Sturge-Weber syndrome
(Encephalotrigeminal Angiomatosis)

PATOPHYSIOLOGY
- residual embryonal blood vessels with secondary effects on surrounding brain tissue.
  - normally, in 6th week vascular plexus develops around cephalic portion of neural tube, under ectoderm destined to become facial skin; vascular plexus regresses around 9th week of gestation.
  - failure of normal regression → angiomata.
  - neurologic dysfunction results from secondary effects:
    a) vascular steal around angiomata → hypoxia, ischemia
    b) venous occlusion, thrombosis, infarction.
  - secondary effects are manifested by recurrent seizures (even when short) → progressive dystrophic calcification*, gliosis, atrophy → neurologic deterioration, seizures!^

ATHOPHYSIOLOGY
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N.B. calcifications are located primarily in cerebral substance rather than in vessel walls.

TURGE SYNDROME
- congenital spodrome phacomatosis with capillary venous angiomas in leptomeninges, skin of face, eye.

PATHOLOGY, CLINICAL FEATURES
- All lesions (if unilateral) tend to be ipsilateral!

ETIOLOGY
- no recognizable genetic contribution; somatic mutations affecting:
  a) structure blood vessels (vessel circumference decreased, while vessel density increased)
  b) innervation of blood vessels (malformed vessels innervated only by noradrenergic, sympathetic fibers)
  c) expression of extracellular matrix (fibronectin) and vasoactive molecules (endothelin-1 expression in malformed vessels).

EPIDEMIOLOGY
- 1 per 50,000

PATHOLOGY, CLINICAL FEATURES
- No increased propensity for cancer!!

1. Leptomeningeval angiomata:
  - unilateral (65%) > bilateral (15%)
  - most common in parietal and occipital regions.
  - ipsilateral features - cerebral hemiatrophy, hemihypertrophy of skull and sinuses, enlarged choroid plexus, abnormal myelination.
  - cortical veins are either absent or replaced by few enlarged cortical veins.
  - neurologic manifestations:
    1) seizures (72-93%) - typically focal; may be intractable; 75% before age of 1 year, 95% begin before 5 years.
    2) focal deficits (esp. hemiparesis [25-56%], homonymous hemianopsia [44%]) - may be transient ("stroke-like episodes"), but otherwise slowly progressive.
    3) vascular headaches ("symptomatic migraine") (44-77%)
    4) developmental disorders (50-75%) (developmental delay, learning disorders, mental retardation) - more common when angiomata are bilateral.
  - N.B. major intracranial hemorrhage is rare!

2. Cutaneous angiomata ("port-wine stain")'s: nevus flammeus (87%) in skin of face.
  - N.B. most patients with facial port-wine stains do not have SWS!
  - N.B. absence of port-wine stain implies neither presence nor severity of intracranial leptomeningeval angiomatosis (only 8% of facial port-wine stains have this association)
  - typically in V1 and V2 distributions of CNS.
  - N.B. none is affected if port-wine stain does not involve V1 area!
  - unilateral (48-86%); ipsilateral to CNS lesion) > bilateral (14-51%).
  - presents at birth – suspicion of diagnosis in neonate!
  - can be progressive (light pink macule → dark red or purple nodular lesion).

Glaucoma (30-71%) → buphthalmos (hydrophthalmia) → blindness.
  - N.B. glaucoma typically occurs only when port-wine stain involves eyelids; if port-wine stain is unilateral, glaucoma is ipsilateral!
  - causes: mechanical angle obstruction, episcleral venous pressure↑, secretion↑ of aqueous fluid (by choroidal hemangioma or ciliary body).

may be present at birth but can develop at any age.

4. Eye hemangiomas – choroidal (40%), conjunctival, episcleral.

**ROACH SCALE CLASSIFICATION**

<table>
<thead>
<tr>
<th>Type I</th>
<th>- both facial and leptomeningeal angiomata; may have glaucoma.</th>
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<td>Type II</td>
<td>- facial angiomata alone (no CNS involvement); may have glaucoma.</td>
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<td>Type III</td>
<td>- isolated leptomeningeal angiomata; usually no glaucoma.</td>
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**DIAGNOSIS**

Structural versus functional mismatch (functional neuroimaging demonstrates greater area of involvement than structural neuroimaging) - especially important when considering epilepsy surgery!

Skull X-ray – pathognomonic: *tram-track* calcifications in gyri or pons pattern (late finding - usually in patients > 2 yrs) - paired parallel lines that follow cerebral convolutions.

N.B. calcification in ipsilateral* outer cortex rather than of blood vessels or white matter!

*ipsilateral to port wine stain

underlying ipsilateral cerebral atrophy → ipsilateral skull-table and orbital thickening, elevation of sphenoid wing and petrous ridge, enlarged ipsilateral paranasal sinuses and mastoid air cells.

"Tram-track" calcifications:

Smaller hemicranium on affected side:

Angiography – does not show angiomata (or early capillary blush)

- lack of superficial cortical veins → nonfilling of dural sinuses (with absence of cortical veins, venous drainage occurs via enlarged tortuous transcortical veins into deep venous system).

CT:

- "tram-track" calcifications under angiomata (in infants and even neonates)
- adjacent cortical atrophy
- Shrunken cerebral lobe with calcified cortex & enlarged draining transcortical draining veins.
- BBB breakdown (during seizures).

CT - left hemiatrophy of cerebral cortex and typical gyral calcification:

MRI:

- T2 – hyperintense leptomeningeal thickening and enhancement.
- gadolinium enhancement of angiomata (appears as enhancement of subarachnoid space, medium covering cortical gyri and filling sulci) – early diagnosis!

N.B. enhancement is difficult to assess on CT in presence of calcification!

- adjacent cortical atrophy, accelerated / delayed myelination around angiomata.
• enlarged ipsilateral choroid plexus (size correlates with angioma extent) & enlarged draining transcortical draining veins.
• progressive sinovenous occlusion → lack of superficial cortical veins (on MRV).

Contrast T1-MRI - right cerebral atrophy, enhancing right occipital cortex, enlarged right choroid plexus:

Contrast T1-MRI - intense pial enhancement and subjacent central atrophy:

SPECT: hyperperfusion (in infancy, before first seizures) → classic hypoperfusion of involved hemisphere (after 1 year of age, even in those without epilepsy).
• steal phenomenon (during seizures).

PET – hypometabolism.

EEG – marked voltage attenuation in region of angioma; background suppression (74%); polymorphic delta activity; epileptiform discharges in remainder of cortex (22%).

Biopsy – typically not performed.

TREATMENT

1. Seizure control improves neurologic outcome
   N.B. epilepsy surgery should not be delayed (ideally – during infancy)!
   controversy regarding optimal timing of surgery: early surgery might preempt cognitive deficits from chronic, intractable epilepsy vs. early surgery might subject some patients to surgery risks.
   • complete seizure control is achieved in 10-50% patients; refractory seizures occur in 11-83%.
   • epileptogenic region is located in cortex adjacent to angioma.
   • localize area of seizure onset preoperatively by video EEG, ECOG, functional neuroimaging (e.g. ischemic regions may act as epileptogenic foci that may not be detected by CT / MRI).
   1) Focal cortical resection – when epileptogenic region is smaller and more localized.
   2) Hemispherectomy (anatomical hemispherectomy or functional hemispherectomy or hemidecortication) – for extensive, unilateral epileptogenic region; hemispherectomy is more successful if done during infancy!
   3) Corpus callosotomy – for bilateral disease (intractable atomic or tonic seizures leading to secondary injury).
   4) Vagus nerve stimulation (VNS) – for those who are not candidates for other surgical procedures.

2. Prophylactic daily low-dose aspirin - for headaches, stroke-like events (may be result of progressive venous thrombosis).
   N.B. varicella and yearly influenza immunizations (varicella / influenza + aspirin → Reye syndrome)

3. Cosmetic laser therapy ASAP for port-wine stain (earlier treatment - fewer laser flashes needed to remove lesion).

4. IOP control

BIBLIOGRAPHY for ch. “Phakomatoses” → follow this LINK >>