Joint Annual Meeting SNG|SSN
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Rare Causes of Stroke

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Unité
Cérébrovasculaire

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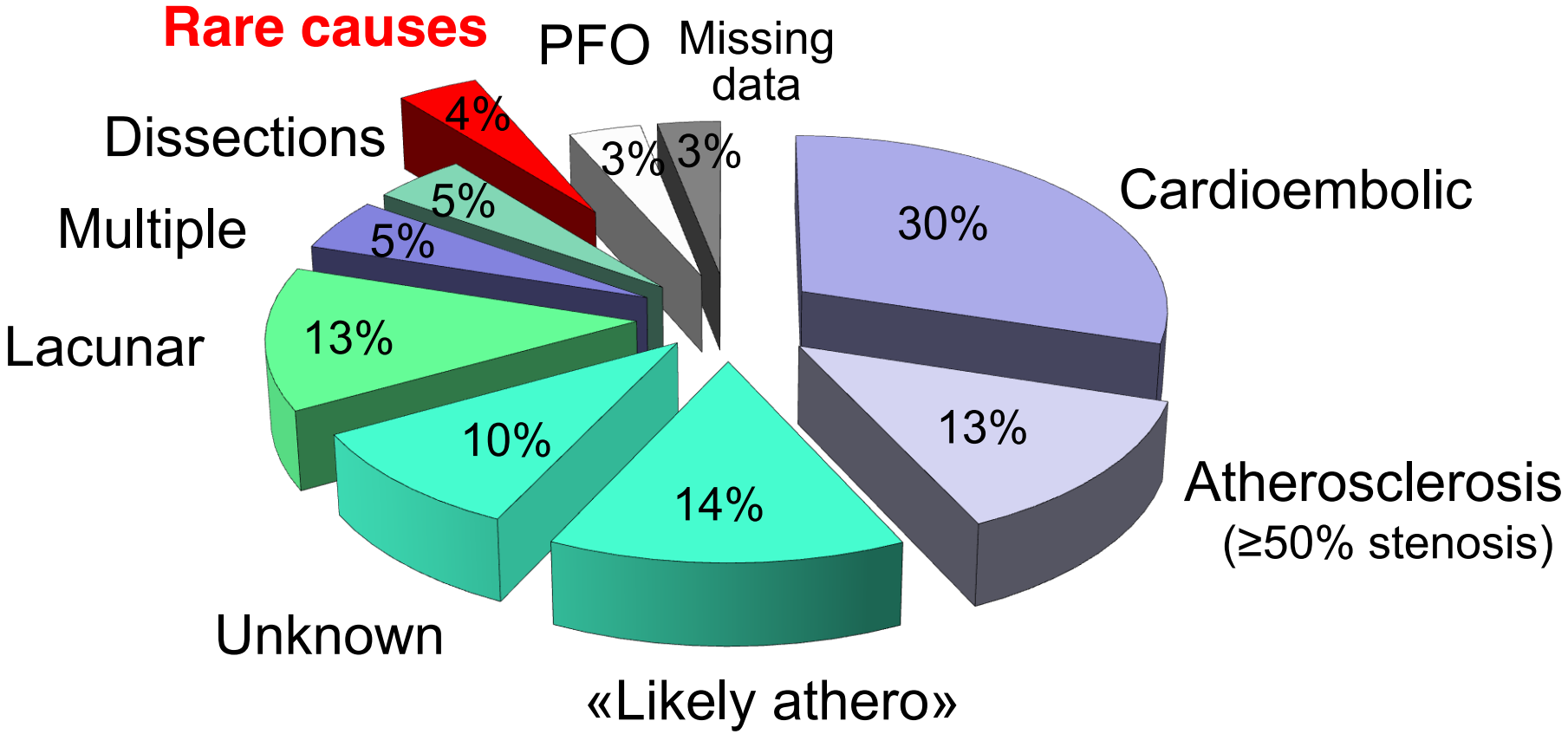
How rare are « rare » ischemic strokes ?

N=2612 consecutive acute strokes 2003-2011



Modified TOAST classification, standardized workup

Source: ASTRA Michel & Eskandari, unpublished

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Rare stroke syndromes

Overview

1. Vasculitis
2. Hypercoagulability and oncologic
3. Drug related stroke
4. Migraine, vasospasms, pregancy
5. Rare cardiac causes
6. Genetic diseases
7. Other non-inflammatory vasculopathies
8. Unusual causes of ICH

Primary systemic vasculitides

- Giant cell
  - Temporal arteritis
  - Takayasu's arteritis
- Necrotizing
  - Polyarteritis nodosa
  - Churg-Strauss syndrome
- Granulomatous
  - Wegener's granulomatosis
  - Lymphomatoid granulomatosis
- With prominent eye involvement
  - Susac's syndrome
  - Cogan's syndrome (also necrotizing)
  - Vogt-Koyanagi-Harada syndrome (VKH)
  - Eales' retinopathy
  - Acute posterior multifocal placoid pigment epitheliopathy

Quiz : 76 y.o. man

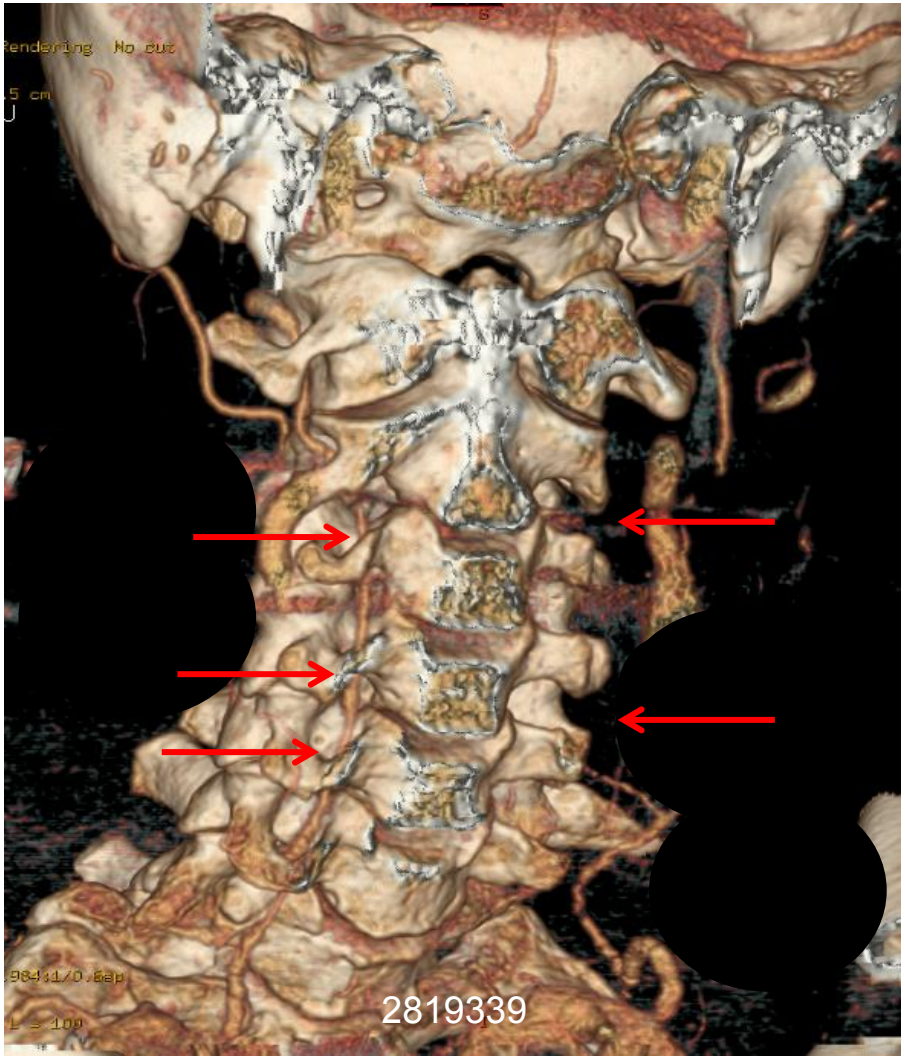
- Doesn't see the doctor
- Now : acute pure left hemiparesis
- NIHSS fluctuating between 8 and 1
- CT/CT-perfusion : normal
- Diagnosis: lacunar warning syndrome

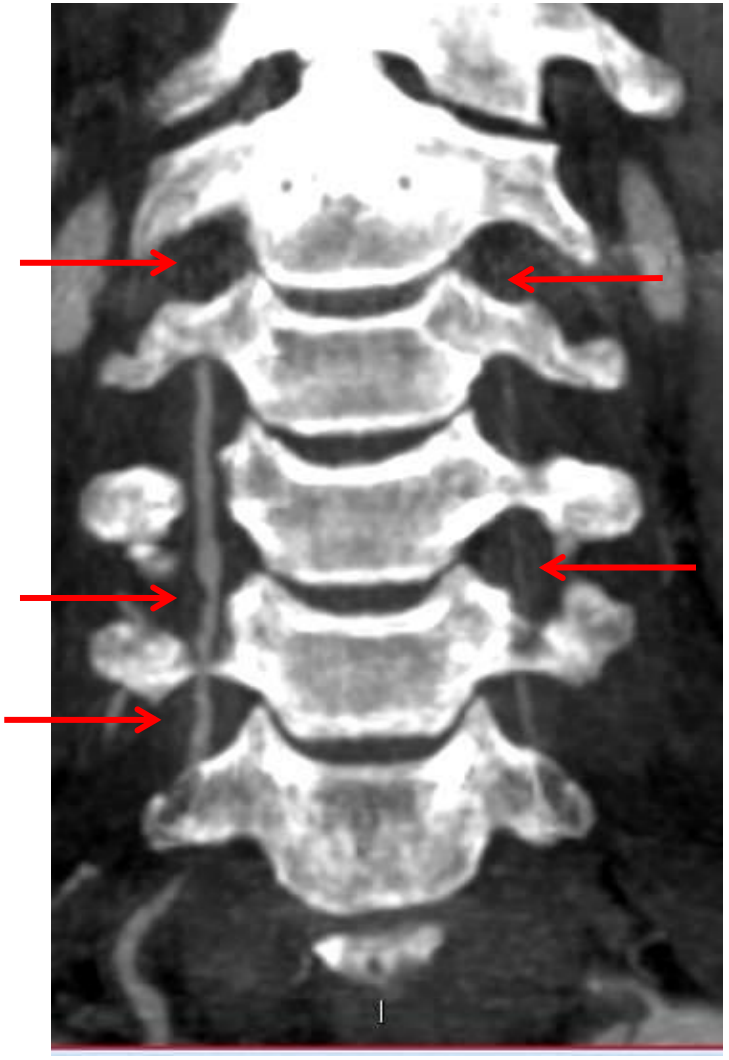
  → Hyperacute CT: normal

  → IV thrombolysis at 2h25min.
- Acute CT-angiography :

76 yo man, lacunar warning syndrome

Pre-thrombolysis CTA

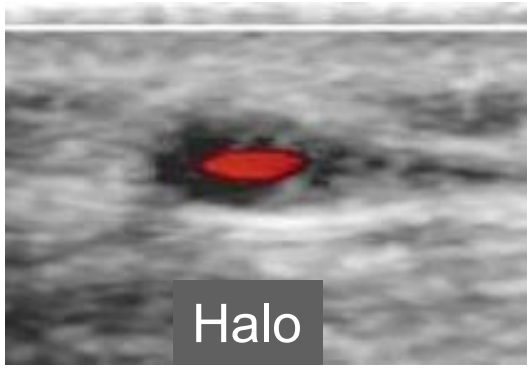


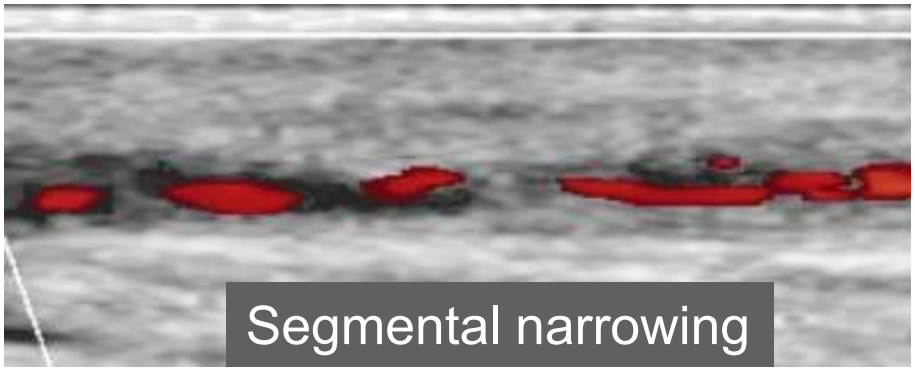


Segmental narrowing both vertebrals

CTA: A. Fumeaux

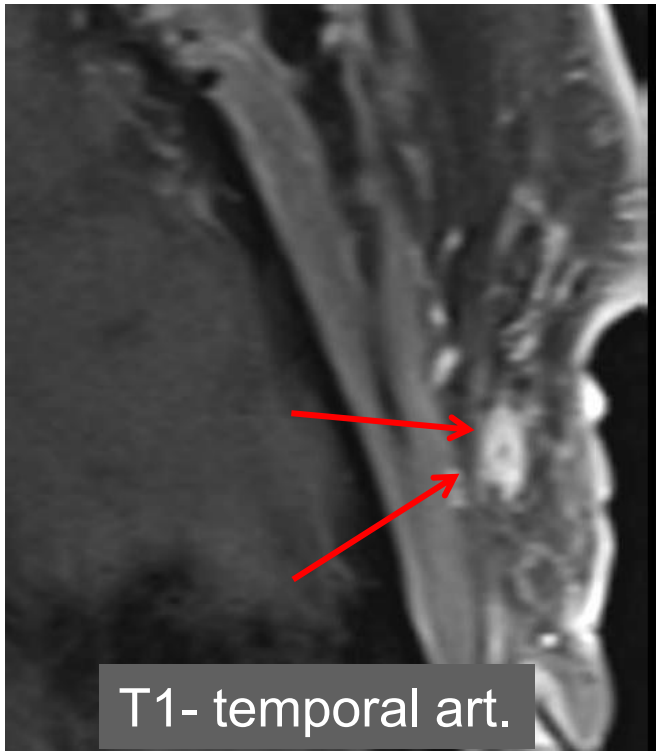
Duplex and temporal arteritis : arterial wall thickening

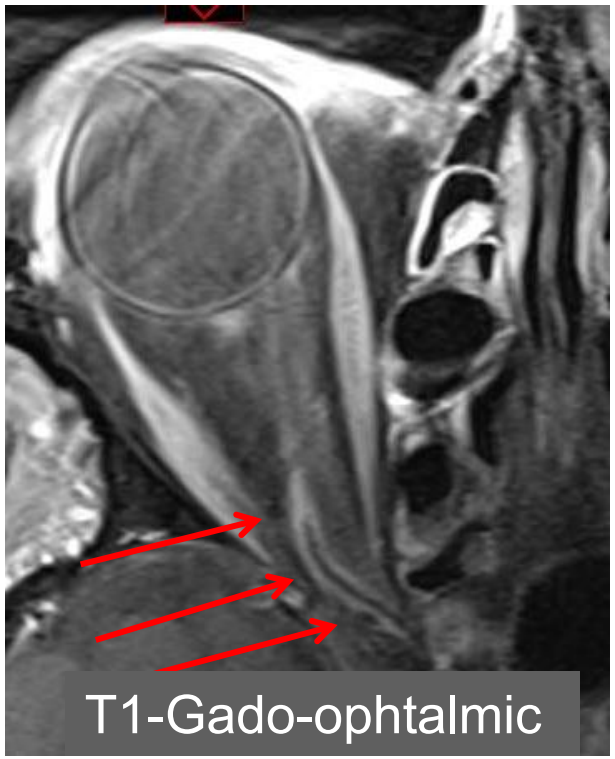




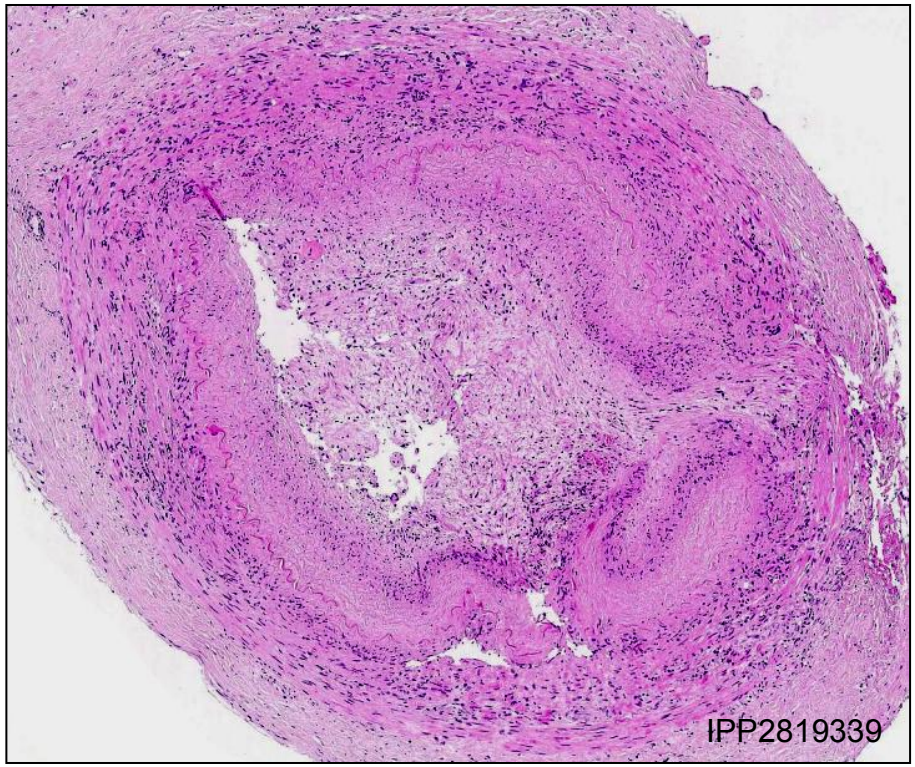
Duplex:
L.Hirt

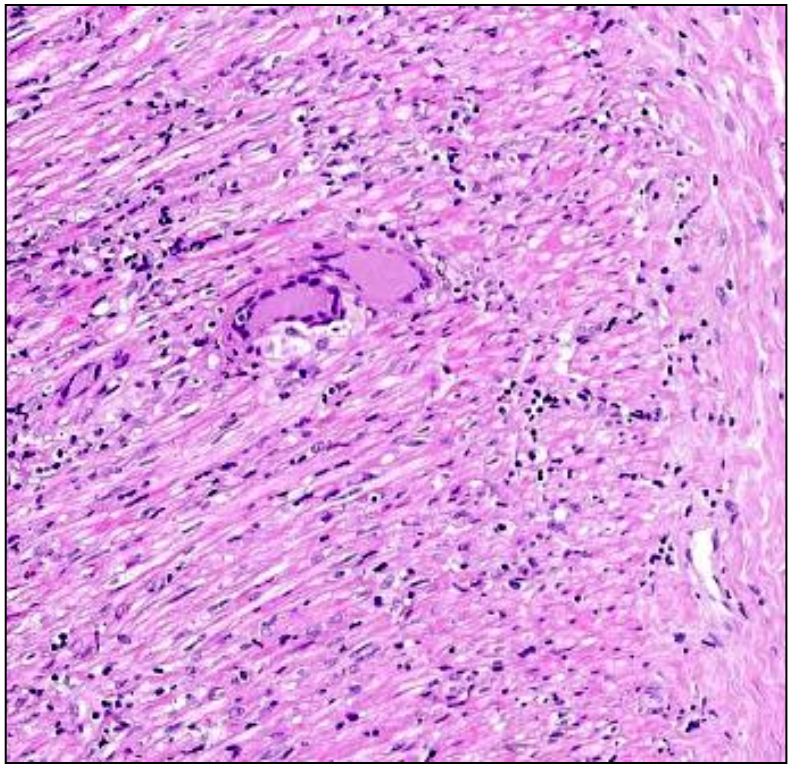
MRI and temporal arteritis : arterial wall thickening





Temporal artery biopsy





Histology: Dr I. Letanovic, CHUV

Giant cell: Temporal arteritis

- Is rare below 60 years
- Continuum TA - PMR
- If stroke (about 3-7%) :
  - Mainly from extracranial vertebral arteritis
  - May occur after corticosteroid have been started
- Diagnosis :
  - Sedimentation rate may be normal (15%)
  - Temporal artery Duplex/CTA/MRA: moderately helpful
  - Biopsy:
    - Take long segment, consider contralateral temporal artery
    - Corticosteroids don't negativize biopsy for 7-14 days

1. Vasculitis

as potential cause of stroke

- Primary systemic vasculitides
- Vasculitides secondary to systemic disease
- Isolated vasculitis of the CNS

Giant cell: Takayasu's arteritis

- Extracranial vaculitis: aortic arch and main arterial trunks, descending aorta and renal arteries
- Clinical:
  - Pulselessness/claudication/paraesthesias upper extremities
  - CNS: dizziness, headache, syncope
  - Systemic symptoms
  - Strokes (20-30%): ischaemic or haemorrhagic
  - ESR↑ in most, renal hypertension
- Diagnosis: major and minor criteria

Takayasu Japanese J Ophtal 1905.
Diagnostic criteria: Arend 1990

Quiz : 26 y.o. lady, good health

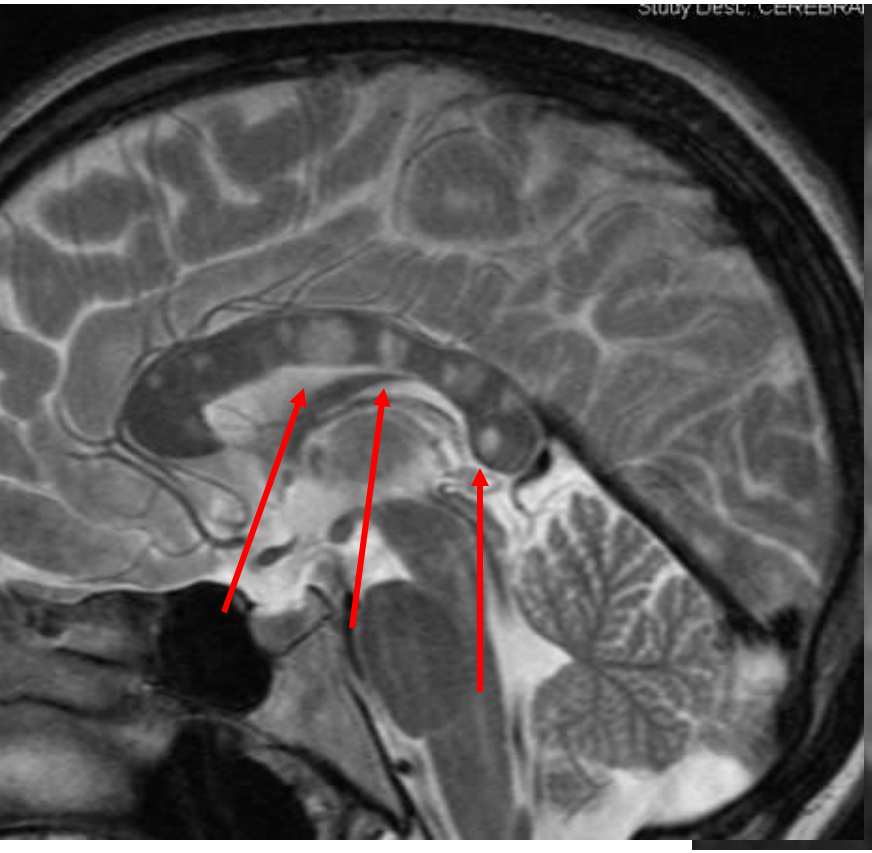
- History : since 1 month :
  - “Smokey” vision
  - Memory problems
  - Unstable gait
  - One episode of diplopia
  - Mild posterior headache
- Exam:
  - Attentional problems
  - Mild bilateral corticospinal and cerebellar signs
  - Left hypoaccousis

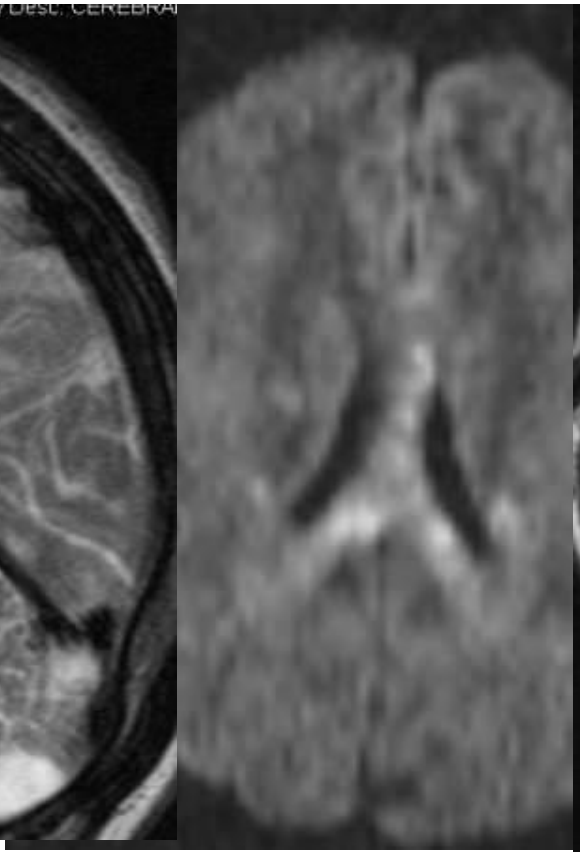
Primary vasculitides
with eye/ear involvement

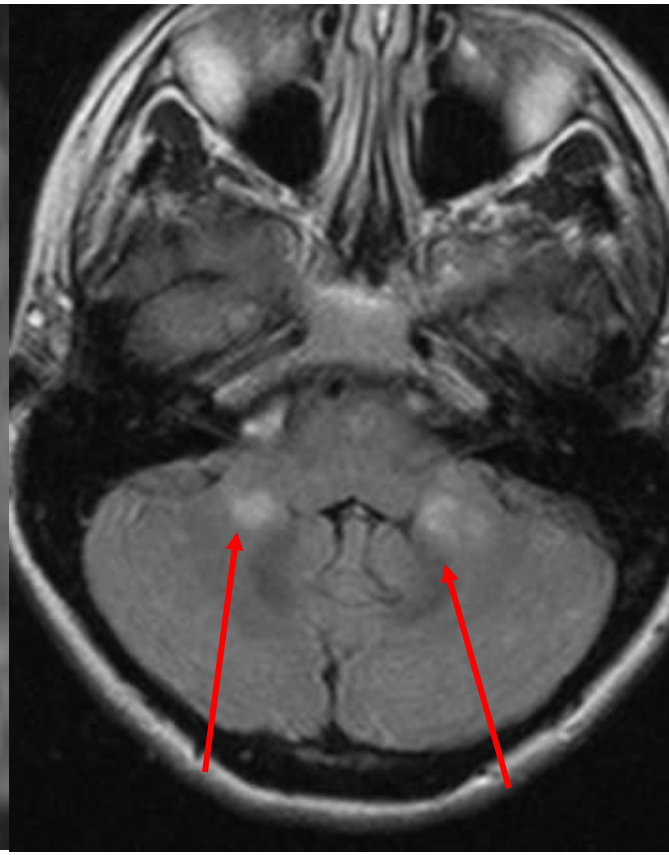
- Cogan's syndrome
- Susac's syndrome
- Vogt-Koyanagi-Harada syndrome

- Eales retinopathy
- Acute posterior multifocal placoid pigment epitheliopathy

26 y.o. lady: MRI





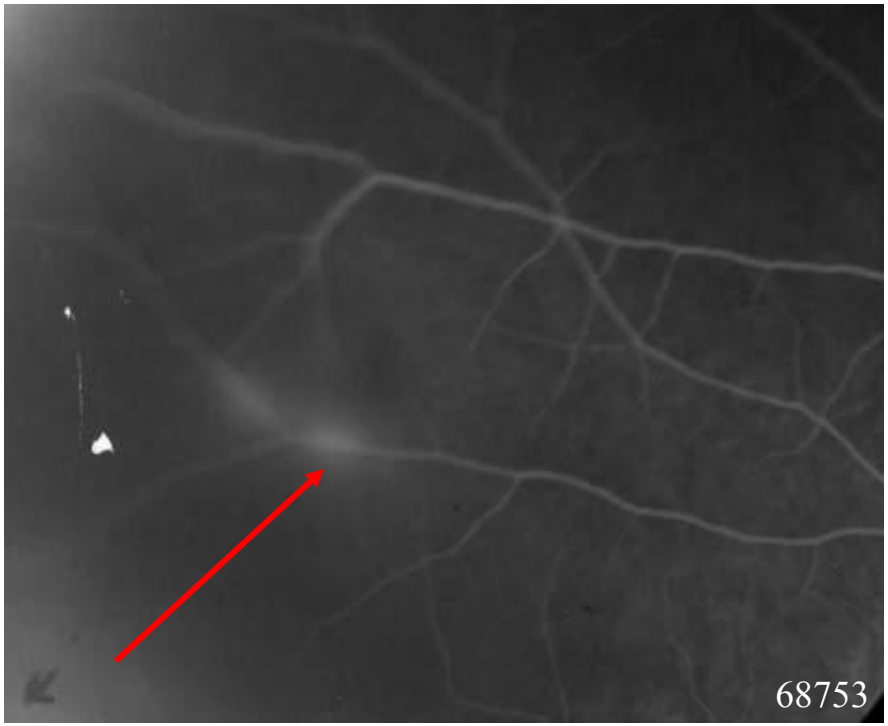


T2W

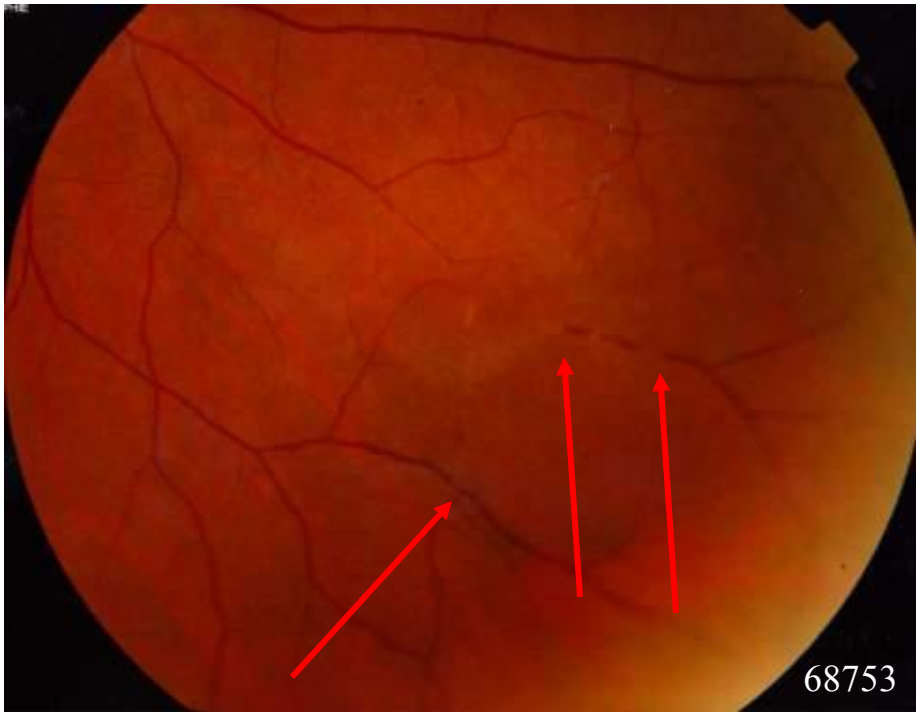
Diffusion (DTI)

FLAIR

Susac's syndrome: retinal findings



Indocyanide angiography
Contrast leak



Fluoro-angiography
Arterial narrowings
Venous obstructions

Courtesy : Dr JA Pournaras, Lausanne eye hospital

Susac's syndrome

Retino-cochleo-cerebral arteriolopathy

- Triade:
  - Small cortical and subcortical strokes
  - Retinal branch occlusion
  - Infarctions of cochlea (→ neurosensory hearing loss)
- Monophasic disease with or without preceeding specific infections
- Differential Dx: multiple sclerosis

Susac Neurology 1979 and 2003; Barker JNNP 1999

Cogan's syndrome

- Triade:
  - CNS-vasculitis
  - Keratitis
  - Deafness
- Rare:
  - Headaches, encephalopathy, lymphocytic meningitis, encephalopathy, seizures
  - Sinus vein thrombosis
  - Peripheral or cranial neuropathy
  - Aortitis, aortic insufficiency
  - GI hemorrhage, hepatospleno, lympadenopathy

Vogt-Koyanagi-Harada syndrome (VKH)

- Triade:
  - CNS&meningeal symptoms
  - Bilateral uveitis
  - Hair changes (poliosis, alopecia)
- Other neurological manifestations (rare)
  - Encephalopathy, coma
  - Seizures
  - Cranial nerve palsy (V-VIII)
- 4 stages:
  - 1) Prodromal (days): meningeal&neurologic manifestations
  - 2) Uveitic (weeks): posterior-> anterior uvea
  - 3) Convalescent (months) : hair/skin changes
  - 4) Chronic recurrent stage

Vogt 1906, Koyanagi 1929, Harada 1926

Vasculitides

secondary to systemic disease

- Systemic Lupus erythemtodes (SLE)
- Sjögren's syndrome
- Behçet's disease
- Sarcoidosis
- Rheumtoid polyarthritis
- Scleroderma
- Mixed connective tissue disease
- Dermatomyositis
- Ulcerative colitis/Crohn's disease

Systemic lupus erythematodes

Mechanisms of stroke

- Ischaemic
  - Libman-Sachs endocarditis
  - Hypercoagulability: antiphopholipids, cytokines ?
  - Cerebral vasculopathy/vasculitis
- Haemorrhagic
- Cerebral venous thrombosis
  - Hypercoagulability: antiphopholipids

Other vasculitides

secondary to systemic disease

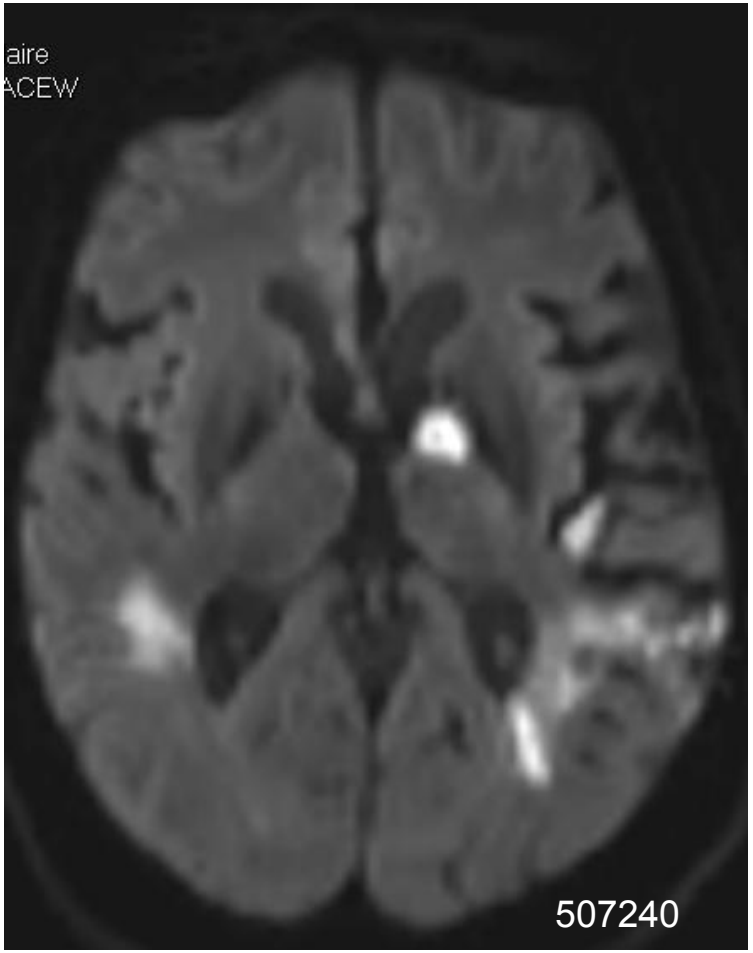
➢ SLE	➢ 11 criteria. Stroke, venous thrombosis
➢ Sjögren's syndrome	➢ Dry eyes/mouth, ANA+ (-> SSA/SSB+)
➢ Behçet's disease	➢ Oral/genital ulcers 3x/y, eye, skin
➢ Sarcoidosis	➢ Respiratory problems, liver, skin, uveitis
➢ Rheumatoid polyarthritis	➢ 4 or 7 criteria (morning stiffness >1h, ≥3 joints, hand joints, rheumatoid nodules)
➢ Scleroderma, MCTD	➢ Skin, multiples autoimmune
➢ Dermatomyositis	➢ Myopathy, dermatitis (extensor-side of joints/eye-lids)
➢ Ulcerative colitis/Crohn's disease	➢ GI symptoms, malabsorption

- Most can develop have CNS and/or PNS vasculitis
- Most can have other immunological disorders affecting near-neurological structures (autoimmune meningitis, uveitis, nerve compression, myositis)

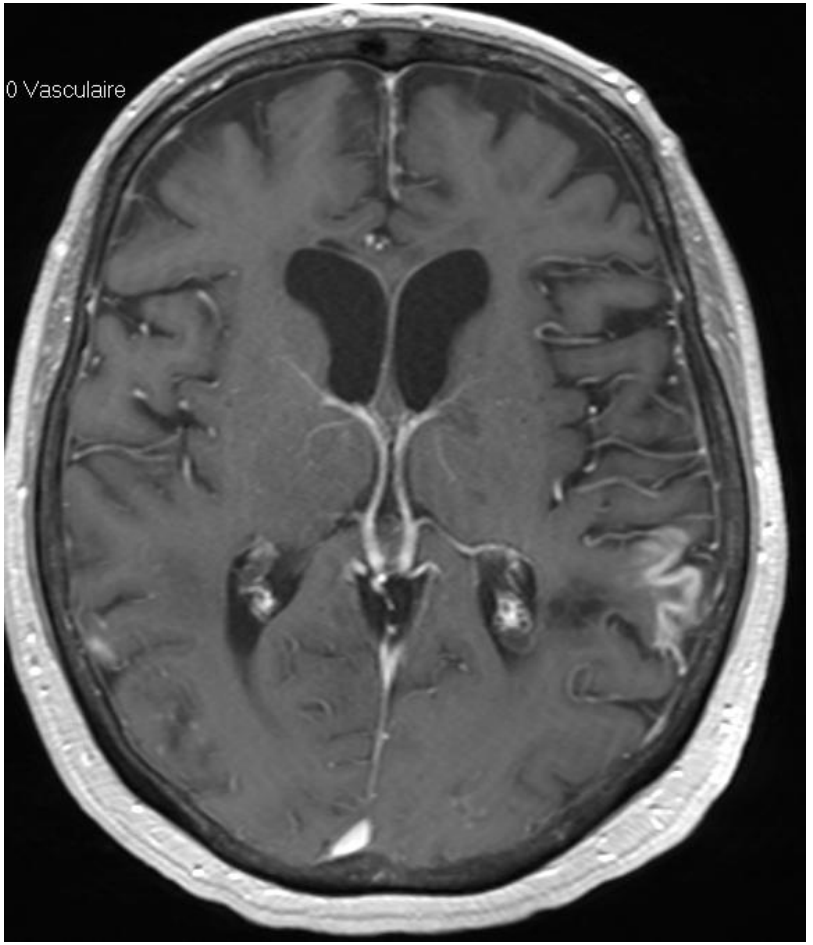
Quiz : 61 y.o. old woman

- Hypertension, smoking
- Controlled Basedow
- Recent removal of a skin kyste (neck)
- Now : 3 days of fluctuating confusion, aphasia?
- On exam:
  - Inattentive, sometimes crying
  - Fluent aphasia, major apraxia
  - Mild right corticospinal signs

61 y.o. woman : MRI



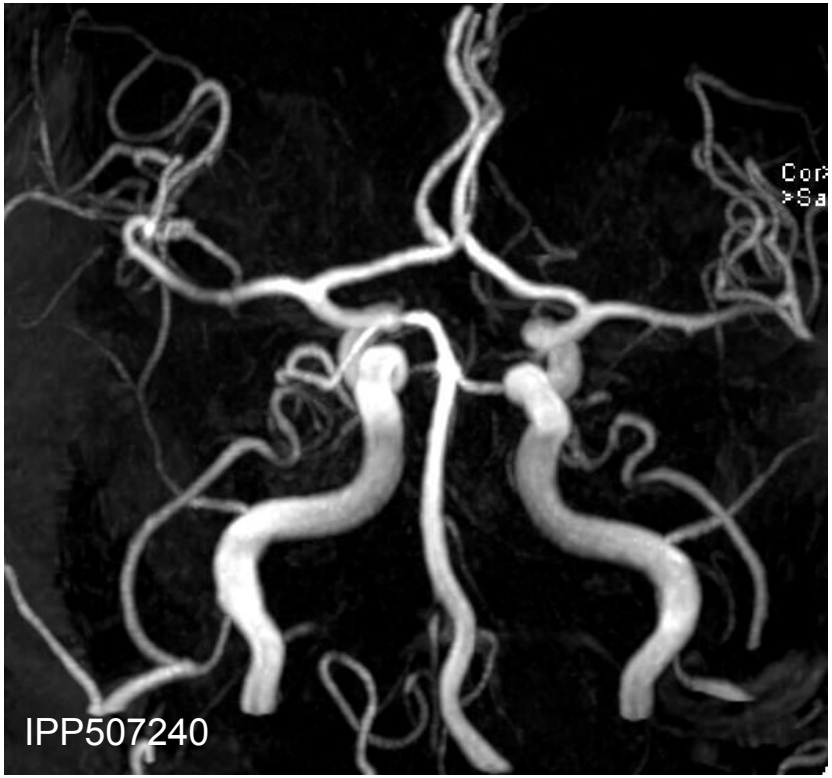
DWI

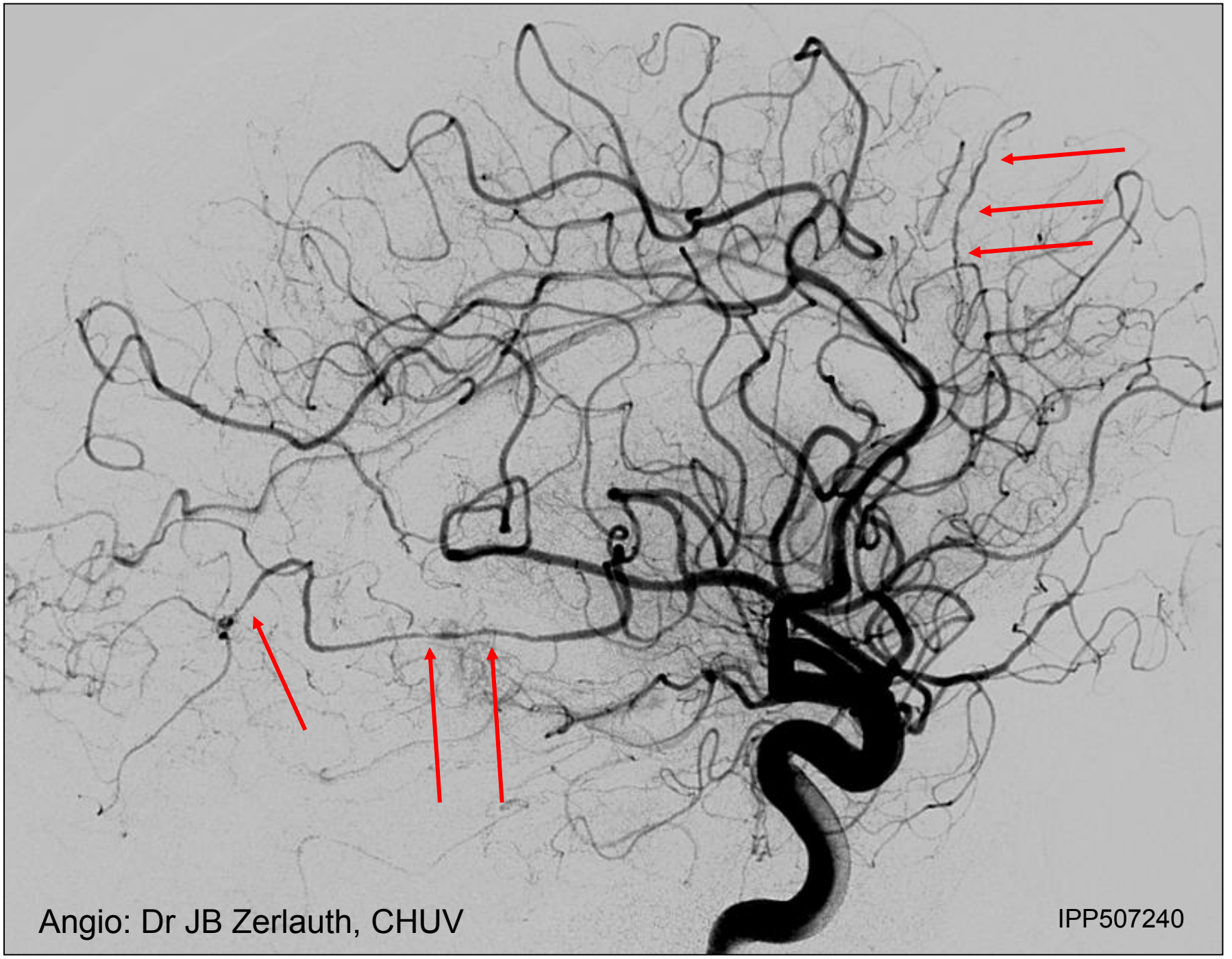


T1-Gadolinium

61 y.o. woman : work-up

- Blood normal
- CRP and sed. rate normal
- ETT & ETO : normal
- Ophta : normal retina
- No cancer
- Homocysteine-, APLA-
- Lumbar punctuer:
  - 70 leukocytes (PMN)




Angio: Dr JB Zerlauth, CHUV
IPP507240

Isolated (primary) vasculitis of the CNS

- Rare, difficult diagnosis
- Presentation: very variable ! Recurrences/progression of
  - Cognitive problems/confusion
  - Focal symptoms and signs
  - Headaches
- Diagnosis: no gold standard
  - Multiple lesions on MRI (80%), leptomeningeal enhancement (60%)
  - Abnormal LP (50%-90%)
  - Segmental narrowing on DS-angiography (50-80%, DDx: spasms, emboli)
  - Brain/meningeal biopsy (80%)
  - Retinal fluorescein angiography
  - Rule out endocarditis, toxics/drugs, malignancy etc.

Infectious and postinfectious vasculitis/vasculopathy

- Meningovascular syphilis
- Neuroborreliosis (Lyme disease)
- Tuberculosis and mycosis
- Bacterial meningitis with strokes
- Neurocysticercosis
- VZV-related; CMV and herpes related
- Chlamydia pneumoniae/Mycoplasma
- HIV: hetereogenous mechanisms
- Hepatitis C and mixed cryoglobulinemia

Meningovascular syphilis

- Any vessel affected, often cognitive problems
- Diagnosis
  - Clinical &
  - Pleocytosis on LP &
  - Elevated IgG or IgM **CSF-index** for treponema

$$\frac{\text{IgG-CSF/IgG-Serum}}{\text{Albumine-CSF/Albumine-Serum}}$$

- Mechanisms of stroke in symphilis:
  - Meningeal vasculitis
  - Marantic endocarditis
  - Aortic dissection

VZV related vasculopathy

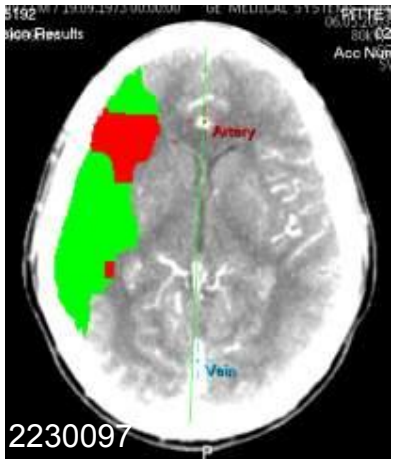
- Adults: 2-6 weeks after shingles mainly of the trigeminal nerve
- Children: 1-3 months after varicella = chickenpox
- Pathogenesis: controversial (infectious vs. immunologic)
- Clinical
  - Ipsilateral deep or superficial MCA-stroke
  - Rarer: disseminated CNS-vasculopathy (mainly if immunosuppressed)
  - Very rare: optic nerve ischaemia, retinal necrosis

2. Hypercoagulable causes of stroke

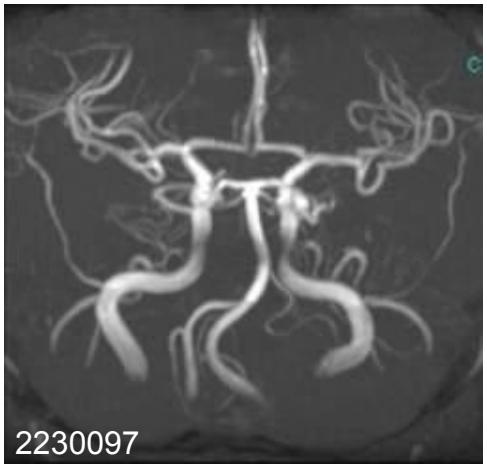
- Antiphospholipid antibody syndrome
- Hyperhomocysteinaemia
- Hyperviscosity syndromes
- Disseminated intravascular coagulation (DIC) and Moschcowitz syndrome (thrombotic thrombocytopenic purpura)
- Disorders of the coagulation cascade
- Mixed cryoglobulinemia (hepatitis C)
- Paraneoplastic (intestinal, lung, gynecologic)

Quiz: 30 y.o. man

- 2003: minor right MCA stroke. PFO & ASIA, smoking, cholesterol
- → PFO-closure

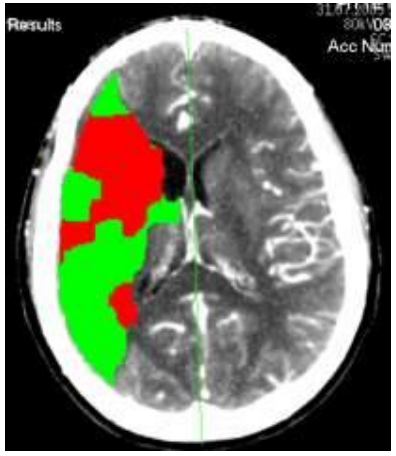


CTP 281 min.

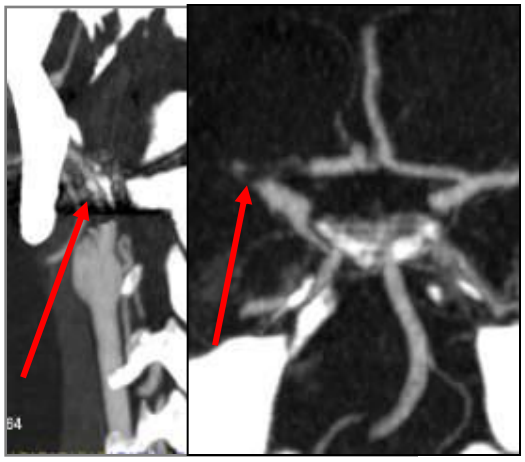


IRM à 12 h

- 2005: massive right MCA stroke → iv-thrombolysis at 135'
- No more R-L shunt, still cholesterol, smoking



CTP à 140'



T-occlusion carotid
No atherosclerosis

Hyperhomocysteinaemia

- Causes
  - *Genetic*: MTHFR (rarely cystathionine-beta-synthase or methionine synthase deficiency* (skin-Bx!)
  - *Genetic childhood form*: also marfanoid features, mental retardation, ectopia lentis
  - *Nutrition/malabsorption*: B6, B12 and folic acid deficiency
- Clinical:
  - Linear increase of stroke and coronary risk with serum levels
  - Incresed risk of venous thrombosis
- Treatment (folic acid, B6, B12):
  - No clear benefits for stroke prevention
  - Individual cases may benefit*

Vitamin stroke trials: Toole/VISP: JAMA 2004; VITATOP, Lancet Neurol 2010
*Novy, Thromb Haemostas 2010

Antiphospolipid antibody syndrome (APLS)

Diagnostic criteria (1 clinical & 1 laboratory)

- Clinical criteria
  - Vascular thrombosis (arterial or venous, any tissue or organ)
  - Otherwise unexplained abortus
    - ≥1 death fetus >10th week, or
    - ≥1 premeature birth <34th week, or
    - ≥3 consectutive spontaneous abortions <10th week
- Laboratory criteria: on 2 occasions ≥ 3 months apart:
  - Lupus antcoagulant antibodies, or
  - Anticardiolipin (IgG or IgM), or
  - Anti-beta-2-Glycoprotein-I (IgG or IgM)

Miyakis et al: International consensus statement. J Thromb Haemost 2006

APLS : clinical presentations

- Primary APLS : no other disease associated
- Secondary APLS : mainly SLE, aussi RA,
- Sneddons' Syndrome : stroke+livedo reticularis+APL
- Catastrophic APLS :
  - at least 3 organs over days to weeks
  - acute thrombotic microangionpathy affecting small vessels
  - similar to haemolytic-uremic syndrome and TTP

Disorders of the coagulation cascade

- Adults: no proven association with ischaemic stroke:
  - Protein C resistance and factor V Leiden mutation (homo- or heterozygous)
  - Protein C and S deficiency, AT-III mutation
  - Prothrombin G20210A mutation, etc.
- Children : possible association with ischaemic stroke
- Associated with cerebral venous thrombosis and possibly with PFO-related stroke
- Fibrinogen mutations: → ischaemic or haemorrhagic strokes
- vWF factor : haemophilia → intracranial haemorrhages

Hyperviscosity syndromes

- Polycythemia vera (+/- thrombocytosis)
- Sickle cell anemia: homozygous only
  - Due to intimal hyperplasia from pathologogical blood-intima interaction
  - Intracranial stenosis (sometimes Moya-Moya-like)
- Hyperproteinemia/monoclonal gammopathies
  - Waldenström's macroglobulinemia
  - Immunoglobuline treatment (also: vasospasm?)
- Nephrotic syndrome
  - Arterial and venous thrombosis
  - Urinary loss of AT-III, elevatied levels of coagulation factors, platelet hyperactivity

Work-up in suspected hypercoagulable states

- Good history and exam
- Full blood count, basic chemistry, serum protein, serum proteinelectrophoresis (ev. fibrinogen)
- Urinalysis
- Pregnancy test
- Serum homocysteine
- PT, aPTT, anticardiolipin IgG and IgM, lupus antcoagulant (if negative: anti-beta-2-glycoprotein-I)
- Consider cancer search:
  - Rectal exam, stool occult blood
  - Chest XR/body scan, mammography
  - Fibrin monomers
  - Urine proteinelectrophoresis

Strokes in cancer patients

Multiple potential mechanisms

→ Increased risk for

- Ischaemic strokes
- Haemorrhagic strokes
- Cerebral vein thrombosis, recurrent venous thrombophlebitis (Trousseau's syndrome)

◆ Mechanisms for ischaemia (mostly in gi-tumors)

- Distant effects of tumor: thrombocytosis, coagulation proteins up/down, chronic DIC, Libman-Sachs, autoimmune (acquire vW disease, APLS, vasculitis)
- Venous statis, surgery, chemotherapy, dehydration
- Rarely: tumor emboli, intravascular lymphoma

◆ Mechanisms for haemorrage

- Autoimmune thrombocytopenia, acquired vW disease
- DIC

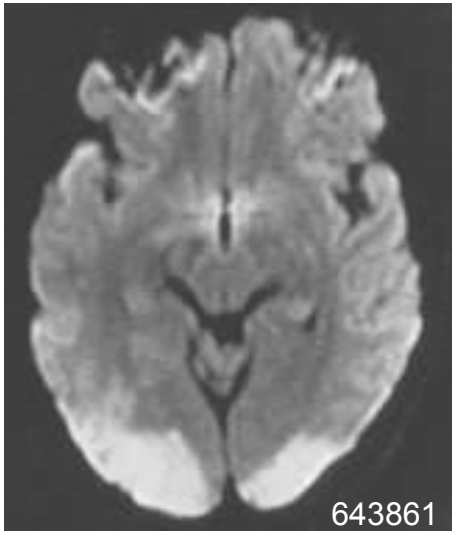
◆ Markers: → d-dimers, fibrin monomers, CCA-1

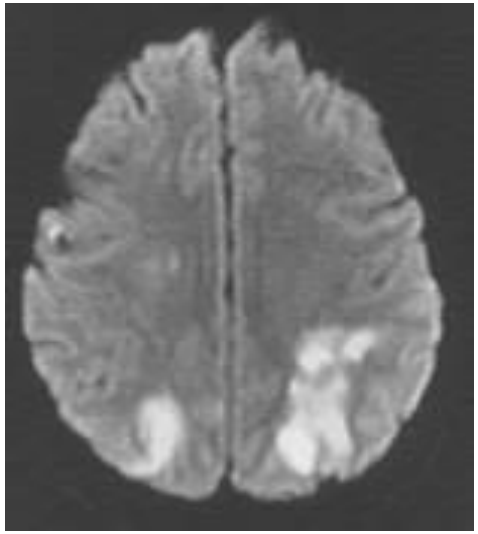
Quiz : 26 y.o. lady

- Known for migraine without aura
- Severe migraine attack with visual symptoms
  - Progressively disoriented over 36 hours
  - Worsening visual problems
  - On exam: partially oriented, Anton's syndrome

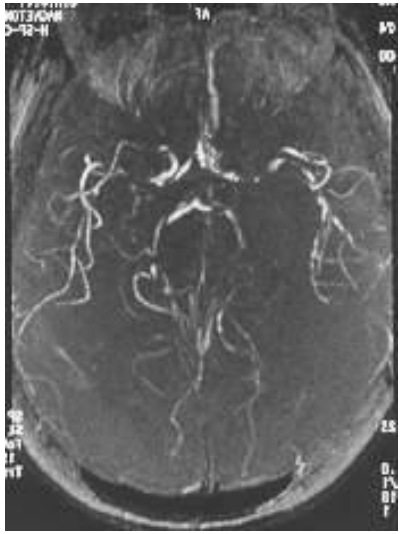
26 y.o. lady

Headaches, confusion, Anton's syndrome

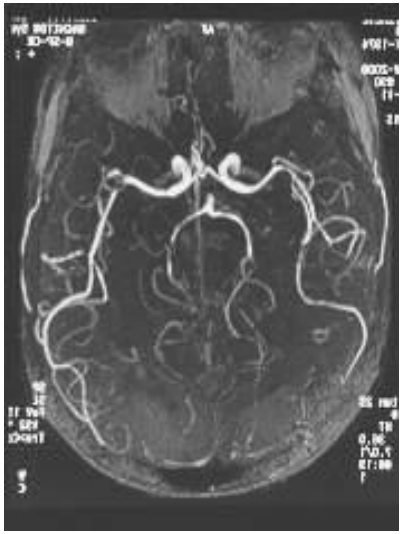




Bilateral posterior > anterior borderzone infarcts



Multifocal vasospasms



After i.a. treatement with nimodipine & balloon

Courtesy: M.Reichhart, A.Uske, CHUV

Cerebral vasospasms: Causes

- Subarachnoid haemorrhage
- Illicit drugs
  - Cocaine, Crack, amphetamines, sympathomimetics
- Medications
  - Ergotamines, triptans
  - Sympathomimetics
  - Immunoglobulines
- Severe hypertension, phaechromocytoma
- Post partum angiopathy, sickle cell anemia, migraine (thunderclap headache)
- Idiopathic : Reversible cerebral segmental vasoconstriction (« Call-Flemming's syndrome »)

Our patient: migraine attack → ergotamines → triptans → vasospasms of multifactorial origine

3. Drug related stroke

- Medications
  - Platinum-based chemotherapy
  - Oral contraception, hormone-replacement therapy
  - Ergotamines, triptans
  - Intravenous immunoglobulines
- Illicit drugs
  - Stimulanting drugs (cocaine, crack, amphetamines, sympathmimetics), phenylpropanolamine, ephedrine, ...

    → ischaemic and haemorrhagic strokes, sometimes vaculitic

4. Migraine, vasospasms, pregancy

- Migraine and stroke
  - ➢ Migrainous stroke: strict IHS-criteria
    - Same aura as usual
    - Acute ischemic lesion on imaging
    - Exclusion of other causes
- Vasospasms and stroke
  - ➢ See previous checklist
- Pregnancy and stroke
  - ➢ What are the causes ?

Pregnancy and puerperium

Cerebrovascular syndromes

- Eclampsia, reversible posterior encephalopathy syndrome, HELLP
- Postpartum cerebral angiopathy
- Postpartum dilated cardiomyopathy
- DIC
- Paradoxical/PFO; amniotic fluid embolism
- Arterial dissection (labor)
- Intracerebral haemorrhage : AVMs
- Subarachnoid haemorrhage : aneurysms
- Pituitary apoplexy
- Cerebral sinus vein thrombosis

Our patient:
→ postpartum cerebral angiopathy

4. Migraine and stroke

- Migraine is an independent risk factor for ischaemic stroke in the young
  - Especially migraine with aura and if smoking
  - Association of migraine with PFO
- Migrainous stroke : diagnosis (IHS 2004)
  - The aura corresponds to the patient's usual aura
  - Infarction must be demonstrated on neuroimaging
  - Symptoms may last < 24 hours and migrainous stroke is present
  - Other causes (dissection, AVMs, ergots, triptans, etc.) must be excluded
- Migraine is frequent, migrainous stroke is rare
- Variant: Headache with neurologic deficits and CSF lymphocytosis (HaNDL)*

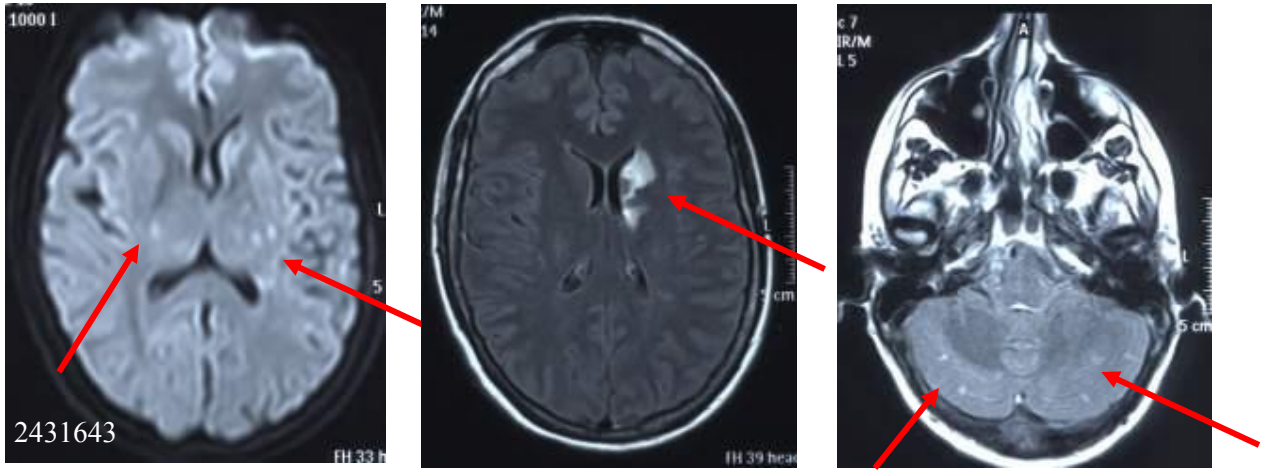
*Gomes-Aranda Brain 1997

5. Rare causes of cardioembolism

- Myxoma, fibroelastoma
- PFO
- Endocarditis
  - Infective
  - Marantic (Libman-Sachs)
- Gaz emboli

Quiz : 30 y.o. woman

- Hashimoto's thyroiditis (6 months ago)
- Transient aphasia and right arm weakness (15 min)
- Acute CT/perfusion-CT/CTA: normal
- Sedimentation rate = 45, CRP normal

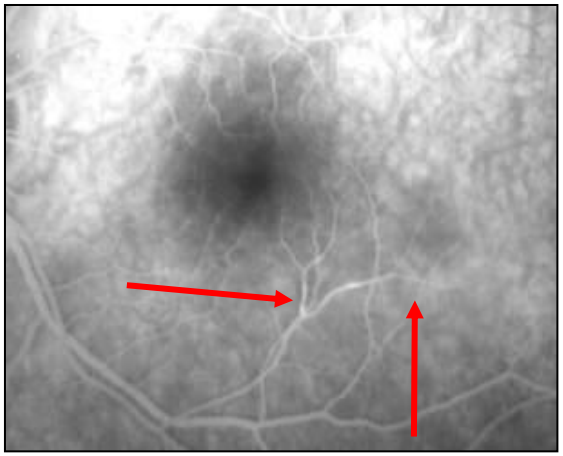


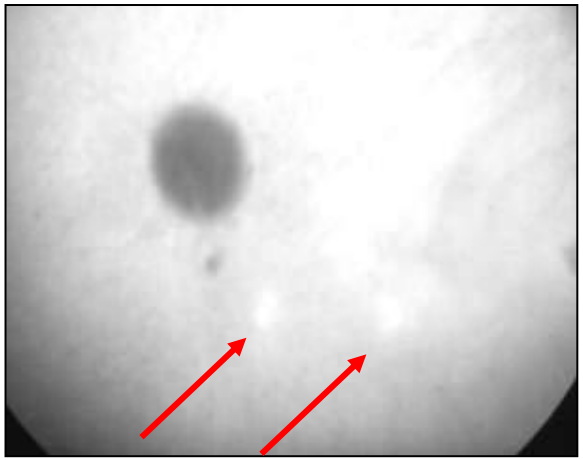
MRI day 2 : multiple small deep lesions, different ages
(Neuroradiology CHUV)

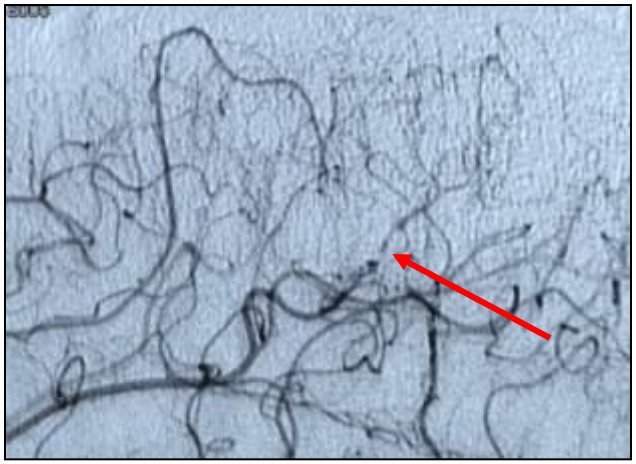
30 y.o. woman : work-up

- Lumbar puncture normal
- Fundoscopy:

Arteriography







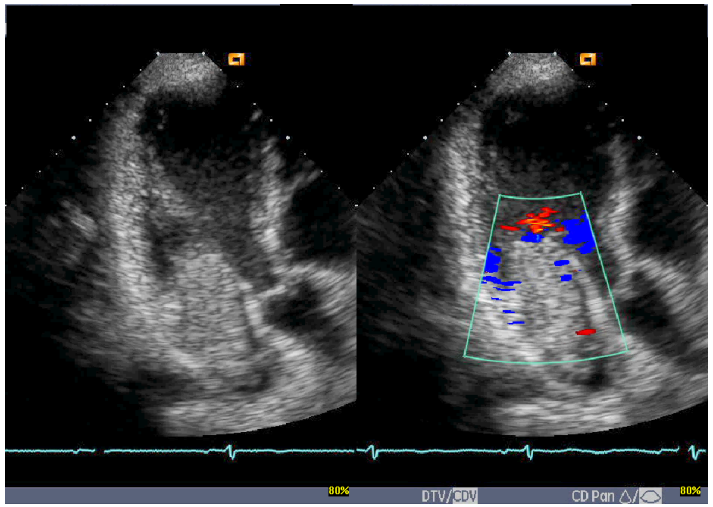
«Vasculitis » in multiple sites, leaking of contrast on fluoresceine and ISG angiography

(Dr Borruat, Neuro-ophthalmology)

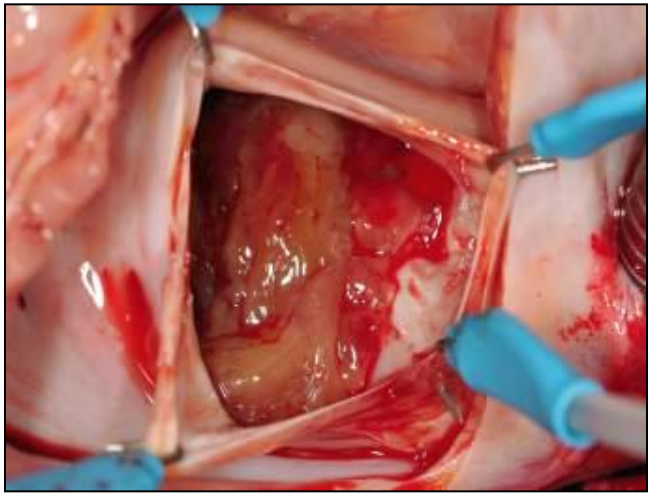
« Vasculitis»

(Dr Binaghi, Neuroradiology)

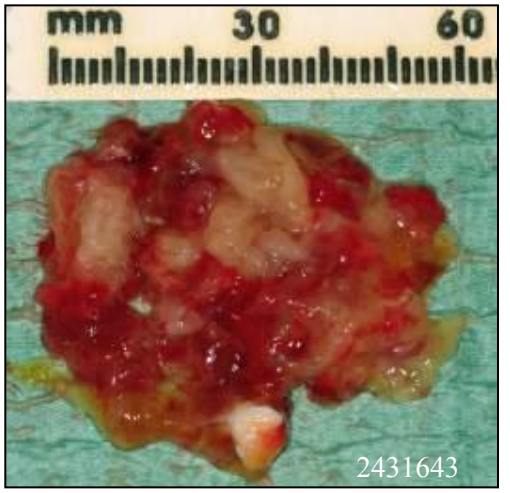
30 yo woman : « CNS vasculitis ? »



TTE (Dr Jeanrenaud, CHUV)



Cardiotomy (Dr Hurni, CHUV)



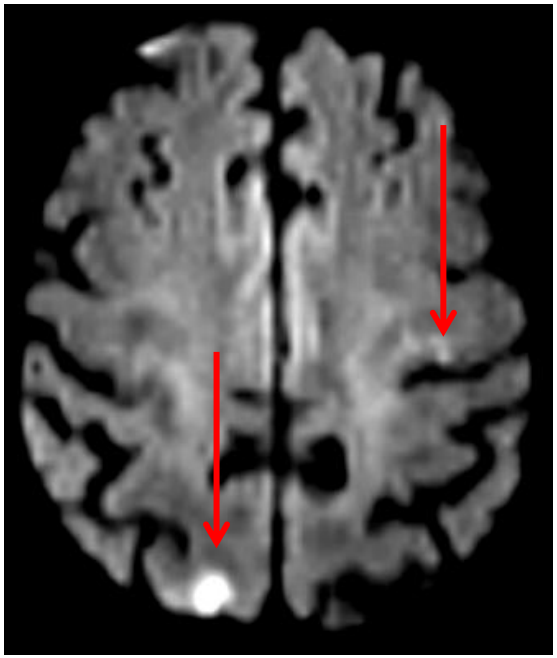
Pathology (CEMCAV)

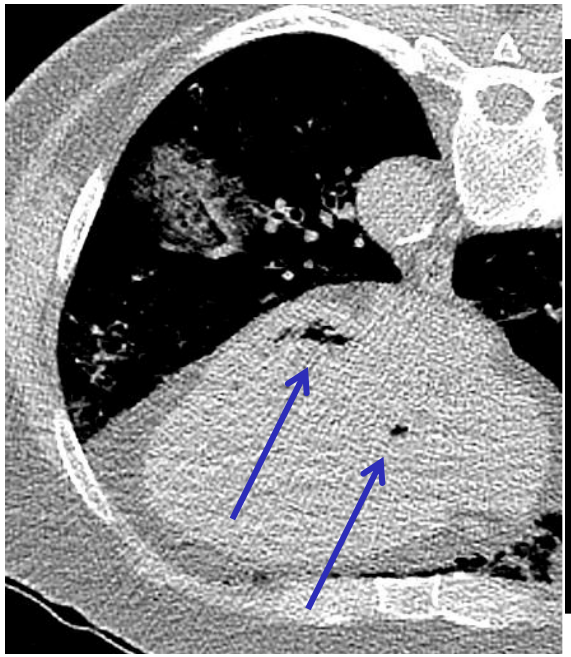
→ Cardiac myxoma

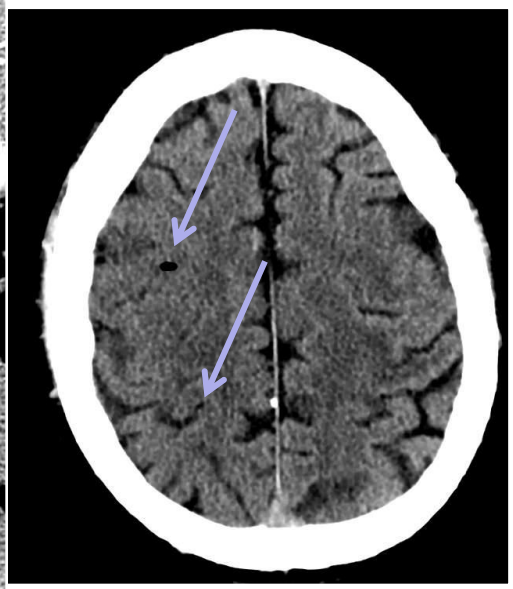
- Inflammatory symptoms
- Rarely malignant
- Occasionnaly multiple or recurrent (Carney-complex)

5. Rare causes of cardioembolism

- 74 yo man; transcutaneous lung nodule biopsy
- End of procedure: syncope, then dysarthria, gait ataxia







Air emboli on CT
(other patient)

Muth NEJM 2000; Tsetou, submitted

6. Genetic causes of stroke

6.1 Genetic collagen disorders

(→ mid-size arteriopathies)

6.2 Genetic small vessel diseases

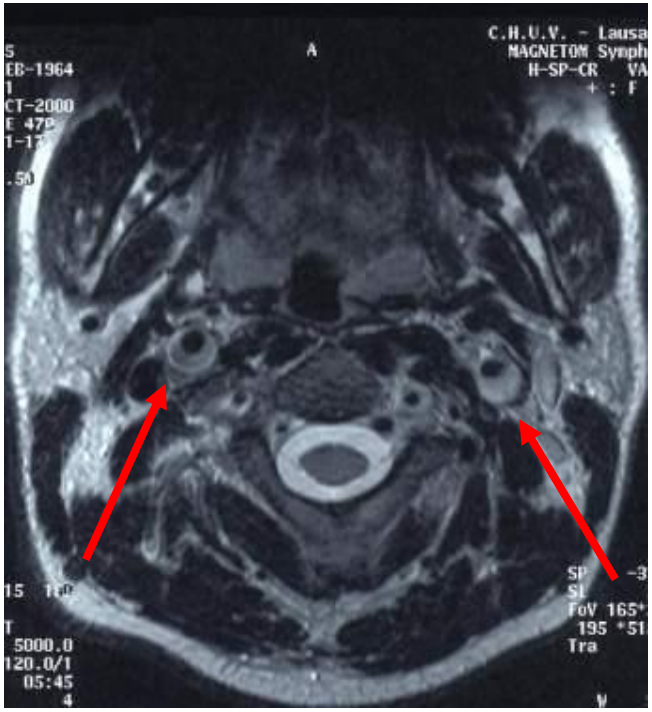
6.3 Genetic metabolic diseases with strokes

6.1 Genetic collagen vasculopathies
(→ mid-seize arteriopathies)

- Examples :
  - Ehler-Danlos IV, Marfan's syndrome, polykystic kidney disease, cystic media necrosis, osteogenesis imperfecta
  - Alpha-1-antitrypsin-deficiency
  - Fibromuscular dysplasia (FMD)
  - Neurofibromatosis (mainly NF-1)
  - Non-specific collagen changes on biopsy
- All these are at increased risk for :
  - Dissections
  - Cerebral saccular aneurysm
  - Dolichoectasia/fusiforma aneurysms
  - Aortic disease, renal/splanchnic arterial disease

Fibromuscular dysplasia (FMD)

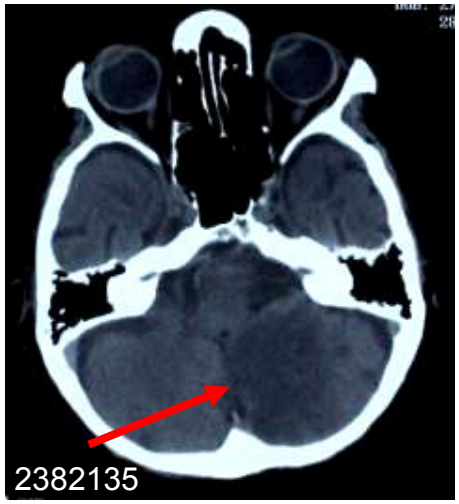
- Extra >> intracranial vessels
- Renal and splanchnic arteries
- Radiology: «String of beads»
- Dissections possible
- Genetics unknown

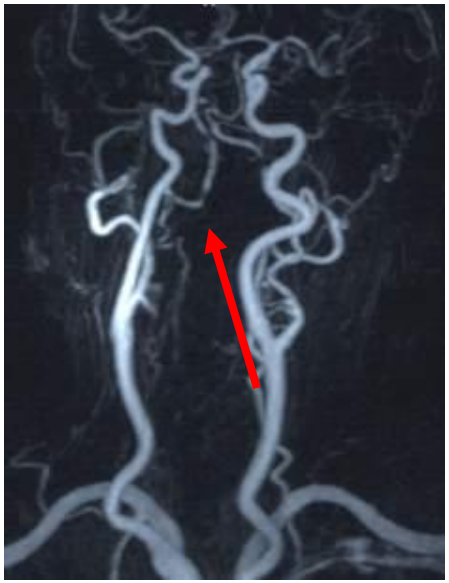


Young lady with bilateral carotid dissections and FMD

Neurofibromatosis - I

- Extra- and intracranial large vessel narrowing
- Posterior > anterior circulation
- Saccular aneursyms
- Diagnostic criteria: 2 of 7

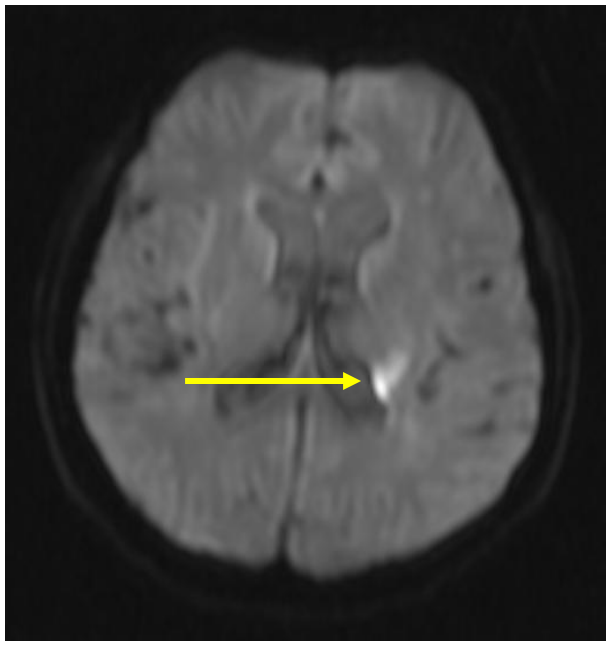


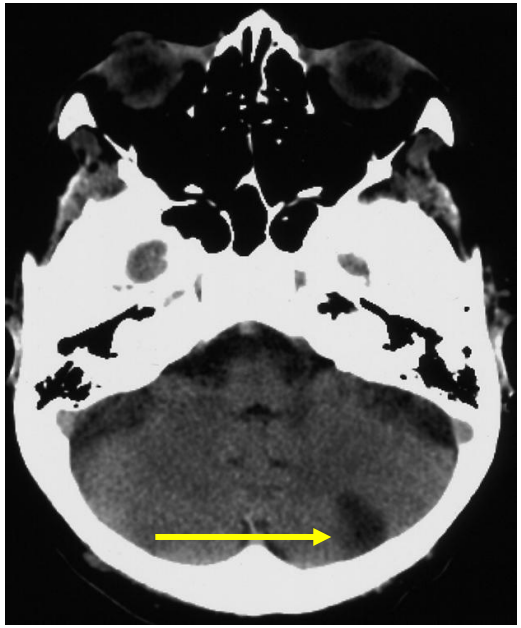


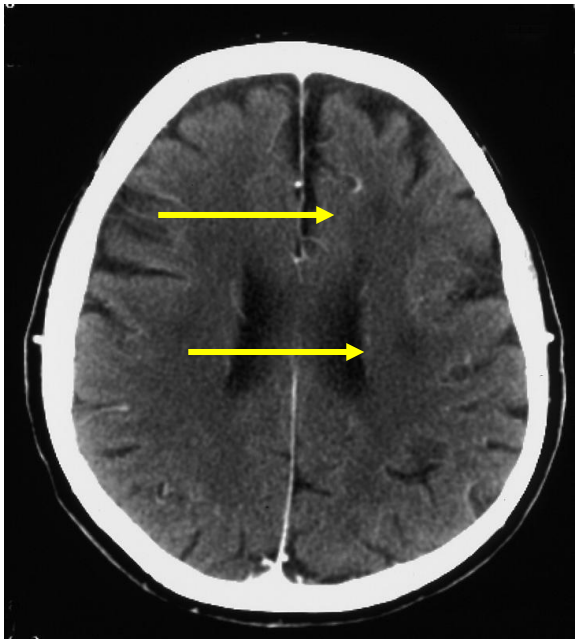
Left PICA and bilateral pontine strokes

Quiz: 66 year old lady

Waking up with acute right ataxia hemiparesis

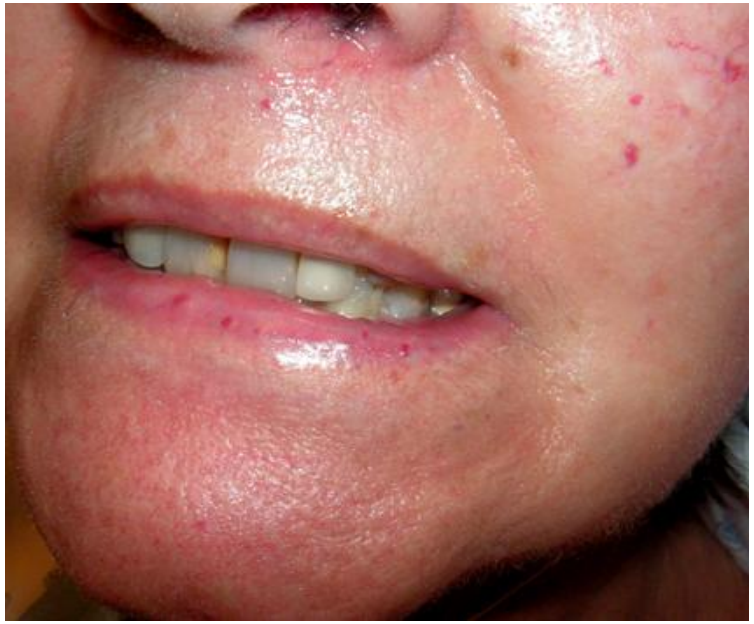


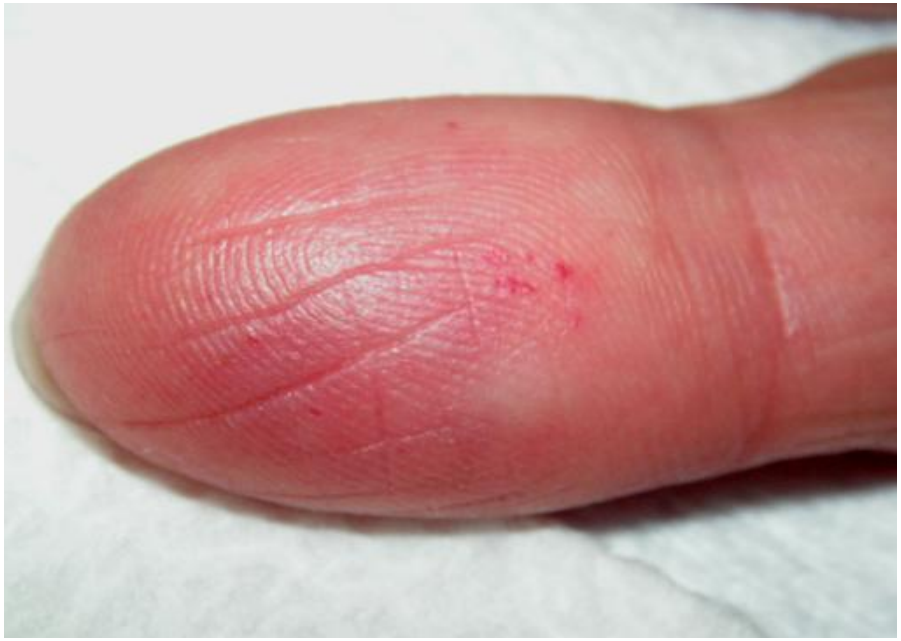




66 yo lady : multiple subcortical lesions

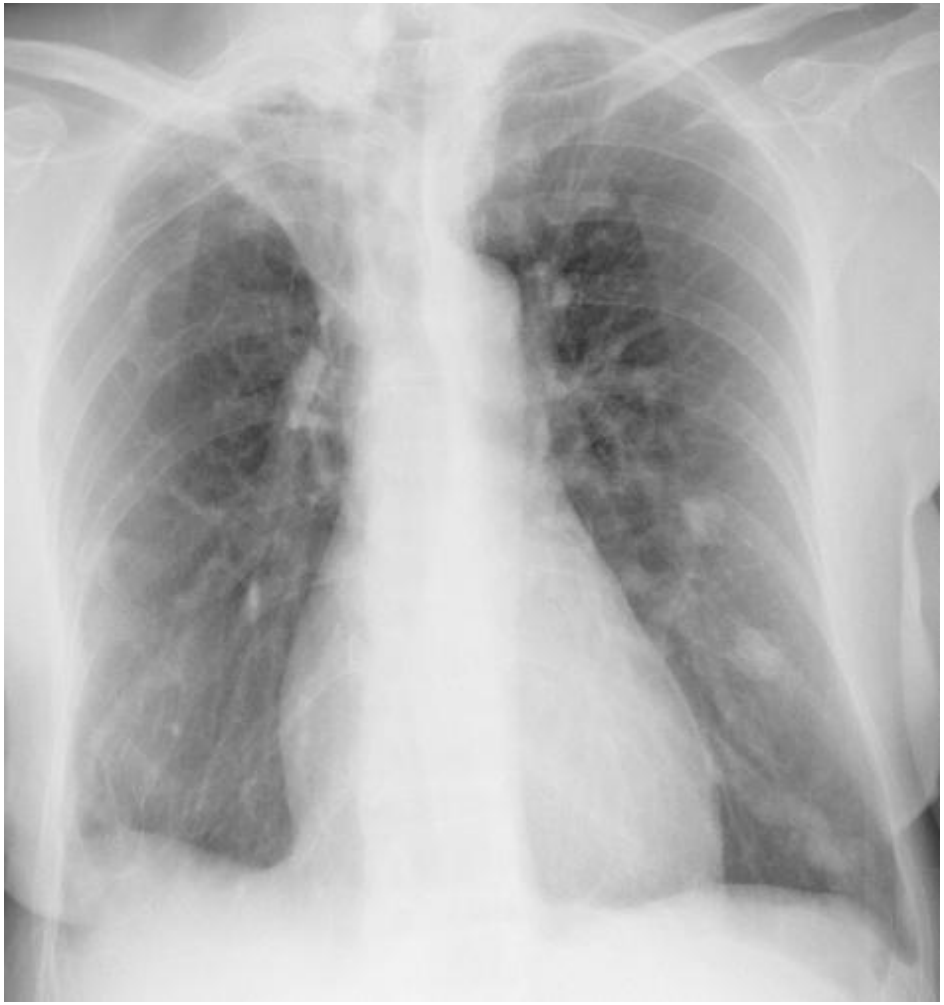
- Migraines with visual aura
- Recurrent epistaxis since childhood
- Dyspnea grade II
- Skin lesions:





Morier & Michel, Arch Neurol 2011

66 yo lady : strokes, epistaxis, skin lesions



Morier & Michel, Arch Neurol 2011

Rendu-Osler-Weber disease

Hereditary hemorrhagic telangiectasia

- Autosomal dominant (chromosome 9)
- Multiple telangiectasias of skin, mucous membranes, epistaxis, viscera
- 10% with neurological complications
  - Related to pulmonary arteriovenous malformations (PAVM)
    - Ischaemic strokes from paradoxical and air embolism, and from hyperviscosity/polyglobulia
    - Brain abcess, bacterial meningitis
    - Gaz emboli
  - AV-malformations with intracerebral haemorrhages and spinal haemorrhages

Rendu 1896, Osler&Weber 1901 and 1908
Morier & Michel, in: Uncommon Causes of Stroke, 2nd edition

Stroke and skin disease

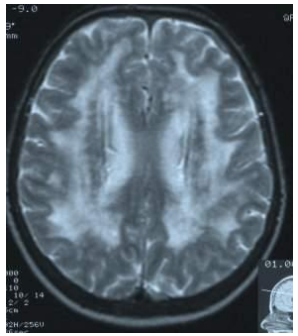
- Vasculitis related to lupus, sarcoidosis etc.
- Infections : Syphilis, Lyme disease
- Genetic collagen vasculopathies (→ mid-size arteries)
  - Rendu-Osler-Weber disease
  - Pseudoxanthoma elasticum
  - Von Hippel-Lindau disease
  - Neurofibromatosis
  - Sturge-Weber syndrome
- Genetic metabolic diseases
  - Fabry's disease
  - Köhlmeier-Degos disease

6.2 Genetic small vessel diseases

- **CADASIL** = Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
- **HERNS** = Hereditary endotheliopathy with retinopathy, nephropathy and stroke
- **HVR** = Hereditary vascular retinopathy
- **CRV** = Cerebroretinal vasculopathy
- **HIHRATL** = Hereditary infantile hemiparesis, retinal arterilar tortuosity, and leukonecephalopathy (COL4A1-mutation)
- **HANAC** = Hereditary Angiopathy with Nephropathy, Aneurysm and Cramps (COL4A1 -mutation, Plaisir NEJM 2007)
- Some cerebral amyloid angiopathies

checklist

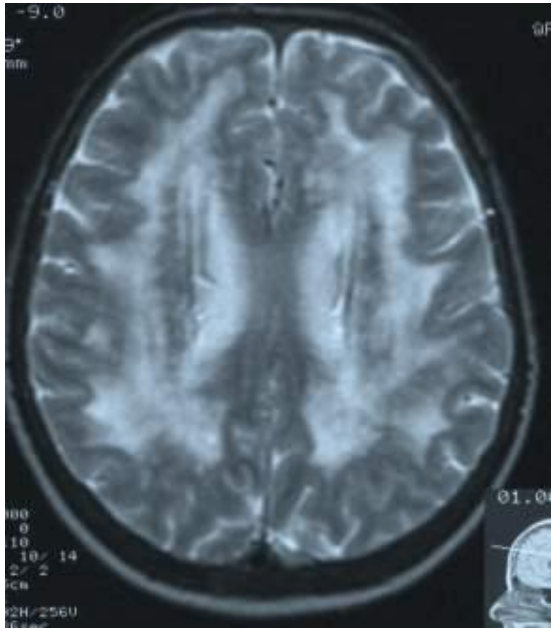
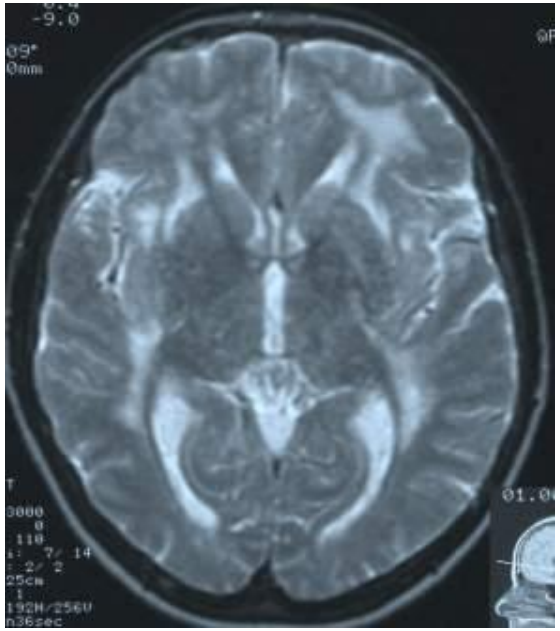
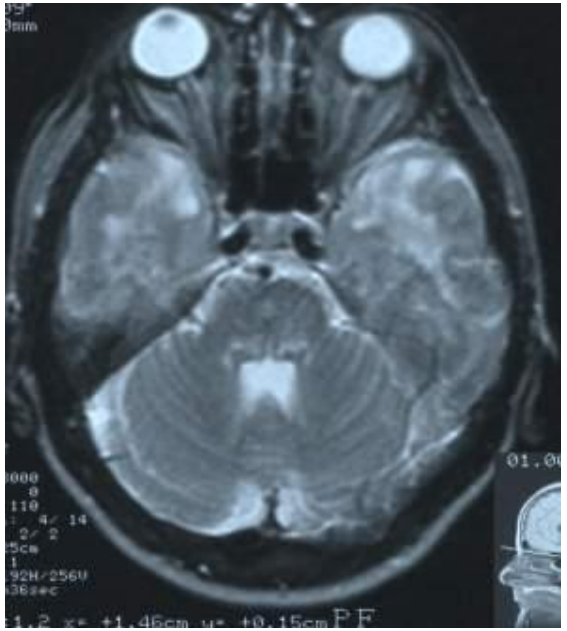
Multifocal or diffuse
ischaemic white matter disease



- Chronic poorly controlled hypertension, other risk factors
- Vasculitis
- Multiple (minor) cardiac emboli
- Hyperhomocysteinemia/uria
- CADASIL and other genetic small vessel diseases
- Cerebral amyloid angiopathy
- Hypercoagulabitiy, antiphospolipid syndrome, SLE
- Mitochondrial diseases
- Fabry's disease
- Post-radiation encephalopathy

Quiz: 64 yo lady

- High cholesterol, history of migraines
- Now : acute gait instability
- Exam: mild bilat. corticospinal signs, cognitive problems

Sion Radiology

CADASIL

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy

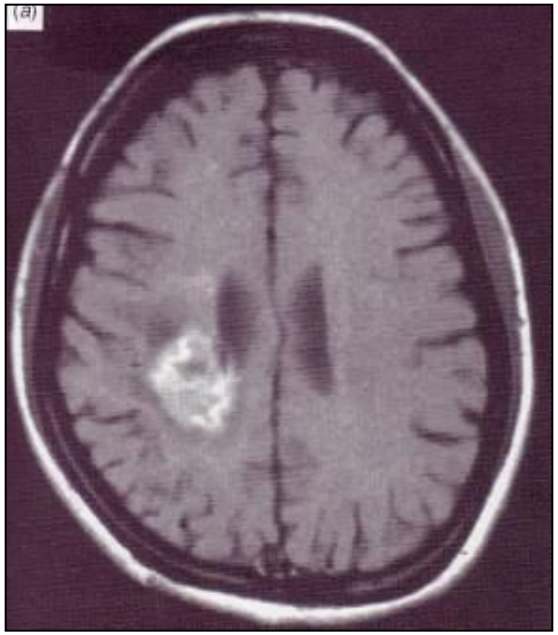
- Pathology
  - Brain, meningeal vessels: thinned; **granular eosinophilic material**, abnormal smooth muscle cells
  - Granular eosinophilic material in most organ vessels

    → genetics or skin biopsy for diagnosis
- CARASIL
  - Same CNS symptoms
  - Back pains/kyphosis/spinal dysplasia, elbow/knee deformities
  - Alopecia, ophtalmoplegia, facial palsy
  - No retinal nor skin involvement

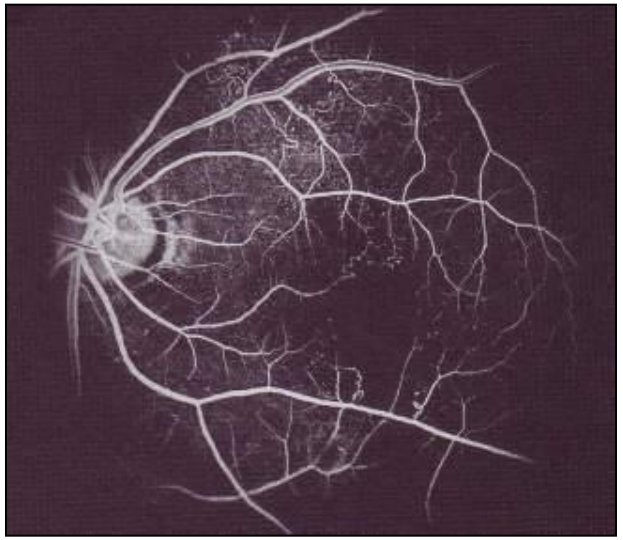
CADASIL: Tournier-Lasserve & Bousser 1993
CARASIL: Yanagawa Neurology 2002

HERNS

Hereditary endotheliopathy with retinopathy, nephropathy and stroke



Gadolinium-MRI



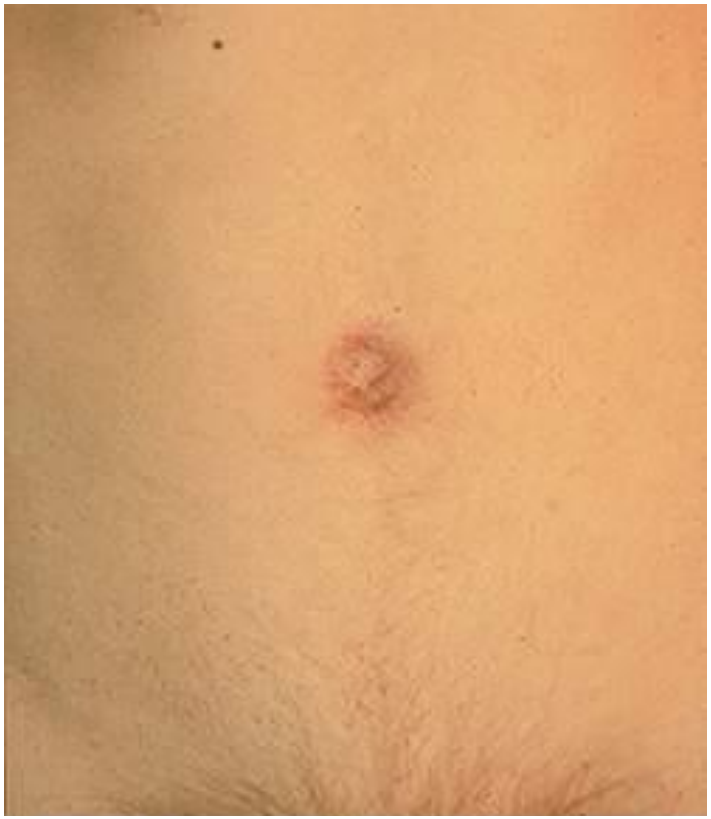
Fluorescein angiogram with dilated toruous telagiectatic vessels and capillary shunts
Jen 1997 Lippincott

- Gadolinium-enhancing masses, renal insuff, proteinuria
- Chr.3p21, gene not identified

Quiz : 40 y.o. man

- Acute ataxic hemiparesis

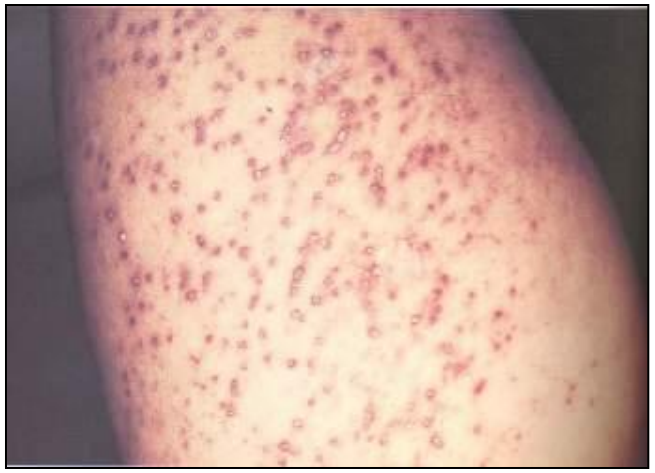
  → right internal capsule lacune
- Occasional feet and hand pains and anhydrosis
- Skin changes



Cabrera-Salazar & Barranger
Medlink Neurology

Fabry's disease
(Angiokeratoma corporis diffusum)

- Ischaemic strokes
  - Small vessel or embolic (cardiac, prothrombotic states)
  - White matter disease/dementia
  - Dolichoectasia
- Polyneuropathy
  - Sensory-autonomic
  - Painful crisis, triggered by heat etc.
- Renal failure
- Heart
  - Infarction, valvular heart disease
  - Hypertrophic cardiomyopathy
- Eye
  - Corneal and lenticular opacities



Caplan & Mohr:
Rare stroke syndromes

Fabry's disease
(Angiokeratoma corporis diffusum)

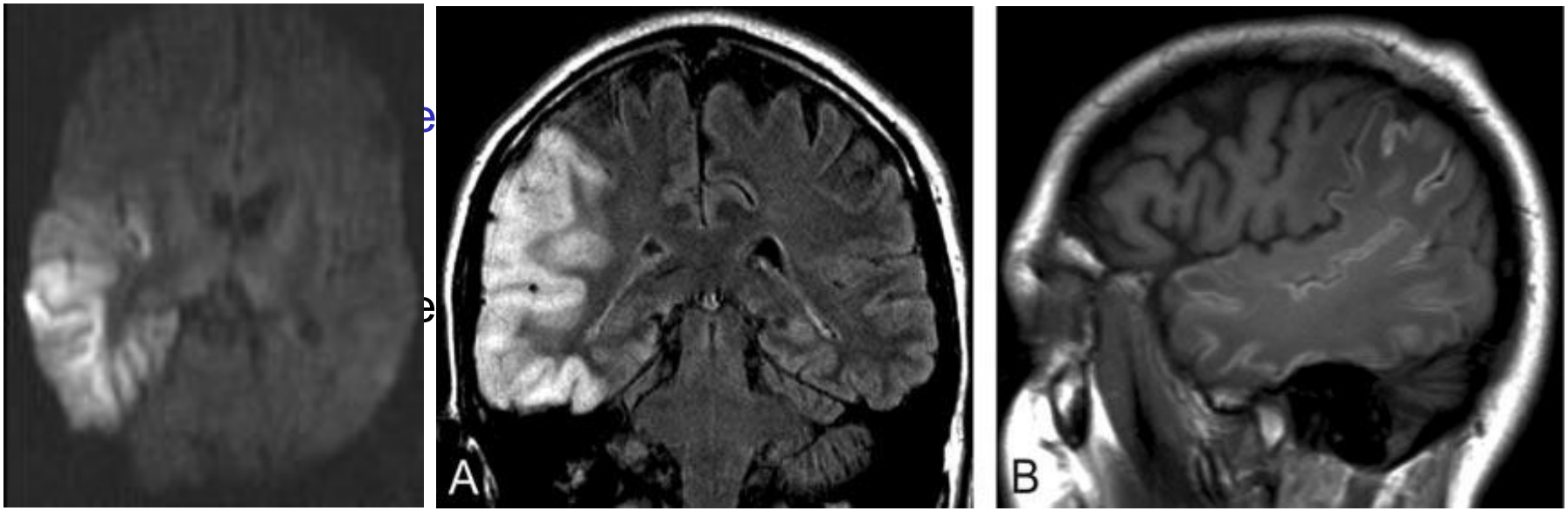
- Alpha-galactosidase deficiency
  → Glycosphingolipid-accumulation in intima etc.
- X-recessive
  → Women : manifestations rare and later
- Treatment
  → Alpha-galactosidase A replacement therapy

6.3 Genetic-metabolic diseases with strokes

- Fabry's disease
- Mitochondriopathies
- Others:
  - Menke's disease (kinky hair disease, copper metabolism)
  - Tangier's disease (lipoprotein metabolism)
  - Organic acid disorders
  - Glutaric aciduria tpyes I and II

Mitochondriopathies

- MELAS = Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes
  - Stroke-like (cortical-subcortical, rather parieto-occipital, not respecting arterial territories, may be alternating R/L)
  - Migraines, focal or generalized (myoclonic) seizures
  - Sometimes precipitated by febrile illness



MELAS, Tzoulis Stroke 2009

Mitochondriopathies : work-up

- Suspect if
  - Family history (maternal), young
  - Unexplained stroke-like episodes, migraines, seizures
  - Short stature, myopathy, neuropathy, cardiomyopathy/conduction defects, cataracts, retinitis pigmentosa, deafness, intestinaopathy, diabetes, hypogonadism, hypothyroidism, purpura, globus pallidus calcification
- Work-up
  - MRI, MR-spectroscopy (lactate), SPECT (parito-occipital)
  - Serum-lactate and pyruvate
  - CSF-lactate
  - ENMG, muscle biopsy
  - Genetic testing

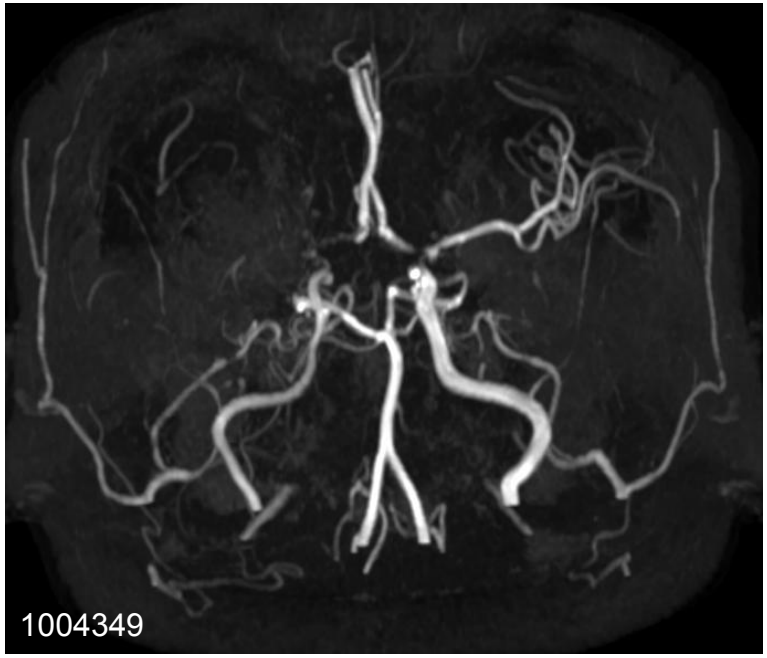
7. Other, non-inflammatory vasculopathies

(partially genetic ?)

- Moya-moya disease
- Cerebral amyloid angiopathies (CAA)
- Dissections with Eagle's syndrome
- Dolichoectasia and fusiform aneurysms
- Köhlmeier-Degos disease

Moya-moya disease

« Puff of smoke »



42 yo lady, R MCA TIAs

- 6 stages (Suzuki 1986)
- Slowly progressive narrowing or occlusion bilateral distal carotids, then other intracranial arteries
- Histo: Proliferative intima and media vasculopathy (intra- and extracranial)
- Radiological : collateral networks in basal ganglia
- Clinical:
  - *Children*: rather ischaemic strokes
  - *Adults*: more haemorrhagic strokes
  - Diffuse cerebral symptoms, focal symptoms with hyperventilation

Moya-Moya : Etiology

- Moya-Moya disease: idiopathic (genetic ?)
- Moya-Moya syndrome:
  - Temporal arteritis, SLE, PAN, other vasculitides, Kawasaki, Sjögren
  - Eosiniphilic granuloma
  - Atherosclerosis, smoking, renal artery stenosis
  - Sickle cell disease, thalassemia
  - Dissection, fibromuscular dysplasia, pseudoxanthoma elasticum, retinitis pigmentosa, neurofibromatosis, PCK
  - Tuberous sclerois, Turner, Down's, glycogen storage dis type I
  - Oral contraceptive use, prot C and S def, hyperhomocysteinaemia, type II plasminogen deficiency
  - Anaeorbic meningitis, Tbc-meningitis, pharyngitis, tonsillitis, leptospirosis, EBV, proprionibacterium acnes
  - Parasellar neoplasms, craniocerebral trauma, cranial irradiation, AVMs, saccular aneurysm

Adams/ Hachinski/ Norris: Ischemic Cerebrovascular Diseases 2001

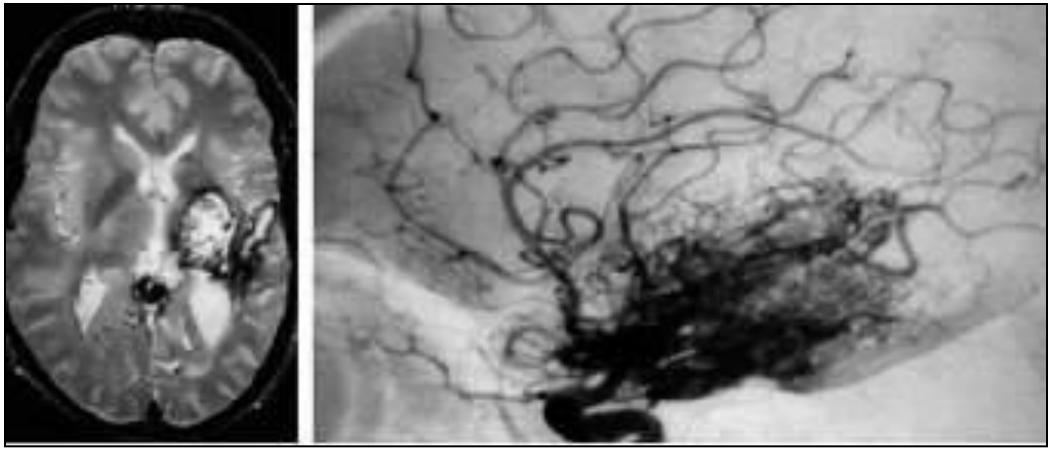
8. Intracerebral Haemorrhages

Rare causes

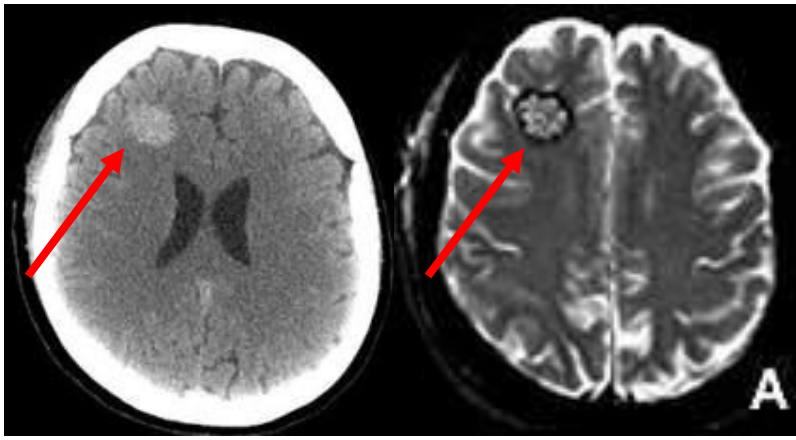
- **Vascular malformations**
  - Saccular aneurysms
  - Arterio-venous malformations
  - Cavernous angioma
  - Moya-Moya
- **Vasculitis** (Takayasu, others)
- **Very low cholesterol and vWF**
- **Hemorrhagic transformation (of an ischaemic stroke)**
- **Haemorrhage into tumor/metastasis**

- **Coagulopathies**
  - Blood disorders (platelets, hemophilia, leucemias)
  - DIC
- **Sinus vein thrombosis** with secondary haemorrhage
- **Substances**
  - Alcohol
  - Stimulanting drugs (cocaine, amphetamines, ...)
  - Sympathomimetics (phenylprop, ephedrine, ...)

Cerebral vascular malformations



Choi&Mohr, Lancet Neurol 2005



Elliot, Medlink Neurology

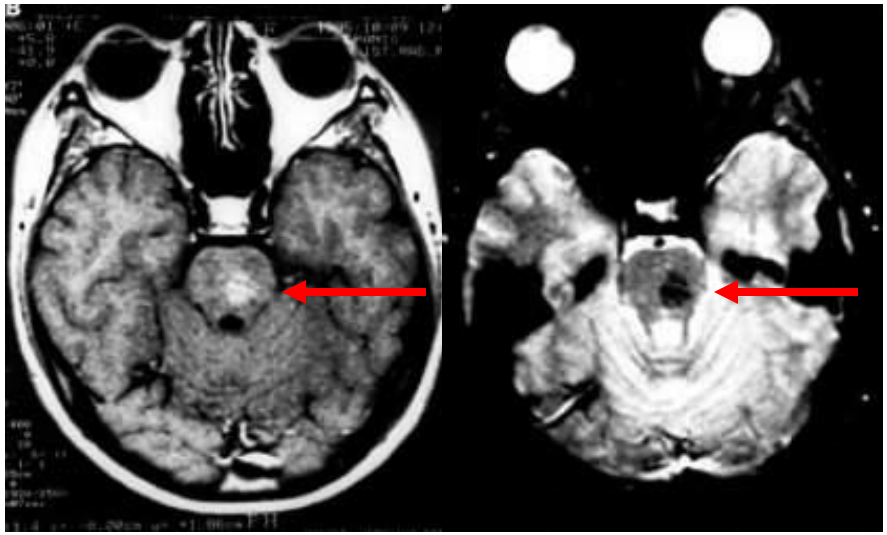
1. Arteriovenous Malformations

ICH, SAH, seizure, progressive focal symptoms, increased ICP, 1.5-3% yearly bleeding rate

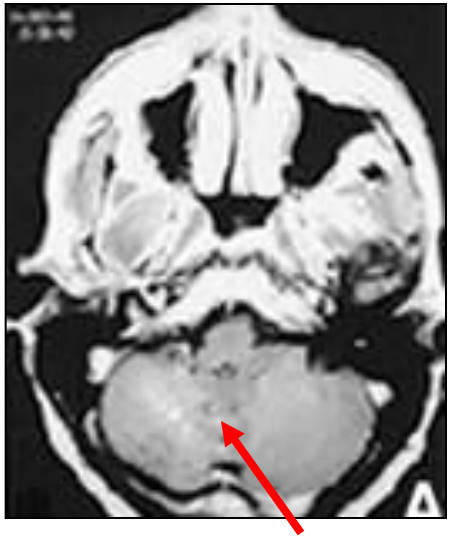
2. Cavernous angiomas

Mostly hemispheres
Sometimes familial (CCM1 etc.), 1% yearly bleeding rate

Cerebral vascular malformations



Scaclione JNNP 2001



Dayoub Medlink Neurology

3. Capillary telangiectasias

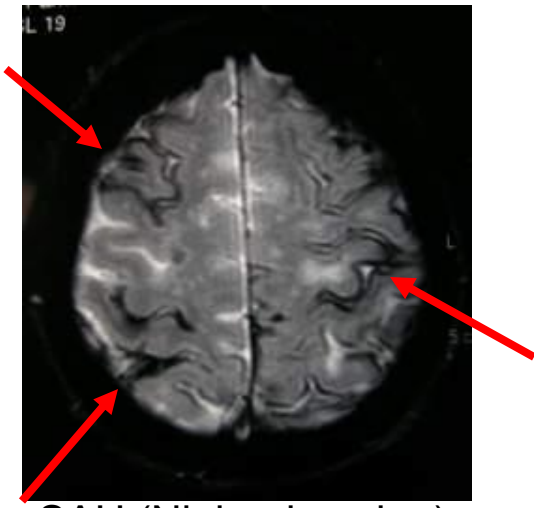
Mostly benign, brainstem/cerebellum

4. Venous angiomas

Rare ICH or seizures

ICH: further radiological work-up if ….

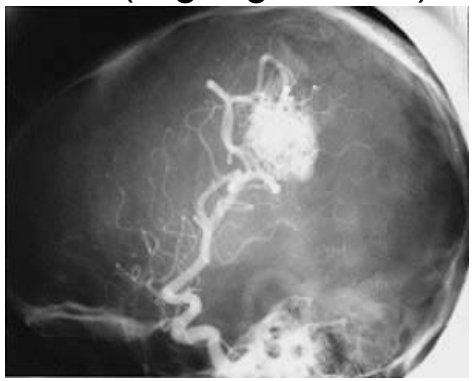
- Suspicion of
  - AVM, aneurysm
  - Vasculitis, tumor/metastasis
  - Sino-venous thrombosis
  - Amyloid angiopathy



SAH (Nighoghossian)

→ Angiography (CTA, MRA, or conventional) if suspicion of AVM, vasculitis, aneurysm, sino-venous thrombosis

→ MRI if suspicion of tumor or CAA



AVM

Modified from: Steiner/ESO CVD 2007§

M E R C I !

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