Sturge-Weber Syndrome Patient Registry: Delayed Diagnosis and Poor Seizure Control

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Objective To examine the symptomatology and treatment of Sturge-Weber syndrome (SWS) from a large patient registry to identify common symptoms, clinical outcomes, and areas of unmet clinical need.

Study design An online patient questionnaire was completed by 628 patients with clinically diagnosed SWS and/or a port-wine birthmark over a 19-year period. Statistical analysis focused on seizures as a primary outcome measure, as well as associated neurologic, ophthalmologic, and dermatologic attributes to understand some of the natural history of the disorder.

Results The majority (92%) of patients had a port-wine birthmark, and 60% of the patients had neurologic symptoms, including seizures and stroke-like episodes. Glaucoma was present in 48% of the patients. Other common symptoms included behavioral (46%) and hearing (or vestibular) disorders (24%). Delayed diagnosis of SWS beyond 1 year after presentation of initial symptoms occurred in 16% of the patients, with 68% having clear preexisting comorbidities, especially headaches. Birthmarks on the forehead and scalp were associated with seizures ($P < .001$), whereas bilaterality of birthmarks was not. Only 49% of patients being treated for epilepsy were free of seizures.

Conclusions Seizures and glaucoma were the primary drivers for a diagnosis of SWS in patients with delayed diagnosis, and hearing (or vestibular) and behavioral problems were also prevalent. The diagnosis of SWS was delayed when the predominant symptom was headache. Seizure control was quite poor in many patients with SWS. Our findings highlight an important need for detailed, longitudinal data to improve our understanding of SWS and develop better treatment strategies for patients with this disorder. *(J Pediatr 2019;215:158-63)*.

Sturge-Weber syndrome (SWS) is a sporadically occurring neurocutaneous disorder (OMIM #185300) caused primarily by a somatic activating mutation in the *GNAQ* gene encoding the G protein alpha subunit Gαq, R183Q.[1] SWS occurs in 1 in 20 000-50 000 individuals, with equal prevalence in males and females and across all races.[1]

Primary clinical features of SWS include the presence of a facial nevus, termed port-wine birthmark, and dural or leptomeningeal vascular malformations involving the brain and eye, although the presence of both is not necessary for a diagnosis.[2,3] SWS manifests with a wide spectrum of symptomatology and severity and with multiple comorbidities, leading to heterogeneous clinical outcomes and an incomplete understanding of the natural history of the disease.[4] The severity of the disorder is hypothesized to be a function of the spatiotemporal occurrence of the *GNAQ* mutation during embryonic development, which often translates to unilateral or bilateral physical presentation of the disease in terms of port-wine birthmark size and brain involvement.[4] Mutations that occur earlier in gestation may lead to a larger port-wine birthmark and involvement of more brain regions. Localization of the birthmark to the forehead, corresponding to the embryonic vascular development of the face, leads to more severe neurologic outcomes.

Despite the wide spectrum of symptoms involving the skin, eye, and brain, to date there has been no large-scale effort to study the natural history of disease. The published studies measuring longitudinal clinical spectrum and outcomes are limited in sample size, and many are based on clinical review,[2,5,6] leaving many fundamental questions unanswered regarding the natural history and comorbidities of SWS. To address this knowledge gap, the Sturge-Weber Foundation established a web-based registry[7] in which self-reported data are collected as questionnaire responses, with the following objectives: (1) to gather epidemiologic data on diagnosis and characterize symptoms at presentation; (2) to profile comorbidities and clinical outcomes; (3) to study the relationship between physical presentation and natural history; and (4) to compile treatment strategies and identify areas of unmet clinical need.

SWS	Sturge-Weber syndrome

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Methods

Between 2000 and 2018, patients or family members of patients with SWS and/or port-wine birthmarks (forehead and/or eye region) completed an online questionnaire following a protocol approved by the Advarra Institutional Review Board. Of the 2000 participants, only 628 provided sufficient information in accordance with our inclusion criteria listed below and were included in our analyses. The analyses were performed on deidentified data. The questionnaire was presented in an open survey format in which visitors to the website could register and participate.

Responses were collected from the registry data for a variety of categories, including demographic characteristics, diagnosis, and neurologic, ophthalmologic, dental, and other medical history (**Table I**; available at www.jpeds.com). Data were processed and analyzed with R 3.5.0 (R Project for Statistical Computing, Vienna, Austria). Given the modular nature of the questions (eg, demographics, neurologic problems, medications) in the questionnaire, only records from participants with >80% completion of a particular section of questions were included in the analysis of that section. Missing information for incomplete records was flagged as "missing" and not counted toward proportion calculations when considering variables of interest. For intersectional analyses, only records with information in assessed sections were analyzed. Thus, each analysis (see below) was of subsets of the total data entries based on available response data. Records with inconsistent information across sections were removed from the analysis.

Patients with delayed diagnosis were defined as patients aged >1 year who were diagnosed after at least 1 year between the age of diagnosis of SWS and the age at which any symptoms, such as port-wine birthmark or headaches, first manifested.

Simple linear and generalized linear models were used to test associations between symptoms. Specifically, simple linear regression was used to identify associations between age of diagnosis and age of onset for general, neurologic, or ophthalmologic symptoms. Logistic regression in the form of a multivariable generalized linear model with a logit link function was used to assess associations between seizures and port-wine birthmark location and laterality. Univariable logistic regression was used to analyze associations between seizures and laterality.

Results

The 628 patients whose entries passed curation and quality control included 372 females (59%) and 256 males (41%), and 74% were diagnosed within the first year of life (**Table II**). The majority (92%) of patients had a port-wine birthmark on the face, with 59% presenting with bilateral birthmarks. Among the patients with port-wine birthmark on the face, 30% had resulting growth asymmetry (**Table III**; available at www.jpeds.com).

Table II. Demographic characteristics

Characteristics	Value, n (%)
Total number of patients	628
Sex	
Female	372 (59.24)
Male	256 (40.76)
Age at diagnosis	
at birth	146 (24.83)
birth-2 wk	50 (8.5)
2 wk-4 wk	15 (2.55)
1 mo-3 mo	56 (9.52)
3 mo-6 mo	68 (11.56)
6 mo-9 mo	29 (4.93)
9 mo-12 mo	25 (4.25)
1 y	46 (7.82)
2 y	20 (3.4)
3 y	13 (2.21)
4 y	10 (1.7)
5 y	6 (1.02)
6 y	9 (1.53)
8 y	9 (1.53)
9 y	4 (0.68)
10 y	4 (0.68)
11 y	2 (0.34)
12 y	5 (0.85)
13 y	2 (0.34)
14 y	3 (0.51)
15 y	2 (0.34)
16 y	7 (1.19)
17 y	3 (0.51)
18 y	2 (0.34)
19 y	3 (0.51)
20-30 y	17 (2.89)
30-40 y	11 (1.87)
40-50 y	12 (2.04)
50-60 y	6 (1.02)
60-70 y	3 (0.51)
Missing/unsure	40
PWB and neurologic symptoms	
No PWB, no neurologic symptoms	19 (3.03)
PWB only	229 (36.46)
Neurologic symptoms only	29 (4.62)
PWB and neurologic symptoms	351 (55.89)
Glaucoma	
Yes	271 (48.31)
No	290 (51.69)

PWB, port-wine birthmark.

Neurologic symptoms, including seizures and stroke-like episodes, were present in 60% of the patients (**Table II**), with 50% of these experiencing seizures (**Table IV**; available at www.jpeds.com). Approximately 48% of the patients developed glaucoma in their lifetime (**Table II**). Beyond these, a wide range of symptoms, imaging findings, and comorbidities were recorded in the registry (**Table IV**). Almost one-half (46%) of the patients reportedly had some form of behavioral disorder, including 19% diagnosed with depression. Hearing and vestibular (or other ear) problems were significant in 24% of the patients.

Delayed Diagnosis

Of the 556 patients with available data on the age of diagnosis, 16% had a delayed diagnosis of SWS. For these patients, the diagnosis was made at least 1 year after symptoms were first observed, including the presence of

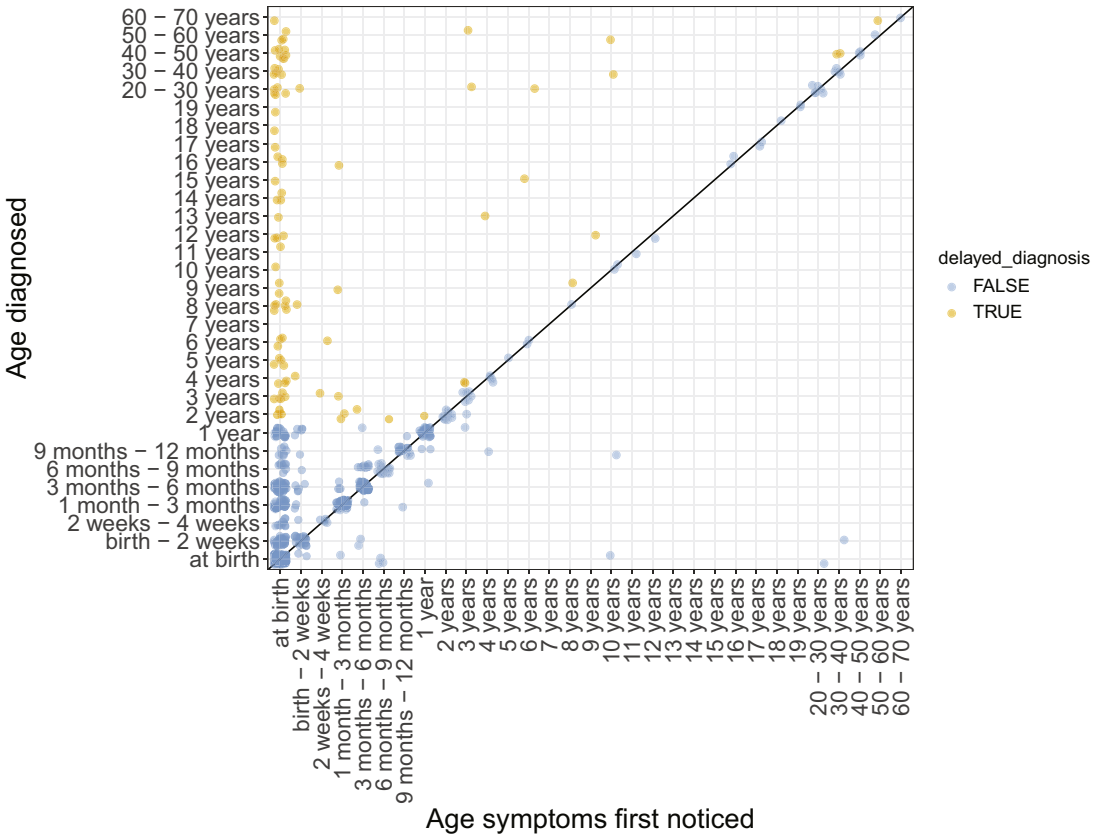

Figure 1. Delay in diagnosis in a subset of patients. For each patient, the age of diagnosis was compared with the age when symptoms were first noted. Each point represents a patient. Points in orange indicate patients who had a gap of at least 1 year between first manifestation of symptoms and diagnosis.

port-wine birthmark or other conditions (**Figure 1**). Of note, many of these patients had symptoms present at birth and went undiagnosed for years. Of the 556 patients, 466 (including 79 of the 90 with delayed diagnosis) also had detailed information regarding ophthalmologic, hearing, behavioral, and neurologic comorbidities. In the majority of these patients with delayed diagnosis, the diagnosis was made at the onset of neurologic or ophthalmologic conditions (**Figure 2**; available at www.jpeds.com), with the exception of headaches. Importantly, 68% of these patients had comorbidities that could be attributed to SWS during this period of misdiagnosis, including hearing (or vestibular or other ear conditions) and behavioral disorders (**Table V**; available at www.jpeds.com). Many of the children with a port-wine stain or frequent headaches were not diagnosed with SWS until a more serious clinical event occurred, such as glaucoma or seizure.

Relationship between Seizures and Birthmark Location

Using a multivariable generalized linear model with a logit link function for logistic regression, we modeled seizures as a function of location and laterality. Seizures were positively associated with port-wine birthmarks located on the forehead ($P = 3.3 \times 10^{-7}$), scalp ($P = .03$), nose ($P = .0377$), and ear ($P = .00417$) (**Table VI**). We also observed negative associations between seizures and port-wine birthmarks on the upper eyelid, cheek/nose, and neck. Bilaterality of the port-wine birthmark on the face was not associated with seizures in both univariable and multivariable analyses.

Poor Seizure Control in SWS

The most prominent neurologic complication of SWS is epilepsy, and early seizure onset is a prognostic indicator of poor outcome.[8,9] Therefore, a primary goal of treatment in these cases is seizure control. A total of 250 patients completed questions regarding seizure medication, of whom 213 had complete and concordant information for analysis of efficacy.

At the time of survey completion, 82% were taking seizure medications. Of those, 39% were prescribed 2 or more medications at the time of the survey (**Table VII**; available at www.jpeds.com). Seizure control with medication was poor, with only 10% of patients with complete resolution of seizures and able to stop medication (**Table IV**). Of patients still on medication during the survey, only 49% were seizure-free on medication, and 38% had some

Table VI. Multivariate generalized linear model associations with seizures and birthmark location/laterality

Variables	Estimate	SE	*Z*-score	*P* value	Significance
Region					
Forehead	1.3	0.254	5.11	3.25E-07	*
Scalp	0.327	0.151	2.17	.03	†
Upper.eyelid	−0.563	0.251	−2.24	.0249	†
Lower.eyelid	0.298	0.201	1.48	.138	
Nose	0.311	0.15	2.08	.0377	†
Cheek.nose	−1.01	0.228	−4.44	8.82E-06	*
Upper.lip	0.0716	0.189	0.379	.704	
Lower.lip	−0.0624	0.214	−0.292	.77	
Chin	0.221	0.237	0.932	.351	
Ear	0.612	0.214	2.86	.00417	‡
Neck	−0.64	0.232	−2.76	.00575	‡
Laterality					
Laterality (unilateral)	−0.0414	0.15	−0.276	.783	
Cheek.nose	−1.01	0.228	−4.44	8.82E-06	*
Chin	0.221	0.237	0.932	.351	
Ear	0.612	0.214	2.86	.00417	‡
Forehead	1.3	0.254	5.11	3.25E-07	*
Lower.eyelid	0.298	0.201	1.48	.138	
Lower.lip	−0.0624	0.214	−0.292	.77	
Neck	−0.64	0.232	−2.76	.00575	‡
Nose	0.311	0.15	2.08	.0377	†
Scalp	0.327	0.151	2.17	.03	†
Upper.eye	−0.563	0.251	−2.24	.0249	†
Upper.lip	0.0716	0.189	0.379	.704	
Unilateral	−0.0414	0.15	−0.276	.783	

*$P < 0.001$.
†$P < 0.05$.
‡$P < 0.01$.

(>50%) seizure control (**Figure 3**, A). Patients prescribed a single medication had better seizure control than those taking 2 or more medications (**Figure 3**, B). The most commonly prescribed medications included levetiracetam, oxcarbazepine, and carbamazepine (**Figure 3**, C and **Table VIII** [**Table VIII** available at www.jpeds.com]).

Among the 250 patients who answered questions regarding seizure medication, 71% had cycled through 2 or more medications (**Table IX**; available at www.jpeds.com) and 18% reported stopping 1 or more medications due to side effects (**Table X**; available at www.jpeds.com). Proportional to the number of patients prescribed a given medication, phenytoin was not well tolerated, with 20% stopping it due to side effects.

Discussion

We studied the registry data of more than 600 patients with SWS who reported a wide range of symptoms and comorbidities. Beyond the previously characterized neurologic and ophthalmologic symptoms,[3] a large number of patients had hearing, vestibular or other ear problems, and behavioral disorders. Although individual case reports have recorded such information,[10,11] and several studies have characterized these symptoms through retrospective reviews,[12,13] the symptoms have not been characterized in a larger cohort until now. Analysis of this registry information has identified symptomology in patients with SWS that may help promote earlier diagnosis and clinical interventions.

A previous study of 277 patients with SWS characterized a large number of comorbidities. Day et al reported a higher prevalence of neurologic comorbidities (eg, seizures, strokes, epilepsy) than we identified, along with a comparable prevalence of non-neurologic comorbidities.[14] This discrepancy is likely attributable to patient selection, because Day et required neuroimaging support for brain involvement for patient recruitment, and neurologic comorbidities are highly associated with brain involvement.[14]

Our self-reporting patient cohort identified a significant subgroup diagnosed with SWS at least 1 year after symptoms first manifested, including the presence of port-wine birthmark, headaches/migraines, hearing (or vestibular) disorders, and behavioral abnormalities. Because some of these are not considered typical SWS symptoms, caregivers may have missed these clues to underlying SWS in patients without typical seizures or stroke-like episodes.[15] This observation is important, because initiation of treatment strategies aimed at preventing seizures and stroke-like episodes requires early, presymptomatic diagnosis.[4] Of note, an important distinguishing factor was migraines, which is a risk factor for ischemic attacks[16] and is associated with prolonged visual auras and hemiplegic attacks in SWS.[4] Furthermore, the prevalence of migraines in SWS exceeds that in the general population, and headache management could have clinical benefits beyond symptomatic relief.[17]

We observed a positive association between seizures and the presence of a port-wine birthmark on the forehead and scalp, consistent with recent findings.[18] Although this finding

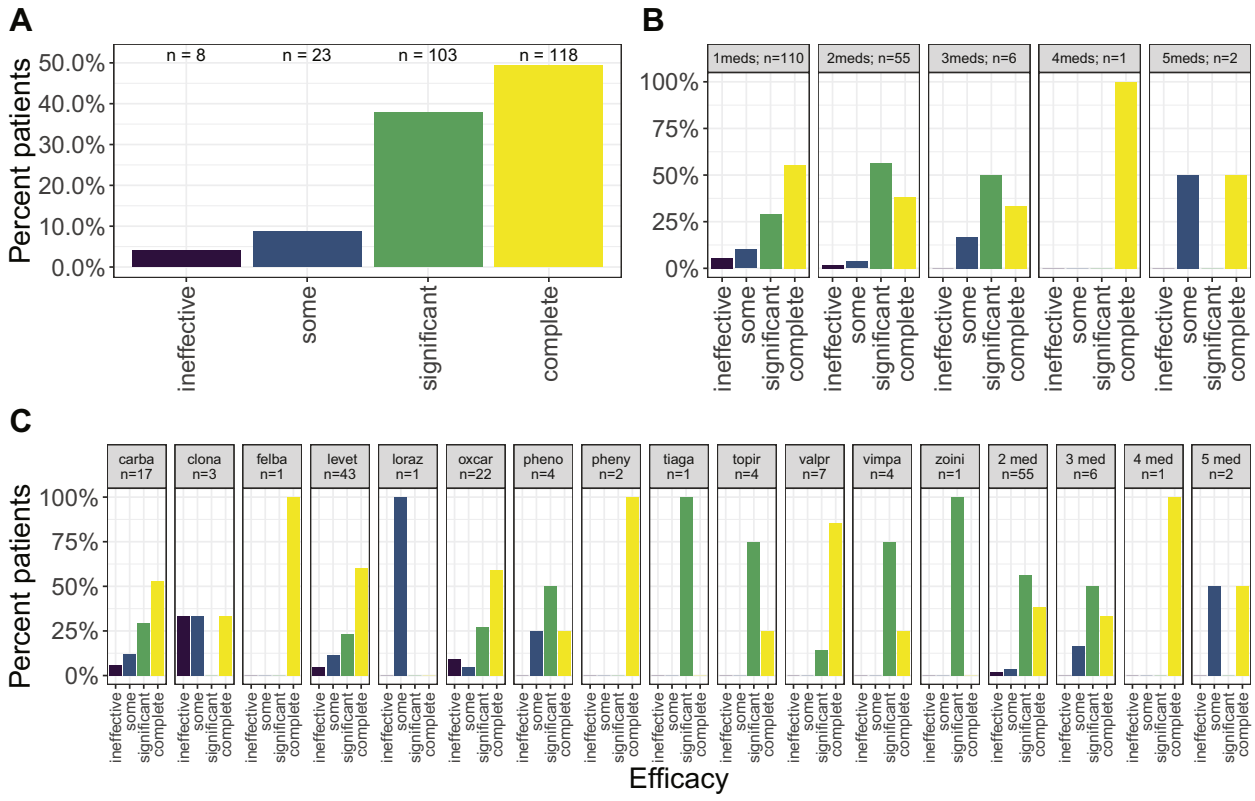

Figure 3. Efficacy of seizure medications of patients on medication at the time of the survey **A**, in all patients, regardless of medication regimen; **B**, by medication count; and **C**, by individual medication regimen. *Carba*, carbamazepine; *clona*, clonazepam; *felba*, felbamate; *levet*, levetiracetam; *loraz*, lorazepam; *oxcar*, oxcarbazepine; *pheno*, phenobarbital; *pheny*, phenytoin; *tiaga*, tiagabine; *topir*, topiramate; *valpr*, valproic acid; *vimpa*, vimpat; *zoini*, zonisamide.

does not guarantee brain involvement, the knowledge that there is a greater likelihood for brain involvement in some patients will lead to earlier diagnoses and allow patients and caregivers to prepare for and be aware of future symptoms known to be associated with that sign. The location of the birthmark,[18] coupled with the presence of atypical SWS symptoms, could be important markers to suggest brain imaging tests for patients with a port-wine birthmark to diagnose brain involvement.

We did not observe a relationship between seizures and bilaterality in both univariable and multivariable analyses, which may be due to an overall selection bias of patients with more severe phenotypes. We would have liked to assess the severity and frequency of seizures, but these data are not captured by the registry, which speaks to the need to develop further surveys or clinical databases to capture ongoing, repeated data. We propose that a future version of the SWS patient registry should include such information as well as detailed input from caregivers in a longitudinal framework to allow a better description of the natural history of the disease.

Seizure control is an important goal in the clinical management of SWS and is associated with improved development. Unlike most patients with epilepsy, among whom roughly two-thirds are well controlled on seizure medications,[19] only one-half of patients with SWS had complete seizure control. Many patients had cycled through multiple medications to find the most appropriate medication regimen. We observed that more patients on monotherapy had complete seizure control compared with patients on 2 or more medications, likely reflecting the poor response to seizure medications in the latter group.

The primary limitation of this study stems from its self-reporting nature. Although subjective symptoms reported by patients and their families are likely reliable, a major challenge with patient-reported registries of more complex medical problems is decreased reliability in accurate reporting. There is also likely to be selection bias toward patients with more severe clinical presentations of SWS, as perhaps indicated by the observed majority of individuals with bilateral port-wine birthmark. Responses also may be inaccurate, with various sources of error, including lack of understanding of medical terminologies used, recall bias, and other inaccuracies. We have taken measures to limit such errors, including removing questions that could lead to ambiguous responses and discarding complete patient entries when errors are recognized (eg, discordant seizure information). Despite these limitations, we have still shown that there is valuable and accurate information that can be used to study the symptomology of SWS. Other limitations of the study

include the imprecise measures for seizures, missing drug dosage information, lack of evidence for brain involvement, and absence of longitudinal data. These restrictions prevented us from performing more comprehensive analyses, such as assessing current treatment modalities, including aspirin and antiseizure medications. Efforts are currently underway by the Sturge-Weber Foundation Clinical Care Network of 27 centers to develop such a longitudinal database with detailed clinical, imaging, and outcome measures that will better map the natural history and suggest treatment strategies. ■

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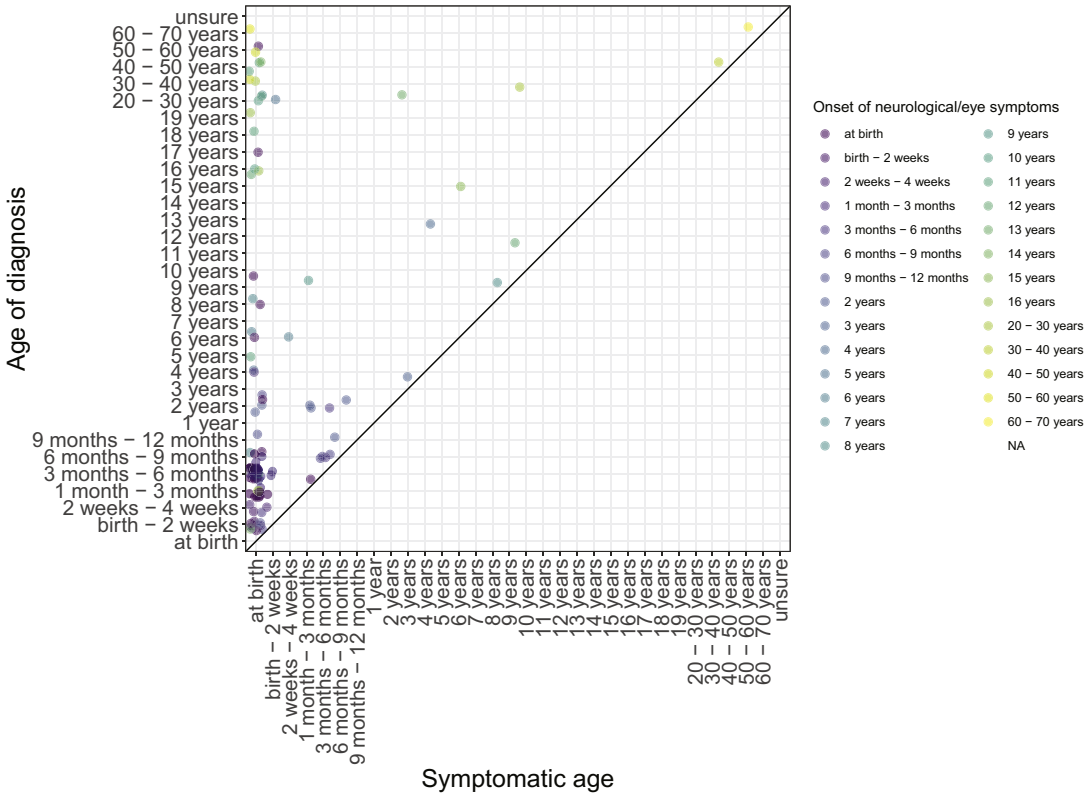

Figure 2. Diagnosis was associated with onset of neurologic and ophthalmologic symptoms in patients with delayed diagnosis. For each patient, the age of diagnosis was compared with the age at which symptoms were first noted. Points are colored by the age of onset for either a neurologic or an ophthalmologic condition.

Table I. Summary of questionnaire categories and keys in the registry

Categories	Question keys
birthmark_asymmetry	asymmetry
birthmark_asymmetry	binary
birthmark_other	binary
birthmark_other	other
demographics_info	age
demographics_info	birthplace
demographics_info	consent
demographics_info	gender
demographics_info	location
demographics_info	race
demographics_info	respondent
demographics_info	status
demographics_info	vitalstatus
development_child	overweight
development_child	shortstature
development_children	birthmarks
development_children	developmentaldelay
development_children	number
development_current	height
development_current	weight
development_female	period
development_female	reproductive
development_infancy	failuretothrive
development_infancy	growthdelay
development_newborn	fullterm
development_newborn	length
development_newborn	tx
development_newborn	weight
diagnosis_sws	age.diagnosed
diagnosis_sws	age.symptoms
diagnosis_sws	genetic.testing
diagnosis_sws	method
diagnosis_sws	professional
diagnosis_sws	subtype
eye_condition	binary
eye_condition	corrective
eye_condition	diagnosis
eye_condition	medication
eye_condition	othermedication
eye_surgery	detailed
family_condition	autoimmune
family_condition	behavior
family_condition	birthmark
family_condition	heart
family_condition	hormone
family_condition	orthopedic
family_condition	seizure
family_mother	pregnancy
family_mother	reproductive
family_sibling	birthmarks
family_sibling	devdelay
medical_autoimmune	diagnosis
medical_behavioral	diagnosis
medical_cardiopulmonary	diagnosis
medical_diabetes	diagnosis
medical_diabetes	tx
medical_endocrine	diagnosis
medical_endocrine	tx
medical_gi	diagnosis
medical_hearing	diagnosis
medical_lipid	diagnosis
medical_lipid	tx
medical_orthopedic	diagnosis
medical_therapies	medication
medical_therapies	tx
neurological_issue	agedx
neurological_issue	binary
neurological_issue	diagnosis
neurological_problem	agebegin
neurological_problem	binary
neurological_problem	diagnosis
neurological_problem	resolution
neurological_seizures	binary
neurological_seizures	medication
neurological_seizures	surgery
neurological_seizures	VNS.implant
neurological_test	ageres
neurological_test	binary
neurological_test	diagnosis
oral_dental	birthmark
oral_dental	bleeding
oral_dental	surgery
oral_dental	symptoms
pwb_location	body
pwb_location	face
pwb_location	
qol_academic	highest
qol_employment	status
qol_headache	academic
qol_headache	status
qol_living	condition
qol_wakefulness	status
research_biospecimen	donated
research_trial	clinical_trial

(*continued*)

Table III. Demographic data

Variables	Number
Sex	
Female	372
Male	256
Race	
American Indian or Alaska Native	7
Asian Indian	14
Black or African American	21
Chinese	12
Filipino	5
Korean	2
Multiracial	37
White	471
Other	32
Other Asian	9
Other Pacific Islander	1
Refuse to answer	5
Unknown	1
Missing	11
SWS subtype	
Port-wine birthmark only	76
Type 1 classic SWS	228
Type 2 SWS spectrum	80
Type 3 forme fruste	27
SWS and Klippel-Trenaunay	38
Other	35
Unsure	142
Missing	2
Birthmark extent	
Face	
Minor	174
Average	206
Extensive	196
None	33
Missing	4
Body	
Minor	50
Average	53
Extensive	56
None	446
Missing	8
Birthmark laterality	
Face	
Left	129
Right	112
Bilateral	339
None	33
Body	
Left	474
Right	28
Bilateral	78
None	33
Other birthmarks	
Café au lait	49
Capillary hemangioma	49
Forme fruste	16
Nevus of ota	6
Telangiectasia	23
Other	28
Unsure	46
None	411
Birthmark growth asymmetry	
Face	179
Extremities	48
Trunk	19
Other	55
Unsure	54
None	273
Diagnosing professional	
Dentist	1
Dermatologist	12
General practitioner/primary care physician/internist	15
Geneticist	2
Multiple	210
Neonatologist	6
Neurologist	196
Obstetrician	3
Ophthalmologist/optometrist	56
Pediatrician	50
Surgeon	2
Unsure	45
Missing	30
Diagnostic method	
Imaging	153
Multiple	244
Physical examination by healthcare provider	155
Unsure	44
Missing	32

Table IV. Comorbidities of SWS

Disorders	Number (%)
Autoimmune	
Eczema psoriasis	70 (13.54)
Fibromyalgia	7 (1.35)
Multiple sclerosis	2 (0.39)
Rheumatoid arthritis	10 (1.93)
Other	27 (5.22)
None	410 (79.3)
Total unique patients	517
Lipid disorders	
High LDL cholesterol	51 (9.86)
Hyperlipidemia	6 (1.16)
Hypertriglyceridemia	4 (0.77)
Low HDL cholesterol	13 (2.51)
Unknown	81 (15.67)
None	379 (73.31)
Total unique patients	517
Gastrointestinal	
Autistic enterocolitis	7 (1.35)
Chronic constipation	42 (8.12)
Chronic diarrhea	16 (3.09)
Gastroesophageal reflux	67 (12.96)
Inflammatory bowel disease	15 (2.9)
Irritable bowel syndrome	29 (5.61)
Peptic ulcers	12 (2.32)
Silent reflux	15 (2.9)
None	391 (75.63)
Total unique patients	517
Cardiopulmonary	
Allergies	131 (25.34)
Angina	23 (4.45)
Arrythmia	27 (5.22)
Arteriosclerosis	15 (2.9)
Asthma	68 (13.15)
Cardiomyopathy	14 (2.71)
Heart murmur	51 (9.86)
High blood pressure	68 (13.15)
High cholesterol	62 (11.99)
Rheumatic fever	14 (2.71)
Tachycardia	25 (4.84)
None	312 (60.35)
Total unique patients	517
Hearing, vestibular, and ear	
Dizziness and/or vertigo	103 (19.92)
Ear pain	103 (19.92)
Sensorineural hearing loss	70 (13.54)
Tinnitus	117 (22.63)
None	395 (76.4)
Total unique patients	517
Orthopedic	
Flexible scoliosis	12 (2.32)
Fractures	41 (7.93)
Genu recurvatum	8 (1.55)
Joint swelling	26 (5.03)
Kyphosis	7 (1.35)
Lordosis	8 (1.55)
Muscle bone joint pain	73 (14.12)
Scoliosis	35 (6.77)
Torticollis	15 (2.9)
None	391 (75.63)
Total unique patients	517
Diabetes	
Prediabetes	14 (2.71)
Type I	1 (0.19)
Type II	16 (3.09)
Unsure	9 (1.74)
None	477 (92.26)
Total unique patients	517
Behavioral	
Addiction	32 (6.19)
ADHD or ADD	88 (17.02)
Aggression	70 (13.54)
Anxiety	131 (25.34)
Autism spectrum disorder	41 (7.93)
Bipolar	19 (3.68)
Depression	101 (19.54)
Manic depressive	15 (2.9)
Obsessive compulsive	43 (8.32)
Oppositional defiant	31 (6)
Panic attacks	53 (10.25)
Self-injury	39 (7.54)
Tourette syndrome	7 (1.35)
None	276 (53.38)
Total unique patients	517
Endocrine	
Calcium deficiency	29 (5.61)
Cortisol	19 (3.68)
Cushing syndrome	9 (1.74)
Early menopause	14 (2.71)
Early puberty	30 (5.8)
Growth hormone deficiency	24 (4.64)
Hashimoto disease	10 (1.93)
Hyperthyroidism	15 (2.9)
Hypothyroidism	34 (6.58)
Late puberty	23 (4.45)
Obesity	63 (12.19)
Short stature	39 (7.54)
Vitamin D deficiency	61 (11.8)
None	348 (67.31)
Total unique patients	517
Neurologic symptoms and findings	
Imaging findings	
Atrophy	139 (27.42)
AVM	85 (16.77)
Calcification	203 (40.04)
Chiari malformation	42 (8.28)
Symptoms	
Hemiparesis	123 (24.26)
Hemiplegia	71 (14)
Hydrocephalus	42 (8.28)
Ischemic stroke	71 (14)
Migraine	131 (25.84)
Stroke	63 (12.43)
None	190 (37.48)
Total unique patients	506
Seizures	
Yes	298 (50)
Unsure	35 (5.87)
No	263 (44.1)
Total	596
Seizure resolution	
Yes	26 (10.4)
No	224 (89.6)
Total with resolution information	250
Missing	48
Ophthalmologic	
Amblyopia	22 (3.92)
Anatomic blindness	12 (2.14)
Buphthalmos	25 (4.46)
Cataract	43 (7.66)
Choroidal hemangioma	43 (7.66)
Conjunctival abnormality	11 (1.96)
Cortical blindness	48 (8.56)
Glaucoma	271 (48.31)
Iris same	3 (0.53)
Optic nerve change	29 (5.17)
Strabismus	25 (4.46)
Visual field improvement	13 (2.32)
Unsure	33 (5.88)
None	201 (35.83)
Total unique patients	561

(*continued*)

Table IV. Continued

Disorders	Number (%)
Oral/dental	
Delayed eruption	39 (7.47)
Dry mouth	22 (4.21)
Early eruption	50 (9.58)
Missing permanent teeth	21 (4.02)
Missing primary teeth	5 (0.96)
Periodontal disease	42 (8.05)
Pointed teeth	12 (2.3)
Poor alignment of teeth	145 (27.78)
Poor jaw alignment	85 (16.28)
Problems with tooth decay	79 (15.13)
Small teeth	24 (4.6)
Tooth discoloration	67 (12.84)
Other	39 (7.47)
Unsure	38 (7.28)
None	202 (38.7)
Total unique patients	522

ADD, attention deficit disorder; *ADHD*, attention deficit hyperactivity disorder; *AVM*, atrioventricular malformation; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein

Table V. Count summary of the symptoms present before formal SWS diagnosis in patients with delayed diagnosis

Symptoms before diagnosis	Number
None	25
Behavioral	7
Otolaryngologic	3
Ophthalmologic	10
Neurological	5
Otolaryngologic, behavioral	3
Ophthalmologic, behavioral	6
Ophthalmologic, otolaryngologic	2
Ophthalmologic, otolaryngologic, behavioral	1
Neurologic, behavioral	5
Neurologic, otolaryngologic	1
Neurologic, otolaryngologic, behavioral	1
Neurologic, ophthalmologic	5
Neurologic, ophthalmologic, behavioral	2
Neurologic, ophthalmologic, otolaryngologic	1
Neurologic, ophthalmologic, otolaryngologic, behavioral	2
Total	79

Table VII. Number of medications prescribed at the time of questionnaire completion

Number of current medications	Number of patients (%)
0	39 (15.6)
1	114 (45.6)
2	72 (28.8)
3	20 (8)
4	3 (1.2)
5	2 (0.8)
Total	250 (100)

Table VIII. Medications prescribed at the time of questionnaire completion

Medication	Number (%)
Levetiracetam	43 (24.71)
Oxcarbazepine	22 (12.64)
Carbamazepine	17 (9.77)
Topiramate	4 (2.3)
Valproic acid	7 (4.02)
Phenobarbital	4 (2.3)
Vimpat	4 (2.3)
Clonazepam	3 (1.72)
Phenytoin	2 (1.15)
Lorazepam	1 (0.57)
Felbamate	1 (0.57)
Tiagabine	1 (0.57)
Zonisamide	1 (0.57)
2 medications	55 (31.61)
3 medications	6 (3.45)
4 medications	1 (0.57)
5 medications	2 (1.15)
Total	174

Table IX. Number of medications prescribed to patients throughout their lifetime

Number of lifetime medications	Number of patients (%)
1	73 (29.2)
2	58 (23.2)
3	46 (18.4)
4	29 (11.6)
5	19 (7.6)
6	16 (6.4)
7	2 (0.8)
8	4 (1.6)
9	2 (0.8)
10	1 (0.4)
	250 (100)

Table X. Reported medication side effects

Medication	Total patients	Patients with side effects, n (%)
Carbamazepine	98	5 (5.1)
Clonazepam	36	2 (5.56)
Felbamate	8	1 (12.5)
Levetiracetam	163	11 (6.75)
Lorazepam	36	2 (5.56)
Oxcarbazepine	105	7 (6.67)
Phenobarbital	100	15 (15)
Phenytoin	70	14 (20)
Topiramate	47	7 (14.89)
Valproic acid	43	4 (9.3)
Vimpat	25	3 (12)