Sturge-Weber syndrome (Encephalotrigeminal Angiomatosis)

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STURGE-WEBER SYNDROME - congenital SPORADIC phacomatosis with capillary venous ANGIOMAS in ***leptomeninges***, ***skin of face***, ***eye***.

PATHOPHYSIOLOGY

- ***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 angioma → hypoxia, ischemia
  b) venous occlusion, thrombosis, infarction.
- secondary effects are *aggravated by recurrent seizures* (even when short) → progressive dystrophic calcification*, gliosis, atrophy → neurologic deterioration, seizures↑.

> Although leptomeningeal angioma is static anatomic lesion, syndrome has progressive nature!

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

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

INCIDENCE - 1 per 50,000

PATHOLOGY, CLINICAL FEATURES

> All lesions (if unilateral) tend to be ipsilateral!

No increased propensity for cancer!!!

1. **Leptomeningeal angiomas**
   - **unilateral** (85%) > 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 ("strokelike 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 angiomas are bilateral.

     N.B. major intracranial hemorrhage is rare!

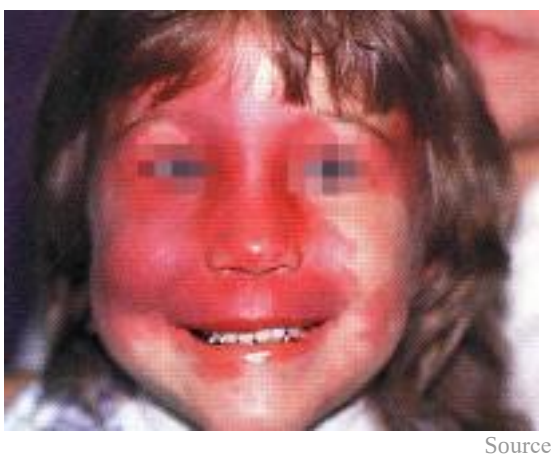
2. **Cutaneous angioma** ("port-wine stain" s. nevus flammeus) (87%) in skin of face.

   N.B. most patients with facial port-wine stains do not have SWS!

   N.B. presence of port-wine stain implies neither presence nor severity of intracranial leptomeningeal angiomatosis (only 8% of facial port-wine stains have this association)

   - typically in V_1 and V_2 distributions of CN5.

     CNS is not affected if port-wine stain does not involve V_1 area!
   - **unilateral** (49-86%; 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).



Source of picture: H. Richard Winn "Youmans Neurological Surgery", 6th ed. (2011); Saunders; ISBN-13: 978-1416053163 >>

3. **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

Type I - both *facial* and *leptomeningeal* angiomas; may have glaucoma.
Type II - *facial* angioma alone (no CNS involvement); may have glaucoma.
Type III - isolated *leptomeningeal* angiomas; usually no glaucoma.

DIAGNOSIS

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

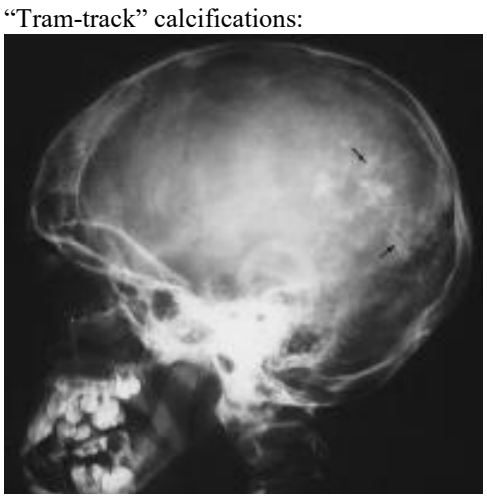
Skull X-ray – pathognomonic subcortical *"tram-track" calcifications* in gyriform pattern (late finding – usually in patients > 2 yrs) - paired parallel lines that follow cerebral convolutions.

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

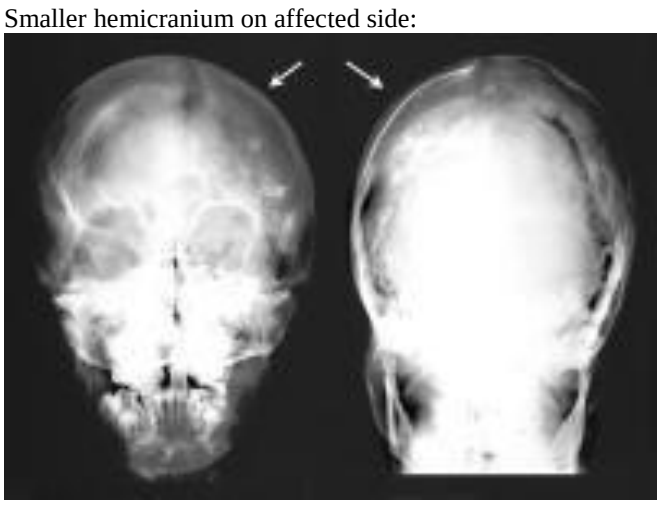
*ipsilateral to port wine stain

- 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:



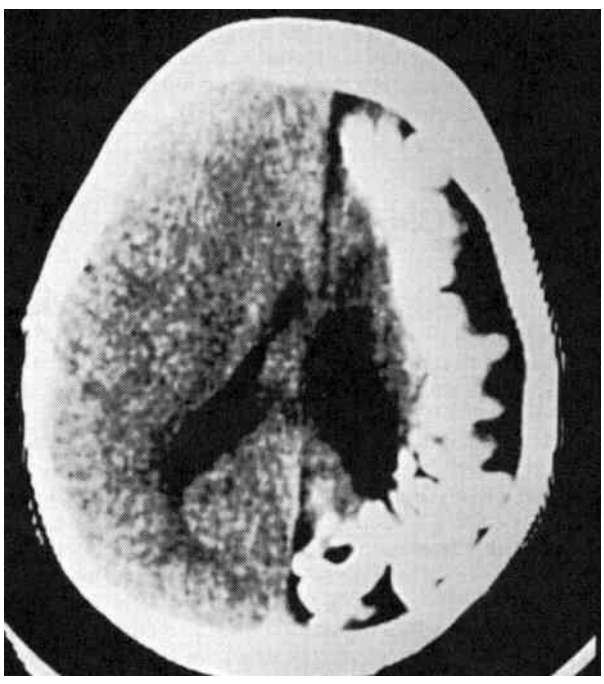
Angiography – does not show angioma! (or early capillary blush)

- 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).

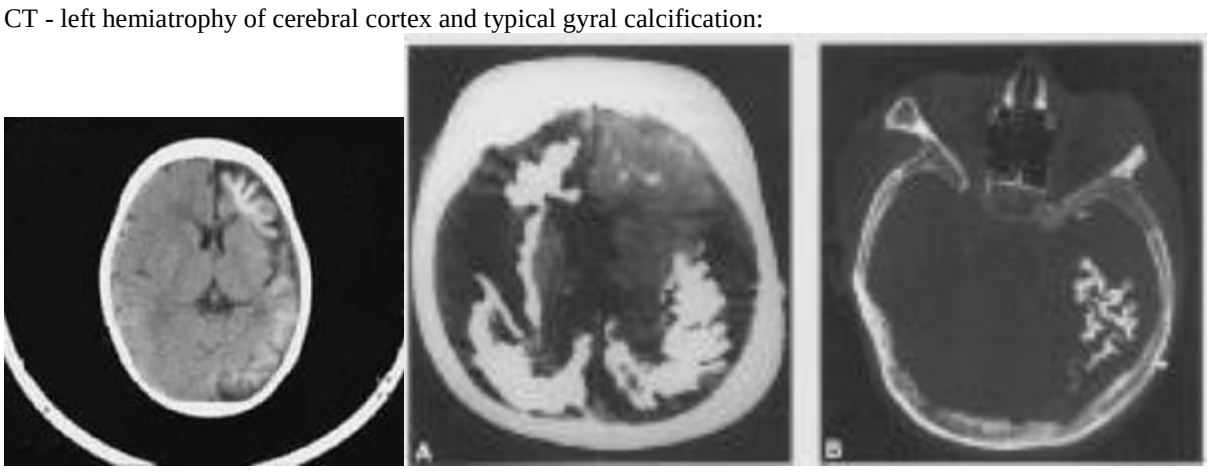
CT:

- *"tram-track" calcifications* under angioma (in infants and even neonates)
- adjacent cortical atrophy.

  Shrunken cerebral lobe with calcified cortex
- enlarged ipsilateral choroid plexus & enlarged draining transcortical draining veins.
- BBB breakdown (during seizures).



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



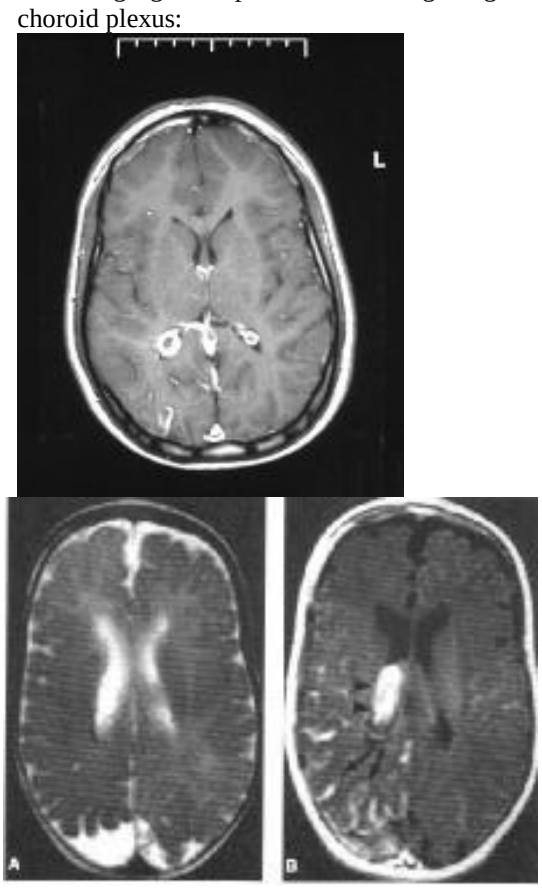
MRI:

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

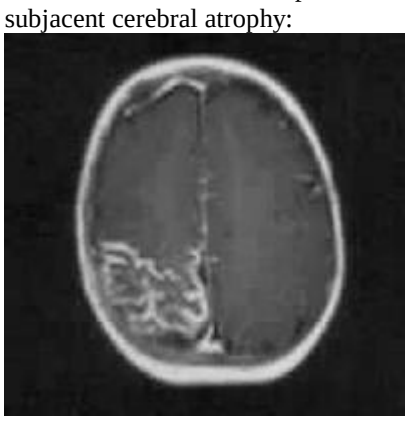
  N.B. enhancement is difficult to assess on CT in presence of calcification!
- adjacent **cortical atrophy**, accelerated / delayed myelination around angioma.

- 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 cerebral 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 atonic 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 >>