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Type I Sturge-Weber Syndrome with Bilateral Megalocornea in a Three Years Old Girl

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Abstract: ***Sturge-Weber syndrome (SWS) is a sporadic condition characterized by presence of port wine vascular nevus (PWS) on the upper part of the face and ipsilateral leptomeningeal angioma. The incidence estimated at 1/50,000 persons. Common symptoms are seizures, hemiparesis, vascular headache, developmental delay, glaucoma, and hemianopsia. We reported a three years old girl with type I SWS. She had PWS on right side of her face, leptomeningeal angiomatosis, and suspected secondary glaucoma with bilateral megalocornea. She was hospitalized because of seizures and developed transient hemiparesis. CT scan and MRI revealed abnormal calcification on asymmetric right fronto-temporo-parietal area, leptomeningeal angiomatoses and multiple small cavernous hemangioma on the tip of anterior corn of the bilateral lateral ventricle and right thalamus. EEG revealed mild general hypofunction. Patient was treated with carbamazepine and consulted to Ophthalmology, Dermatology, and Neurosurgery Departments but there were no surgery treatment at that time. Long term management was needed to prevent continuing brain damage and complications.***

Keywords: Sturge-Weber syndrome, children, bilateral megalocornea

1. Introduction

Sturge Weber syndrome (SWS) as described by Sturge in 1879 and Kalischer in 1897 is a sporadic condition characterized by a port-wine vascular nevus on the upper part of the face, salutatory neurologic deterioration and eventual neurodevelopmental delay. The hallmark intracranial vascular anomaly is a leptomeningeal angiomatosis that involves one or more lobes in one or both hemispheres [1], [3]. This sporadic disorder is thought to be caused by a somatic mutation but the genes remain unidentified [4]. Incidence of SWS currently estimated at 1 case in 50,000 persons [3]. Port-wine stain (PWS) on the face occurs in approximately 3 in 1,000 births and only 5% of infants affected with this type of cutaneous lesion have SWS [1].

SWS were classified into three types based on the presence of PWS, leptomeningeal angiomatosis, and glaucoma [4]. Some common findings related to SWS are focal or generalized seizures, hemiparesis and hemi atrophy, vascular headache, developmental delay and mental retardation, glaucoma, and hemi-anopsia [1]. SWS need multidisciplinary management and it is important for clinician to know this disease's clinical features and its complication in order to provide proper management. The aim of this study was to report a case of a three year old girl with SWS type I and bilateral megalocornea. Megalocornea is very rarely detected in SWS cases [5].

2. Case Report

A three years old girl, was admitted to Pediatric Emergency Unit at Sanglah Hospital on December 22, 2014, for complaining of seizure. Seizure was initially focal, starting from the left eye and left hand and occurred approximately ten minutes, without fever obtained.

Seizure then became frequent with jerky movement on left extremities. Patient was treated with intra rectal diazepam and intravenous diazepam and then loading dose intravenous phenytoin because of status epilepticus. Seizure was controlled after midazolam intravenously and admitted to Pediatric Intensive Care Unit. Patient was hospitalized with suspected diagnosis SWS for seven days. Patient was treated with carbamazepine and advised for routine visit to pediatric department for further investigation. Unfortunately, patient did not control routinely and without any medication.

The past history, patient had seizure since four months old. Seizure was occurred eight times without fever. Post seizure, patient was always alert. Patient was hospitalized twice with seizures until present. Patient also complained headache on admission but she can't explain the headache type and location. Patient discharged from hospital and seizure was controlled with carbamazepine orally.

Patient also had transient hemiparesis of left extremities with activity limitation, symptoms resolved after resting period. Right eye looked slightly bigger than the left one, and was noticed since newborn. There was no complained of pain or visual acuity. Physical examination revealed port wine stain in the complete right half of the face, including right half of the neck, paresis on seventh cranial nerves (right side), and hemiparesis of the left side of the body **(Figure 1)**. There were no meningeal sign neither pathologic reflex. Muscle power slightly decreased with hypotonic. Patient had caries dentist and increased vascularity on the right side of the cavity. Laboratory result revealed complete blood count within normal limit, normal blood sugar was normal and without electrolyte imbalance.

Eye examination showed bilateral megalo-cornea with cornea horizontal diameter 16 millimeters on right eye and 12 millimeters on left intraocular eye, and cornea vertical diameter 11 millimeters on right eye and 11 millimeters on

left eye. Under general anesthesia, intra-ocular pressure examination revealed normal with 17.3 mmHg on the right eye and 7.8 mmHg on left eye and cup disc ratio (CDR) of the optic nerve were 0.5 on both eyes showing nerve atrophy. Patient was diagnosed with megalocornea and suspected for secondary glaucoma. There were no specific treatment at the time and patient was advised for re-evaluation at ophthalmology department for the next six months.

Head CT scan was performed and revealed multiple calcification in intra-axial right and left frontal lobe and right temporo-occipito-parietal lobe lead to SWS feature **(Figure 2)**.

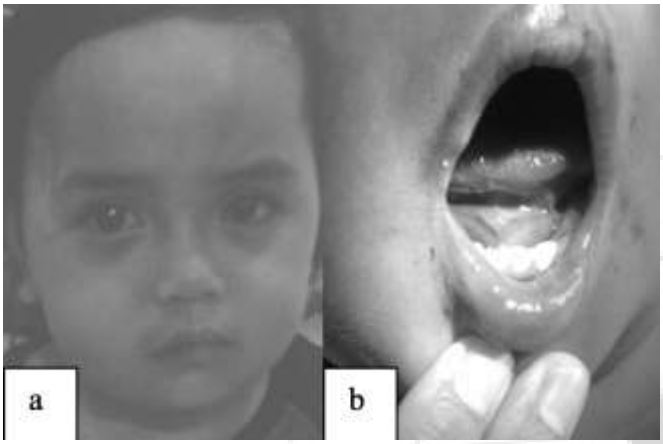

Figure 1: a. Port wine stain on the right side of the face and bilateral megalocornea b. Port wine stain on oral cavity mucosa (arrow).

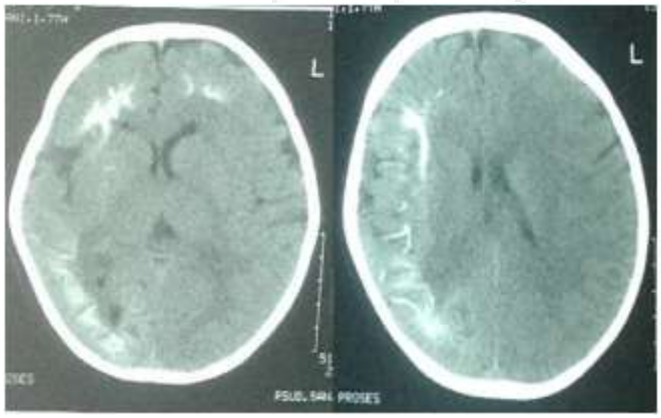

Figure 2: CT scan revealed calcification on leptomeninges in intra-axial right and left frontal lobe and right temporo-occipito-parietal lobe

Magnetic Resonance Imaging (MRI) showed abnormal intra cerebral calcification on bilateral frontal sub-cortical area and asymmetric right fronto-temporo-parietal area, with external cerebral atrophy on asymmetric right fronto-temporo-parietal area. With intravenous Gadolinium contrast addition, MRI revealed prominent leptomeningeal angiomatosis and multiple small cavernous hemangioma on the tip of anterior corn of the bilateral lateral ventricle and right thalamus. There was also soft tissue thickening on right maxilla-frontal area (skin hemangioma). This MRI result supports the diagnosis of SWS **(Figure 3)**.

The inter-ictal electroencephalogram (EEG) on December 31, 2014 revealed abnormal EEG. The background EEG showed alpha activity, with frequency of 4-5 Hz and 2-3 Hz, moderate voltage. There were no asymmetry and no focal epileptiform discharge. No clinical significant of EEG abnormalities during photic stimulation. The conclusion was abnormal EEG with mild general hypo-function **(Figure 4)**.

Patient was consulted to Dermatology Venereology Department for the PWS. The cutaneous lesion was described as red plaque with defined border and geographical form, which extend from right forehead to right chin. With diascopy test, the lesion appeared pale with pressure. Planning therapy for the PWS was observation and laser therapy suggested when patient reach adult age. Patient was also consulted to Neurosurgery Department, at the time there was neither specific treatment nor neurosurgery.

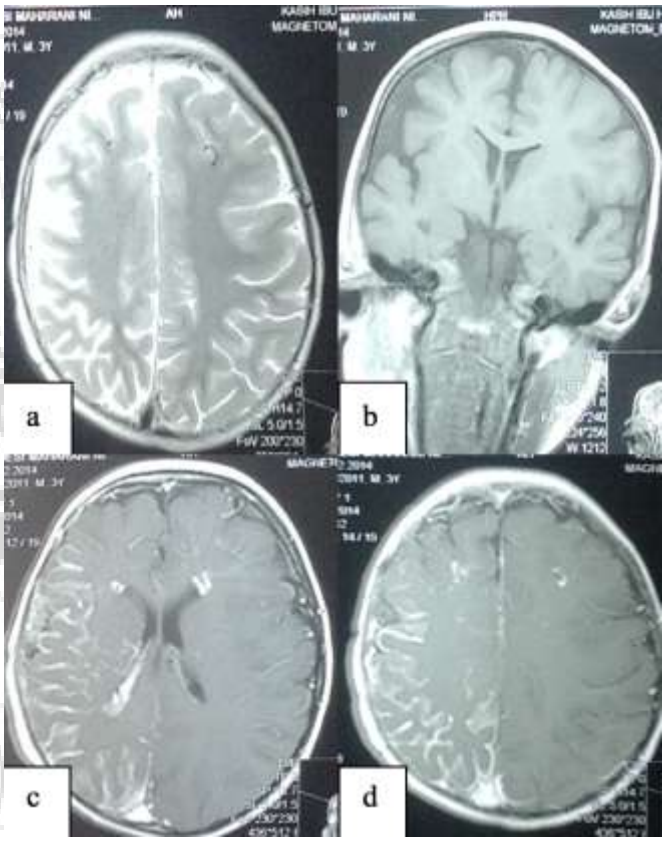

Figure 3: a. MRI revealed abnormal calcification on bilateral frontal sub-cortical area and asymmetric right fronto-temporo-parietal area.b. cerebral atrophy on asymmetric right fronto-temporo-parietal area. c and d. MRI with Gadolinium contrast revealed prominent leptomeningeal angiomatosis.

3. Discussion

Sturge-Weber syndrome is classified into neurocutaneous syndromes, a group of disorders with manifestation on the skin and central nervous system. Skin manifestation appears since newborn and experts called it phakomatoses. These disorders originate from defect that occurs on primitive ectoderm differentiation [1], [4].

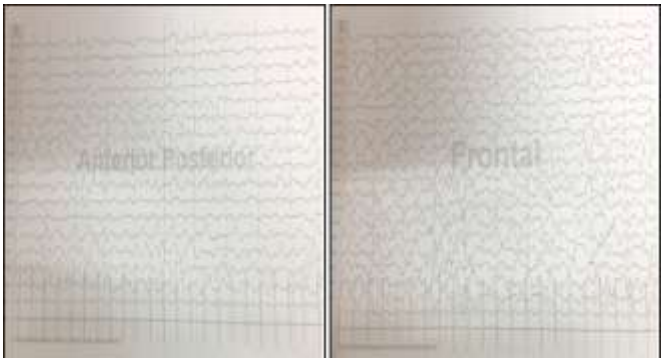

Figure 4: EEG was revealed abnormal with mild general hypofunction, without epileptiform discharged.

Pathogenesis of SWS is caused by somatic gene mutation and there was not enough evidence to prove that SWS was hereditary. Research by Shierley et al in 2013 find that somatic mosaic mutations disrupting vascular development cause both the SWS and PWS. There was 88% somatic mutation in GNAQ on SWS patient in this research [6]. **In our case,** there were no family history with the same symptoms. It was coherent with the hypothesis that SWS is sporadic and caused by somatic gene mutation.

SWS manifestation can be found on skin, eye, and nervous system. The cutaneous port-wine nevus is present at birth and involves at least one eyelid or the supraorbital region of the face. It is initially pale red and gradually assumes the deep port-wine color. It is unilateral in 70% of children and ipsilateral to the venous angioma of the pia, typically in the ophthalmic (V1) and maxillary (V2) distribution of trigeminal nerve [3]. The angioma can be extended to other facial areas including the lips, gingival, palate, tongue, pharynx, and larynx. The neck, trunk, and extremities also can be involved, either ipsilaterally or contra laterally to the facial angioma [4]. **In our case,** PWS was on the distribution area of right trigeminal nerve from right forehead to neck and also oral cavity mucosa and the palatum.

The most common neurologic complication of SWS is epilepsy. Approximately 80% of individuals with SWS have epilepsy, with partial seizures being the most common seizure type. Almost 75% of seizures occur by the first birthday, but adults with SWS can develop new onset seizures. Fever and infection may trigger the onset of seizures in many children with SWS [4]. These are usually the initial neurologic manifestation and frequently begin in the first year of life. Seizures can progressively become more refractory to medication and can be followed by transient or permanent hemiparesis. Hemiparesis, often with homonymous hemianopia, ultimately develops. **In our case,** seizures developed for the first time at the age of four months. Seizures were usually preceded by upper respiratory tract infection. Type of seizures of the patient was focal/partial seizures.

Other findings common to patients with SWS are vascular headache (40% to 60%), developmental delay and mental retardation (50% to 75%), glaucoma (30% to 70%), hemianopsia (40% to 45%), and hemiparesis (25% to 60%) [1], [6]. **In our case,** on recent admission, patient had hemiparesis, glaucoma, and also developmental delay.

Severe headaches and migraines are more frequent in SWS than in the general population. Severe headaches may precede the stroke-like episodes and have also been related temporarily to seizure clusters. The temporal relation between migraine-like headache, recurrent seizures, and hemiparesis in SWS is consistent with observations in animal models that dural stimulation causes distention of cranial vessels, stimulation of trigeminal afferents, and there lease of vasoactive peptides at nerve terminal. The leptomeningeal angioma may predispose children to neuronal hyper excitability that accounts for migraine [3], [4]. **In our case,** patient complained headache on admission but she can't explain the headache type and location due to her young age. Headache was followed by hemiparesis on the left side that resolved during treatment in hospital.

Transient deficits in motor, visual, and cognitive function are under-recognized as a complication of SWS. These episodes last hours to days and are regularly thought to be epileptic rather than stroke-like in nature. Although seizures frequently accompany stroke-like episodes, they typically follow the onset of motor deficits rather than precede them, as in a Todd's paralysis. Stroke-like episodes should be aggressively managed with hydration, rectal diazepam, and intravenous phenytoin or phenobarbital to reduce the risk or occurrence and severity of associated seizures. It has been speculated that such events result from either venous microcirculatory stasis or thrombotic occlusion of larger veins. Patients with stroke-like episodes have a gradual improvement in motor function over days to weeks, although careful motor testing often shows permanent motor and sensory deficits. Retrospective studies show that aspirin is beneficial, but no randomized, controlled trials have been completed in SWS. Occupational and physical therapy are beneficial to treat the transient stroke-like episodes and progressive hemiparesis adequately [3], [10], [11], [12]. **In our case,** patient complained hemiparesis on left side, followed by focal seizures. During treatment in hospital, hemiparesis was resolved and patient was able to walk after a week.

Most children with a facial cutaneous vascular malformation do not have SWS. When the cutaneous malformation is unilateral or bilateral and includes the ophthalmic division of the trigeminal nerve, the likelihood of SWS increases. The overall risk of SWS associated with any kind of facial cutaneous vascular malformation is approximately 8%. Children with involvement of the eyelids are at elevated risk for eye and brain disease. Rarely, some children with SWS lack a facial cutaneous vascular malformation but have the neurologic and/or ophthalmic components. Roach classify SWS into 3 types considering PWS, leptomeningeal angioma, and glaucoma. Type I is when individual has a facial PWS, leptomeningeal angioma, and may have a glaucoma, type II is when individual has a facial PWS, no leptomeningeal angioma, and may have glaucoma, and type III is when individual has leptomeningeal angiomatosis, no facial PWS, and rarely glaucoma [4]. **In our case,** we found PWS on the right side of the face in the area enervated by

trigeminal nerve, leptomeningeal angioma, and secondary glaucoma. Patient was classified into type 1 SWS.

Abnormalities of the skin, leptomeningeal, choroid, and cortex in SWS, can be traced to malformation of an embryonic vascular plexus, arising within the cephalic mesenchyme between the epidermis (neuro-ectoderm) and the telencephalic vesicle. Interference with the development of vascular drainage of these areas at approximately 5 to 8 weeks of gestation subsequently affects the face, eye, leptomeninges, and brain. The angiomatosis is accompanied by poor superficial cortical venous drainage, with enlarged regional trans-medullary veins developing as alternate pathways. The ipsilateral choroid plexus may become engorged. Vascular stasis promotes chronic hypoxia of both cortex and underlying white matter. Ultimately, tissue loss and dystrophic calcification occur. Diagnosis of SWS is made on the basis of the presence or absence of ophthalmologic or neurologic disease [4]. Children with PWS in the trigeminal nerve distribution should have the following imaging studies completed: a non-contrast enhanced computed tomography (CT) scan and a contrast-enhanced MRI scan of the head. The MRI with contrast is ideal to define the vascular anatomy characteristic of SWS. The features most often seen are the enhancement of the leptomeningeal angioma, enlarged trans-medullary veins, choroid plexus hypertrophy, white matter abnormalities (perhaps secondary to ischemia), atrophy and cortical calcification [1], [4], [8]. Other imaging studies that may prove helpful in selected cases are single photon emission computed tomography (SPECT), positron emission tomography (PET), and magnetic resonance spectroscopy (MRS) [1]. **In our case,** we found calcification on leptomeninges through the head CT-scan examination. Abnormal calcification on bilateral frontal sub-cortical area, asymmetric right fronto-temporo-parietal area, and cerebral atrophy on asymmetric right fronto-temporo-parietal area showed in MRI. With intravenous contrast addition MRI revealed prominent leptomeningeal angiomatoses and multiple small cavernous hemangioma on the tip of anterior corn of the bilateral lateral ventricle and right thalamus.

Electroencephalogram is routinely obtained in patients with SWS and epilepsy. There is slowing ipsilateral to cerebral involvement, with associated spikes and sharp waves. During episodes of transient, stroke-like episodes, the EEG frequently shows slowing without active epileptiform activity [4]. **In our case,** EEG was revealed abnormal with mild general hypofunction without epileptiform discharge.

Approximately one half of patients with SWS can achieve complete seizure control. It is essential to increase the dose for weight gain as control can be lost if adequate antiepileptic drugs (AED) doses are not maintained in the moderate to high range. Except for intravenous management of seizures in SWS, phenobarbital and phenytoin are no longer recommended for use in children with SWS. If intravenous phenobarbital has been necessary to achieve seizure control, it is slowly tapered orally over several months and replaced with a different AED. Carbamazepine was found to be effective in controlling partial seizure compared with valporate [9]. If seizures recur in children with SWS receiving carbamazepine, we can add topiramate, with the ultimate goal of providing seizure control with monotherapy topiramate. Leviteracitam, valproate, or clonazepam are excellent alternatives to topiramate. Epilepsy surgery should be considered very carefully in patients with frequent, debilitating seizures in whom antiepileptic drugs have been ineffective. In fact, older age at surgery correlated with an improved outcome. Maria et al recommend two or more AEDs for over six months before considering surgical management [4]. **In our case,** patient was prescribed carbamazepine at first hospitalization. But patient didn't took the AED routinely which caused frequent seizures occurred. On the last admission, patient was treated with diazepam, phenobarbital, phenytoin and midazolam according to epileptic status algorithm. Carbamazepine was given for long term management of seizures. At the time, seizure was controlled so there was not necessary for epileptic surgery.

In SWS, vascular abnormalities of the conjunctiva, episclera, retina, and choroid may occur. Patients with the most severe anomalies in conjunctiva and episclera vessels are at greater risk of glaucoma. About 30 to 70% of patients with SWS will develop glaucoma. The presence of a cutaneous vascular malformation in the distribution of the ophthalmic division of the trigeminal nerve increases the probability of glaucoma. Glaucoma is diagnosed in infancy in most children with SWS, but 40% of patients develop the complication as adolescents or in adult years. A neonate with a PWS over the V1 distribution should have an ophthalmologic evaluation as soon as possible. Follow-up screenings every 3 months for the first year, semiannually the second year, and annually thereafter will detect increased intraocular pressure. This increased intraocular pressure will eventually cause buphthalmus although it is rare. Most commonly, the affected eye is ipsilateral to the PWS. Management for glaucoma in SWS requires beta blockers, carbonic anhydrase drops, and multiple surgeries [13]. Choroid thickening may also occur and may cause vision loss and require laser photocoagulation for retinal detachment later in adolescence or adulthood. Ongoing ophthalmologic care is essential to current management of SWS [4], [14]. **In our case,** patient was diagnosed with megalocornea and suspected for secondary glaucoma due to SWS syndrome. There were sign of optical nerve atrophy but intraocular pressure remained normal. There was no specific treatment at the time. Patient was advised for routine evaluation to Ophthalmologist to monitor her eye condition.

All children with a PWS should have a full dermatologic evaluation. The PWS ranges from light pink to dark purple and is actually caused by an excess of capillaries underneath the affected skin (capillary vascular malformation). The current treatment of PWS is laser treatment, most often using a pulsed dye laser. Treatment is encouraged for reasons that extent beyond cosmetic issues. Children with a large PWS are more likely to have social and behavioral issues. If PWS are untreated, it will frequently develop hypertrophy of the tissue, blebbing and cobblestoning which depending on location, impair vision, speech or the airway and result in bleeding. The PWS may often grows and becomes hyper-pigmented and nodular, fewer treatments are required if started in early infancy. Results with modern lasers are excellent, and it is often difficult to detect the PWS later [4].

In our case, Patient was consulted to Dermatologist and was planned to undergo laser therapy when patient get older.

Developmental delay, learning disabilities, and mental retardation are often seen in children with SWS, more so in those who have seizures. Children with SWS also have an increased risk for having emotional and behavioral difficulties, including attention deficit hyperactivity disorder (ADHD). Poor school performance associated with one or more of the above problems have been a major concern of parents. Most individuals with SWS require neuropsychological assessment of intellectual and academic skills, social skills, and mood to guide educational interventions [4]. Cognitive delay was significantly correlated with seizure intensity in the early period. High seizure intensity in young patients with SWS is a prognostic marker for mental deterioration [15], [16]. Children with epilepsy are at increased risk for psychopathology and clinicians should consider both neurological and psychosocial factors, including the family system, when treating psychopathology in children with epilepsy [17]. **In our case,** patient experienced seizures since the first year and there was developmental delay. Early intervention was needed to prevent difficulties in emotional, behavioral, and intellectual aspect.

4. Summary

We reported a case of SWS type I with bilateral megalocornea. Patient presented port wine stain on the right half of the face, secondary glaucoma and leptomeningeal angiomatoses in the brain. The type of seizure was partial seizure and patient was treated with carbamazepine. The patient was consulted to ophthalmologist, dermatologist, and neurosurgeon.

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