Sturge–Weber syndrome and variability of clinical presentation

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ABSTRACT

Introduction: Sturge–Weber syndrome (SWS) is a congenital syndrome characterised by intellectual disability, glaucoma, a characteristic port-wine stain on the skin around the route of the ophthalmic branch of the trigeminal nerve and the affection of the leptomeninges in the brain in the form of abnormal capillary venous vessels. The aim of this study is to look at the clinical features as well as the correlation of SWS with other comorbidities in hospitalised children.

Materials and methods: Records of admitted children over the period 2000–2019 were retrospectively studied. Epidemiological variables, gender and age at the time of diagnosis, changes in the skin, central nervous system affection and ophthalmological changes were analysed and recorded.

Results: Eleven cases of SWS were identified and included in the study. Age at the time of diagnosis ranged from 1 to 36 months. EEG showed specific grapho-elements, with partial seizures presenting in five cases out eight total cases with epilepsy. Ophthalmological complications were common, with glaucoma and choroidal haemangioma being the most common. Cognitive problems were found in seven cases, headache in eight cases and hemiparesis in four.

Conclusion: SWS is associated with other medical conditions. The study has described some of the features of SWS and found its correlation with epilepsy and other neurological problems, glaucoma, headache, hemiparesis and cognitive problems.

KEYWORDS:
Glaucoma, Port wine stain, Leptomeningeal angioma, epilepsy

INTRODUCTION

Sturge-Weber syndrome (SWS) is a congenital syndrome characterised by intellectual disability, glaucoma, a characteristic port-wine stain on the skin around the route of the ophthalmic branch of the trigeminal nerve and the affection of the leptomeninges in the brain in the form of abnormal capillary venous vessels.[1] It is caused by a somatic mutation in the gene GNAQ.[2] According to the National Organisation for Rare Disorders, SWS occurs in one of every estimated 20,000 to 50,000 live births.[3] The medical term for this disease is encephalotrigeminal angiomatosis but it can also be named as craniofacial angiomatosis.[3] Sturge–Weber can cause a number of complications, including seizures, developmental delays, muscle weakness on one side of the body, paralysis, cognitive impairment and eye problems.[3,4] In some children, however, the abnormal vessels characteristic for the disease can be asymptomatic.[6,7] Two out of every three children with SWS will have seizures. They may start at birth or in the first year of life. They are usually focal (also called partial) motor seizures involving jerks of one side of the body only. The seizures may become generalised and evolve into other types of seizures, such as atonic seizures 'drop attacks', myoclonic seizures or infantile spasms.[2,3] The abnormal blood vessels may also involve the eye directly and result in an abnormality of the drainage of fluid within the eye.[8,7]

According to the American Association for Paediatric Ophthalmology and Strabismus, an estimated 50% of children with SWS develop glaucoma during infancy or later in childhood. Glaucoma is an eye disease often caused by increased pressure in the eye. This can cause vision impairment, sensitivity to light and eye pain.[9,10]

Learning disabilities are present in two out of three children with SWS. In some children, severe learning disabilities develop. The more frequent and the more severe the seizures, the greater the severity of the learning disabilities.[11,12] The diagnosis of SWS is usually relatively easy. This is because of the characteristic 'port-wine' birth mark on one side of the face and neck is seen at or soon after birth. However, sometimes the diagnosis is more difficult. This is when the birth mark is very pale or occurs only over the scalp and is covered by the child's hair. A computerised tomography (CT) scan of the brain will usually show the typical abnormalities of the blood vessels on the surface of the brain better than a magnetic resonance imaging (MRI) brain scan.[7,11,13,14]

Treatment is mainly directed towards trying to control the frequent seizures and monotherapy does not produce good results. In these cases, early consideration should be given to epilepsy brain surgery. The surgery involves disconnecting part of the brain in the region of the abnormal blood vessels. This is called a 'hemispherotomy.'[6,2,15] Treatment of glaucoma, if it develops, is possible and laser treatment may be very effective for the birth marks.[8,16]

Through this study, we aimed to evaluate the clinical features of the disease in our country, its correlation with epilepsy and

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Table I: Structure of patients with SWS by sex and comorbidity

Sex	No.	%	*p* value
Female	5	45.5	0.76
Male	6	54.5	
Total	11	100.0	
Comorbidity			
Without comorbidity	3	27.3	0.13
With comorbidity (epilepsy)	8	72.7	
Total	11	100.0	

[a]Chi-square test was applied

Table II: Descriptive statistics for patients with SWS – age of diagnosis (n=11)

Age at diagnosis (day)		Statistic	Std. Error
Mean		540.27	124.43
95% Confidence Interval for Mean	Lower Bound	263.02	
	Upper Bound	817.52	
5% Trimmed Mean		539.41	
Median		365.00	
Std. Deviation		412.69	

Table III: Clinical characteristics of patients with SWS and neurological symptoms (n=8)

Type of seizures	No.	%	*p* value
Partial seizures	5	62.5	0.28
Mixed seizures	3	37.5	
EEG manifestations			
Specific electrical manifestations into one hemisphere	5	62.5	0.28
Specific electrical manifestations into two hemispheres	3	37.5	
Treatment			
Carbamazepine	2	25.0	0.61
Valproic acid+Levetiracetam	2	25.0	
Carbamazepine+Levetiracetam+Clonazepam	4	50.0	
Complications			
Ophthalmological	6	54.5	
Cognitive problems	7	63.6	
-lack of concentration, learning disorder	4	36.4	
-severe behavioral disorders	3	27.3	
Headaches	8	72.7	
-migraine headache	6	54.5	
-tension headaches	2	18.2	
Hemiparesis	4	36.4	
Changes in the face and nervous system	3	27.3	

[a]Chi-square test was applied.

Table IV: Treatment of patients with ophthalmological problems (n=6)

Ophthalmological treatment	No.	%	*p* value
Surgery (trabeculotomy-trabeculectomy)	4	66.7	0.41
Conservative treatment	2	33.3	
Total	6	100.0	

[a]Chi-square test was applied.

other neurological problems, glaucoma, headache, hemiparesis, and the impact of the disease on psychomotoric developmental delay.

MATERIALS AND METHODS

This is a retrospective cohort study and includes analysis of medical records of children admitted during the period of 2000–2019. Following this analysis, 11 cases with Sturge Weber syndrome have been identified, according to International Classification of Diseases (ICD-10). The study was undertaken at the University Clinical Centre of Kosovo, the referral and the only tertiary health care institution, covering cases referred from the entire country.

The data taken from the medical records include epidemiological variables, gender, age at the time of diagnosis, changes in the skin, changes in central nervous

system and ophthalmological changes. Other signs of central nervous system affection (development of epilepsy or not, hemiparesis, psychomotor disturbances, headache attacks), treatment of seizures, treatment of ophthalmological problems, imagery changes (central nervous system computerised tomography and magnetic resonance imaging) and electroencephalography changes, were analysed too.

In order to undertake and publish the study, informed consent and approval by Ethics and Professional Committee of Hospital and Clinical University Centre of Kosova were obtained, holding a decision number 3426, on November 11th, 2019.

The following statistical parameters have been used: the structure index, cumulative structure, simple arithmetic mean, standard deviation, standard error, confidence interval with a significance level of 95% (CI 95%). For the purpose of testing the differences for categorical data, chi-square test (chi-test), for the exact level of significance (p) has been used. The statistical tool used to analyse the date was Statistical Package for the Social Sciences (SPSS).

RESULTS

11 cases have been included in the study, six males and five females with a ratio of 55% to 45% (Table I).

When analysing the association of the disease with comorbidities, it has been identified that 8 cases (73%) have been associated with epilepsy. Age at the time of diagnosis ranged from 1 to 36 months, with a mean of 18 months (Table II).

Most of the seizures, 5 cases (63%), were partial while 3 cases (37%) were combined (atonic, partial with secondary generalisation, and generalised (Table III). EEG showed specific grapho-elements in one of the hemispheres in 4 cases (50%) (Table III). In 4 other cases (50%), specific grapho-elements are seen in both hemispheres. Specific grapho-elements include spike, spike-wave complex and low voltage in one of the hemispheres, slow wave activity and polyspike (Table III). With regard to the therapy, anticonvulsive drugs of different spectre have been used. Carbamazepine has been used successfully as monotherapy in 2 cases (25%), sodium valproate combined with levetiracetam resulting in partial seizure control in 2 cases (25%). Three antiepileptic drugs (carbamazepine, levetiracetam, clonazepam) have been used in 4 other cases (50%) with no full seizure control (Table III). Brain surgery such as hemispherectomy has not been undertaken in any of the cases. Hemiparesis was found in 4 cases (36%) and usually in contralateral side to facial and brain changes. Three cases (17%) presented with only facial changes and brain changes (Table III). Cognitive problems have been found in 7 cases (64 %). Cognitive problems were in direct correlation with the onset of seizures, the early the seizures started, more severe the cognitive problems. Also, cognitive problems were more severe in patients using two and more antiepileptic drugs. The commonest problems include attention deficit, learning disability in 4 cases (57%) and severe behavioural problems in 3 cases (43%) (Table III). Often, the level of behavioural problems depends on associated symptoms found in different patients, the more clinical manifestations, the greater the severity of behavioural problems. Headache of different nature has been found in 8 cases (73%), mostly migraine-type headache in 6 cases (75%) and tension type in 2 cases (25%) (Table III).
Ophthalmological complications are common. Six cases have associated glaucoma and choroidal haemangioma (55 %) (Table III).

In most of the patients, glaucoma was congenital and associated with choroidal haemangioma. Usually, ophthalmological changes were unilateral and ipsilateral to the facial changes. In order to prevent atrophy of optic nerve and increased intraocular pressure (IOP), combined surgical therapy was conducted in 4 cases (67%) and conservative therapy in 2 cases (33%). Trabecolotomy-trabeculectomy has been performed as a surgical method, and prostaglandins, beta blocker and anhydrase inhibitors (Table IV).

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DISCUSSION

Sturge-Weber syndrome is a rare disease, first mentioned by Schirmer (1860), and then described more by Sturge in 1879.[14] SWS has been classified in the group of rare diseases. According to the National Organisation for Rare Disorders, SWS occurs in one of every estimated 20,000 to 50,000 live births.3 There is no significant difference between male and female (6:5 in favour of male).[7] Glaucoma presents in 55% of the cases and is often associated with choroidal haemangioma, which also matches with data of many authors.[8,7,17] In most of the cases, a combination of surgical and conservative methods have been used to treat glaucoma.[15] About 73% of the patients have associated epilepsy, presenting with different type of seizures, in particular partial at the beginning of the disease evolving into secondary generalisation in older patients. The earlier the onset of seizures, the greater resistance to anticonvulsive therapy was noted.[5,11,17,2] Two and more anticonvulsive drugs have been used in most of the cases (75%) with no full seizure control. EEG revealed a range of changes, from focal to generalised, including different grapho-elements such as slow wave activity, spike wave complex, polyspike and low voltage. The same changes have been described by different authors.[5,11,17.2] Headache was present in 8 cases (73%), mostly migraine type.[6,13,14] Hemiparesis is seen in 4 cases (36%), involving contralateral side to changes in brain hemispheres.[11] A significant number of patients have psychomotoric developmental delay of different types (64%).[12] The level of psychomotoric delay depends on the time of seizure onset and number of abnormalities in other systems.

Sturge-Weber syndrome belongs to facomatosis group of diseases. The disease is associated with abnormalities in other systems, too. About 74% of cases are associated with epilepsy. EEG changes in most of the cases are partial. Treatment is complex because monotherapy does not produce good results. Carbamazepine is the most effective drug. The most common ophthalmological problem (55%) includes glaucoma and choroidal haemangioma. Glaucoma requires surgical and conservative intervention. Headache is quite common (73%), mostly migraine type. Cognitive problems are found in 64% of the cases, including speech disturbances, aggressive behaviour, and memory problems. Hemiparesis is not rare in children with SWS, it has been found in 34% of the cases. 17% of the cases presented with only facial and brain changes and no symptoms that could impact the quality of life. Diagnostic methods mostly used are computerised tomography, magnetic resonance imaging, doppler brain ultrasonography and fundoscopy.

The study has detected cases with rare SWS and its associated conditions as described in the literature, and described their complexity, especially in terms of inability to achieve the full seizure control, through monotherapy or combined drugs, in those presenting with seizures.

LIMITATION

In order to achieve a better seizure control, no hemispherectomy has been performed in any of the cases therefore a limitation is noted in terms of bringing our experience in this regard. Although the total number of cases was not high, most of the associated conditions were found in these cases, which gives an opportunity to further analyse each of them and extend the studies in the future to their specific management and outcomes.

CONCLUSION

To our best knowledge, this is the first study conducted in our country related to SWS in paediatric population. The results present the clinical characteristics of our patients, including the comorbidities and complications. As such, they are beneficial and useful for our further studying and planning.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Shirley MD, Tang H, Gallione CJ, Baugher JD, Frelin LP, Cohen B, et al. Sturge–Weber syndrome and port-wine stains caused by somatic mutation in GNAQ. New Engld J Med 2013; 368(21): 1971-9.
2. Kaplan EH, Kossoff EH, Bachur CD, Gholston M, Hahn J, Widlus M, et al. Anticonvulsant efficacy in Sturge-Weber syndrome. Paediatr Neurol 2016; 58: 31-6.
3. Neto FX, Junior MA, Ximenes LS, Jacob CC, Junior AG, Palheta CP. Clinical features of Sturge-Weber syndrome. Intl Arch Otorhinolaryngol 2008; 12(4): 565-70.
4. Murakami N, Morioka T, Suzuki SO, Hashiguchi K, Amano T, Sakata A, et al. Focal cortical dysplasia type IIa underlying epileptogenesis in patients with epilepsy associated with Sturge-Weber syndrome. Epilepsia 2012; 53(11): e184–8.
5. Bachur CD, Comi AM. Sturge-weber syndrome. Curr Treat Option Neurol. 2013; 15(5): 607-17.
6. Bodensteiner JB, Roach ES, editors. Sturge-Weber syndrome. Mt. Freedom: Sturge-Weber Foundation; 1999.
7. Mantelli F, Bruscolini A, La Cava M, Abdolrahimzadeh S, Lambiase A. Ocular manifestations of Sturge–Weber syndrome: pathogenesis, diagnosis, and management. Clin Ophthalmol (Auckland, NZ) 2016; 10: 871.
8. Andrew Kemp OD, Marcus Gonzales OD, Joe DeLoach OD, Zanna Kruoch OD. Targeting Intraocular Pressure in Glaucoma: a Teaching Case Report. Optometric Educ 2017; 42(3). [cited Sep 2022]. Available from: https://journal.opted.org/article/targeting-intraocular-pressure-in-glaucoma-a-teaching-case-report/
9. Sarwat Salim MD, Luchsinger W. Sturge-Weber syndrome and secondary glaucoma.
10. Gupta S. Sturge Weber syndrome with secondary glaucoma. J Clin Ophthalmol Optom 2017; 2: 102.
11. Brazier J, Ara R, Azzabi I, Busschbach J, Chevrou-Séverac H, Crawford B, et al. Identification, review, and use of health state utilities in cost-effectiveness models: an ISPOR good practices for outcomes research task force report. Value Health. 2019; 22(3): 267–75.
12. Raches D, Hiscock M, Chapieski L. Behavioural and academic problems in children with Sturge-Weber syndrome: differences between children with and without seizures. Epilepsy Behav 2012; 25(3): 457–63.
13. Perez AM, Rojas MR, Martin VP, Carral JD, Saez IC, Rodriguez AD, et al. Analysis of Sturge–Weber syndrome: a retrospective study of multiple associated variables. Neurología (English Edition). 2017; 32(6): 363-70.
14. Manivannan N, Gokulanathan S, Ahathya RS, Gubernath D, Shanmugasundaram R. Sturge-Weber syndrome. A retrospective study of multiple associated variable. 2012; J Pharm BioAll Sci 4: 349-52.
15. Yuen NS, Wong IY. Congenital glaucoma from Sturge-Weber syndrome: a modified surgical approach. Korean J Ophthalmol. 2012; 26(6): 481-4.
16. Su WW. Acute primary angle-closure in Sturge-Weber syndrome. Am J Ophthalmol Case 2018; 10: 101-4.
17. Juhász C. Predicting and preventing epilepsy in Sturge-Weber syndrome. Paediatr Neurol Brief 2016; 30(11): 43.