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Sturge-Weber syndrome

Synonyms: fourth phacomatosis ('mother-spot') or encephalotrigeminal angiomatosis

What is Sturge-Weber syndrome?

Sturge-Weber syndrome (SWS) is a neurocutaneous disorder classically presenting with:

- A facial port-wine stain affecting the facial skin (in the distribution of some or all divisions of the trigeminal nerve).[1]
- Vascular eye abnormalities.
- An ipsilateral occipital leptomeningeal angioma.
- The leptomeningeal malformations lead to venous hypertension and subsequent hypoperfusion of the underlying cortex.

Children with SWS often develop progressive problems including glaucoma, seizures, stroke, and intellectual disability. A genetic mutation disrupting vascular development causes both the Sturge-Weber syndrome and port-wine stains.[2] [3] The severity and extent of presentation are thought to be determined by the developmental time point at which the mutation occurred.

Causes of Sturge-Weber syndrome (pathogenesis)

- SWS is a phacomatosis, ie one of a group of congenital and hereditary diseases characterised by the development of hamartomas in various tissues. Other examples include tuberous sclerosis and neurofibromatosis. SWS cases appear randomly without clear evidence of familial inheritance.

- It is caused by a somatic mosaic mutation in the GNAQ gene located on chromosome 9q21, affecting neural crest cells emanating from the forebrain region, and resulting in vascular abnormalities of the cutaneous forehead, cerebral cortex, and eye.[4]
- Neurological deterioration is thought to be secondary to impaired blood flow to the brain and is worsened by the presence of seizures.[3]
- Normally (ie where there is no SWS) a vascular plexus develops around the cephalic portion of the neural tube, under the area of ectoderm which is destined to become facial skin.
- This plexus develops in the sixth week and regresses around the ninth week of gestation.
- Residual vascular tissue in SWS forms the angiomata of the leptomeninges, face, and ipsilateral eye and also has secondary effects on surrounding brain tissue, including:
    - Hypoxia.
    - Ischaemia (caused by 'vascular steal phenomenon').
    - Venous occlusion, thrombosis and infarction.
- Recurrent seizures, status epilepticus, intractable seizures, and recurrent vascular events may aggravate cortical ischaemia.
- This leads to more calcification, gliosis, and atrophy, which in turn increase the chance of seizures and neurological deterioration.

Classification of Sturge-Weber syndrome

The cutaneous angioma is called a port-wine stain. These are usually seen in the ophthalmic and maxillary distributions of the trigeminal nerve, although it is now realised that development follows the embryological pattern of facial development, rather than the neurodevelopmental pattern.[1]

SWS is referred to as complete when both central nervous system and facial angiomas are present, and incomplete when only one area is affected. The Roach Scale has been traditionally used for classification, although a proposed prognostic system of classification suggests that the best predictor of adverse outcomes is a port wine stain involving the 'forehead area', stretching from the midline of the forehead to a line joining the outer canthus of the eye to the top of the ear, and including the upper eyelid. This involves all three divisions of the trigeminal nerve, and corresponds well to the embryonic vascular development of the face.[1]

Abnormal MRI is a better predictor of all clinical adverse outcome measures than port-wine stain distribution:[1]

Roach classification

Type I

- Both facial and leptomeningeal angiomas.
- May have glaucoma.

Type II

- Facial angioma alone.
- May have glaucoma.

Type III

- Isolated leptomeningeal angioma.
- Usually no glaucoma.

How common is Sturge-Weber syndrome? (Epidemiology)

- Sturge-Weber syndrome affects 1 in every 20,000 to 50,000 live births.[5]
- Males and females are equally affected.
- There is no racial predilection.

Symptoms of Sturge-Weber syndrome (presentation)[6]

Not all infants with facial naevi have SWS. Incidence of SWS has been reported to be 8-33% in those with a port-wine stain.

- The characteristic skin manifestation of Sturge-Weber syndrome is a port-wine birthmark, a congenital vascular malformation composed of malformed capillary-like vessels, which is present at birth as a typically unilateral, bilateral, or centrally located well-demarcated, pink to red patch on the face.[4]
- Although classical SWS encompasses a triad of clinical manifestations, incomplete forms are not uncommon and the presentation is variable.
- SWS always involves the upper face and eyelid, although it may also appear on the lower face, trunk and oropharyngeal mucosa.
- More than two thirds of patients with SWS present with a unilateral capillary malformation; approximately 25% exhibit the port-wine birthmark in the sensory territories of all three trigeminal branches of both sides.
- Macular lesions can be progressive.
- The ipsilateral eye to the naevus commonly shows buphthalmos and glaucoma.
- There may be macrocephaly and choroidal haemangiomata.

- Focal tonic-clonic seizures typically appear in the first year on the opposite side to the naevus.
    - The incidence of epilepsy in patients with SWS is 75-90%, and around 75% of these will appear in the first year of life.
    - The seizures may become generalised and evolve into other types, such as drop attacks, myoclonic or infantile spasms.
    - The seizures are often very frequent, and prolonged seizures may occur.
    - In many cases seizures are associated with slowly progressive hemiparesis.
    - The incidence is approximately 33%.
    - The severity of weakness is closely related to the severity of the seizures.
    - As the child grows the weakness may become more severe and permanent.
    - The seizures may be resistant to drug treatment.
- Developmental delay and general learning disability are related to the degree of neurological involvement. These conditions occur in 50-60% of patients and are more likely in patients with bilateral involvement.[1] [3] [6]
- Headaches occur secondary to vascular disease. The symptoms are similar to a migraine headache.

Diagnosis of Sturge-Weber syndrome

- The diagnosis of SWS is suspected when a newborn has a facial port-wine birthmark.
- Diagnosis of SWS is made if the cutaneous port-wine stain is associated with either brain or eye involvement.
- This risk is about 25% when the skin port-wine birthmark involves most of the ophthalmic distribution of the trigeminal nerve on the face.

- The risk increases to 33-50% with bilateral or more extensive facial port-wines stains.
- Some patients do not have facial port-wine stain but are diagnosed on the basis of clinical findings and leptomeningeal angiomata alone.

Investigations

Imaging[7]

The diagnostic algorithm should start with ultrasound, followed by non-invasive MRI or CT, and finally invasive investigations like angiographies when indicated.

MRI is the imaging modality of choice. The routine use of computed tomography (CT) scans in children with new-onset SWS-related seizures or new neurological symptoms is not recommended due to low yield and the potential risks of radiation exposure. If a CT scan is done, an MRI with and without contrast administration should follow to establish the diagnosis of SWS and provide detailed insight on brain vascular and parenchymal abnormalities.

Electroencephalogram (EEG)

- This is used for evaluation of seizures and for localisation of seizure activity in refractory seizures when epilepsy surgery is considered.
- Typical findings include reduced background activity, polymorphic delta activity and epileptiform features.

Management of Sturge-Weber syndrome

Treatment is symptomatic with antiepileptics, antiglaucoma drugs and laser therapy for port-wine stain. Low dose aspirin has been studied in the prevention of stroke like episodes and seizures. Surgical intervention is reserved for patients with refractory seizures and uncontrolled glaucoma.[8]

See also the article on Port-wine Stain.

Pharmacological treatments

Carbamazepine is an anticonvulsant effective for treatment of complex partial seizures:

- The major mechanism of action is reduction of sustained high-frequency repetitive neural firing.
- The chance of achieving seizure control with medical therapy in SWS varies. There is a wide range of reported seizure control in studies, with no overall consensus.
- The age of seizure onset may be a prognostic sign for ultimate seizure control. Early onset is associated with refractory seizures and developmental delay.

Surgical treatments

- Pulsed dye laser (PDL) treatment is used for port-wine stain:[9]
    - This laser treatment is particularly effective in improving facial port-wine stains in infants ≤6 months of age.[10]
    - This is often recommended for lesions near the eyes or orifices, or if the lesions bleed, ulcerate or become infected.
    - Significant re-darkening of port-wine stains has been noted at 10-year follow-up.[11]
    - External laser treatment of vascular abnormalities may not be effective if they are deep, because the laser beam does not penetrate far beneath the skin.[12]
    - Intralesional photocoagulation is a laser treatment that involves inserting a laser fibre into the lesion to deliver the light deep within it.[13]
- Combined use of PDL therapy and topical imiquimod may produce superior results to PDL alone.[14]

- Surgical options are available for focal seizures refractory to medical treatment: [13]

    - Surgical procedures include focal cortical resection, hemispherectomy, corpus callosotomy and, recently, vagal nerve stimulation (VNS).
    - Criteria for medical intractability should be fulfilled before considering surgery.

Prognosis [15]

Although, apparently neurologically normal in the first year of life, over half of cases are found to have severe learning disability in later childhood. This is in part due to prolonged generalised seizures and use of anticonvulsants, but abnormalities of vascular supply and 'vascular steal syndromes' may also play a significant role in producing a degree of cortical atrophy.

Although it is possible for the birthmark, and the associated atrophy in the cerebral cortex, to be present without symptoms, most infants develop convulsive seizures during their first year of life. There is a greater likelihood of intellectual impairment when seizures start before the age of 2 and are resistant to treatment.

As might be expected, studies have found that cortical volume analysis (representing cortical atrophy) on MRI correlates well with impairment and prognosis.

Dr Mary Lowth is an author or the original author of this leaflet.

Further reading

- Sturge-Weber UK
- Singh AK, Keenaghan M; Sturge-Weber Syndrome. StatPearls, Jan 2023.
- Sturge–Weber syndrome; DermNet. Jan 2020.
- Port-wine stain; Primary Care Dermatology Society. June 2022.

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