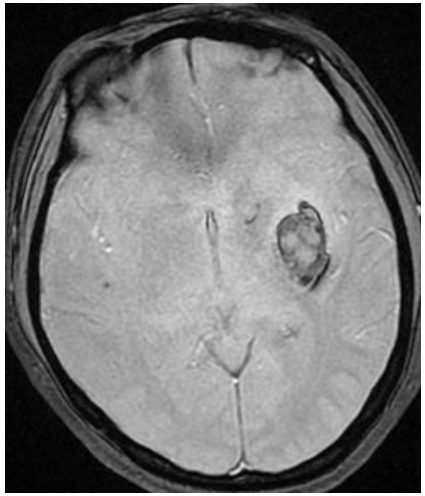
Microvessels
WMH and bleeds











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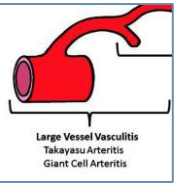
Other causes



- **Cancer associated angiitis**

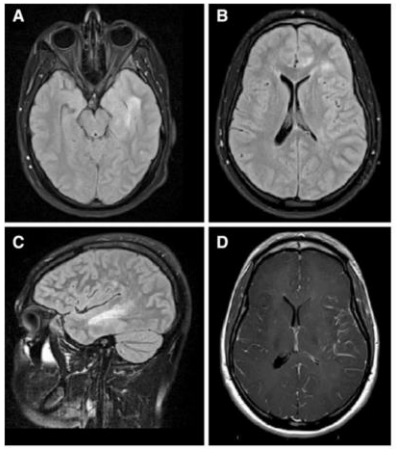
Paraneoplasic
Direct vascular insult or invasion
Lymphoma / Leukemia

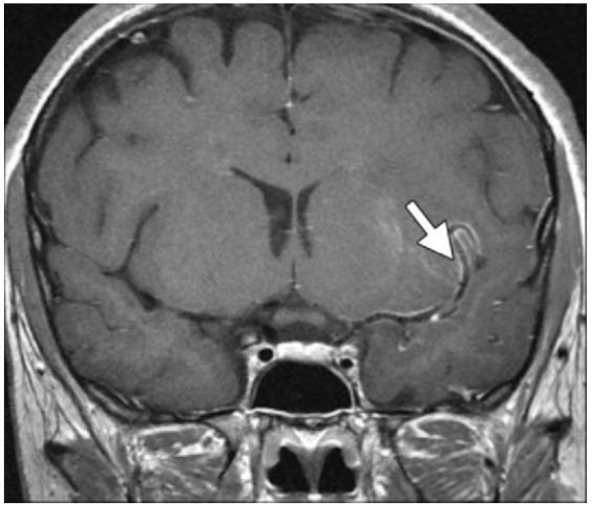
- **Radiation-induced angiitis**

Context
Slow progression

- **Toxic angiitis**

Cocain / Heroin
Chemotherapy
….

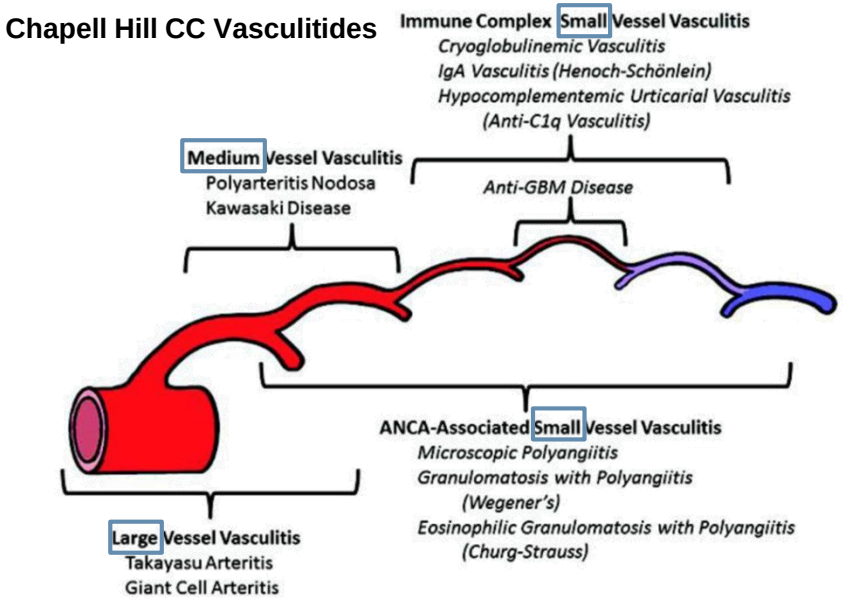




Morotti A. Hodgkin and CNS vasculitis. J Neurol (2013)

Non-infectious vasculiitis and Stroke

By vessel size



Nosologic spectum

Vasculitis associated with <u>systemic disease</u> or <u>probable etiology</u>

Temporal GCA. Takayashu.
Drug-associated (DA) immune complex / DA
ANCA-associated / Cancer-associated

Variable vessel vasculitis (VVV)

Behcet's disease (BD)
Cogan's syndrome (CS)

Single-organ vasculitis (SOV)

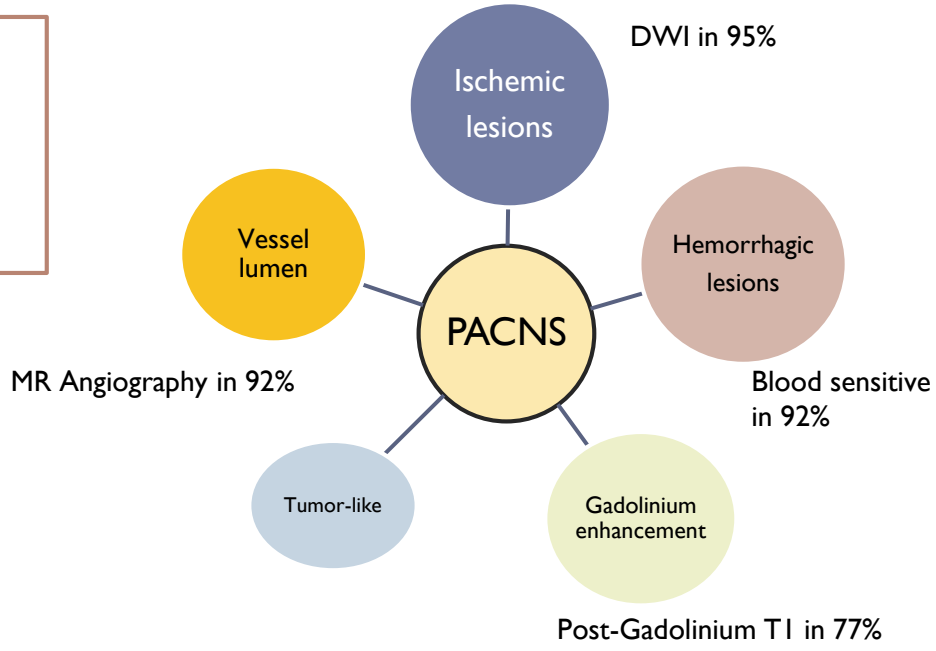
Cutaneous leukocytoclastic angiitis
Cutaneous arteritis
Primary central nervous system vasculitis
Isolated aortitis / Others

Adult Primary Angiitis of CNS (aPACNS)

- Rare – challenging to diagnose / Severe evolution wo ttt
  - Calabrese and Mallek criteria
- COVAC: French Min. of Health supported multicentric cohort
  - Launched in 2010

- Adult patients
- CNS vascular anomalies (biopsy/DSA)
- Differential diagnoses ruled out
- 6+ months of follow-up

Age at diagnosis (years)	45 ±12.9
Male Gender	34 (56.7%)
Clinical Symptoms at presentation	
- Focal Deficit(s)	**50 (83.3%)**
- Headaches	31 (52.7%)
- Cognitive disorder	24 (40%)
- Seizure(s)	23 (38.3%)
- Impaired vigilance	13 (21.7%)
- Psychiatric symptoms	13 (21.7%)

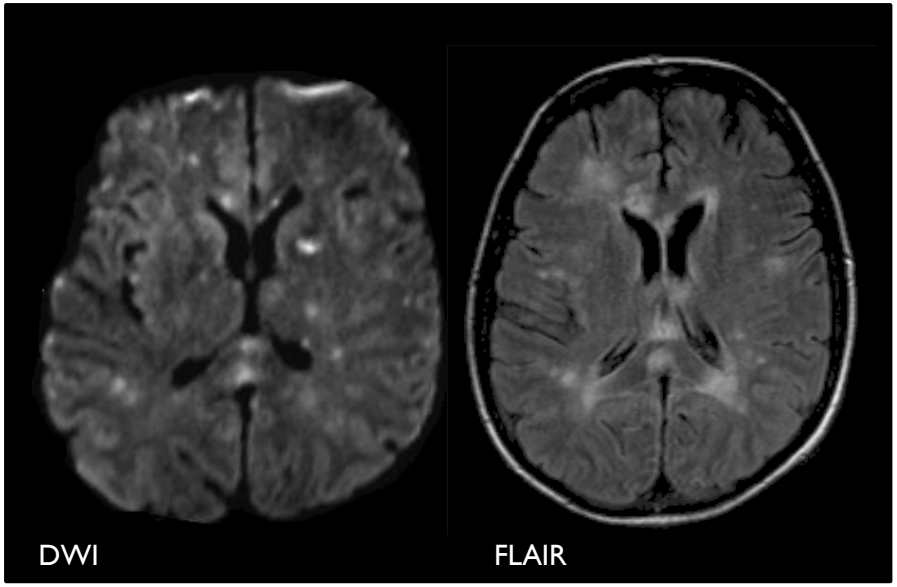


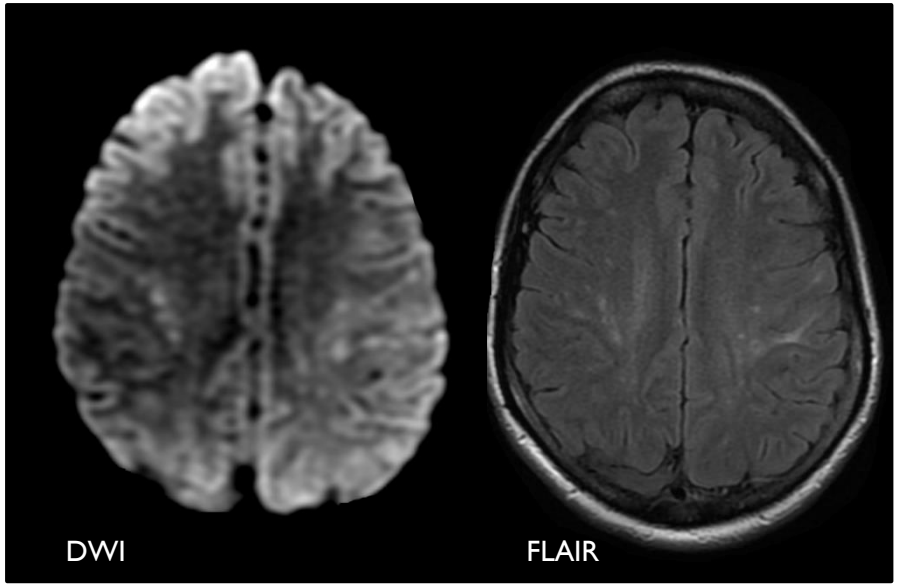
60 patients included

Calabrese LH et al. 1988. Medicine (Baltimore)

aPACNS – Ischemic lesions

- 75% of patients acute ischemic lesions
- Lesions more frequently
  - Multiple / Disseminated (½ of patients)

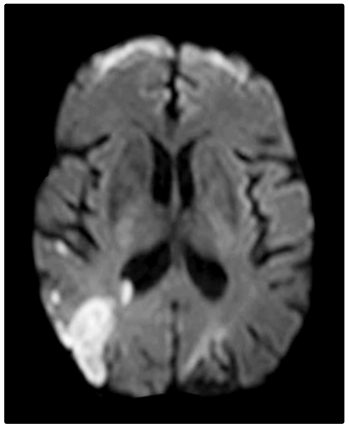


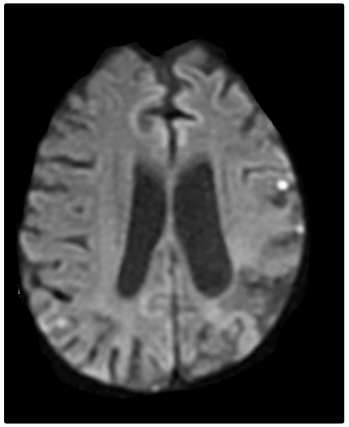


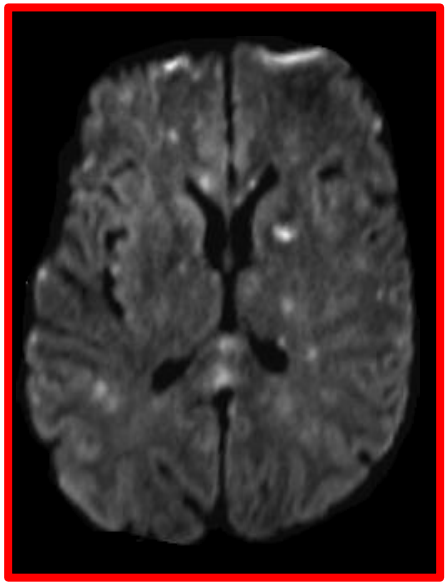
Boulouis G, et al. Primary Angiitis of the Central Nervous System: Magnetic Resonance Imaging Spectrum of Parenchymal, Meningeal, and Vascular Lesions at Baseline. Stroke. 2017;48(5):1248–1255.

aPACNS – Ischemic lesions

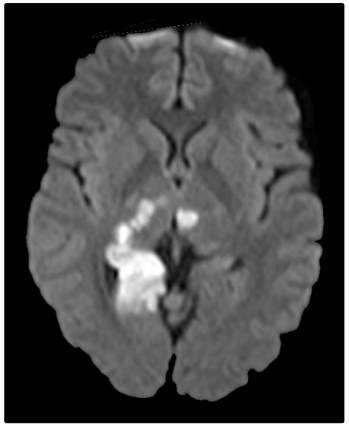
- 75% of patients acute ischemic lesions
- Lesions more frequently
  - Multiple / Disseminated (½ of patients)
  - Supra-tentorial only (70% of patients)
  - Subcortical (72% of patients)
  - Bilateral (54% of patients)



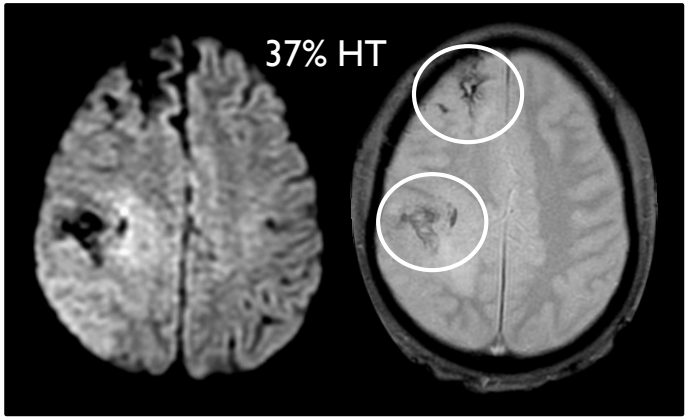




PACNS related infarcts can have ANY aspect



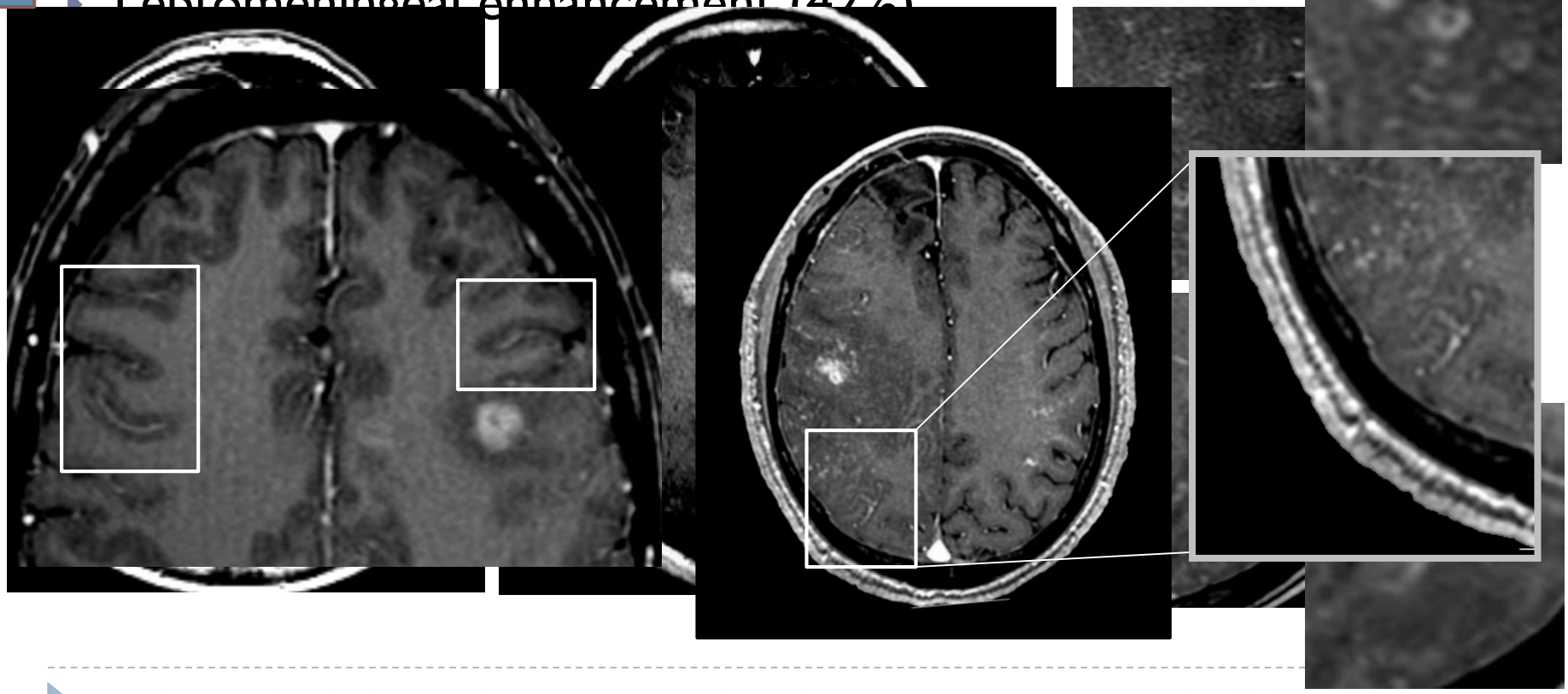
(More ?) important rate of hemorrhagic transformation



Boulouis G, et al. Primary Angiitis of the Central Nervous System: Magnetic Resonance Imaging Spectrum of Parenchymal, Meningeal, and Vascular Lesions at Baseline. Stroke. 2017;48(5):1248–1255.

aPACNS – Gadolinium uptake

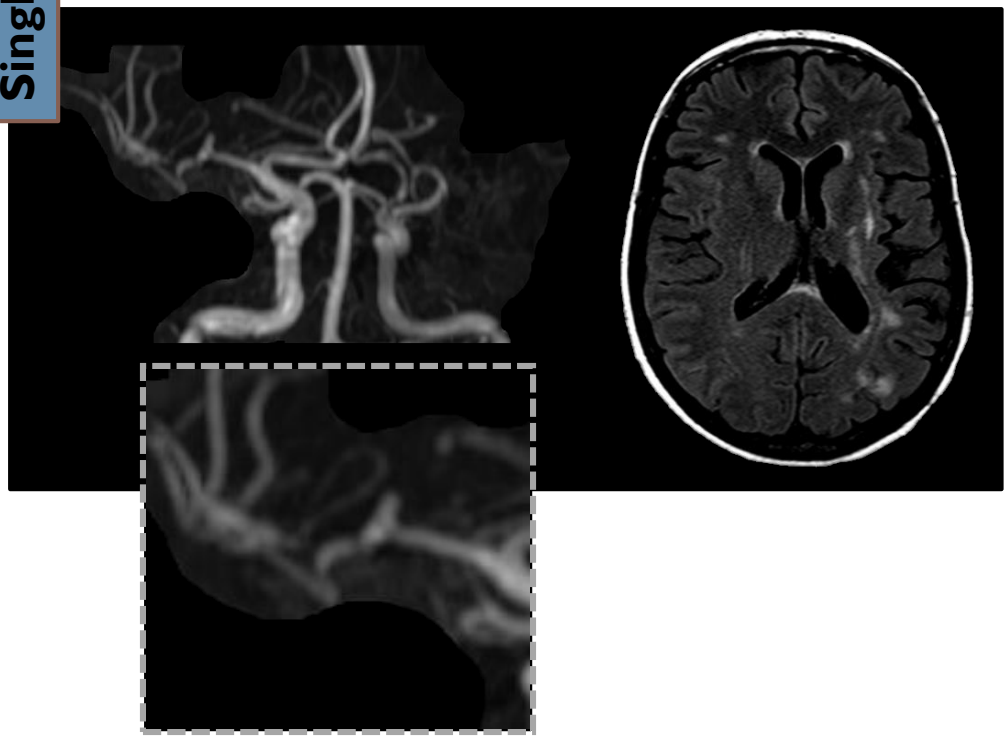
- Parenchymal enhancement (75%)
  - BBB disruption in sub-acute infarcts (60%)
  - Non ischemic enhancement (40%)
- Leptomeningeal enhancement (42%)



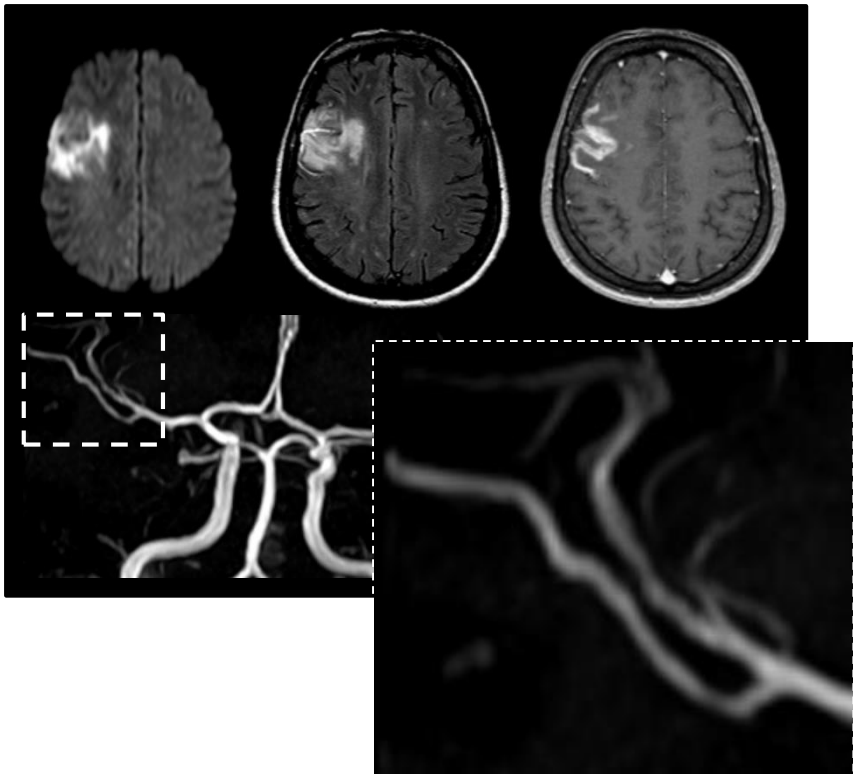
Boulouis G, et al. Primary Angiitis of the Central Nervous System: Magnetic Resonance Imaging Spectrum of Parenchymal, Meningeal, and Vascular Lesions at Baseline. Stroke. 2017;48(5):1248–1255.

Vessel lumen imaging

- 76% of patients with abnormal MR Angiography
  - Proximal = Distal distribution (53% vs 54%)



Proximal: M1/A1/P1 and upstream

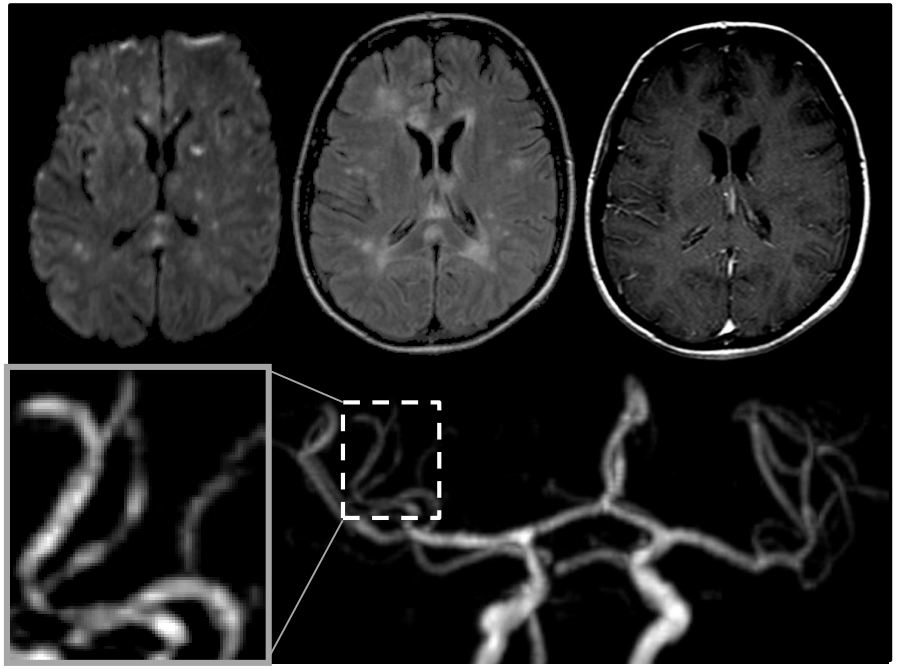


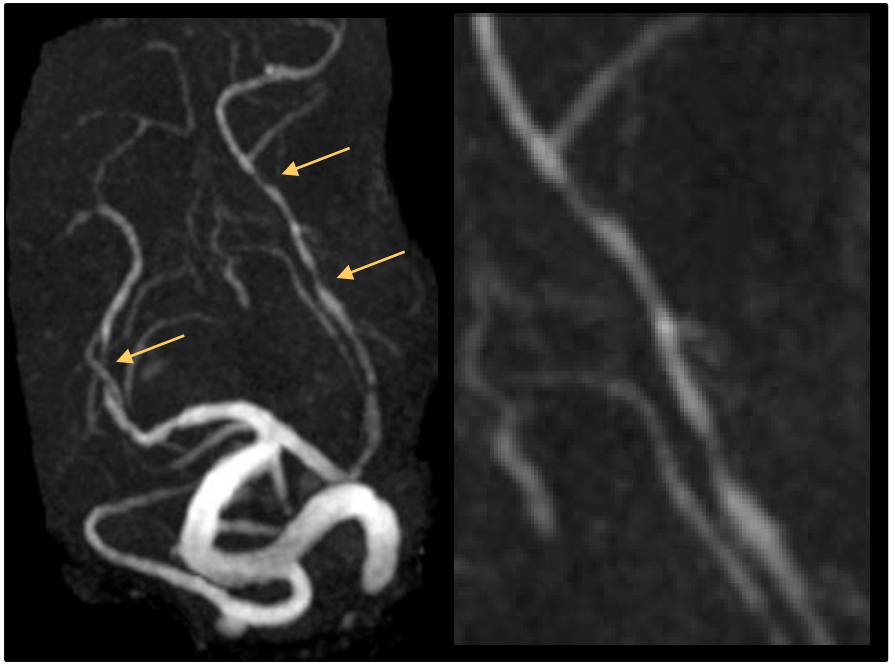
Distal: M2/A2/P2 and downstream

Boulouis G, et al. Primary Angiitis of the Central Nervous System: Magnetic Resonance Imaging Spectrum of Parenchymal, Meningeal, and Vascular Lesions at Baseline. Stroke. 2017;48(5):1248–1255.

Vessel lumen imaging

- 76% of patients with abnormal MR Angiography
  - Proximal = Distal distribution (53% vs 54%)
  - Beading uncommon (20%)
- Very Low DSA yield in patients with normal MRA (Affected vessels <200microns)





PACNS main differential: RCVS

- Favoring RCVS
  - Baseline presentation
    - Thunderclap headache
    - Female sex
    - Absence of motor deficit
    - Absence of brain infarct
    - Subarachnoid bleed
  - Follow-up
    - Recurrent thunderclap headache
    - Early reversibility of vasospasm

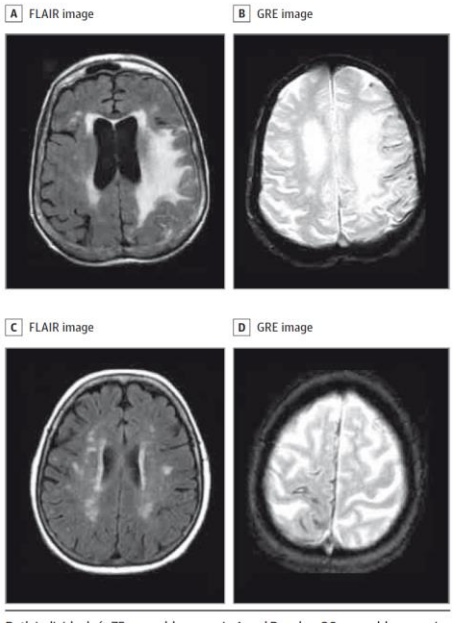
Persisting vascular anomalies after 6 months
Almost certainly **rules out** RCVS

Reversible cerebral vasoconstriction syndromes and primary angiitis of the central nervous system: clinical, imaging, and angiographic comparison. Ann Neurol 2016. Singhal et al.
Primary Angiitis of the Central Nervous System or Reversible Cerebral Vasoconstriction Syndrome : a clinical-radiological differentiation tool. De Boysson. 2018. Submitted.

Single Organ Vasculitis

Single-organ vasculitis (SOV)

- aPACNS
- CAA-Related inflammation
- Amyloid related Imaging Anomalies (ARIA)
  - Amyloid modifying treatment



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

Eitan Auriel, MD, MSc; Andreas Charidimou, MD, PhD; M. Edip Gurol, MD, MSc; Jun Ni, MD; Ellis S. Van Etten, MD; Sergi Martinez-Ramirez, MD; Gregoire Boulouis, MD; Fabrizio Piazza, PhD; Jacopo C. DiFrancesco, MD, PhD; Matthew P. Frosch, MD, PhD; Octávio M. Pontes-Neto, MD, PhD; Ashkan Shoamanesh, MD; Yael Reijmer, PhD; Anastasia Vashkevich, BA; Alison M. Ayres, BA; Kristin M. Schwab, BA; Anand Viswanathan, MD, PhD; Steven M. Greenberg, MD, PhD

Table 1. Criteria for the Diagnosis of CAA-ri

Diagnosis	Criteria
Probable CAA-ri	1. Age ≥40 y 2. Presence of ≥1 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 3. 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 4. Presence of ≥1 of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis[a] 5. Absence of neoplastic, infectious, or other cause
Possible CAA-ri	1. Age ≥40 y 2. Presence of ≥1 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 3. MRI shows WMH lesions that extend to the immediately subcortical white matter 4. Presence of ≥1 of the following corticosubcortical hemorrhagic lesions: cerebral macrobleed, cerebral microbleed, or cortical superficial siderosis[a] 5. Absence of neoplastic, infectious, or other cause

Cerebral vasculitis

- When a (bizarre) stroke … think of it
- Initial Imaging diagnosis: **Primarily MRI based +++**
- Ideal dedicated imaging protocol, using a 3T Magnet
  - High –Res DWI (**Ischemia**)
  - Multi-slab TOF (**Intracranial Vessels**, Foramen magnum to vertex)
  - FLAIR (**White Matter Lesions**, ***acute subarachnoid blood***)
  - 3DT2* (SWAN/SWI/VenoBold, **Blood residues**)
  - V_{essel} W_{all} I_{maging}, Black-blood 3DT1 w/o and w/ gadolinum
- DSA required
  - When non-invasive work-up negative, if high suspicion
    - But yield is low
  - To map lesions severity

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11.01.2018
Lausanne University Hospital

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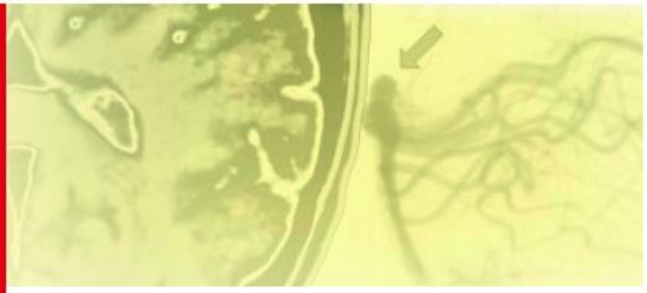
12.01.2018
Lausanne University Hospital

Symposium of the Swiss Stroke Nursing Network
12.01.2018
Lausanne University Hospital

NEW!



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Vasculitis and Stroke
Causes and Imaging

Dr G. Boulouis, MD-MSc
Centre Hospitalier Sainte Anne, Paris, France

THANK you FOR YOUR ATTENTION