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Intracerebral hemorrhage in Sturge Weber Syndrome: A case report

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ABSTRACT

Background. Encephalotrigeminal angiomatosis also called Sturge Weber Syndrome (SWS) is neurocutaneous abnormality with angioma affecting the leptomeninges and the face skin, commonly in the eyes and maxillary distribution of trigeminal nerve. The characteristic of SWS is dilated face skin veins, and referred to nevus flammeus and port wine stain.

Case reports. We report a case of Sturge Weber Syndrome in a 41 years old male with uncontrolled hypertension and smoking, left-sided weakness, and left-sided facial port wine stain.

Conclusions. Neurological examination was suggestive of SWS and further radiological examination confirmed the diagnosis.

Keywords: intracerebral hemorrhage, encephalotrigeminal angiomatosis, Sturge Weber Syndrome

Abbreviations (in alphabetical order):

CT	– Computed tomography
EEG	– Electroencephalography
FDG-PET	– Fluorodeoxyglucose Positron Emission Tomography
MRI	– Magnetic Resonance Imaging
PWS	– Port Wine Stain
qEEG	– Quantitative Electroencephalography
SWI	– Susceptibility Weighted Imaging
SWS	– Sturge Weber Syndrome
VEGF	– Vascular Endothelial Growth Factor

INTRODUCTION

Sturge Weber Syndrome (SWS) is a rare neurovascular congenital abnormality which impacts the skin, eyes, and brains. SWS is related to the mutation of gene GNAQ. The incidence of the syndrome between 1/50.000 until 1/230.000 live births. Sturge Weber syndrome is a non-heritable condition, but instead presents predominantly in sporadic cases, both in males and females, in all racial and in all ethnic origins. The neurological manifestations of SWS can involve tonic, myoclonic, or atonic seizures, mental disability, a learning problem, brain cell atrophy and calcifications, visual field defections, and glaucoma. SWS is a multifaceted impairment, in which endocrine, psychiatric, ophthalmological, rehab, dermatology and many more clinical concerns are prevalent and attention deficit hyperactivity disorder [1,2]. SWS is a globally prevalent condition. Most often, the condition is easily recognized at delivery or in the beginning of babyhood according to superficial clinical signs on their own. But, the ongoing morbidity progresses from a lifetime of the secondary underlying alteration and complication. Typically, the patient with SWS develops facial capillary malformations, also recognized as port wine birthmarks or nevus flammeus. Leptomeningeal vessel defects commonly present in the trigeminal nerve region. SWS is the third most prevalent a neurocutaneous syndrome subsequent to those of neurofibromatosis and tuberic sclerosis.

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SWS patients with intracranial hemorrhage were very rare. Angiomatous defects, venous angiomas over plexus of the choroid, and the sinus thrombosis are recognized as prevalent in SWS patients though the correlation among SWS and intracranial hemorrhage is unclear in other situations [3,4]. The patient will has impaired blood supply to the brain and is at increased risk of developing venous strokes and stroke like episodes. Capillary malformation and leptomeningeal angiomastosis can result from a failure in the primitive vein system in initial stages of developmental [4,5]. Whereas, intracranial hemorrhages in patients suffering from SWS rarely occur. We are reporting a rare case of SWS presenting with intracerebral hemorrhage with concomitant risk factors of uncontrolled hypertension.

CASE REPORT

A 41-year-old male suddenly hemiplegia in the left side was admitted to our emergency department after 4 hours onset. Its neurological status was scored according to GCS 13 (E3V4M6) on the left side weakness. Upon delivery, he developed a trademark SWS port wine stain birthmark on the left side of his face affecting the eye, submaxillary, and mandibular division of the trigeminal nerve, as in (Figure 1). He has no clinical history of any ophthalmic or neurological signs including seizure, glaucoma, and stroke like episodes, aside from visual disturbances in his left eye. He was not treated with anticonvulsants or antiaggregant agents, and had none past heart problem history or any cancerous tumors. He had history of uncontrolled blood pressure and smoking. During admission, his blood pressure was 220/110 mmHg

FIGURE 1. The illustration of port-wine birthmark in our patient

and with pulse rate 72 pulses a minute in a normally rhythmic sinus rhythm, elevated body temperatures was 37.1° C. His neurologic condition was scored as GCS 13 (E3V4M6) with left side hemiparesis, and focal seizure in the left extremities, and the National Institute of Health Stroke Scale scored is 16.

Laboratories findings showed: hemoglobin 13.8 g/dl, the hematocrit 41.2%, blood urea nitrogen 32.5 mg/dl, and creatinine 1.20 mg/dl. Thrombocytes activation factor and coagulation rate are both normal. Computed tomography showed right thalamic hemorrhage with perilesion edema, as in Figure 2. The patient was managed conservatively with tranexamic acid, furosemide, nicardipine, amlodipine, cande-

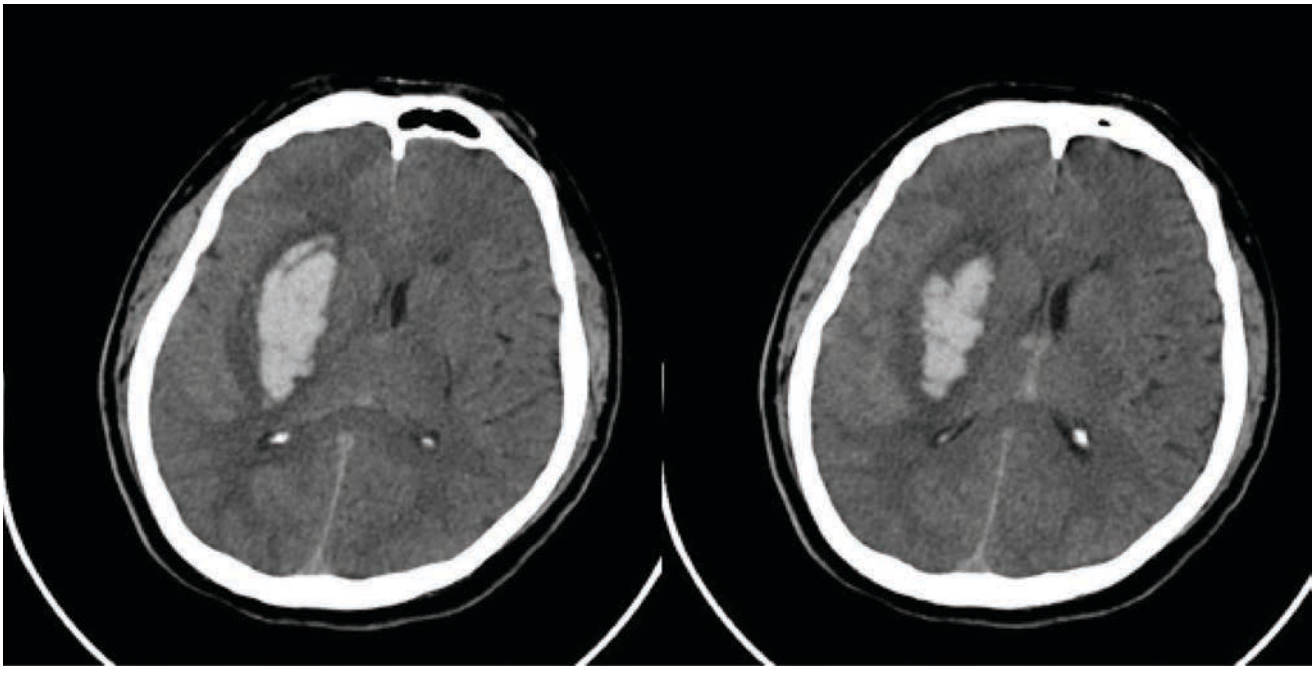

FIGURE 2. The brain CT showed right thalamic hemorrhage

sartan, and anti-seizure medication. His consciousness disturbance improved slowly to GCS 15 (E4V5M6). Left side hemiparesis It slowly eased, and began to walk with support of the side rail. After 10 days the patients was discharged. In 6 month evaluation, the modified Rankin scale was 2. He continue the anti-hypertension and anti-seizure medication.

DISCUSSION

We reported rare cases of intracerebral hemorrhage in SWS. Spontaneous intracranial hemorrhage has been documented in cases reported by Anderson and Duncan in 1974, Pozzati et al. in 1983, Dolkart and Bhat in 1995, Aguglia et al. in 2008, Lopez et al. in 2013, and Nakajima et al. in 2014. The median age of affected patients was 15.1 years, ranging from 1 to 62 years old. Most cases of intracranial hemorrhage occur during childhood, in one's twenties, and thirties.

SWS is a manifestation of congenital neurocutaneous syndromes which presents as facial angiomas (also called wine stains) in the higher facial areas and frequent intracranial leptomeningeal angiomatosis. Patients with SWS commonly having temporary episodes of hemiparesis, or stroke like episodes, which may be most puzzling serious neurologic symptoms in patients affected by Sturge Weber syndrome (SWS). Although this episode is similar to an ischemic stroke, the clinical presentation is quite variability, and MRI of the brain rarely shows persistent infarcts that usually occur in cerebrovascular originating from arteries [6,7]. Several disorders present with clinical features similar to Sturge-Weber syndrome (SWS) and should be considered in its differential diagnosis. Klippel-Trenaunay-Weber syndrome features port-wine stains on the face and extremities, alongside hemihypertrophy of soft and bony tissues, resembling SWS. It is sporadic like SWS and can involve solid visceral tumors, commonly affecting the kidney, adrenal gland, or liver. There have been rare reports of overlap between SWS and Klippel-Trenaunay-Weber syndrome. Beckwith-Wiedemann syndrome includes facial port-wine birthmarks, macroglossia (enlarged tongue), omphalocele (abdominal wall defect), and visceral overgrowth, with a notable risk of visceral tumors. Severe hypoglycemia from pancreatic islet-cell hyperplasia is a common and potentially life-threatening feature. Dyke Davidoff Masson syndrome shares neuroimaging findings resembling SWS, where one cerebral hemisphere shows atrophy due to carotid artery infarction before or shortly after birth. This syndrome also presents with cerebral hemiatrophy and enlarged calvarial diploic space on imaging. Severe siderosis and calcifications from intrathecal methotrexate therapy and meningitis are also considerations in the differential diagnosis, particularly when cortical calcifications are observed on CT scans. However, these conditions typically do not exhibit the unilateral, specific geographic localization seen in SWS.

Computed tomography (CT) is effective for identifying calcifications and visualizing changes such as cortical atrophy and leptomeningeal enhancement with contrast. However, due to its use of ionizing radiation, routine CT scans are not recommended for children. Instead, MRI of the brain with contrast is preferred as it offers detailed imaging without radiation exposure. The most commonly affected brain regions in Sturge-Weber Syndrome are the occipital and posterior parietal/temporal lobes. MRI findings depend on the disease stage. In the early phase, there is transient hyperperfusion with accelerated myelin development, leptomeningeal enhancement (seen as zigzagging enhancement along brain folds), and restricted diffusion in cases of acute ischemia. In the late phase, there is increased T2 signal indicating gliosis, reduced leptomeningeal enhancement, and cortical atrophy. Superficial cortical veins are diminished, while deep medullary/subependymal veins and choroid plexus appear enlarged. Gyriform calcifications are best visualized on T2 or susceptibility weighted imaging (SWI) as areas of signal loss along the brain folds in a serpentine pattern. Children with cutaneous and ocular signs of SWS and normal brain MRI at one year of age are unlikely to develop brain complications later. Choroidal angiomas can be seen on MRI as enhanced areas along the posterior choroid layer of the eye. Fluorodeoxyglucose positron emission tomography (FDG-PET) can assess cerebral metabolism in SWS patients, showing increased metabolic activity in early stages and decreased activity in later stages of the disease [8,9]. Capillary or venular malformation, also known as PWS (Port Wine Stain) or nevus flammeus, is the distinctive skin feature observed in Sturge-Weber syndrome (SWS). This birthmark appears at birth, varies in size, typically appears on one side but can be bilateral, and ranges in color from pale pink to deep purple. It can sometimes be mistaken for salmon patches (nevus simplex), which are lighter, less defined pink patches often found centrally on the face including the forehead, philtrum, upper eyelids, vertex, and neck. PWS is characterized by its unilateral distribution, more vivid coloration, and well-defined edges, which set it apart from salmon patches. The risk of neurological or eye complications associated with facial PWS depends on its size and location. Birthmarks affecting the frontal region, which aligns with the sensory innervation areas of the trigeminal nerve branches (V1, V2, and V3), pose a greater risk compared to those found on the lower face. In Sturge-Weber syndrome (SWS), intracranial angiomatosis usually appears on the same side as the port-wine stain (PWS) but can sometimes affect both sides. It typically in-

volves the occipital and occipitoparietal lobes, and occasionally extends to the entire hemisphere. Histologically, this condition is characterized by abnormal, twisted blood vessels and thickened leptomeninges.

There are also abnormalities in the enlarged deep veins that drain these areas. The underlying brain tissue may show atrophy, neuronal loss, astrocytosis, cortical developmental anomalies, and calcifications around blood vessels or in the cerebral cortex, which are believed to be caused by insufficient oxygen supply. In individuals with SWS, the leptomeningeal vessels show elevated levels of fibronectin and vascular endothelial growth factor (VEGF), along with increased endothelial cell proliferation and apoptosis. The main clinical symptoms of leptomeningeal angiomatosis include seizures (in 75-90% of cases), gradually worsening weakness on one side of the body (in 25-60% of cases), migraine-like headaches (in 30-45% of cases), delayed cognitive development (in 50-60% of cases), and episodes resembling strokes, such as temporary paralysis on one side, visual field disturbances, and behavioral problems. Seizures in SWS are primarily caused by irritation of the cerebral cortex due to the vascular malformation, resulting in conditions like hypoxia, ischemia, and gliosis. These seizures typically manifest as complex partial seizures or partial seizures with secondary generalization. Progressive neurological decline in children with SWS is attributed to ischemic damage due to altered cerebral blood flow and increased metabolic demands resulting from prolonged seizure activity. In Sturge-Weber syndrome (SWS), ocular vascular malformations involve enlarged and twisted venous vessels affecting structures like the conjunctiva, episclera, retina, and choroid. These abnormalities can lead to optic nerve damage and vision loss. Glaucoma is a frequent ocular complication in SWS, believed to result from increased pressure in the episcleral veins, which is supported by the presence of blood in the Schlemm canal, or due to anomalies in the anterior chamber that hinder normal drainage of aqueous humor, causing elevated resistance.

Glaucoma may be present from birth or develop later in life. In early-onset cases, around 60% are associated with anterior chamber angle abnormalities, while in younger individuals and adults, about 40% are linked to elevated episcleral venous pressure. Choroidal hemangioma is found in 40% to 50% of individuals with Sturge-Weber Syndrome (SWS) and can manifest as either circumscribed or diffuse lesions. Occasionally, these vascular lesions in the choroid display a distinctive appearance described as a reddish hue resembling tomato ketchup. During childhood, the choroid typically remains stable however, in adolescents and adults, it may undergo significant thickening. Less commonly reported ocular issues in SWS include heterochromia iridium (variation in iris coloration), retinal detachment, strabismus (misalignment of the eyes), homonymous hemianopsia (loss of half of the visual field), phakomatosis pigmentovascularis (presence of both vascular and pigmented skin lesions), and neovascularization in the iris and choroid, as well as displacement of the lens. [10]. The identity of the underlying somatic chromosome mutational and presumable hyperactivity of the pathways downstream, as well-known as the biomarker developments and the measures of adherence in SWS, have facilitated recent prospective drug trials for these patients. Meanwhile, the R183Q GNAQ mutations have typically shown to be linked to SWS. Sturge-Weber syndrome is primarily linked to a specific genetic mutation known as R183Q in the GNAQ gene. This mutation causes Gαq, a protein involved in transmitting signals from G protein-coupled receptors to cellular processes, to be hyperactive. Normally, Gαq switches between active (GTP-bound) and inactive (GDP-bound) states. The R183Q mutation disrupts this process by reducing the stability of the inactive GDP-bound state, preventing the protein from properly turning off. This leads to continuous activation of downstream signaling pathways, particularly the Ras/Raf/MEK/ERK pathway and mTOR activity. These pathways play crucial roles in cell growth, differentiation, and vascular development. The dysregulation caused by the R183Q mutation results in abnormal vascular development, which is a hallmark of Sturge Weber Syndrome. Specifically, the constant activation of signaling pathways interferes with the normal formation and maintenance of blood vessels. This disruption leads to the formation of vascular malformations observed in affected individuals, such as the characteristic port wine birthmarks and the abnormal blood vessel growth in the brain, which can cause neurological symptoms.

The molecular consequences of the R183Q mutation in GNAQ ultimately manifest as the vascular anomalies characteristic of Sturge Weber Syndrome. The capillary defects and leptomeningeal angiomatosis may be contributed to the malfunction of primary cephalic veins plexuses to retrogress. In the earliest phase of its development, the primal vein systems are split into the external section that nourishes and drains the face of skin and the scalp, the medial part that nourishes the meninges, and visceral part, that nourishes and drains the brain. It suggests that during this phase, the embryological closely linked ectoderm, fated to shape the higher part of face skin, to the neural tube parts that will constitute the parietal-occipital part of brain, possibly explaining the affiliation among face capillary malformation and leptomeningeal angioma, might provide an understanding of the connection between face capillary malformation and leptomeningeal angiomatosis and

the development of leptomeningeal angioma [10]. SWS is categorized as being complete if engages the CNS and angiomes of the facial region, and being uncomplete if it engages just one area without the other. Based on a different measure, the Roach scale, SWS is divided up into three groups: (1) Case I - Both face and also leptomeningeal angiomas, may eventually result in glaucoma, (2) Case II - Face angioma itself, may eventually result in glaucoma, (3) Case III - An outlying leptomeningeal angioma, typically not leading to glaucoma [11].

Contrast-enhanced magnetic resonance imaging is being utilized to diagnosis the patients having leptomeningeal vessel deformities, deep venous dilation, and brain atrophy apparent on SWS of brain involve. The area and site of MRI brain engagement as correlated with intelligence. Since the MRI is less sensitive on SWS cerebral engagement in young infants, EEG and quantitative EEG can screen for evidence of SWS cerebral involvement. EEG assesses redundant spikes, sharps, attenuations, and ictal activities. qEEG may quantify pulses on either side of hemisphere and screening for meaningful pulsatile pulses asymmetries. The approach of qEEG provides up to 40% of diagnostic insights in screening the risk of SWS cerebral engagement, versus predicting on the basis of the amount of size and breadth of birthmark only. qEEG can assist in determining the best time for diagnostic MRI and in the prevention of risk for newborns with at risk of facial capillary defects [12,13]. In our patient the uncontrolled blood pressure can be the important trigger and confounding factors

CONCLUSION

To summarize, we report a very uncommon intracranial hemorrhage cases among SWS patients. Uncontrolled blood pressure may be the important confounding factor. Outcome of SWS patients is suffering from intracranial hemorrhage is not favorable.

Ethics:
The authors certify that they have obtained verbal patient consent. The patient identity cannot be identified.

Conflict of interest:
We certify that none of the writers of this work have any conflicts of interest. The conduct, preparation, collecting, analysis, interpretation, and writing of the report were all done without any financial assistance.

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