Sturge-Weber Syndrome

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Sturge-Weber syndrome is a sporadic neurocutaneous disease characterized by facial port-wine stain, ocular abnormalities (glaucoma and choroidal hemangioma) and leptomeningeal angioma. Although the precise pathogenesis is unknown, available data regarding genetics, embryogenesis, and pathologic features are briefly reviewed. Clinical features vary from mild incomplete forms to full-blown disease with facial stain, seizures, and glaucoma. Frequencies of associated complications are reviewed. To plan treatment and further follow-up, diagnosis of glaucoma and intracranial involvement, even if asymptomatic, is fundamental in children at risk. Early neuroimaging features are important to recognize. Management of patients with Sturge-Weber syndrome is focused on treating associated neurologic and ocular abnormalities.

STURGE-WEBER SYNDROME (SWS) (OMIM #185300) or encephalotrigeminal angiomatosis is a sporadic neurocutaneous disorder characterized by a facial capillary malformation, ipsilateral leptomeningeal angioma and vascular eye abnormalities. However, many incomplete forms, lacking one feature of this triad, exist. The clinical features of this syndrome were first described by Sturge in 1879, and Parkes Weber described the cortical calcifications on X-rays in 1922.[1,2] The facial capillary malformation in SWS has often been referred to as facial port-wine stain (PWS), due to the characteristic dark red color similar to the Portuguese liquor. The facial PWS typically involves the forehead and upper eyelid, in a distribution that resembles the area innervated by the first branch (ophthalmic branch) of the trigeminal nerve (V1).

PATHOGENESIS

It has been suggested that SWS results from failure of the primitive cephalic venous plexus to regress during the first trimester of pregnancy.[3-5] At this stage in embryogenesis, the close proximity of the ectoderm destined to form the facial skin to the portion of the neural tube destined to form the parietooccipital area of the brain may explain the association of a facial PWS and leptomeningeal angioma.[3-5]

Other authors suggest that there is either a failure of superficial cortical veins to develop or early thrombosis of these veins. As a result, there is redirection of blood to the developing leptomeninges and into the deep venous system. Despite this redirection there is insufficient venous drainage, leading to progressive venous stasis and vessel dilatation producing chronic hipoxia.[6]

The pathogenesis of PWS remains controversial. It seems clear that there is only dilatation of blood vessels without proliferation. The cause of blood vessels ectasia does not seem to be secondary to a defective vessel wall (see Histopathology section) but may be related to a deficiency in sympathetic innervation of the vessel and failure to regulate vasoconstriction.[7,8]

GENETICS

SWS occurs sporadically with equal frequency in boys and girls. There are only a couple of familial cases reported in the literature; a father and son both affected by SWS and a mother with PWS in the distribution of the third branch of the trigeminal nerve, whose son had SWS.[9,10] It has been proposed that SWS is the result of a somatic mutation in the affected areas.[11,12] Discordance in monozigotic twins is consistent with this hypothesis. Chromosomal rearrangement and trisomies in chromosomes 4 and 10 have been detected in the affected skin of 2 patients with SWS who lacked these findings in normal skin and blood.[13]

Familial occurrence of capillary malformations in an autosomal dominant manner has been described in the literature. The locus for this hereditary form has been mapped on chromosome 5q, and a candidate gene has been identified.[14-16] However, in these familial cases, capillary malformations are multiple, small, pink to red patches that are not restricted to the face and are clinically different from PWS of SWS.

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HISTOPATHOLOGY

On histopathologic examination of skin biopsies of PWS in SWS, dilated and ectatic thin-walled vessels in the superficial vascular plexus are observed.[17,18] There is no increase in the number of vessels. In some cases, there is an underlying "cavernous hemangioma" with proliferation and ectasia of thin-walled vessels in the deeper dermis, subcutaneous adipose tissue, and skeletal muscle. The cobblestoned, roughened surface of older lesions is due to progressive ectasia of blood vessels. In some cases, small angiomatous nodules may appear that usually represent pyogenic granulomas.[19,21] In a few instances, the angiomatous nodules correspond to acral arteriovenous tumors and acquired tufted angiomas.[22,23]

Vessel morphology is typical of capillaries, postcapillary venules and small veins. There is no decrease in the components of the vessel wall (fibronectin, factor VIII, or type IV collagen) to explain decreased support and secondary dilatation.[24] Immunohistochemical analysis with monoclonal antibodies specific for endothelium (PAL-E, anti-Factor VIII related antigen, anti-ICAM-1 and anti-ELAM-1) show no substantial differences from normal blood vessels.[25] In one study, S-100 immunoperoxidase staining revealed a significant decrease in nerve density in the wall of blood vessels, which may explain dilatation.[8]

Histologic studies of leptomeningeal angiomas has revealed thickened leptomeninges with tortuous blood vessels. The underlying brain may be atrophic, with intense gliosis and calcifications both in the cortex and white matter. Calcium deposits are seen initially only in the vessel wall and later on in perivascular tissue or rarely within the neurons.[26-28] Focal cortical dysgenesis has been found in some cases.

Histological studies of trabeculectomy specimens in patients with SWS have shown abnormal collagen deposition and abundant vessels in the intra-trabecular spaces, as well as morphological abnormalities in the Schlemm canal.[29-31] The presence of hemangiomas in the trabecular meshwork is a highly characteristic finding of SWS and is never associated with congenital glaucoma of other etiologies.

CLINICAL MANIFESTATIONS

There are a number of reviews of SWS that address clinical manifestations and frequencies of different complications.[10,32-29] Clinical manifestations can be divided into cutaneous, neurologic, or ocular manifestations.

Cutaneous Manifestations

Port-wine stains or *nevus flammeus* in SWS are well-demarcated red macular stains present at birth. (Fig 1). With increasing age, the stain darkens in color and becomes raised and thickened. Sometimes multiple, small, red to purple nodules develop on the surface that confer a cobblestone pattern to the lesions (Fig 2). In a few instances, larger nodules develop representing pyogenic granulomas or acral arteriovenous tumors.[20,22,23,40,41]

Facial port-wine stains, whether or not associated with SWS, usually have a sharp midline demarcation, although some extension over the midline may be observed (Fig 1). The pattern of the cutaneous PWS, although repetitive from patient to patient, does not conform exactly to any known dermatomal or vascular distribution and does not reproduce the embryological facial prominences. However, in the literature the distribution of the facial nevus has always been correlated to the branch of the trigeminal nerve that innervates most of the involved skin. Following this convention, PWS in patients with SWS always involve the skin innervated by the first arch of the trigeminal nerve (V1, forehead and upper eyelid).[32,33,38,42] This is in contrast with the more common V2 distribution of facial port wine stains, not associated with SWS.[32,33,38] (Fig 3). Tallman et al reviewed 274 patients with facial PWS, and found 4 patients (1%) with PWS in the V2 or V2 + V3 distribution had associated eye or neurologic complications.[38] These 4 patients all had involvement of the lower eyelid. These findings have not been confirmed in other large series where patients without V1 involvement do not appear to be at risk of complications.[32,33,36,42] This discrepancy may be due to the fact that in most series involvement of the lower eyelid is considered V1 distribution, while in Tallman's series, the lower eyelid is considered V2. In addition, he also classifies some patients with upper eyelid involvement as V2.[38]

Involvement of V1 alone is uncommon (2%-4% in patients without SWS, and up to 20% in patients with SWS). In many patients, there is additional involvement of V2 or V2 and V3 (2%-23%).[32,33,36,38,42] Bilateral lesions can be seen in 10% to 30% of the patients[10,32,33,38] (Fig 4). Extrafacial involvement in patients with facial

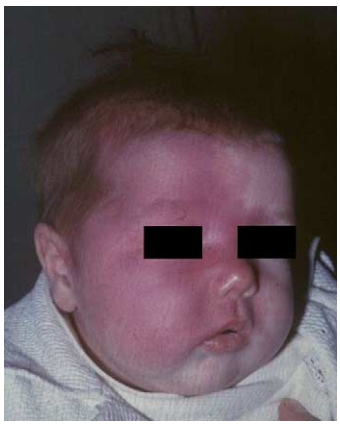


Fig 1. Pink to red macular stain involving most of the right side of the face. The port wine stain crosses the midline. Note mild buphthalmos (distention secondary to increased intraocular pressure) of the right eye.

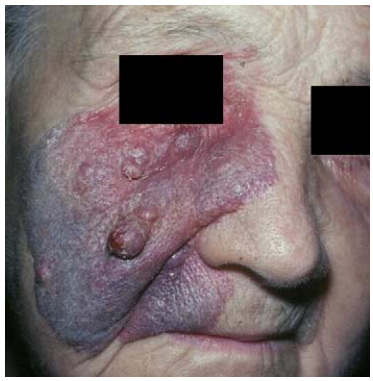


Fig 2. Facial port wine stain in a V1, V2 distribution (note upper eyelid involvement). There is darkening and nodularity at advanced age.

PWS may be seen and is much more common when the lower face is involved or with bilateral lesions.[43]

Soft tissue hypertrophy and facial bone overgrowth may occur, especially when the maxillary and mandibular areas are involved.[44-46] In these cases, there is often gum hyperplasia and maleruption of teeth that may cause periodontal and dental problems.[47,48] Phenytoin-induced gum hyperplasia may aggravate the symptoms.

Overall, the risk of associated ocular and/or neurologic manifestations in patients with involvement of V1 varies from 32% to 65%.[32,33,38] The risk increases with extensive and bilateral lesions. However, some authors have not found a correlation between the size of facial PWS and the

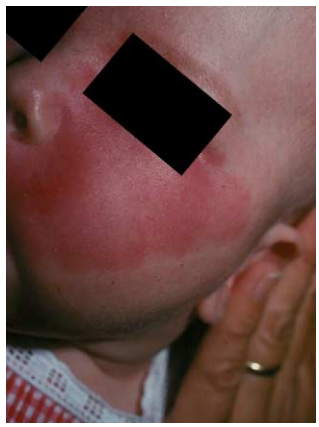


Fig 3. Facial PWS in a malar distribution. Note that there is involvement of lower eyelid and small extension to upper eyelid. Some authors would consider this distribution V1 + V2 due to lower eyelid involvement, while other would considered it V2.

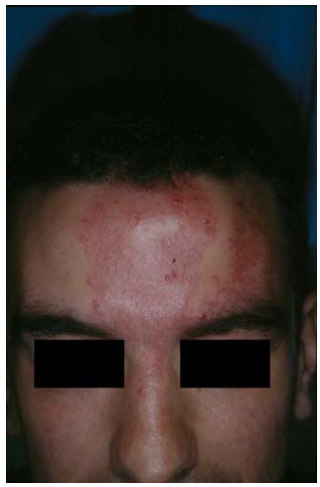


Fig 4. Patient with PWS extending over midline in a V1 distribution. He had bilateral leptomeningeal angiomatosis.

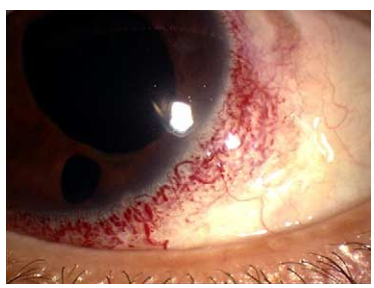


Fig 5. Dilatation and tortuosity of episcleral vessels.

size of pial angioma.[10,49] Glaucoma and neurologic manifestations (23%-38%) occur more commonly than either glaucoma alone (3%-8%) or neurologic manifestation alone (5%-19%).[33,38] The inconsistencies in the reported frequencies can be explained by differences in the modes of ascertainment and by the age distribution of the study populations.

Neurologic Manifestations

Seizures are the most common neurologic manifestations and have been reported to occur in 23% to 83% of patients with SWS.[10,36,37,50,51] Again, such differing prevalences are probably due to variations in the age of patients in different studies. Seizures are an early manifestation of SWS and may first present anywhere between birth to adolescence. However, in the majority of patients, they develop before 2 years of age.[37] Seizures occur either on the contralateral side of the PWS or are generalized. Focal motor seizures predominate but secondary generalization may develop. Generalized seizures are primarily tonic-clonic seizures, but atonic seizures and absence seizures may also occur. Infantile spasms may be the first epileptic manifestation in infants.[10,49] In many patients, the seizures begin during febrile episodes. With advancing age seizures tend to become more severe, frequent, and complex. Status epilepticus may also be observed.

Certain subsets of patients may have more severe neurologic involvement. Patients with bilateral leptomeningeal angiomatosis, which occur in 7% to 26% of patients, have more severe seizures, developmental delay and focal deficits.[10,52] Early onset of seizures may correlate with poorer prognosis and difficult epilepsy control.[10,37] However, Arzimanoglou at al, in their series, found that late onset was associated with a greater degree of intractability.[51]

Developmental delay and progressive mental retardation are reported in half of the patients with SWS.[36,37] Children with SWS may need some special education but only one third of patients may be severely mentally handicapped.[10] There is a direct correlation between age of onset of seizures and degree of intellectual impairment. Children without epilepsy or with onset of seizures after 48 months of age have normal development and intelligence.[36] The occurrence of prolonged seizures, lasting for more than 1 hour, correlates with further severe epilepsy, motor deficits and mental deterioration.[49]

Recurrent headaches are another common manifestation present in one third to one half of the patients.[36,53] Additional neurologic manifestations include contralateral hemiparesis, hemiplegia and hemianopsia (Table 1).[10,37] In many instances, neurologic deficits follow prolonged seizures. Acute hemiparesis not associated with an obvious seizure may occur in a few patients and have been related to vessel thromboses.[54]

Ocular Manifestations

Glaucoma is the most common ocular manifestation, and develops in as much as one third of the patients.[55-57] Sujansky et al found an even higher incidence of 60% in their cohort of 52 adult patients with SWS.[36] Glaucoma is usually ipsilateral to the facial PWS, although bilateral glaucoma with unilateral PWS stain may be seen.[58] The age of onset ranges from birth to 41 years with a median of 5 years.[36] Glaucoma in SWS develops insidiously, with a chronic or subacute increase in ocular pressure. There is a single case report with acute glaucoma in SWS.[59] Increases in the episcleral venous pressure and developmental anomalies in the anterior chamber angle have been considered to be the main causal factors for the glaucoma associated with SWS.[29,30,57]

Diffuse choroidal hemangioma ipsilateral to the PWS is another characteristic feature of SWS that may be found in up to 71% of SWS cases.[57] It is usually seen as a red, flat to moderately elevated mass producing a classic "tomato ketshup" appearance on fundoscopic examination. This image is in contrast to choroidal hemangiomas not associated with SWS that are discrete and raised. With time, choroidal hemangiomas produce sec-

Table 1. Neurologic and ocular associations of Sturge-Weber Syndrome

Neurologic	Ocular
Seizures (focal > generalized)	Glaucoma
Intellectual impairment	Choroidal hemangioma
Hemiparesis (transient or permanent)	Episcleral/conjunctival hemangioma
Hemianopsia	Iris heterochromia
Migraine headache	Buphthalmos
	Retinal pigment degeneration
	Retinal detachment
	Optic disc coloboma
	Cataract
	Nevus of Ota

ondary changes in the overlying retina such as retinal pigment epithelium degeneration, fibrous metaplasia and cystic retinal degeneration leading to visual loss and visual field defects. Continuing exudation of the hemangioma may cause retinal detachment. Choroidal hemangiomas are almost always associated with leptomeningeal hemangiomas; therefore, neuroimaging is mandatory when fundoscopic evaluation reveals a choroidal hemangioma. Only 2 cases of choroidal hemangioma without intracranial involvement have been reported.[57,60]

Other ocular abnormalities that have been reported in SWS include dilatation and tortuosity of conjunctival and episcleral vessels, (Fig 5) buphthalmos, iris heterochromia, optic disc coloboma and cataract. Nevus of Ota may coexist in patients with SWS.[55,61]

Visual loss in patients with SWS is secondary to glaucoma or from damage to the retrogeniculate pathways by the angiomatous lesions. Optic neuropathy may develop rarely and contribute to progressive visual loss.[62] Homonimous hemianopsia may also be secondary to occipital lobe involvement. Central vein occlusion has been reported in young adults with SWS without any other predisposing factors other than high intraocular pressure.[63]

Atypical Forms and Variants of Sturge-Weber Syndrome

Leptomeningeal angioma without facial nevus has been reported and is considered a variant of SWS.[4,5,64-73] In 3 reported cases the leptomeningeal angioma was present in an unusual frontoparietal temporal location sparing the occipital lobe.[65,66] Glaucoma has not been reported in patients lacking facial PWS.

In SWS, leptomeningel angioma and choroidal hemangiomas are typically ipsilateral to the facial PWS. Leptomeningeal angioma contralateral to facial PWS, unilateral leptomeningeal angioma with bilateral facial PWS, and bilateral choroidal hemangioma with unilateral PWS have been reported rarely.[10,58,72,74-76]

Patients with SWS may have other vascular abnormalities (Klippel-Trenaunay syndrome) or other neurocutaneous syndromes, including phakomatosis pigmentovascularis.[77-83] Intracranial manifestations of SWS have been described in patients with Klippel–Trenaunay syndrome.[84] In fact, some authors consider SWS and Klippel–Trenaunay syndrome to be the same disorder differing only in severity and location.[85] A patient with hypomelanosis of Ito with pial angiomatosis has been reported.[73]

NEUROIMAGING STUDIES

Radiologically, a leptomeningeal (pial) vascular malformation, commonly located in the parieto-occipital area, cerebral atrophy and calcifications may be seen. Neuroradiologic data in SWS has been reviewed extensively.[6,86,87] Cerebral lesions in SWS are ipsilateral to the facial PWS. Bilateral intracranial involvement is uncommon even in patients with bilateral PWS.[10]

On CT scans, homolateral cortical atrophy may be seen, which may be associated with a compensatory hypertrophy of the frontal bone and frontal sinus.[88] (Fig 6). Cortical and intracranial calcifications underneath the leptomeningeal angiomas are best seen on CT-scans.[89,90] They have a characteristic gyriform or "s" shape. They may we found at the cortex as well as at the meningeal arteries, cortical, and subcortical veins. They are commonly associated with cortical atrophy in the same area. Atrophy and calcifications are considered to be an indirect consequence of chronic ischemia of the cortex due to vascular stasis in the

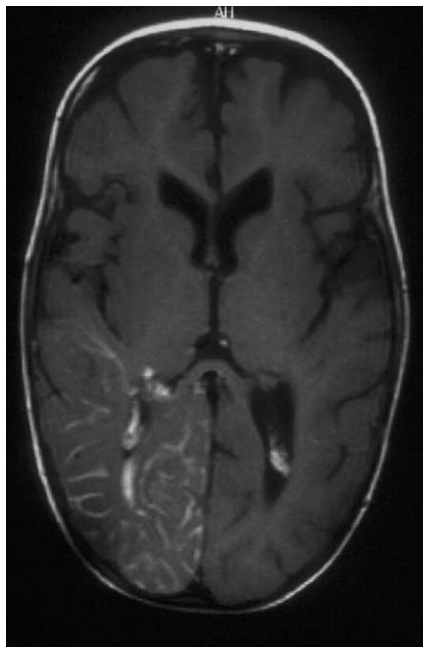
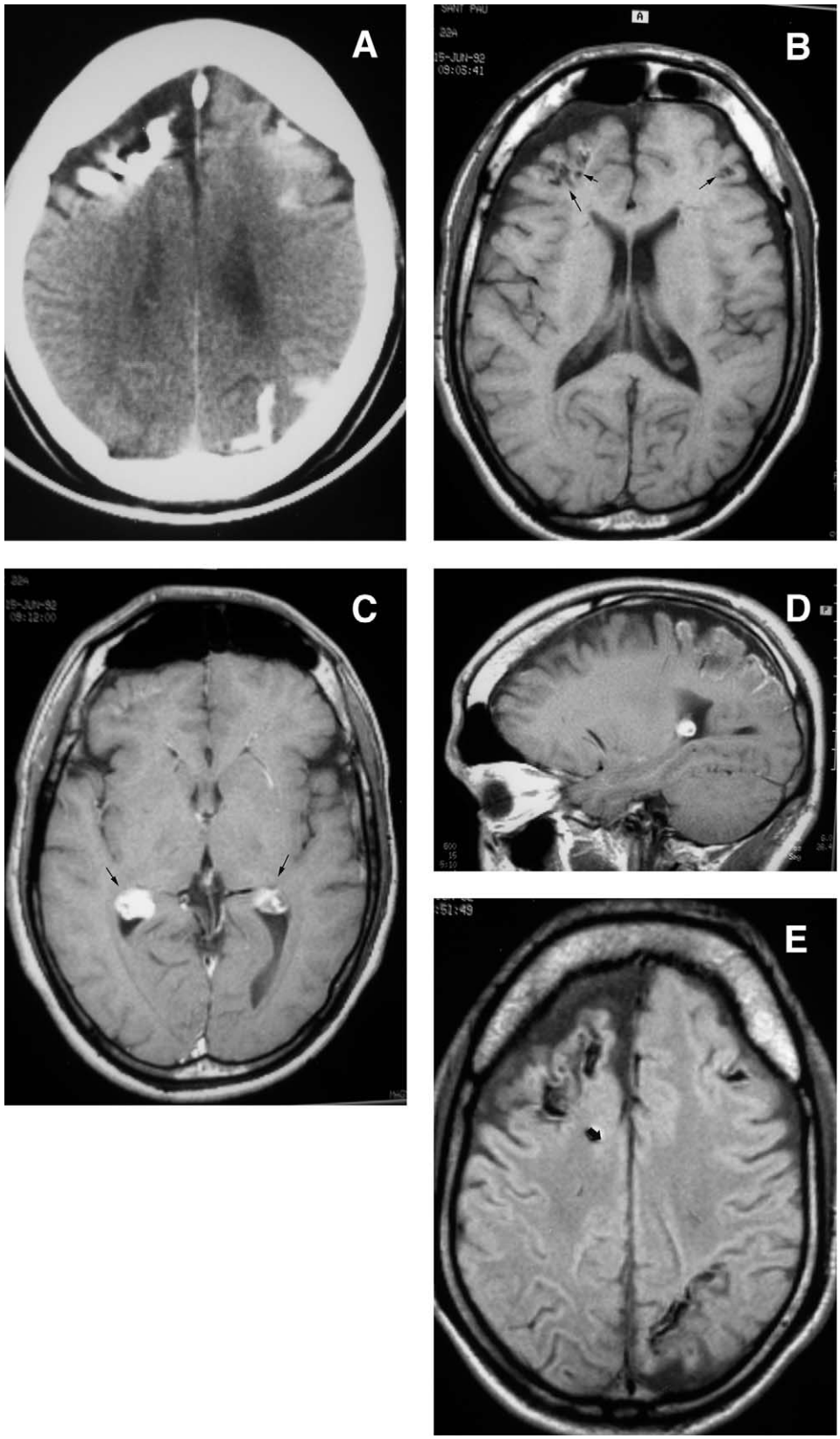


Fig 6. T1 weightened MRI after gadolinium injection. Enhancement of leptomeningeal angioma at the occipital lobe.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area of leptomeningeal angioma. In severe forms they may develop rapidly. Calcifications may be seen at birth, but in many instances they may not be visible until an older age.[87] Direct visualization of the pial malformation after contrast injection may be difficult on CT scans.[91] Areas of contrast enhancement may differ in successive CT scans and may even disappear. It has been shown that cortical enhancement is usually present if performed shortly after an episode of severe seizures or hemiplegia but is absent or considerably less marked if performed later.[87] An ipsilateral prominent choroid plexus may be seen on contrast-CT, with or without calcifications. Sometimes this is the only sign of Sturge-Weber on CT scans.[87,88,92] CT scan may also show thickening of the ocular globe as a manifestation of choroidal disease, especially in unilateral cases where the opposite side can be used for comparison.[52,93] However, in bilateral cases, CT is less useful because it is difficult to distinguish between enhancement and beam-hardening effects. CT scan after contrast injection may demonstrate dilatation of the deep venous structures.[91]

MRI, especially after contrast injection, is the preferred and most sensitive imaging technique for diagnosis and evaluation of SWS. MRI without contrast may show cerebral atrophy both in T1 and T2 sequences, diploic prominence, and enlarged choroid plexus (Fig 7). Calcifications may be seen in T2, especially, in gradient-echo images, as areas of low signal.[89,90,94] Accelerated myelination may produce the areas of hypointensity in T2, and this may be the earliest sign of SWS in children under 6 months of age. In others, hyperintensity on T2 representing areas of gliosis may be seen.

After injection of gadolinium, there is diffuse pial enhancement is seen in T1 weighted images. This is the single most reliable criterion for diagnosis of SWS. Contrast enhanced fluid-attenuated inversion recovery (FLAIR) sequences improve the detection of leptomeningeal angiomatosis because they suppress the signal intensity of normal vascular structures.[95] There are 2 patients reported in the literature with SWS without pial enhancement on MRI.[51,96] They were older children of 11 and 14 years of age. The lack of leptomeningel enhancement might be due to progressive obliteration of leptomeningeal vessels, a well-documented phenomenon in SWS.[96]

Enlargement of the choroid plexus of the affected side is another characteristic feature of SWS and is best seen on contrast MRI.[52,72,87,93] The size of the choroid plexus seems to correlate with the extent of leptomeningeal involvement.[72] For some authors, the choroid plexus is enlarged because there is a choroidal hemangioma while for others it represents dilatation due to impaired drainage by the engorged deep venous system.[93] Abnormalities in the draining venous system with dilatation of deep venous system can be in both contrast enhanced and non-contrast MRI.[91,97]

Diffuse choroidal hemangioma can be identified more easily with contrast MRI than with CT scans or non-contrast MRI.[52,93] Fat suppression images are very useful when evaluating the orbits.

Cerebral angiography, although usually not performed, demonstrates the venous anomalies of SWS including a lack of superficial cortical veins, non-filling superior sagital sinus and thickening and tortuosity of the deep subependimal and deep medullary veins.[10,98] Intracranial arteries appear of smaller size in the affected hemisphere secondary to cerebral atrophy.

Skull radiographs are no longer obtained for evaluation and early diagnosis of SWS (Fig 8). However, if obtained a typical pattern of calcification resembling a "railroad track" may be seen, and is usually demonstrable at a mean age of 7 years.[50] Other indirect signs that may be demonstrated on skull radiographs include cranial asymmetry, thickening of the cranial diploe and increased sinus sizes on the side of the PWS.

Functional neuroimaging studies of glucose metabolism by position emission tomography (PET) or cerebral perfusion by SPEC, have been introduced recently in the evaluation of SWS and may show disturbances before clinical symptoms appear.[86,99] In initial stages, they show a transient

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Fig 7. (A) CT scan in a patient with bilateral involvement Bilateral atrophy. Diffuse calcification in the frontal lobes. (B) T1 weighted MRI in a patient with bilateral involvement. Bilateral atrophy and compensatory hypertrophy of frontal bone and sinuses. Areas of calcification in the bilateral frontal lobes appear as areas of signal voids (arrow heads). (C) T1-weighted MRI after gadolinium injection. Enhancement of prominent choroid plexus most marked on the right side. Leptomeningeal enhancement. (D) T2-weighted MRI. Bilateral atrophy, areas of calcification in the frontal lobe appear as signal voids.

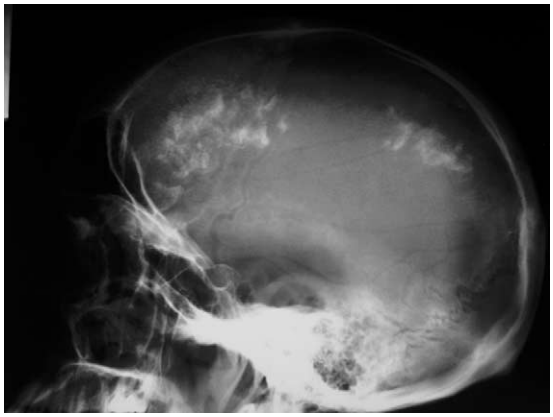

Fig 8. Prominent calcification on skull X-rays. Thickening of the cranial diploe and increased frontal sinus size.

hypermetabolism (PET) in the affected cortex secondary to hyperperfusion (SPEC). At advanced stages there is hypometabolism and hypoperfusion. These studies are not performed routinely for diagnostic purposes although they may potentially give some insight into the pathogenesis of SWS and information regarding the functional repercussion of the pial angiomatosis.[100-102]

ELECTROENCEPHALOGRAPHY

EEG (electroencephalography) in patients with SWS shows asymmetry of the background amplitude in the waking record involving the affected hemisphere. This asymmetry may be detected early but becomes more pronounced as cerebral atrophy becomes more severe. Epileptiform activity can be obtained in patients having clinical seizures.

DIAGNOSIS AND WORK-UP

Diagnosis of SWS can be made on clinical grounds by the association of facial nevus and neurological features and/or glaucoma. However, because glaucoma should be treated before symptoms manifest, newborns at risk with a facial PWS in the V1 distribution should have an eye exam with fundoscopy and measurements of intraocular pressure (Fig 9). Glaucoma may not develop until late childhood; therefore, lifelong assessment of eye pressure is mandatory. Choroidal hemangioma is also important to diagnose in children with SWS, because it may predispose to retinal detachment and to choroidal hemorrhage during or after surgery for glaucoma. Choroidal hemangioma may be difficult to diagnose clinically on fundoscopic examination. Contrast-MRI is the most sensitive way to demonstrate the crescentic enhancement in the posterior wall of the ocular wall. Eye ultrasonography is a noninvasive technique that may demonstrate choroidal thickening with or without associated retinal detachment.

Infants at risk, should also have neuroimaging studies, even if asymptomatic, because there is a potential role for prophylactic antiepileptic treatment if extensive intracranial involvement is detected (Fig 9). Contrast-MRI is the optimal and

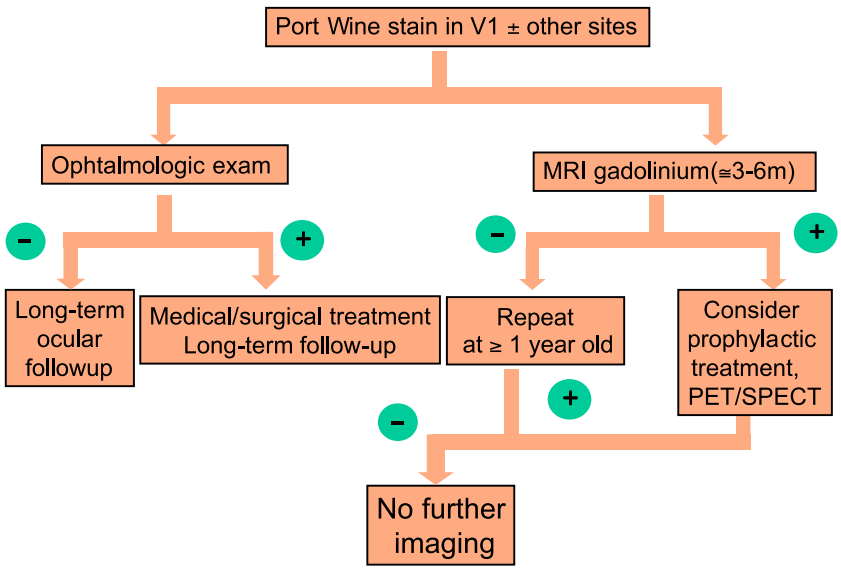

Fig 9. Work-up.

most sensitive neuroimaging technique for the screening in infants at risk for SWS.[86] CT scan is not sensitive enough in infants as cortical calcifications and atrophy appear later. In the neonatal period, pial angiomatosis may be difficult to identify even after contrast-MRI. Accelerated myelination in the involved hemisphere, with areas of white matter hyperintensity on T2 may be an early diagnostic feature before 6 months of age. If this early neuroradiological evaluation is negative, it is recommended to obtain a MRI with contrast later in the course as progressive dilatation of meningeal vessels with increasing age leads to better recognition of a leptomeningeal angioma.

TREATMENT

Control of epilepsy is the major goal in treatment of SWS patients.[51] Medical treatment with carbamazepine, sodium valproate, phenobarbitol, or phenytoin have all been tried. Vigabatrin may also be useful. Epilepsy control in SWS is difficult and usually requires the administration of more than one drug.[51] Poor control correlates with progressive mental deterioration and motor deficits.[10,37] Ideally, treatment should prevent first seizures.[49,103] There are no prospective randomized studies about the prophylactic use of anticonvulsants. In a non-randomized study, seizures that started later were less severe and cognitive function was better in the prophylactically treated group.[49] Although no general recommendation regarding prophylactic treatment can be made it may worth considering it in children at higher risk, ie, those with large leptomeninegeal angioma.

For children with refractory unihemispheric seizures, hemispherectomy has been proposed as a form of therapy.[104-110] In reviewing surgical outcomes in 32 patients with SWS who underwent hemispherectomies, 81% were seizure-free after surgery. Hemiparesis was not more severe than before surgery.[108] Cognitive deterioration may even improve after surgery.[104] Therefore, surgery should be considered early, before mental status deterioration, if it becomes clear that epilepsy is untreatable. Some authors have proposed venous thrombosis as a cause for clinical deterioration in patients with SWS, and aspirin therapy has been advocated.[54,97]

Control of glaucoma may be achieved with medical treatment alone (beta-blockers and carbonic anhydrase inhibitors) and should be considered the initial treatment of choice.[111-113] In patients not responding to medical treatment, different surgical procedures have been performed including cyclocryotherapy, YAG laser goniotomy, surgical goniotomy, and trabeculotomy or trabeculectomy. Choroidal effusion and hemorrhage are common complications of surgery. Late postoperative complications as a result of persistent hypotony may result in loss of vision. Molteno or Ahmed implants may be necessary if these fail or even at first intervention.[114] Retinal detachment secondary to the choroidal hemangioma is usually treated with external beam radiation. Recently photodymanic therapy has been used.[115]

Facial port wine stain can be treated with pulsed dye laser in the same way that is treated in children without SWS.[116] Facial PWS in V1 respond better than in other locations. Both local anesthesia and general anesthesia may be used. Anesthesia should be planned to avoid increases in ocular pressure or intracranial pressure.[117]

REFERENCES

1. Sturge WA: A case of partial epilepsy apparently due to a lesion of one of the motor centers of the brain. Trans Clin Soc London 12:112, 1879

2. Parkes Weber F: Right-sided hemihypertrophy resulting from right-sided congenital spastic hemiplegia with a morbid condition of the left side of the brain revealed by radiogram. J Neurol Neurosurg Psychiatry 37:301-311, 1922

3. Comi AM: Pathophysiology of Sturge-Weber syndrome. J Child Neurol 18:509-516, 2003

4. Maiuri F, Gangemi M, Iaconetta G, et al: Sturge-Weber disease without facial nevus. J Neurosurg Sci 33:215-218, 1989

5. Taly AB, Nagaraja D, Das S, et al: Sturge-Weber-Dimitri disease without facial nevus. Neurology 37:1063-1064, 1987

6. Griffiths PD: Sturge-Weber syndrome revisited: The role of neuroradiology. Neuropediatrics 27:284-294, 1996

7. Rosen S, Smoller BR: Port-wine stains: A new hypothesis. J Am Acad Dermatol 17:164-166, 1987

8. Smoller BR, Rosen S: Port-wine stains. A disease of altered neural modulation of blood vessels? Arch Dermatol 122: 177-179, 1986

9. Debicka A, Adamczak P: Przypadek dziedziczenia zespolu Sturge'a-Webera. Klin Oczna 81:541-542, 1979

10. Pascual-Castroviejo I, Diaz-Gonzalez C, Garcia-Melian RM, et al: Sturge-Weber syndrome: Study of 40 patients. Pediatr Neurol 9:283-288, 1993

11. Hamm H: Cutaneous mosaicism of lethal mutations. Am J Med Genet 85:342-345, 1999

12. Happle R: Lethal genes surviving by mosaicism: A possible explanation for sporadic birth defects involving the skin. J Am Acad Dermatol 16:899-906, 1987

13. Huq AH, Chugani DC, Hukku B, et al: Evidence of somatic mosaicism in Sturge-Weber syndrome. Neurology 59: 780-782, 2002

14. Eerola I, Boon LM, Watanabe S, et al: Locus for susceptibility for familial capillary malformation ("port-wine stain") maps to 5q. Eur J Hum Genet 10:375-380, 2002

15. Breugem CC, Alders M, Salieb-Beugelaar GB, et al: A locus for hereditary capillary malformations mapped on chromosome 5q. Hum Genet 110:343-347, 2002

16. Eerola I, Boon LM, Mulliken JB, et al: Capillary Malformation-Arteriovenous Malformation, a New Clinical and Genetic Disorder Caused by RASA1 Mutations. Am J Hum Genet 73:1240-1249, 2003

17. Finley JL, Noe JM, Arndt KA, et al: Port-wine stains. Morphologic variations and developmental lesions. Arch Dermatol 120:1453-1455, 1984

18. Barsky SH, Purwoko R, Jitsukawa K: The nature and evolution of port-wine stains: A computer assisted study. J Invest Dermatol 74:154-157, 1980

19. Katta R, Bickle K, Hwang L: Pyogenic granuloma arising in port-wine stain during pregnancy. Br J Dermatol 144:644-645, 2001

20. Lee JB, Kim M, Lee SC, et al: Granuloma pyogenicum arising in an arteriovenous haemangioma associated with a port-wine stain. Br J Dermatol 143:669-671, 2000

21. Swerlick RA, Cooper PH: Pyogenic granuloma (lobular capillary hemangioma) within port-wine stains. J Am Acad Dermatol 8:627-630, 1983

22. Kim TH, Choi EH, Ahn SK, et al: Vascular tumors arising in port-wine stains: two cases of pyogenic granuloma and a case of acquired tufted angioma. J Dermatol 26:813-816, 1999

23. Carrasco L, Pastor A, Farina C, et al: Acral arteriovenous tumor developed within a nevus flammeus in a patient with Sturge-Weber syndrome. Am J Dermatopathol 25:341-345, 2003

24. Finley JL, Clark RA, Colvin RB, et al: Immunofluorescent staining with antibodies to factor VIII, fibronectin, and collagenous basement membrane protein in normal human skin and port wine stains. Arch Dermatol 118:971-975, 1982

25. Neumann R, Leonhartsberger H, Knobler R, et al: Immunohistochemistry of port-wine stains and normal skin with endothelium-specific antibodies PAL-E, anti-ICAM-1, anti-ELAM-1, and anti-factor VIIIrAg. Arch Dermatol 130:879-883, 1994

26. Di Trapani G, Di Rocco C, Abbamondi AL, et al: Light microscopy and ultrastructural studies of Sturge-Weber disease. Childs Brain 9:23-36, 1982

27. Norman MG, Schoene WC: The ultrastructure of Sturge-Weber disease. Acta Neuropathol (Berl) 37:199-205, 1977

28. Simonati A, Colamaria V, Bricolo AM, et al: Microgyria associated with Sturge-Weber angiomatosis. Childs Nerv Syst 10:392-395, 1994

29. Cibis GW, Tripathi RC, Tripathi BJ: Glaucoma in Sturge-Weber syndrome. Ophthalmology 91:1061-1071, 1984

30. Weiss DI: Dual origin of glaucoma in encephalotrigeminal haemangiomatosis. Trans Ophthalmol Soc U K 93:477-493, 1973

31. Akabane N, Hamanaka T: Histopathological study of a case with glaucoma due to Sturge-Weber syndrome. Jpn J Ophthalmol 47:151-157, 2003

32. Boixeda P, de Misa RF, Arranzola JM, et al: Angioma plano facial y síndrome de Sturge-Weber. Med Clin (Barc) 101:1-10, 1993

33. Enjolras O, Riche MC, Merland JJ: Facial port-wine stains and Sturge-Weber syndrome. Pediatrics 76:48-51, 1985

34. Kihiczak NI, Schwartz RA, Jozwiak S, et al: Sturge-Weber syndrome. Cutis 65:133-136, 2000

35. Paller AS: The Sturge-Weber syndrome. Pediatr Dermatol 4:300-304, 1987

36. Sujansky E, Conradi S: Outcome of Sturge-Weber syndrome in 52 adults. Am J Med Genet 57:35-45, 1995

37. Sujansky E, Conradi S: Sturge-Weber syndrome: age of onset of seizures and glaucoma and the prognosis for affected children. J Child Neurol 10:49-58, 1995

38. Tallman BF, Tan OT FAU, Morelli JG FAU, et al: Location of port-wine stains and the likelihood of ophthalmic and/or central nervous system complications. Pediatrics 87: 323-327, 1991

39. Bebin EM, Gomez MR: Prognosis in Sturge-Weber disease: Comparison of unihemispheric and bihemispheric involvement. J Child Neurol 3:181-184, 1988

40. Castanedo-Cazares JP, Lepe V, Moncada B: Pyogenic granuloma within port-wine stains. Eur J Dermatol 12:616, 2002

41. Valeyrie LF, Lebrun-Vignes BF, Descamps VF, et al: Pyogenic granuloma within port-wine stains: An alarming clinical presentation. Eur J Dermatol 12:373-375, 2002

42. Stevenson RF, Thomson HG FAU, Morin JD: Unrecognized ocular problems associated with port-wine stain of the face in children. Can Med Assoc J 111:953-954, 1974

43. Inan C, Marcus J: Sturge–Weber syndrome: Report of an unusual cutaneous distribution. Brain Dev 21:68-70, 1999

44. Ahluwalia TP, Lata J, Kanwa P: Sturge Weber syndrome with intraoral manifestations. A case report. Indian J Dent Res 9:140-144, 1998

45. Ramli N, Sachet M, Bao C, et al: Cerebrofacial venous metameric syndrome (CVMS) 3: Sturge-Weber syndrome with bilateral lymphatic/venous malformations of the mandible. Neuroradiology 45:687-690, 2003

46. Ilgenli T, Canda T, Canda S, et al: Oral giant pyogenic granulomas associated with facial skin hemangiomas (Sturge-Weber syndrome). Periodontal Clin Investig 21:28-32, 1999

47. Aviv I, Assif D, Horowitz I, et al: Sturge-Weber syndrome–a combined surgical, periodontal and prosthetic treatment. Ann Dent 46:27-30, 1987

48. Yukna RA, Cassingham RJ, Carr RF: Peridontal manifestations and treatment in a case of Sturge-Weber syndrome. Oral Surg Oral Med Oral Pathol 47:408-415, 1979

49. Ville D, Enjolras O, Chiron C, et al: Prophylactic antiepileptic treatment in Sturge-Weber disease. Seizure 11:145-150, 2002

50. Uram MF, Zubillaga C: The cutaneous manifestations of Sturge-Weber syndrome. J Clin Neuroophthalmol 2:245-248, 1982

51. Arzimanoglou A, Aicardi J: The epilepsy of Sturge-Weber syndrome: Clinical features and treatment in 23 patients. Acta Neurol Scand Suppl 140:18-22, 1992

52. Griffiths PD, Boodram MB, Blaser S, et al: Abnormal ocular enhancement in Sturge-Weber syndrome: correlation of ocular MR and CT findings with clinical and intracranial imaging findings. AJNR Am J Neuroradiol 17:749-754, 1996

53. Klapper J: Headache in Sturge-Weber syndrome. Headache 34:521-522, 1994

54. Roach ES, Riela AR, McLean WT, et al: Aspirin therapy for Sturge-Weber syndrome. Ann Neurol 18:387, 1985

55. Celebi S, Alagoz G, Aykan U: Ocular findings in Sturge-Weber syndrome. Eur J Ophthalmol 10:239-243, 2000

56. Stevenson RF, Morin JD: Ocular findings in nevus flammeus. Can J Ophthalmol 10:136-139, 1975

57. Sullivan TJ, Clarke MP, Morin JD: The ocular manifestations of the Sturge-Weber syndrome. J Pediatr Ophthalmol Strabismus 29:349-356, 1992

58. Amirikia A, Scott IU, Murray TG: Bilateral diffuse choroidal hemangiomas with unilateral facial nevus flammeus in Sturge-Weber syndrome. Am J Ophthalmol 130:362-364, 2000

59. Maruyama I, Ohguro H, Nakazawa M: A case of acute angle-closure glaucoma secondary to posterior scleritis in patient with Sturge-Weber syndrome. Jpn J Ophthalmol 46:74-77, 2002

60. Madlom MM, Hoggard N, Griffiths PD, et al: Facial naevus flammeus with choroidal haemangioma and without intracranial involvement. Dev Med Child Neurol 45:139, 2003

61. Recupero SM, Abdolrahimzadeh S, De Dominicis M, et al: Sturge-Weber syndrome associated with naevus of Ota. Eye 12(Pt 2):212-213, 1998

62. Sadda SR, Miller NR, Tamargo R, et al: Bilateral optic neuropathy associated with diffuse cerebral angiomatosis in Sturge-Weber syndrome. J Neuroophthalmol 20:28-31, 2000

63. Knapp CM, Sarodia U, Woodruff GH: Central retinal vein occlusion associated with Sturge Weber syndrome. Eye 16:657-659, 2002

64. Ambrosetto P, Ambrosetto G, Michelucci R, et al: Sturge-Weber syndrome without port-wine facial nevus. Report of 2 cases studied by CT. Childs Brain 10:387-392, 1983

65. Comi AM, Fischer R, Kossoff EH: Encephalofacial angiomatosis sparing the occipital lobe and without facial nevus: On the spectrum of Sturge-Weber syndrome variants? J Child Neurol 18:35-38, 2003

66. Dilber C, Tasdemir HA, Dagdemir A, et al: Sturge-Weber syndrome involved frontoparietal region without facial nevus. Pediatr Neurol 26:387-390, 2002

67. Gururaj AK, Sztriha L, Johansen J, et al: Sturge-Weber syndrome without facial nevus: A case report and review of the literature. Acta Paediatr 89:740-743, 2000

68. Liang CW, Liang KH: Sturge-Weber syndrome without facial nevus. Chin Med J (Engl) 105:964-965, 1992

69. Martinez-Bermejo A, Tendero A, Lopez-Martin V, et al: Angiomatosis leptomeningea occipital sin angioma facial. Debe considerarse como variante del sindrome de Sturge-Weber? Rev Neurol 30:837-841, 2000

70. Pascual-Castroviejo I, Pascual-Pascual SI, Viano J, et al: Sturge-Weber syndrome without facial nevus. Neuropediatrics 26:220-222, 1995

71. Sen Y, Dilber E, Odemis E, et al: Sturge-Weber syndrome in a 14-year-old girl without facial naevus. Eur J Pediatr 161:505-506, 2002

72. Griffiths PD, Blaser S, Boodram MB, et al: Choroid plexus size in young children with Sturge-Weber syndrome. AJNR Am J Neuroradiol 17:175-180, 1996

73. Garcia Muret MP, Puig L, Allard C, et al: Hypomelanosis of Ito with Sturge-Weber syndrome-like leptomeningeal angiomatosis. Pediatr Dermatol 19:536-540, 2002

74. Cersoli M, Campanile S, Campanile A, et al: Unusual findings in Sturge-Weber syndrome. AJNR Am J Neuroradiol 10:S85, 1989

75. Chaudary RR, Brudnicki A: Sturge-Weber syndrome with extensive intracranial calcifications contralateral to the bulk of the facial nevus, normal intelligence, and absent seizure disorder. AJNR Am J Neuroradiol 8:736-737, 1987

76. Widdess-Walsh P, Friedman NR: Left-sided facial nevus with contralateral leptomeningeal angiomatosis in a child with Sturge-Weber syndrome: case report. J Child Neurol 18:304-305, 2003

77. Vissers W, Van Steensel M, Steijlen P, et al: Klippel-Trenaunay syndrome and Sturge-Weber syndrome: Variations on a theme? Eur J Dermatol 13:238-241, 2003

78. Kiley MA, Oxbury JM, Coley SC: Intracranial hypertension in Sturge-Weber/Klippel-Trenaunay-Weber overlap syndrome due to impairment of cerebral venous outflow. J Clin Neurosci 9:330-333, 2002

79. Donofrio P, Ayala F: Klippel-Trenaunay-Weber syndrome–Report of a case associated with an incomplete form of Sturge-Weber syndrome. Clin Exp Dermatol 9:518-521, 1984

80. Leung AK, Lowry RB, Mitchell I, et al: Klippel-Trenaunay and Sturge-Weber syndrome with extensive Mongolian spots, hypoplastic larynx and subglottic stenosis. Clin Exp Dermatol 13:128-132, 1988

81. Sharma P, Arya AV, Azad RV: Unusual retinal manifestation in a combination of Sturge-Weber and Klipplel-Trenaunay syndrome–A case report. Indian J Ophthalmol 38:195-197, 1990

82. Saricaoglu MS, Guven D, Karakurt AM, et al: An unusual case of Sturge-Weber syndrome in association with phakomatosis pigmentovascularis and Klippel-Trenaunay-Weber syndrome. Retina 22:368-371, 2002

83. Uysal G, Guven A, Ozhan B, et al: Phakomatosis pigmentovascularis with Sturge-Weber syndrome: A case report. J Dermatol 27:467-470, 2000

84. Williams DW III, Elster AD: Cranial CT and MR in the Klippel-Trenaunay-Weber syndrome. AJNR Am J Neuroradiol 13:291-294, 1992

85. Happle R: Sturge-Weber-Klippel-Trenaunay syndrome: What's in a name? Eur J Dermatol 13:223, 2003

86. Boukobza M, Enjolras O, Cambra M, et al: Syndrome de Sturge-Weber. Données actuelles de l'imaginerie neuroradiologique. J Radiol 81:765-771, 2000

87. Terdjman P, Aicardi J, Sainte-Rose C, et al: Neuroradiological findings in Sturge-Weber syndrome (SWS) and isolated pial angiomatosis. Neuropediatrics 22:115-120, 1991

88. Welch K, Naheedy MH, Abroms IF, et al: Computed tomography of Sturge-Weber syndrome in infants. J Comput Assist Tomogr 4:33-36, 1980

89. Marti-Bonmati L, Menor F, Poyatos C, et al: Diagnosis of Sturge-Weber syndrome: comparison of the efficacy of CT and MR imaging in 14 cases. AJR Am J Roentgenol 158:867-871, 1992

90. Tournut P, Turjman F, Guibal AL, et al: MRI in Sturge-Weber syndrome. J Neuroradiol 19:285-292, 1992

91. Benedikt RA, Brown DC, Walker R, et al: Sturge-Weber syndrome: cranial MR imaging with Gd-DTPA. AJNR Am J Neuroradiol 14:409-415, 1993

92. Wasenko JJ, Rosenbloom SA, Duchesneau PM, et al: The Sturge-Weber syndrome: comparison of MR and CT characteristics. AJNR Am J Neuroradiol 11:131-134, 1990

93. Stimac GK, Solomon MA, Newton TH: CT and MR of

angiomatous malformations of the choroid plexus in patients with Sturge-Weber disease. AJNR Am J Neuroradiol 7:623-627, 1986

94. Sperner J, Schmauser I, Bittner R, et al: MR-imaging findings in children with Sturge-Weber syndrome. Neuropediatrics 21:146-152, 1990

95. Griffiths PD, Coley SC, Romanowski CA, et al: Contrast-enhanced fluid-attenuated inversion recovery imaging for leptomeningeal disease in children. AJNR Am J Neuroradiol 24:719-723, 2003

96. Fischbein NJ, Barkovich AJ, Wu Y, et al: Sturge-Weber syndrome with no leptomeningeal enhancement on MRI. Neuroradiology 40:177-180, 1998

97. Cure JK, Holden KR, Van Tassel P: Progressive venous occlusion in a neonate with Sturge-Weber syndrome: Demonstration with MR venography. AJNR Am J Neuroradiol 16: 1539-1542, 1995

98. Bentson JR, Wilson GH, Newton TH: Cerebral venous drainage pattern of the Sturge-Weber syndrome. Radiology 101:111-118, 1971

99. Reid DE, Maria BL, Drane WE, et al: Central nervous system perfusion and metabolism abnormalities in Sturge-Weber syndrome. J Child Neurol 12:218-222, 1997

100. Lee JS, Asano E, Muzik O, et al: Sturge-Weber syndrome: correlation between clinical course and FDG PET findings. Neurology 57:189-195, 2001

101. Chiron C, Raynaud C, Tzourio N, et al: Regional cerebral blood flow by SPECT imaging in Sturge-Weber disease: An aid for diagnosis. J Neurol Neurosurg Psychiatry 52:1402-1409, 1989

102. Chugani HT, Mazziotta JC, Phelps ME: Sturge-Weber syndrome: A study of cerebral glucose utilization with positron emission tomography. J Pediatr 114:244-253, 1989

103. Salman MS: Is the prophylactic use of antiepileptic drugs in Sturge-Weber syndrome justified? Med Hypotheses 51:293-296, 1998

104. Arzimanoglou AA, Andermann F, Aicardi J, et al: Sturge-Weber syndrome: Indications and results of surgery in 20 patients. Neurology 55:1472-1479, 2000

105. Falconer MR, Rushworth RG: Treatment of encephalotrigeminal angiomatosis (Sturge-Weber disease) by hemispherectomy. Arch Dis Child 35:433-447, 1960

106. Hoffman HJ, Hendrick EB, Dennis M, et al: Hemispherectomy for Sturge-Weber syndrome. Childs Brain 5:233-248, 1979

107. Ito M, Sato K, Ohnuki A, et al: Sturge-Weber disease: Operative indications and surgical results. Brain Dev 12:473-477, 1990

108. Kossoff EH, Buck C, Freeman JM: Outcomes of 32 hemispherectomies for Sturge-Weber syndrome worldwide. Neurology 59:1735-1738, 2002

109. Ogunmekan AO, Hwang PA, Hoffman HJ: Sturge-Weber-Dimitri disease: Role of hemispherectomy in prognosis. Can J Neurol Sci 16:78-80, 1989

110. Tuxhorn IE, Pannek HW: Epilepsy surgery in bilateral Sturge-Weber syndrome. Pediatr Neurol 26:394-397, 2002

111. Awad AH, Mullaney PB, Al Mesfer S, et al: Glaucoma in Sturge-Weber syndrome. J AAPOS 3:40-45, 1999

112. van Emelen C, Goethals M, Dralands L, et al: Treatment of glaucoma in children with Sturge-Weber syndrome. J Pediatr Ophthalmol Strabismus 37:29-34, 2000

113. Yang CB, Freedman SF, Myers JS, et al: Use of latanoprost in the treatment of glaucoma associated with Sturge-Weber syndrome. Am J Ophthalmol 126:600-602, 1998

114. Hamush NG, Coleman AL, Wilson MR: Ahmed glaucoma valve implant for management of glaucoma in Sturge-Weber syndrome. Am J Ophthalmol 128:758-760, 1999

115. Anand R: Photodynamic therapy for diffuse choroidal hemangioma associated with Sturge Weber syndrome. Am J Ophthalmol 136:758-760, 2003

116. Leaute-Labreze C, Boralevi F, Pedespan JM, et al: Pulsed dye laser for Sturge-Weber syndrome. Arch Dis Child 87:434-435, 2002

117. Batra RK, Gulaya V, Madan R, et al: Anaesthesia and the Sturge-Weber syndrome. Can J Anaesth 41:133-136, 1994