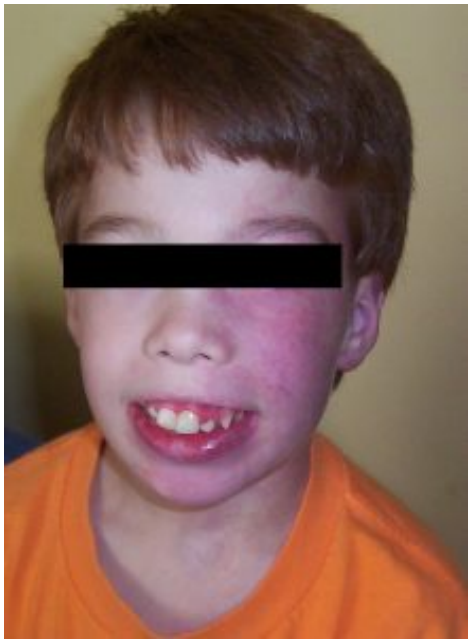
COURSE 10: DIAGNOSIS AND MANAGEMENT OF STURGE-WEBER SYNDROME

Dr. Anne Comi

Introduction: Diagnosis and management of Sturge-Weber syndrome (SWS)



This module has been designed to address the definition, cause, and diagnosis of Sturge-Weber syndrome, as well as the treatment of the syndrome's neurologic aspects.

Sturge-Weber syndrome is abnormal capillary venous blood vessels in the brain, skin, and eye. It is a vascular malformation and not a hemangioma.

SWS is caused by a somatic mosaic mutation in GNAQ gene. SWS occurs sporadically. About 1 in 20-50,000 children are born with SWS; it affects both boys and girls of every race and ethnic background.

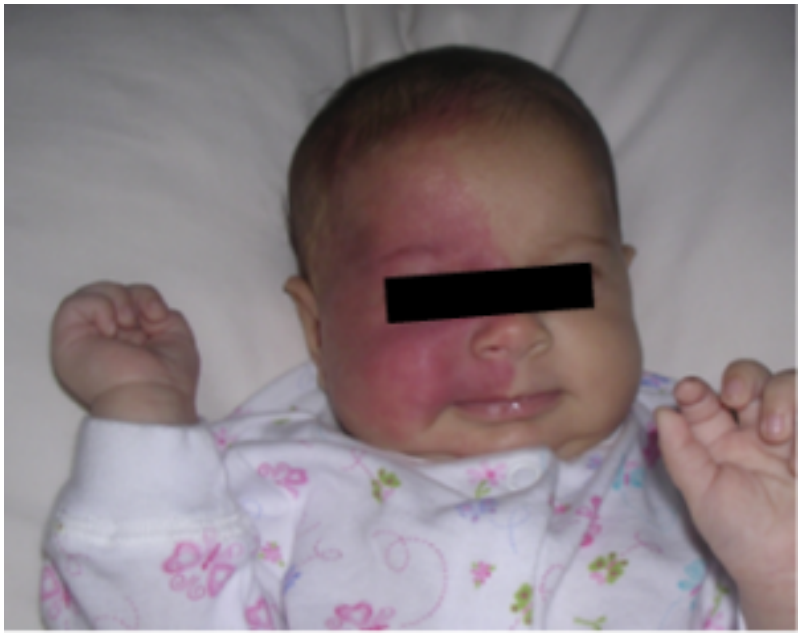
Brain involvement is diagnosed on neuroimaging. Neurologic symptoms include seizures, strokes, migraines, hemiparesis, and visual field deficits. Treatment may include the aggressive use of anticonvulsants and low-dose aspirin. The Atkins or ketogenic diets are also helpful. The use of low-dose aspirin is not universally agreed upon, but is increasingly used. Surgery is an option for patients refractory to medical management.

Objectives

Upon successful completion of this activity, participants should be able to:

- Identify the main clinical features of Sturge-Weber syndrome
- Describe the neuroimaging approaches to the diagnosis of Sturge-Weber syndrome
- Define the underlying cause of Sturge-Weber Syndrome and isolated port wine birthmarks
- List the neurologic symptoms of Sturge-Weber syndrome
- Explain the available treatments for Sturge-Weber syndrome

Facial port wine birthmark



- Port wine birthmark present from birth; it is a capillary malformation, *not* a hemangioma.
- A birthmark on the forehead or upper eyelid suggests a risk of Sturge-Weber syndrome with brain or eye involvement.
- A port wine birthmark frequently fades some after birth, but does not resolve.
- An infant with a port wine birthmark on the upper face has a 20-50% risk of SWS brain and/or eye involvement.
- Treated with laser, although recent research with mTOR inhibitors suggests that a combination of topical mTOR inhibitor with laser may be more effective.

Eye involvement in Sturge-Weber syndrome

Abnormal blood vessels in the eye and abnormally formed drainage structures of the eye can result in glaucoma (increased eye pressure) and vision loss.

Refer to pediatric ophthalmologist as soon as possible after birth. Patients should be closely monitored by an ophthalmologist after initial evaluation.

The peak periods for glaucoma are infancy and young adulthood. Glaucoma:

- Is treated with eye drops and surgery.
- Can be difficult to control and lead to optic atrophy or retinal detachment and blindness.

There is no evidence that early laser treatment for the skin impacts the eye. Eye shields are used during laser treatment to prevent ocular damage.

Neurologic involvement in Sturge-Weber syndrome

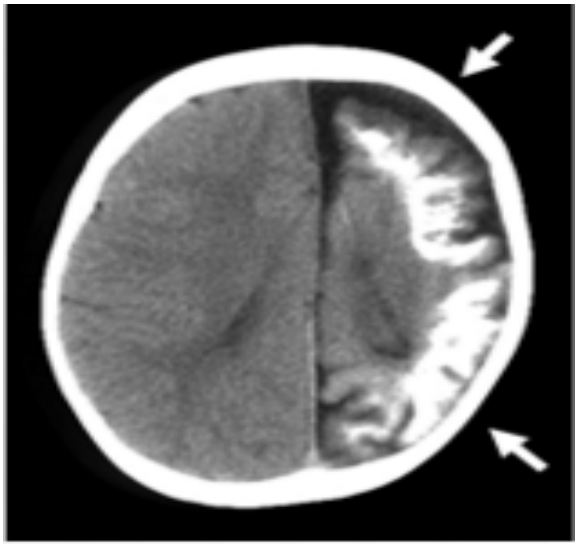
- Pre-symptomatic infants are often normal. Seizures are the most common presentation of
- Sturge-Weber syndrome. Strokes and stroke-like episodes are common, as are focal neurological episodes.
- Older patients frequently complain of headaches, migraines, and complicated migraines.
- 85% of patients have unilateral brain involvement.
- Intellectual disability occurs in 30-50% of patients.
- Psychological impairments, such as attention, mood, and behavior problems, are common.

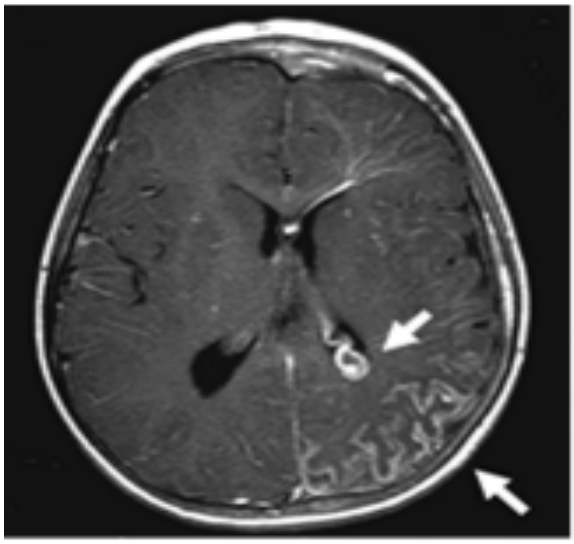
Diagnosing brain involvement

In order to diagnose Sturge-Weber syndrome, an MRI of the brain (with and without contrast) is required. The MRI will demonstrate the:

- Leptomeningeal enhancement
- Choroid plexus glomus
- Atrophy
- CT of brain best shows cortical and subcortical calcifications

Other useful MRI sequences are: MRA/MRV, SWI (susceptibility weighted imaging), perfusion imaging, and post-contrast flair-increase sensitivity to exclude AVM. Serial MRIs are not warranted in the absence of a negative initial MRI and no neurologic symptoms.



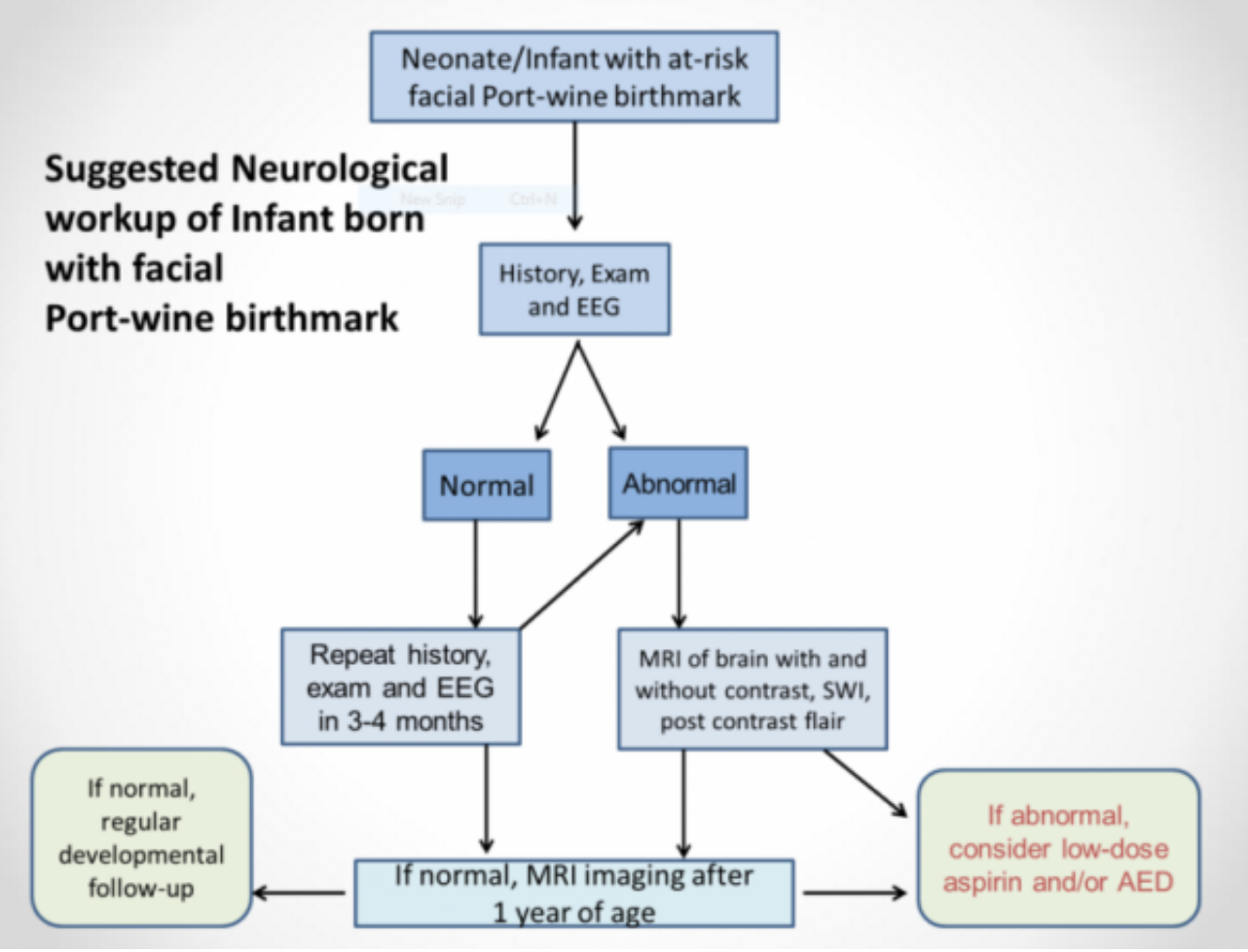


Variant of SWS without port wine birthmark

- Roughly 10% of patients do not have the birthmark
- They do not have a high risk of eye involvement
- Tends to present later
- Tends to spare the occipital lobe
- Better prognosis
- Remember to give an MRI with and without contrast in order to diagnose

Suggested neurological workup

An infant with a facial port wine birthmark should have a history, exam, and EEG. If these are normal, they can be repeated in 3-4 months. If again normal, an MRI (with and without contrast) is needed after one year of age. If the MRI (with and without contrast) is normal, then the child can have normal pediatric follow-up. If the exam, history, or EEG are concerning, then an MRI should be done. If this imaging results in the diagnosis of Sturge-Weber syndrome brain involvement, then treatment should be considered.



Sturge-Weber syndrome: pathogenesis

- SWS is not inherited from a parent.
- SWS cannot be passed on to an affected individual's child. Families do not have to be concerned about having another child with SWS.
- Testing the blood in most cases won't find the mutation.
- Testing the mutation in the affected skin of a baby won't diagnose brain involvement.

Seizure management

Rectal diazepam is provided for acute seizure management starting at 3 months of age. Start seizure medicine after first focal seizure.
Emergency room care:

- Loading with lorazepam, leviteracitam, or phosphenytoin and start chronic anticonvulsant such as oxcarbazepine or leviteracitam.
- IV fluid bolus even if the patient does not appear clinically dehydrated.

Monitor weight gain every few months and increase medicine to keep mg/kg dose the same.
Low-dose aspirin, 3-5 mg/kg/day, is frequently used.
Atkins or ketogenic diet safe and effective. Fluid restriction is not recommended.

Headache management

Headaches are common in Sturge-Weber syndrome. A mainstay of migraine treatment is trigger removal and the use of preventative medications (Kossoff 2005).

- Inadequate sleep is a common trigger.
- Use medications like topiramate, lamotrigine, or divalproex sodium; each prevents both seizures and migraines.
- Abortive treatment with ibuprofen is often effective.
- Hydration is important.
- Triptans can be safely used and may be effective.

Surgery for SWS brain involvement

- Hemispherectomy is better than focal resections for stopping seizures but has more risks. Need for VP shunt not uncommon with anatomical hemispherectomy. Wait until after a year of age, if possible, to reduce risk.
- Vagal nerve stimulator is an option for individuals who are not a candidate for resection.
- Medically refractory seizures are the main indication for neurosurgery. Progressive developmental delay is a controversial indication.
- Some studies suggest that early treatment (<2 years) may improve outcome; others suggest that this is not the case.

COURSE 10 QUIZ

1. Child 2 is a 10 year-old female, previously healthy and developmentally normal, although she receives extra services in school. She has no dysmorphic features and no birthmarks. She is brought to the emergency room following a 15-minute focal seizure with impaired consciousness during a sleepover at a friend's house. After the seizure was aborted with ativan, weakness of right side which was involved in the seizure was noted and persisted for several days. A patient with isolated Sturge-Weber syndrome brain involvement is NOT at high risk for:

A. Stroke-like episodes
B. Seizures
C. Migraines
D. Glaucoma

2. Child 1 is a 9 month-old male born with a right-sided facial port-wine birthmark on his forehead and both the upper and lower eye lids. He was diagnosed with glaucoma at 6 months of age and was started on two different eye drops to decrease the pressure. He presents to the ER with a history of left hand and foot twitching, and eyes deviated to the left for over 5 minutes. Diastat was given by the parents and phosphenytoin was administered in the ER. The most common presentation of Sturge-Weber syndrome brain involvement is:

A. Stroke-like episodes
B. Migraines
C. Seizures
D. Intra-cranial hemorrhage

3. Child 2 is a 10 year-old female, previously healthy and developmentally normal, although she receives extra services in school. She has no dysmorphic features and no birthmarks. She is brought to the emergency room following a 15-minute focal seizure with impaired consciousness during a sleepover at a friend's house. After the seizure was aborted with ativan, weakness of right side which was involved in the seizure was noted and persisted for several days. Frequent migraines in patients with Sturge-Weber syndrome brain involvement are best treated with:

A. Trigger reduction and use of migraine preventative medications that are also seizure preventative medications.
B. Narcotic pain medications.
C. Seizure medications.
D. CT scan of the brain.

4. Child 1 is a 9 month-old male born with a right-sided facial port-wine birthmark on his forehead and both the upper and lower eye lids. He was diagnosed with glaucoma at 6 months of age and was started on two different eye drops to decrease the pressure. He presents to the ER with a history of left hand and foot twitching, with eyes deviated to the left for over 5 minutes. Diastat was given by the parents and phosphenytoin was administered in the ER. Most patients with Sturge-Weber syndrome have:

A. Neither side of the brain involved with the vascular malformation.
B. Both sides of the brain involved with the vascular malformation.
C. One side of the brain involved with the vascular malformation.
D. It is unknown whether most patients with SWS have one or both sides of the brain involved.

5. Child 2 is a 10 year-old female, previously healthy and developmentally normal, although receiving extra services in school. She has no dysmorphic features and no birthmarks. She is brought to the emergency room following a 15-minute focal seizure with impaired consciousness during a sleepover at a friend's house. After the seizure was aborted with ativan, weakness of right side which was involved in the seizure was noted and persisted for several days. This child, who does not have a port wine birthmark, but presents with new onset focal seizures should have the following done to exclude Sturge-Weber syndrome:

A. Genetic testing.
B. A neurologic exam.
C. CT scan of the brain.
D. MRI of the brain with and without contrast.

6. Child 1 is a 9 month-old male born with a right-sided facial port-wine birthmark on his forehead and both the upper and lower eye lids. He was diagnosed with glaucoma at 6 months of age and was started on two different eye drops to decrease the pressure. He presents to the ER with a history of left hand and foot twitching, with eyes deviated to the left for over 5 minutes. Diastat was given by the parents and phosphenytoin was administered in the ER. Sturge-Weber syndrome brain involvement in this infant is diagnosed with:

A. MRI of the brain with and without contrast, SWI, and post-contrast flair imaging.
B. Head CT of the brain showing calcifications.
C. Sequencing blood sample from the patient for the mutation in GNAQ.
D. Sequencing DNA from a skin tissue biopsy for the mutation in GNAQ.

7. Child 1 is a 9 month-old male born with a right-sided facial port-wine birthmark on his forehead and both the upper and lower eye lids. He was diagnosed with glaucoma at 6 months of age and was started on two different eye drops to decrease the pressure. He presents to the ER with a history of left hand and foot twitching, with eyes deviated to the left for over 5 minutes. Diastat was given by the parents and phosphenytoin was administered in the ER. In this child with Sturge-Weber syndrome brain involvement, an anticonvulsant should be started:

A. When the birthmark is diagnosed as a facial port-wine birthmark putting the child at risk for Sturge-Weber syndrome brain involvement.
B. After the first focal seizure occurs.
C. After repeated seizures occur.
D. At birth.

8. Child 2 is a 10 year-old female, previously healthy and developmentally normal, although she receives extra services in school. She has no dysmorphic features and no birthmarks. She is brought to the emergency room following a 15-minute focal seizure with impaired consciousness during a sleepover at a friend's house. After the seizure was aborted with ativan, weakness of right side which was involved in the seizure was noted and persisted for several days. Aggressive treatment of seizures in Sturge-Weber syndrome includes:

A. Emergency room management of all seizures.
B. Use of multiple seizure medications in all patients with Sturge-Weber syndrome.
C. Increasing anticonvulsant dose for weight gain to keep the mg/kg/day dose the same in young children.

9. Child 2 is a 10 year-old female, previously healthy and developmentally normal, although she receives extra services in school. She has no dysmorphic features and no birthmarks. She is brought to the emergency room following a 15-minute focal seizure with impaired consciousness during a sleepover at a friend's house. After the seizure was aborted with ativan, weakness of right side which was involved in the seizure was noted and persisted for several days. The patient's seizures have become refractory to multiple anticonvulsants and to low-dose aspirin. Brain involvement is bilateral. Other options for treatment include:

A. Implanted cortical device for seizure control.
B. High protein diet.
C. Vagal nerve stimulator.
D. None of the above.

10. Child 1 is a 9 month-old male born with a right-sided facial port-wine birthmark on his forehead and both the upper and lower eye lids. He was diagnosed with glaucoma at 6 months of age and was started on two different eye drops to decrease the pressure. He presents to the ER with a history of left hand and foot twitching, with eyes deviated to the left for over 5 minutes. Diastat was given by the parents and phosphenytoin was administered in the ER. Sturge-Weber syndrome is caused by a somatic mutation in the gene GNAQ. This means that which of the following statements are true:

A. The mutation occurs at conception.
B. Identical twins exist where one has Sturge-Weber syndrome and the other does not.
C. The mutation is inherited.
D. The mutation is found in the blood.

AUTHOR
PROFILES

Anne M. Comi M.D., Director, Hunter Nelson Sturge-Weber Center

Dr. Anne M. Comi is an Associate Professor of Neurology and Pediatrics at the Johns Hopkins School of Medicine and at the Kennedy Krieger Insitute. She directs the Hunter Nelson Sturge-Weber Center at the Kennedy Krieger Institute. She oversees both laboratory and clinical research into the basis of, diagnosis, and treatment of Sturge-Weber syndrome.

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COURSE 10 QUIZ ANSWER KEY

1. D
2. C
3. A
4. C
5. D
6. A
7. B
8. C
9. C
10. B