Joint Annual Meeting SNG|SSN
Basel, October 10th, 2012

Rare Causes of Stroke

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How rare are « rare » ischemic strokes?

N=2612 consecutive acute strokes 2003-2011

- Cardioembolic: 30%
- Atherosclerosis (≥50% stenosis): 13%
- «Likely athero»: 14%
- Lacunar: 10%
- Multiple: 5%
- Dissections: 4%
- PFO: 3%
- Missing data: 3%

Rare causes: 13%

Source: ASTRAL, Michel & Eskandari, unpublished
Rare stroke syndromes

Overview

1. Vasculitis
2. Hypercoagulability and oncologic
3. Drug related stroke
4. Migraine, vasospasms, pregnancy
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 vertebrais

CTA: A. Fumeaux
Duplex and temporal arteritis: arterial wall thickening

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

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 preceding 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, lymphadenopathy

DG Cogan 1945
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
- Rheumatoid polyarthritis
- Scleroderma
- Mixed connective tissue disease
- Dermatomyositis
- Ulcerative colitis/Crohn’s disease
Systemic lupus erythematoses

Mechanisms of stroke

- **Ischaemic**
  - Libman-Sachs endocarditis
  - Hypercoagulability: antiphospholipids, cytokines?
  - Cerebral vasculopathy/vasculitis

- **Haemorrhagic**

- **Cerebral venous thrombosis**
  - Hypercoagulability: antiphospholipids
Other vasculitides
secondary to systemic disease

- SLE
- Sjögren’s syndrome
- Behçet’s disease
- Sarcoidosis
- Rheumatoid polyarthritis

- Scleroderma, MCTD
- Dermatomyositis
- Ulcerative colitis/Crohn’s disease

- 11 criteria. Stroke, venous thrombosis
- Dry eyes/mouth, ANA+ (→ SSA/SSB+)
- Oral/genital ulcers 3x/y, eye, skin
- Respiratory problems, liver, skin, uveitis
- 4 or 7 criteria (morning stiffness >1h, ≥3 joints, hand joints, rheumatoid nodules)
- Skin, multiples autoimmune
- Myopathy, dermatitis (extensor-side of joints/eye-lids)
- 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 puncture:
  - 70 leukocytes (PMN)
Angio: Dr JB Zerlauth, CHUV
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: heterogeneous 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
    - \[rac{\text{IgG-CSF}}{\text{IgG-Serum}}\]
    - \[rac{\text{Albumine-CSF}}{\text{Albumine-Serum}}\]

- **Mechanisms of stroke** in syphilis:
  - 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

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

CTP 281 min.

IRM à 12 h

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
  - Increased 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
Antiphospholipid 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)

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 microangiopathy 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 pathological 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, elevated 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 anticoagulant (if negative: anti-beta-2-glycoprotein-I)
- Consider cancer search:
  - Rectal exam, stool occult blood
  - Chest XR/body scan, mammography
  - Fibrin monomeres
  - Urine proteinelectrophoresis
Strokes in cancer patients

Multiple potential mechanisms

→ Increased risk for
  ➢ Ischaemic strokes
  ➢ Haemorrhagic strokes
  ➢ Cerebral vein thrombosis, recurrent venous thrombophlebitis
    (Trouseau’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 stasis, surgery, chemotherapy, dehydration
  ➢ Rarely: tumor emboli, intravascular lymphoma

◆ Mechanisms for haemorrhage
  ➢ 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. treatment 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, phaeochromocytoma
- 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, pregnancy

- 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:

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

(Dr Borruat, Neuro-ophthalmology)

Arteriography

« 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
  - Occasionally 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

Olin Circulation 2011
Neurofibromatosis - 1

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

Morie & Michel, Arch Neurol 2011
66 yo lady: strokes, epistaxis, skin lesions

Mori & 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
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 arteriolar tortuosity, and leukoencephalopathy (COL4A1-mutation)
- **HANAC** = Hereditary Angiopathy with Nephropathy, Aneurysm and Cramps (COL4A1 -mutation, Plaisir NEJM 2007)
- Some cerebral amyloid angiopathies
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
- Hypercoagulabiliy, antiphospholipid 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
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-enhancing masses, renal insuff, proteinuria
- Chr.3p21, gene not identified

Fluorescein angiogram with dilated toruous telangiectatic vessels and capillary shunts
Jen 1997 Lippincott
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 types 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 »

- 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

42 yo lady, R MCA TIAs
Moya-Moya: Etiology

- **Moya-Moya disease**: idiopathic (genetic?)
- **Moya-Moya syndrome**:
  - Temporal arteritis, SLE, PAN, other vasculitides, Kawasaki, Sjögren
  - Eosinophilic granuloma
  - Atherosclerosis, smoking, renal artery stenosis
  - Sickle cell disease, thalassemia
  - Dissection, fibromuscular dysplasia, pseudoxanthoma elasticum, retinitis pigmentosa, neurofibromatosis, PCK
  - Tuberous sclerosis, Turner, Down's, glycogen storage dis type I
  - Oral contraceptive use, prot C and S def, hyperhomocysteinaemia, type II plasminogen deficiency
  - Anaerobic meningitis, Tbc-meningitis, pharyngitis, tonsillitis, leptospirosis, EBV, prionibacterium 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, ...)

Hanley Stroke 2005
Cerebral vascular malformations

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

Choi&Mohr, Lancet Neurol 2005
Elliot, 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

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

Modified from: Steiner/ESO CVD 2007§
M E R C I !

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