

Cerebral Vasculopathies

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FIBROMUSCULAR DYSPLASIA (FMD)

Fibrous dysplastic tissue (fibroplasia) + smooth muscle proliferation* → areas of **segmental arterial narrowing (nonatherosclerotic, noninflammatory)**.

*alternates with rings of medial thinning

- rare condition.
- affects *one ÷ all three layers in arterial walls* (most commonly – media).
- both extracranial and intracranial large arteries (esp. bilateral ICAs at level of C₂ vertebra rarely extending above skull base; vs. origin of vessels in atherosclerotic narrowing).
- **produces ischemia** (both by hemodynamic effects and by thromboembolism).
- frequent (20-50%) association with **aneurysms** (FMD is often found during SAH evaluation).
- may cause **arterial dissections**.

CLINICAL FEATURES

- commonly found in middle-aged women.
- most often **asymptomatic CAROTID BRUIT**.
- may present as **TIA / stroke** without any evident compromise of vascular lumen (possibly due to *functional constriction*).
- common involvement of renal arteries → **renovascular hypertension!** (**RENAL ARTERY BRUIT**).
- FMD may remain stable (good long-term prognosis), but form seen in renal arteries can progress in 35% patients.

DIAGNOSIS

- **arteriography** - multiple rings of **constricting fibromuscular bands** alternating with dilatation (“STRING-OF-BEADS” appearance).



TREATMENT

- stroke recurrence is quite low, even with no therapy.
- antiplatelets / anticoagulants, bypass surgery / surgical dilatation.

MOYAMOYA DISEASE (Basal Occlusive Disease with Telangiectasia)

- noninflammatory slowly progressive **bilateral occlusion of intracranial terminal ICA** (at bifurcation to ACA & MCA) → formation of **collateral network through basal penetrating (lenticulostriate) branches**.

- additional collaterals are transdural anastomoses (between cortical MCA branches and scalp arteries).
- **pathology** - endothelial hyperplasia and fibrosis (intimal thickening), abnormalities of internal elastic lamina in perforating arteries (due to greatly increased flow through these small vessels).

ETIOLOGY

- unknown.
- believed to be hereditary - **autosomal dominant with incomplete penetrance** (depends on age and genomic imprinting) - suspected gene locus - q25.3, on chromosome 17.
- moyamoya vessels (i.e. **MOYAMOYA SYNDROME**) are also found in:
 - 1) **sickle cell disease!!!**
 - 2) neurofibromatosis
 - 3) FMD
 - 4) radiotherapy (to sellar and parasellar tumors)
 - 5) young women who smoke cigarettes and take oral contraceptives.

EPIDEMIOLOGY

- rare condition (0.1 per 100,000 general population in Japan).
- although first described in young Asians, it is widespread.
- bimodal age INCIDENCE - 6 years and 4th decade.

CLINICAL FEATURES

Children < 15 years - **TIA*** (hemiparesis, headache, seizures, other focal deficits); commonly develop **infarctions**.

*often precipitated by physical exercise or hyperventilation.

Young adults - brain **hemorrhages** (thalamus, basal ganglia, deep white matter, occasionally SAH*).

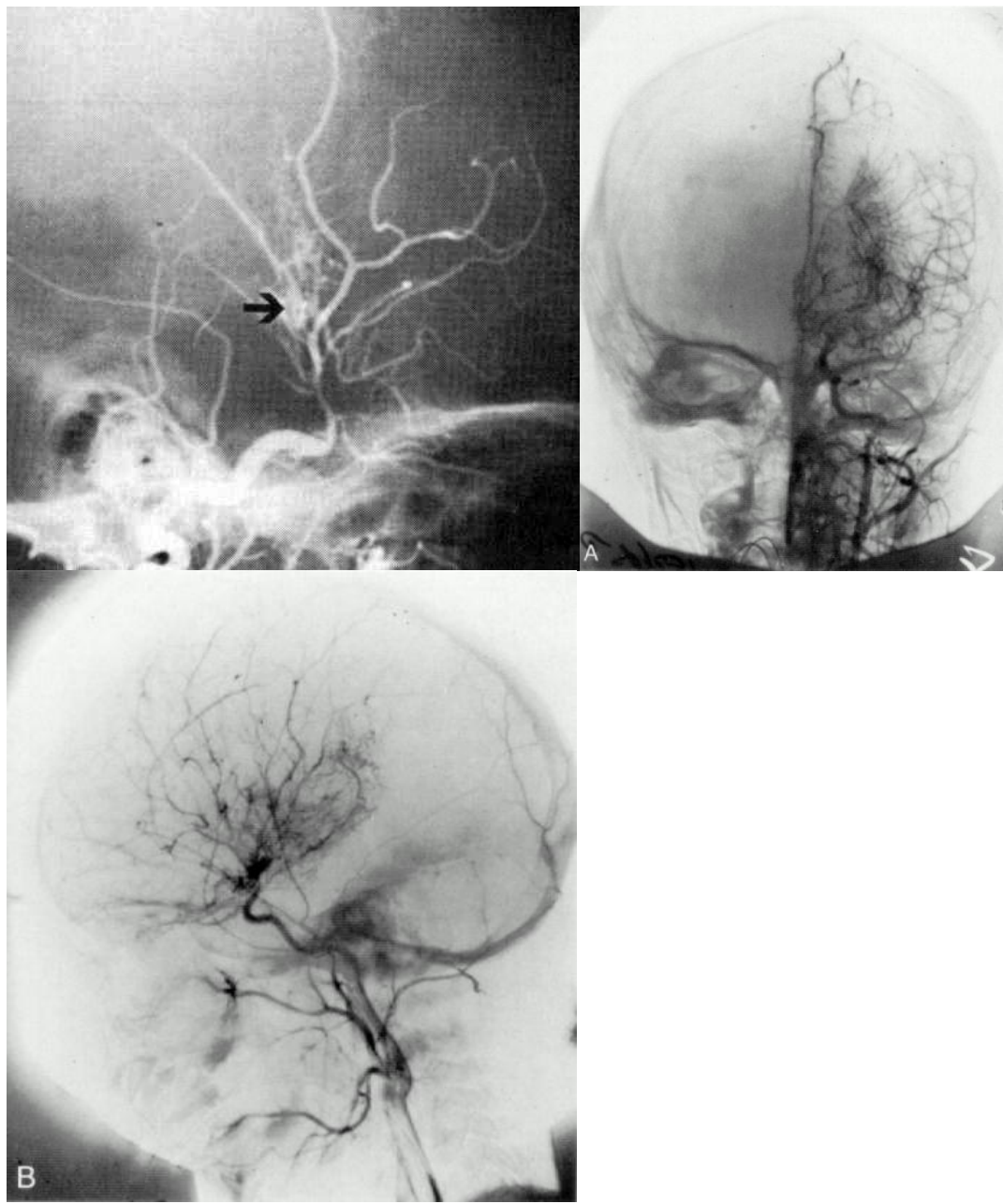
*rupture of transdural anastomotic channels

- some patients stabilize clinically (often after developed disabilities), but moyamoya is progressive disease (poor prognosis).

DIAGNOSIS

Angiography (standard method of diagnosis!):

- progressive occlusion of intracranial ICAs bilaterally; MCA and ACA branches are also frequently involved.
- collateral vessels appear as *cloud of smoke* (*moyamoya* – Jap. “puff of smoke”).



MRA - noninvasive alternative to angiography.

TREATMENT

- various *surgical revascularization* procedures:

- Direct**; because child arteries are small, it is difficult to create direct anastomosis of external-to-cerebral arteries (cut off vessel size \approx 1 mm).
- Indirect** - **encephaloduroarteriosynangiosis (EDAS)**
 - dura, omentum, or muscle is used to receive and transmit blood from external artery (e.g. superficial temporal artery).

CEREBRAL AUTOSOMAL DOMINANT ARTERIOPATHY with SUBCORTICAL INFARCTS and LEUKOENCEPHALOPATHY (CADASIL)

- mapped to chromosome 19q12 (large gene *Notch3*, that belongs to family of genes involved in specification of cell fate during development).
- **pathology** - media (of leptomeningeal and perforating arteries) is thickened by *eosinophilic granular material* (of unknown origin) within smooth muscle cells.
- **no hypertension or other cerebrovascular risk factors!**

CLINICAL FEATURES

Begins in middle adult life (mean – 45 yrs):

- **vascular presentation** - *recurrent subcortical ischemic events* (lacunar TIAs < lacunar strokes).
- **other symptoms** - progressive or stepwise *subcortical dementia* with pseudobulbar palsy, *migraine* with aura (30%), *depression*.

DIAGNOSIS

MRI (even before clinical onset): **multiple deep white matter infarctions** + extensive areas of **diffuse increased T2 signals** in subcortical white matter and basal ganglia.

TREATMENT

- no specific treatment is currently available.

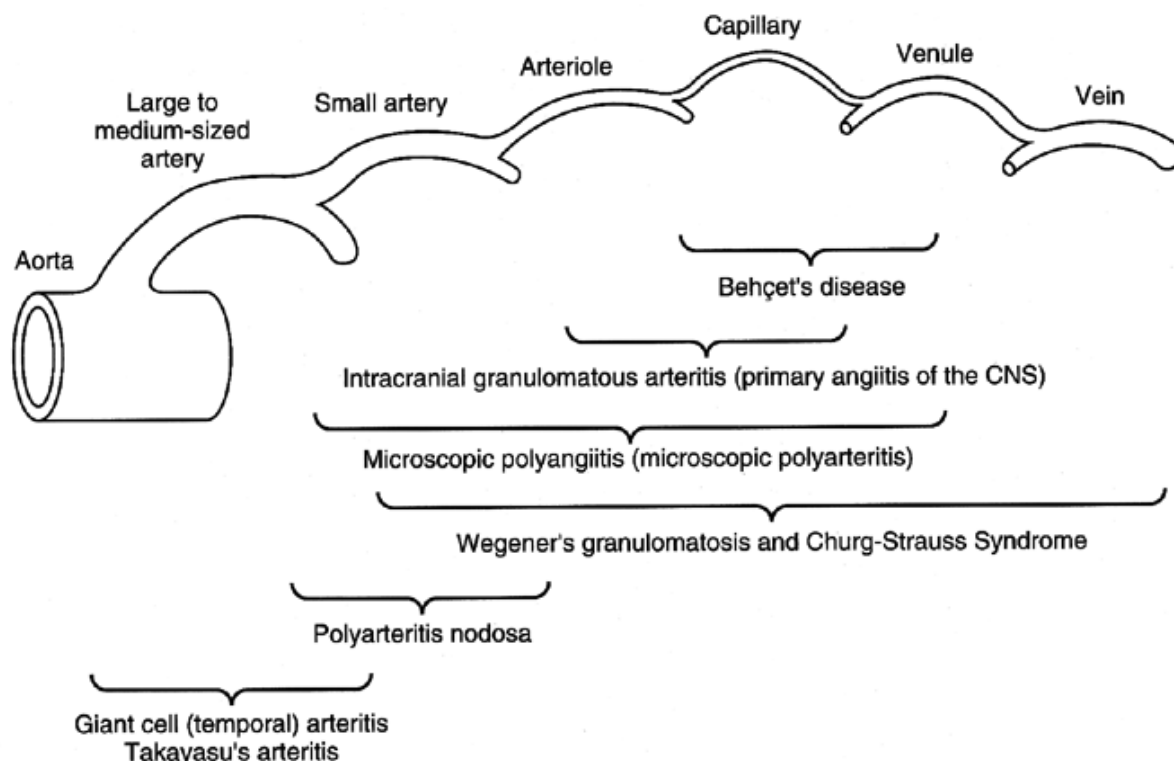
CEREBRAL VASCULITIS

SYSTEMIC ARTERITIDES

- heterogeneous group of inflammatory diseases:

1. Polyarteritis nodosa
2. Sjögren disease
3. SLE
4. Giant cell arteritis

Other causes of cerebral vasculitis – infection (e.g. septic emboli, meningovascular neurosyphilis), malignancy, radiotherapy, cocaine ingestion.



- all involve some **deposition** of humoral and cellular *immune complexes* and **infiltration** of *polymorphonuclear* and *mononuclear* cells in blood vessel walls (SEGMENTAL INFLAMMATION).

CLINICAL FEATURES

- cerebral arteritis becomes symptomatic after systemic (peripheral) manifestations have been present - **(multi)focal cerebral ischemia**:
 - acute** - platelet aggregation and/or clot formation
 - chronic** - through fibrinoid necrosis.
- cognitive disturbances, headache, seizures** (encephalopathy) - occur more frequently than *focal neurologic dysfunction*.
- frequently produce *polyneuropathies*.

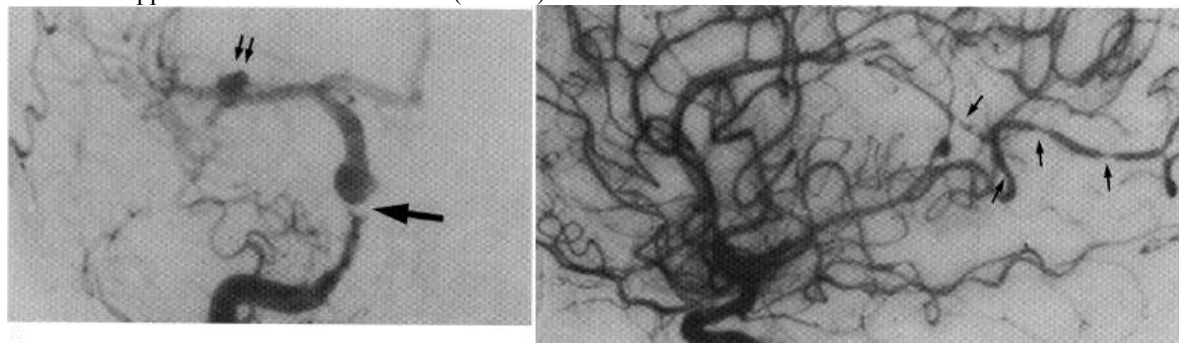
DIAGNOSIS

- mainly smaller parenchymal and leptomeningeal vessels - *high-resolution angiography* is far superior to MRA / CTA (but even angiograms may appear normal in 20-30% cases)
 - Features on angiography (nonspecific) - **stenoses, occlusion, thromboses, beaded appearance**
- brain / meningeal *biopsy* is necessary to make specific diagnosis! (segmental pathology – risk of sampling error)

Arteritis caused by septic cardiac emboli:

A. Carotid arteriogram - filling defect (*arrow*), many vessels are irregular and underfilled, MCA bears mycotic aneurysm (*double arrows*).

B. Beaded appearance of cortical arteries (*arrows*).



GRANULOMATOUS ANGIITIS of NERVOUS SYSTEM (GANS)

number of synonyms: PRIMARY ANGIITIS OF CNS, INTRACRANIAL GRANULOMATOUS ARTERITIS, NONINFECTIOUS GRANULOMATOUS ANGIITIS WITH PREDILECTION FOR CNS

ETIOPATHOLOGY

- absence of systemic disease!**
- small leptomeningeal arteries* are preferentially affected.
- no predilection for branching points of arteries (vs. polyarteritis nodosa).
- arterial wall **inflammatory infiltration** with *mononuclears* (monocytes/histiocytes, lymphocytes, and plasma cells); frequently (85%), granulomatous changes with *multinucleated giant cells* are seen; destruction of vessel wall.
- numerous small infarctions** ± large areas of ischemia, sometimes with superimposed hemorrhage.
- etiology is unknown (viral cause?); no evidence of immune complexes; no identifiable preexisting conditions; postpartum cases described.

CLINICAL FEATURES

- mean age 33-45 yrs. (range 3-74 yrs).
- no systemic symptoms! - clinical manifestations are restricted to brain!
- subacute or insidious; may fluctuate with periods of apparent remission.
- prognosis is guarded (better in postpartum cases; poor if untreated).

Multifocal brain disease with obtundation, severe headaches, and no discernible systemic cause

- Diffuse cerebral dysfunction** (progressive encephalopathy) - **headache** of gradual onset (most common presenting symptom!; often associated with nausea and vomiting), **mental obtundation** (may be preceded by *dementia*).
- Later, **focal cerebral signs** develop (e.g. cranial neuropathies, seizures, cerebellar dysfunction, cauda equina syndrome); strokes are found in 15% cases.
 - isolated cord involvement* has been noted in few patients.

DIFFERENTIAL DIAGNOSIS

- Wegener's granulomatosis** - pulmonary lesions.
- Giant cell (temporal) arteritis** - occurs in older population.
- Infections** (mycobacteria, fungi, meningovascular syphilis, hepatitis B, herpes ophthalmicus!).
- Drugs** (esp. stimulants)
- Noninflammatory vasculopathies** (fibromuscular dysplasia, moyamoya)
- Neoplastic meningitis**

DIAGNOSIS

ESR↑ (66%) ≈ 44 mm/hr (up to 116 mm/hr).

CSF (81%) - *chronic meningitis*: mixed or lymphocytic **pleocytosis** (up to 500), **protein**↑ (> 100 mg/dl in 45-75% cases, up to 825 mg/dl), normal glucose.

- serial LPs may show spontaneous fluctuations in pleocytosis and protein.

EEG (81%) - *diffuse slowing*; occasionally, focal slowing or sharp wave discharges.

CT – normal, low-density lesions, infarcts, gyriform enhancement, hematoma.

MRI - focal *infarctions in multiple vascular territories* (normal MRI is rare, but have been seen in some biopsy-proven cases).

Angiography (with high-resolution film magnification - changes in *small-caliber vessels*):

- "classic arteritis" (65%) - *alternating areas of stenosis and ectasia* ("sausaging" or "beading") in multiple vessels.

N.B. not completely specific (also seen in other vasculopathies)

- less specific abnormalities (19%)
- normal (13%)

Leptomeningeal & cortical biopsy

- indication:
 - 1) normal or atypical angiogram
 - 2) before highly toxic therapy
- focal nature - significant risk for *sampling error* (diagnostic sensitivity 74.4%).

TREATMENT

High dose (60-80 mg/day) **PREDNISONE** + **calcium channel blocker**.

- monitoring - angiography (± repeated biopsies).
- *good clinical response* → tapering in few months.
- *lack of response or recurrence* → add oral **CYCLOPHOSPHAMIDE** (1-2 mg/kg/d) for 6-12 months until all signs of disease have disappeared.

BIBLIOGRAPHY for ch. "Neurovascular Disorders" → follow this [LINK](#) >>