Epilepsy in vascular malformations

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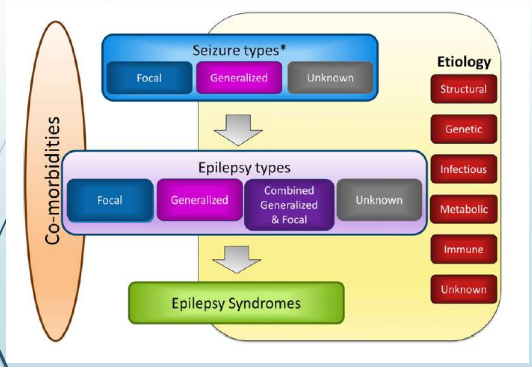
Framework for classification of the epilepsy



I.E. Scheffer et al.

Outlines

- Classification of vascular malformations
- Example of vascular lesion as a symptomatic cause of epilepsy
- Predictive factors for epilepsy in vascular malformation

Symptoms of vascular malformations of the brain

- Depend on the type, size and location of the malformation
- **Headache**
- **Seizure**
- **Bruits, Tinnitus**
- Bleeding from thin vessel walls (of vas malformation) → IICP (nausea, vomiting, headache, loss of consciousness) → **stroke**

2014 ISSVA Classification of Vascular Anomalies

Vascular Tumors	Vascular malformations			
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• Benign • Borderline or locally aggressive • Malignant	Capillary malformation	≥ 2 vascular malformations in 1 lesion		KTS SWS Proteus etc
	Lymphatic malformation			
	Venous malformation			
	Arteriovenous malformation			
	Arteriovenous fistula			

Pediatrics 2015;136.1

SWS: Encephalotrigeminal Angiomatosis

- Facial port-wine stain (PWS)
- Neurological malformations (ipsilateral leptomeningeal capillarovenous anomaly)
- Sometimes, ophthalmologic abnormalities (choroid vascular anomaly or congenital glaucoma)

Port-wine stain PWS: cutaneous capillary malformation

- Incidence of PWS = 0.3 % of newborns (3 per 1,000)
- Present at birth and persist throughout life
- Sex ratio = 1:1
- Unilateral and involves several dermatome of face and neck
- PWS associated with SWS : 1 per 20 to 50,000 live births.
- The overall risk of SWS associated with any kind of facial nevous vascular malformation is 8%

Pediatric Dermatology 2012;29:32-37
Pediatr Neurol 2016;64:52-58

Classification of SWS (Roach scale)

Type	Facial angioma	Leptomeningeal angioma	Glaucoma
I[a]	+	+	+/-
II	+	-	+/-
III	-	+	-/+[b]

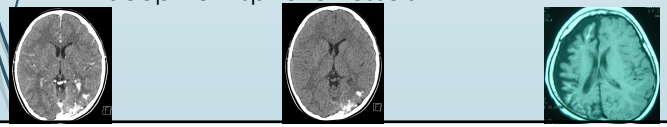
[a] Classic Sturge Weber syndrome
[b] Usually not present

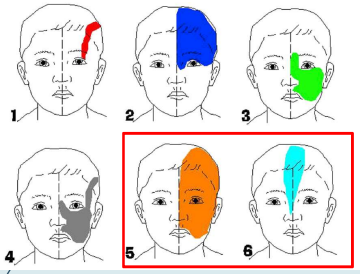
European Journal of Paediatric Neurology 2014;18:257-266
Pediatr Neurol 2016;64:52-58

Imaging finding in SWS

At least one of the following:

1. contrast-enhanced leptomeningeal vascular anomalies
2. choroid plexus enlargement
3. cortical calcifications
4. cerebral atrophy
5. absence of superficial venous drainage or enlarged deep hemispheric vessels





Location that increased risk of SWS

1. Midline crossing *(p<0.001)*
2. Temporal area *(p=0.04)*
3. Nose area *(p=0.005)*

J Am Acad Dermatol 2015;72:473-480

- Involving V1 area
- Associated with upper eyelid involvement
- Extension to the contralateral (40%)
- Homolateral proximal territories (V1 and V2 or V1,V2 and V3: 80%)

Pediatric Dermatology 2012;29:32-37

Can PWS predict SWS ?

Risk of seizure

- In patient with facial PWS in the absence of SWS = risk similar to general population
- In patient with facial PWS with SWS = frequency of seizure is higher (70-90%)

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Predictive factors for epilepsy in pediatric patient with SWS

- Bilateral port-wine (15%) stain is at higher risk of epilepsy
- Unilateral port-wine stain did not increase the risk of epilepsy regardless of its extent
- The presence of DVA(developmental venous anomalies increased the risk of developing epilepsy (p=0.03)

Pediatr Neurol 2016;64:52-58

Epilepsy in SWS (2)

- Prolonged seizures in SWS = worsen cognitive function
- Seizure may be medically intractable in 30-50% of SWS patients
- Seizure in SWS can be progressive as brain atrophy → refractory epilepsy
- FCD is also associated with SWS, drug resistant epilepsy

Frontiers in Neurology 2017
Epilepsia 2010;51:257-267

Epilepsy in SWS(1)

- Occurs in 72% of unilateral cerebral involvement
- Occurs ≥ 90% in bilateral involvement
- Often begin in the 1st year of life and generally by 2 years of age (later in life = 10%)
- Focal onset with secondary generalization
- Seizures commonly occur in clusters or as status epilepticus
- Increased susceptibility for fever induced seizures at any age

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Epilepsy outcome in SWS (3)

- Poor outcome : seizures in early life (< 6 mo)
  : extensive brain pathology
- Better outcome : late onset of seizure (late childhood)

Glaucoma

- PWS in V1 territory had 12.2% of congenital glaucoma
- PWS with V1 and V2 extension had 92% of glaucoma
- SWS with congenital glaucoma (30-40%) occurred in all cases with V1 territory involvement
- Glaucoma is not always ipsilateral to facial PWS

Pediatric Dermatology 2012;29:32-37

Counselling pt with PWS

- If the PWS spares V1= family can be reassured
- If PWS involves V1, ophthalmologic examination should always be performed
- Imaging should be added if PWS (V1) associated with at least one of the following:
  - ophthalmologic,
  - neurologic abnormalities,
  - extension of the stain to the upper eyelid,
  - V2 or V3 territory,
  - contralateral hemiface

Molecular basis of SWS

- Post zygotic somatic mosaic mutation of GNAQ
- Abnormal protein production
- Altered expression of angiogenesis factors: vascular endothelial growth factor, hypoxia-inducible factors alpha 1 and fibronectin
- Result = abnormal vessel development, cerebral calcification, neuronal loss, astrogliosis and cortical dysgenesis

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Cerebral Cavernous Malformations (CCMs) I

- Solitary or multiple nodular aggregated of thin-walled, round, closely packed veins → slow moving blood
- No normal brain tissue structures are enclosed in the lesion between the abnormal veins
- 0.5% of the general population
- Children < 20 years: 25-30%
- Adults 20-40 years: 60%
- Adults over 40 years: 10-15%

Cerebral Cavernous Malformations (CCMs)III

- Established risk factors of seizure
  : supratentorial lesion
  : cortical involvement
  : mesial temporal lesion
- Controversial risk factors of seizure
  : number of cevernomas
  : size of cavernomas
  : presence or absence of hemosiderin rim around lesion
- Treatment: if seizure → AED
  : uncontrolled sz with AED → Sx ?
  : if bleeding → ??

Epilepsia 2013;54:2025-2035

Cerebral Cavernous Malformations (CCMs) II

- **Two forms**: familial and sporadic
- Familial forms: e.g. *KRIT1(CCM1), CCM2, PDCD10(CCM3)*
- Familial forms: Maxican-American families
- Report of cavernoma in post radiation of brain tumor
- **Symptoms**:
  : asymptomatic- 70%
  : symptomatic: **seizure,** HA, stroke etc

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AVM (1)

- Commonest presentation: hemorrhage; 50%
  : epilepsy; 30%
- Small lesion (< 3 cm) presents with hemorrhage
- Large lesion presents with epilepsy
- Other manifestations: progressive neurological deficit

World Neurosurg 2015;84:645-652
Radiopedia.org

AVM(2)

- Overall annual rate of epilepsy: 1%
- Overall annual rate of hemorrhage: 3%
- Unruptured AVM has annual hemorrhage rate of 2.2%
- Ruptured AVM has annual hemorrhage rate of 4.5%
- Recurrent hemorrhage 6-18% in 1st year and declines to pre-hemorrhage rate over 5 years
- Mortality rate of 1% per year

AVM(3)

Seizure may related to

- Overt intracranial hemorrhage
- Hemosiderin deposition following recurrent micro hemorrhage
- Secondary to venous HT
- Ischemia

Predictor of seizure

- Unruptured, large, cortical-based AVM

World Neurosurg 2015;84:645-652

Treatment of AVM

- Conservative treatment
- Microsurgery
- Endovascular embolization
- Radiosurgery