European Journal of Paediatric Neurology 38 (2022) 66–72

Contents lists available at ScienceDirect

European Journal of Paediatric Neurology

journal homepage: www.journals.elsevier.com/european-journal-of-paediatric-neurology

Early MRI diagnosis of Sturge Weber Syndrome type 1 in infants

Coriene E. Catsman-Berrevoets [a,*], Suzanne M. Koudijs [a], Michiel S.J. Buijze [a], Peter C.J. de Laat [c], Suzanne G.M.A. Pasmans [d], Marjolein H.G. Dremmen [b]

[a] Department of Paediatric Neurology, ErasmusMC- Sophia Children's Hospital, Rotterdam, the Netherlands
[b] Department of Neuroradiology, ErasmusMC- Sophia Children's Hospital, Rotterdam, the Netherlands
[c] Department of Paediatrics, ErasmusMC- Sophia Children's Hospital, Rotterdam, the Netherlands
[d] Department of Paediatric Dermatology, ErasmusMC- Sophia Children's Hospital, Rotterdam, the Netherlands

ARTICLE INFO

Keywords:
Sturge Weber syndrome
Prediction
MRI diagnosis
Choroid plexus
Leptomeningeal angiomatosis
Infant
Neonatal

ABSTRACT

Background: Patients with Sturge-Weber syndrome type 1 (SWS1) have a port-wine birthmark (PWB) as cutaneous hallmark. Up to 35% of neonates with a high risk PWB develop SWS1. Clinical manifestations are severe and often progressive. Especially early onset seizures are associated with worse neurocognitive outcome. Identification of pre-symptomatic SWS1 patients is hampered because brain MRI in the first months of life does not always show the for SWS1 characteristic leptomeningeal capillary malformation (LMC).
Objectives: Identification of sensitive and specific MRI predictors for early SWS1 diagnosis.
Methods: In this retrospective single centre study, we included 24 SWS1 patients and 20 controls. We studied specificity and sensitivity for SWS1 diagnosis of LMC and indirect MRI signs such as choroid plexus (CP) size and thickness, abnormal white matter signal, lobar cerebral atrophy, ischemia and cortical calcifications.
Results: In SWS1 patients CP thickness and CP thickness ratio on non-contrast brain MRI was significantly increased. The optimal cut-off value of 5.6 mm on the affected side corresponded with a sensitivity of 91.7% and a specificity of 100% for confirmation of SWS1 diagnosis. In 21% of children aged ≤3 months with a later confirmed SWS1 diagnosis, LMC on initial MRI could not be discerned but CP thickness ≥5.6 mm on the affected side confirmed SWS1 diagnosis.
Conclusions: In this study, CP size ratio and thickness were found to be sensitive and specific signs additional to earlier described criteria to support SWS1 diagnosis in neonates and infants which need to be confirmed in other series.

1. Introduction

Sturge-Weber syndrome (SWS) is a neurocutaneous disorder with as prominent hallmark almost always a facial port-wine birth mark (PWB) [1,2]. SWS and the majority of non-syndromic PWB were found to be associated with a somatic mosaic mutation in the GNAQ-gene on chromosome 9q21 [3]. Somatic GNAQ mutations have also been demonstrated in brain endothelial cells of SWS patients [4]. Mutations occurring early in foetal development likely impact the brain, skin and eyes to lead to the full spectrum of SWS including leptomeningeal capillary malformation (LMC), while mutations occurring in later foetal life may have limited impact and manifest as isolated PWB [1,3,5]. Subtypes of SWS are classified according to the Roach Scale as SWS type 1 (classic SWS1: facial PWB and LMC, often also glaucoma), SWS type 2 (facial PWB without CNS involvement, patients have glaucoma), SWS type 3 (isolated LMC, without facial PWB and usually without glaucoma) [2]. Children with a PWB on the forehead or the upper eyelid, have a 10%- 35% risk of brain involvement (high risk region) [1,2].

The vast majority of children with PWB developing SWS1 present with seizures before the age of two years [6–8]. Approximately 15–25% of children and young adults with SWS1 do not develop seizures although patients have been reported who had a first seizure in late adulthood [6,7,9]. Seizures are initially focal and because of subtlety may go unrecognized for an extended period of time but often evolve to include generalized seizures and frequently children with SWS1 will present with a status epilepticus [6,7]. Seizure control is in general difficult as the majority of patients need at least two different antiepileptic drugs [6]. Early onset seizures especially when they become pharmaco-resistant are associated with worse neurocognitive outcomes

* Corresponding author. Department of Paediatric Neurology, ErasmusMC - Sophia Children's Hospital, Dr Molewaterplein 60, 3015 CN. Rotterdam, the Netherlands.
E-mail address: c.catsman@erasmusmc.nl (C.E. Catsman-Berrevoets).

https://doi.org/10.1016/j.ejpn.2022.04.002
Received 5 May 2021; Received in revised form 15 March 2022; Accepted 10 April 2022
Available online 13 April 2022

List of abbreviations

SWS	Sturge Weber Syndrome
PWB	Port Wine Birthmark
MRI	Magnetic Resonance Imaging
LMC	Leptomeningeal Capillary Malformation
LCA	Lobar cortical atrophy
CP	Choroid Plexus
GNAQ	G protein subunit αq
SPSS	Statistical Package of Social Science
DWI	Diffusion Weighted Imaging
ADC	Apparent Diffusion Coefficient
FLAIR	Fluid-attenuated Inversion Recovery
SWS1	turge Weber syndrome type 1

[10–12]. For this reason, identification of those infants with a facial PWB and LMC is of great importance because parents can be trained to recognise the often subtle first seizures in order to start antiepileptic medication in the earliest stage and thus possibly prevent status epilepticus, farmaco-resistant epilepsy and cognitive decline.

A reliable diagnosis of SWS1 on post contrast magnetic resonance imaging (MRI) in neonates or young infants is not always possible because LMC may not yet be visible in the first months of life [13]. Indirect MRI evidence of cerebral involvement in these young children may however be derived from the presence of ipsilateral choroid plexus (CP) enlargement, signal inversion of the white matter suggesting white matter abnormalities or cerebral atrophy [14–16]. Bar and colleagues suggested a prognostic model to diagnose SWS1 in asymptomatic infants with high sensitivity and specificity especially when LMC was combined with one or more indirect MRI signs [17]. However, neonates and young infants at risk who will ultimately develop SWS1 may still lack direct or indirect MRI signs making an early diagnosis and hence early intervention very difficult. Also in general practice, the diagnostic MRI procedure in these small children may be hampered by difficulties to apply intravenous contrast.

We performed a single centre retrospective MRI study in children with suspicion of SWS1 who were evaluated according to a standard clinical protocol including cerebral MRI. The aim of this study was to validate the findings of Bar et al. [17]. We focussed on quantification of CP measurements in order to raise sensitivity and specificity of early MRI diagnosis even further.

2. Methods

Study design: In this single centre retrospective study we included children 0–18 years that were referred to our multidisciplinary SWS centre because of a facial PWB or vascular birth mark resembling a PWB between January 1st, 2015 and December 31st, 2020 and patients with SWS1 we have in follow up before start of this centre. They had to fulfil the following inclusion criteria: brain MRI available, neurological, dermatological and ophthalmological assessment and follow up at least until age 2 years or later in case initial MRI was normal. Exclusion criteria were: other dermatological diagnosis than PWB or a PWB not including the forehead or the upper eyelid. The initial brain MRI was considered to be made early when performed within the first three months of life and late at any later moment. In case an inconclusive initial brain MRI was made before the first year of life, a second brain MRI made at age 12 months or later was required. When an initial brain MRI was made in a referring centre, this MRI was considered the initial MRI even when there were no post-contrast images available. Assessment focused on occurrence, location and progression of the following neuroimaging features: LMC (if post-contrast sequences were available), CP thickness and CP size ratio, areas with abnormal white matter signal, lobar cortical atrophy (LCA), recent ischemia and cortical calcifications. MRI criteria of these features are represented in Table 1. When at initial MRI, no contrast was administered, we could not establish the presence of LMC and we concentrated on presence of secondary SWS1 characteristics. CP thickness measurements were taken bilateral at the level of the largest diameter of the glomus of the choroid plexus in the lateral ventricle in the axial plane perpendicularly to the wall of the lateral ventricle (Fig. 1). To uncover CP asymmetry, ratio for CP thickness was calculated by dividing the larger CP by the contralateral CP. All measurements were done by a master student (MB) and a senior paediatric neurologist (CCB) aiming at a consensus on correctness of measurements. Relevant patient data were extracted from the electronic patient files. SWS1 diagnosis was considered confirmed when children showed LMC on contrast enhanced brain MRI. SWS1 diagnosis was considered to be excluded when at or after age 12 months brain MRI was normal or no neurological or developmental symptoms or abnormalities were present at age 2 years or later. The latter patients were attributed to the control group.

Statistical analysis: To analyse data, Statistical Package of Social Science (SPSS) version 25 was used. Descriptive statistics including means and proportions were reported. Independent-samples T-test and Independent-samples Mann-Whitney *U* Test were used to compare means for parametric and non-parametric data, respectively. All reported p-values are two-tailed tests of significance with the level of significance defined at < 0.05. Furthermore, a Receiver Operating Characteristic (ROC)-curve analysis was used to determine the discriminatory ability and optimum cut-off values of CP thickness measurements with corresponding sensitivity and specificity [18].

Approvals: The data used for this study are all part of on-going routine clinical evaluations, diagnostic procedures and care for patients referred with (suspicion) of SWS in a specialised SWS outpatient clinic. According to Dutch law, no approval of a Medical Ethical Committee is needed when patient data are studied that are obtained as part of routine patient care.

3. Results

3.1. Patient characteristics

Of 60 eligible children, 44 could be included in this study. Twenty-

Table 1
MRI criteria for the assessment of neuroradiological features found in Sturge Weber Syndrome type 1 patients.

Radiological feature	MRI criteria
Leptomeningeal Capillary Malformation	Serpiginous contrast- enhancement on contrast-enhanced T1-weighted sequence; serpiginous dark areas along the sulci on Susceptibility Weighted Imaging (SWI).
Lobar cortical atrophy	Signs of brain tissue loss on T1-weighted sequence without contrast.
Abnormal white matter signal	Low signal in the white matter on T2-weighted sequence or T2, Fluid-attenuated inversion recovery (FLAIR); low signal areas must follow nerve cell tracts.
Cortical calcifications	Focal hypo-intense spots or subcortical hypo-intense areas along the sulci on SWI. Unwrapped phase images if available used for differentiating venous blood from cortical calcification.
Ischemia	High signal on Diffusion Weighted Imaging (DWI) and low signal on corresponding Apparent Diffusion Coefficient (ADC) map signifying diffusion restriction.
Choroid plexus	T1-weighted sequence with and without contrast enhancement.

Legend: MRI: magnetic resonance imaging, SWI: Susceptibility Weighted Imaging, DWI: Diffusion Weighted Imaging, ADC: Apparent Diffusion Coefficient, FLAIR: Fluid-attenuated inversion recovery,

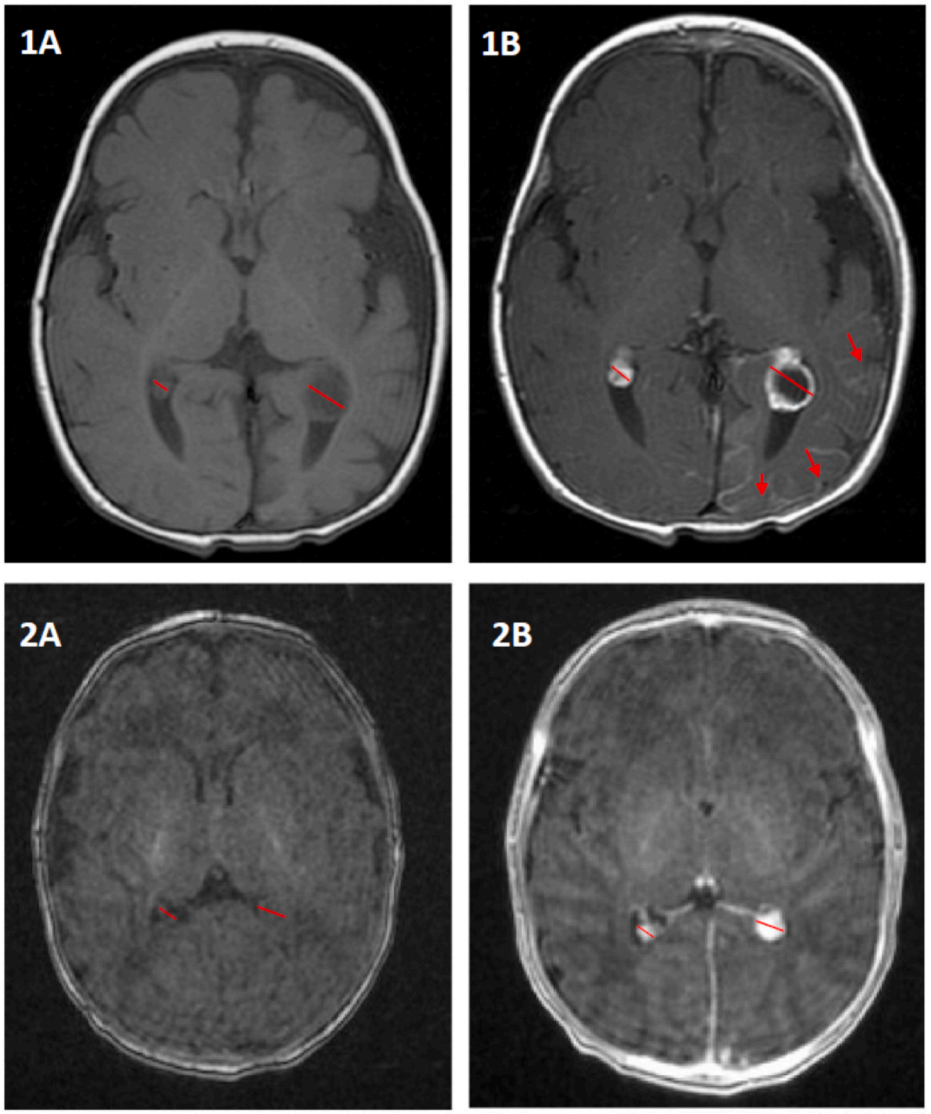

Fig. 1. Examples of axial contrast enhanced T1-weighted MR images of the brain in patient 1 (Fig. 1A and B) with and patient 2 without (Fig. 2A and B) leptomeningeal capillary malformation (arrows) on initial MRI at age 3 months or less. Figs. 1A and 2A represent axial MR images without contrast administration. Figs. 1B and 2B are contrast enhanced MR images. Measurements of choroid plexus thickness in millimetres (red bars) are taken at the largest diameter of the glomus of the choroid plexus in the lateral ventricle in the axial plane. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

four were attributed to the SWS1 group and 20 to the control group. Three patients were excluded because of vascular skin lesions other than PWB, four patients because parents refused MRI, three patients had only a PWB in other facial regions than the forehead or the upper eyelid and six children with normal brain MRI and absent neurological symptoms because of insufficient duration of follow up. (Fig. 2). Patient characteristics can be found in Table 2. Mean age at follow up and the number of boys in the SWS1 group was slightly but not significantly higher compared to the control group. SWS1 and the control group also did not significantly differ in age of initial MRI. The median age at definite SWS1 diagnosis was 8 months (range: 0–38 months). Seventeen patients (71.0%) had an MRI diagnosis before or at 12 months. In 12 of 24 patients an MRI diagnosis was made before epilepsy onset. Three SWS1 patients (12,5%) had not developed epilepsy at the end of the study period at ages 5.9, 5.5 and 2.0 years respectively (Table 2).

3.2. MRI findings in the SWS1 group

Initial brain MRI of the 24 SWS1 patients were made at a mean age 6,8 months (range: 0–38 months). In 11 SWS1 patients, an initial MRI was made at age 3 months or younger. Initial brain MRI in the control group patients were made at a mean age of 19 months (range 0–128 months) of which six before age 3 months. The available MRI sequences of initial brain MRI of all patients are represented in Table 3.

A follow up MRI was made in 19 SWS1 patients at a mean age of 54 months (range 0,8 months–17,8 years). For nine children (43%) in the control group, and specifically those who had a first brain MRI at early age, a follow up MRI was available. Follow up MRI at least included T1-weighted, T2-weighted, contrast enhanced T1-weighted, and diffusion weighted images (DWI)/apparent diffusion coefficient (ADC) sequences.

3.3. Primary criterium for SWS1 diagnosis

Leptomeningeal capillary malformations: LMC was present unilaterally in 12 and bilaterally in four affected patients on initial brain MRI. Parietal (bilaterally 4 patients, unilaterally 7 patients) and occipital (bilaterally 4 patients, unilaterally 8 patients) lobes were affected most frequently. Five of these patients had unilateral LMC along the whole extent of one cerebral hemisphere. In 13 children in the SWS1 group both an initial and follow up contrast-enhanced brain MRI was available. In two of them, LMC was not visible on the initial MRI but became visible on follow up MRI. In nine patients the extent of the LMC had progressed and had become bilateral in eight. Two children showed stable disease.

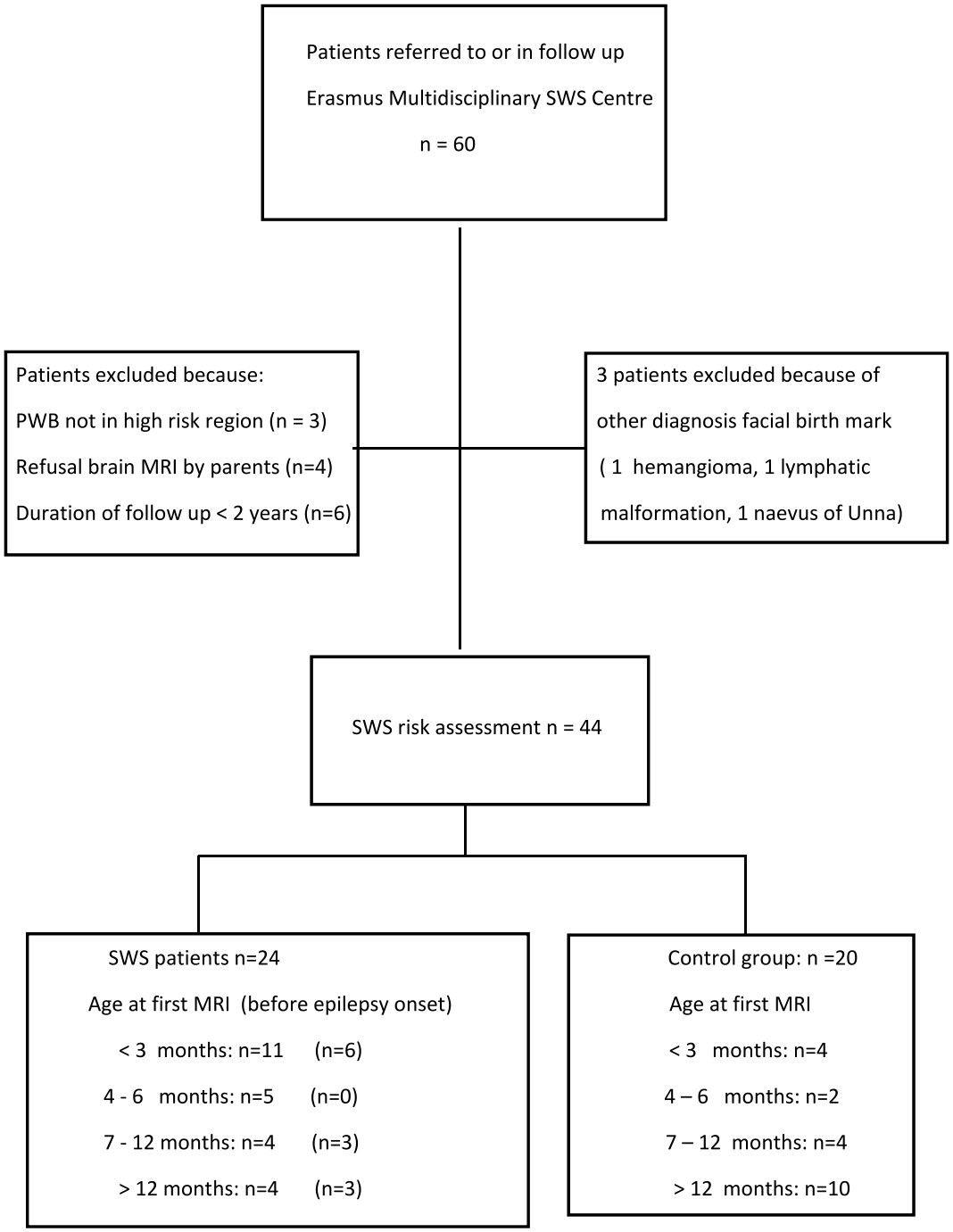

Fig. 2. Flow chart of patient inclusion in the study. Patients were attributed to the SWS1 group when leptomeningeal enhancement was confirmed on MRI. Children were assigned to the control group If no MRI evidence of brain involvement were present at age 12 months or later or no neurological and developmental abnormalities or symptoms were present at age 2 years or later.
n = number of patients.

3.4. Secondary MRI criteria for SWS1 diagnosis

Choroid plexus: All MRI used for analysis of CP thickness in both SWS1 and control groups were made within the first 24 months after birth. All CP measurements on the affected sides were significantly higher in the SWS1 group compared to the control group for MRI with and without contrast administration. Mean CP thickness was 4.2 mm (±1.0) for non-contrast MRI and 4.3 mm (±1.0) for contrast MRI in the control group compared to respectively 7.2 mm (±2,5) and 7.3 mm (±2,5) on the affected sides in the SWS1 group. In the SWS1 group, CP thickness ratio measured (1.44 ± 0.24) for non-contrast and contrast-enhanced MRI. In the control group the CP thickness ratio was 1.09 mm (±0.07). We analyzed the diagnostic accuracy of CP thickness measurements for both non-contrast and contrast MRI as additional prediction tool for early SWS1 diagnosis. CP thickness yielded an optimal cut-off value of 5.6 mm corresponding with a sensitivity of 92.9% and a specificity of 100% for non-contrast MRI and a sensitivity of 92.9% and a specificity of 92.9% for contrast-enhanced MRI.

Abnormal white matter signal**:** In 11 of 24 SWS1 patients (46%) abnormal white matter signal was observed on initial brain MRI. In nine patients this MRI was made at the age of six months or earlier. In three patients abnormal white matter signal became visible on follow up brain

Table 2
Baseline characteristics of included patients.

Characteristics	SWS1 group (n = 24)	Control group (n = 20)	P value
Mean age (at 31 December 2020) Years, months (range)	7,7 (2,0–23,6)	6,0 (2,9–20,6)	0.268
Sex, male number, (%)	15 (62,5%)	9 (45%)	0.307
Mean age at first MRI in months (range)	6,8 (0–38)	19 (0–128)	0.642
Mean age at SWS1 diagnosis in months (range)	8 (0–38)		
Number of patients MRI 0–3 months/ MRI with SWS1 diagnosis[a] (MRI diagnosis before epilepsy onset)	11/6 (n = 4)	4	
Number of patients MRI 4–6 months/ MRI with SWS1 diagnosis[a] (MRI diagnosis before epilepsy onset)	5/3 (n = 0)	2	
Number of patients MRI 6–12 months/ MRI with SWS1 diagnosis[a]. (MRI diagnosis before epilepsy onset)	4/4 (n = 3)	4	
MRI >12 months total number/MRI with SWS1 diagnosis[a] (MRI diagnosis before epilepsy onset)	4/4 (n = 3)	10	
Epileptic seizures	21 (87,5%)		
MRI diagnosis before epilepsy onset	12(50%)		

Data are expressed as mean (range) or absolute numbers (percentage). Statistical significant differences in baseline characteristics between SWS1 group and control group were obtained using independent samples T-test ($P < 0.05$) for scale variables or 2-sided Fisher exact test ($P < 0.05$) for categorical variables. SWS: Sturge Weber Syndrome; MRI = magnetic resonance imaging, n = number of children. [a=]MRI diagnosis following criteria of Bar et al. [17].

Table 3
MRI sequences of first brain MRI in children attributed to the SWS1 (n = 24) and the control group (n = 21).

	SWS1 patients n (%)	Controls n (%)
3D T1	24 (100%)	20 (100%)
T2 (coronal, axial)	24 (100%)	20 (100%)
T2 FLAIR (axial)	18 (75%)	16 (80%)
3DSWI	18 (75%)	16 (80%)
DWI/ADC (axial)	18 (75%)	20 (90%)
3D T1 contrast-enhanced	18 (75%)	20 (90%)
T2 FLAIR contrast-enhanced (axial)	7 (29%)	14 (70%)

Abbreviations: SWS: Sturge Weber Syndrome; MRI = magnetic resonance imaging, SWI: Susceptibility Weighted Imaging, DWI: Diffusion Weighted Imaging, ADC: Apparent Diffusion Coefficient, FLAIR: Fluid-attenuated inversion recovery, n: number.

MRI when this had not been visible on their initial brain MRI made at age 3 months or younger. Abnormal white matter signal was also predominantly found in parietal lobes (unilateral 9 patients, bilateral 1 patient) and occipital (unilateral 8 patients, bilateral 1 patient). Abnormal white matter signal was observed in 75.0% of patients with and 37.5% of patients without prominent medullary or cortical veins. This association was statistically not significant ($p = 0.362$).

Lobar cortical atrophy: Presence of LCA was present in 15 of 24 initial brain MRI in the SWS1 group and was bilateral in three patients. The severity of LCA varied. Some patients displayed a subtle opening of sulci while severely affected children showed evident volume loss of gyri. The parietal lobe was most frequently affected (12 patients). Seventeen SWS1 patients had more than one affected lobe (range: 0–7 atrophic lobes). On follow-up brain MRI, LCA had progressed in 12 patients and was bilateral in four patients. Eight patients showed severe cortical atrophy of the entire unilateral cerebral hemisphere. Two patients had cerebellar atrophy as well.

Ischemia: Only two out of 12 patients (16.6%) had diffusion restriction in areas affected by LMC indicative for recent ischemia. In both patients, indication for MRI was focal status epilepticus. No subsequent MRI studies were made to assess if diffusion restriction was transient and may have been postictal phenomena.

Cortical calcifications: Susceptibility weighted series were available in 16 of 24 SWS1 patients (67%) and T1 weighted images in initial brain MRI of all patients. Four patients with an initial brain MRI at 0, 2.5, 3 and 6 months showed cortical calcifications. Calcifications typically followed a gyriform pattern. On follow up brain MRI nine SWS1 patients showed progressive or new cortical calcifications.

3.5. Early diagnosis of SWS1 based on MRI findings made at age 3 months or earlier

In 11 patients (46.%) initial brain MRI was made at or before age 3 months (Table 4). Following the criteria of Bar et al. (17), in 6 of them SWS1 diagnosis could be confirmed because of the presence of LMC and ≥1 indirect signs. In 4 of these patients MRI diagnosis of SWS1 was made prior to epilepsy onset. In 5 patients LMC was not yet present but ≥1 indirect signs were. In one patient this was discrete widening of parietal cortical sulci and in all five patients asymmetry of CP was present with a CP width of 5.6 mm or more at the affected side (specificity 100%, sensitivity for definite SWS1 diagnosis 35%). If the latter criterium was applied 2 additional (6) SWS1 patients aged 0–3 months would have been identified before epilepsy onset. Follow up MRI showing evident LMC was available for 19 SWS1 patients including those with SWS1 suspicion only on initial MRI. Initial and follow up brain MRI studies of the children in the control group did not show abnormalities.

4. Discussion

We found that in the SWS1 patient group CP thickness and CP thickness ratio on non-contrast brain MRI was significantly increased. The optimal cut-off value of 5.6 mm on the affected side corresponded with a sensitivity of 91.7% and a specificity of 100% for confirmation of SWS1 diagnosis. SWS1 is a severe and often progressive neurocutaneous disease with multiple clinical manifestations. Early onset unrecognized and insufficiently treated seizures are associated with worse neurocognitive outcomes [11,12]. The hallmark of SWS1 brain involvement is the presence of LMC on contrast enhanced MRI [19–21]. Bar et al. found a sensitivity of 85% and specificity of 94% for direct visualization of LMC on contrast MRI in asymptomatic infants before the age of 3 months [17]. Additional use of indirect MRI signs (focal areas with abnormal white matter signal, choroid plexus asymmetry, cortical atrophy)

Table 4
MRI diagnosis of Sturge Weber Syndrome type 1 (SWS1) in children in which an MRI was made at ≤ 3 months of age following the prognostic model of Bar et al. [17].

	SWS1 diagnosis confirmed	SWS1 diagnosis suspected		SWS1 diagnosis uncertain
MRI brain at ≤ 3 months of age	Direct AND ≥1 indirect signs pos	Direct sign pos Indirect sign neg	Direct sign 1 neg Indirect sign pos	Direct sign 1 neg Indirect sign neg
No of SWS1 patients	6	0	5 [3]	0
No of control patients	0	0	0	6 [2]

Legends: Between brackets the number of patients with MRI without Gadolinium enhancement. In the study of Bar et al. leptomeningeal angiomatosis was considered the direct sign. Indirect signs were considered to be abnormal white matter signal such as T1 hypersignal or T2 hypo-signal, asymmetry of the choroid plexus or a localized cerebral atrophy. In the children that showed indirect signs in our study one child with later confirmed SWS1 showed mild parietal cortical atrophy and all SWS1 patients showed choroid plexus asymmetry. pos = positive, neg = negative

increased the sensitivity to 100%. Using the criteria of Bar et al. in our study, sensitivity for SWS1 diagnosis in infants< 3 months was only 35% and specificity 100%. The reason that in three of the five at the time asymptomatic SWS1 patients LMC could not be established was caused by unavailability of contrast enhanced images because contrast could not be applied due to technical issues in the referring centres. CP asymmetry in all five and mild cortical atrophy in one infant suggested indirect MRI signs compatible with a suspected SWS1 diagnosis according to Bar et al. [17]. In all five patients, a follow up contrast-enhanced MRI at the age of 12–14 months confirmed SWS1 diagnosis. This illustrates one of the practical issues in general paediatric neurology practice. Of course, a contrast-enhanced MRI in newborns or young infants with unclear earlier MRI results can be organised but in the children who were referred to us, parents were not all eager to consent to a procedure involving intravenous contrast (sometimes after earlier failure). On the other hand, parents clearly suffered from the insecurity of a possible definite SWS1 diagnosis in the first year of their child.

It is well known that SWS1 is associated with CP enlargement. Previous studies with CT imaging reported CP enlargement in 50–71% of patients [22]. From an embryological point of view, this richly vascularized secretory epithelium is formed by the invagination of the ependymal roof plate into the ventricular cavities [23]. Therefore, choroid plexus enlargement could be considered the direct result of choroidal angiomatosis. Another theory is that ineffective venous drainage leads to choroid plexus engorgement, which is supported by the frequent observation of engorged ependymal veins [24].

In healthy children, no CP magnitude variation exists between gender or age subgroups [25]. One previous study compared CP thickness of 15 children with a SWS1 diagnosis with 15 age-matched controls [23]. In control patients, a mean thickness of 4.0 mm was found (measured at the maximum width of the CP glomus on axial images) with no significant side-to-side size variation. SWS1 patients (all unilateral LMC) demonstrated a significant mean difference in CP thickness of 4.4 mm between the affected and unaffected side [23]. We found a comparable mean CP thickness of 4.3 mm in control patients. In the SWS1 group, the mean CP thickness on the affected side measured 7.3 mm on contrast-enhanced MR images and a CP thickness of 5.6 mm or more was present on initial MRI of all children that were finally diagnosed with SWS1. We found that quantification of CP thickness has significant ability to predict the diagnosis of SWS1 with a CP thickness at an optimum cut-off value of 5.6 mm on non-contrast-MRI yielding the highest discriminatory ability with a sensitivity of 92.9% and specificity of 100%. Because CP thickness remains constant from birth throughout childhood, we suggest that the use of CP thickness measurements on early non-contrast MRI is a safe and non-invasive additional manner to predict SWS1 in neonates and infants with facial PWB. At present we suggest this measurement as a complementary diagnostic tool when contrast MRI is not available or does not as yet show LMC. Our findings, if confirmed in other series may become a reliable diagnostic tool for early SWS1 diagnosis in infancy. Early and reliable diagnosis of SWS1 is important to prepare parents to recognise the onset of seizures in their children as early as possible and start early treatment. It is also pivotal for identification of those children that are at risk for progressive disease and may benefit from early pre-symptomatic neuroprotective treatments with for example antiepileptic drugs or acetylsalicylic acid. Future multicentre international validated trials are urgently needed to establish the clinical value of such regimens and benefits for infants with early signs of SWS1 [25,26]. A reliable method for very early SWS1 diagnosis would be most important to monitor their effects.

The strength of our study is the number of SWS1 patients included and the inclusion of a control group of children with a high risk facial PWB who were referred with a clinical suspicion of SWS1 but in whom the diagnosis could be excluded. The weakness of our study is that although we aimed for a structured MRI follow up programme there still was quite some variation in the timing of initial MRI and available MRI sequences more specifically contrast enhanced series. Especially the initial MRI in very young children in which no contrast series were available illustrate the need for a reliable prognostic measure independent from contrast enhanced MRI series for SWS1 diagnosis. In this study we found that CP size ratio and thickness are sensitive and specific signs additional to the criteria described by Bar et al. [17] to support early SWS1 diagnosis in neonates and young infants. This finding needs to be confirmed in other series.

Declaration of competing interest

None of the authors have any conflict of competing interests to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejpn.2022.04.002.

References

[1] A. Comi, Current therapeutic options in Sturge weber syndrome, Semin.Pediatric Neurol. 22 (2015) 295–301.
[2] R. Waelchli, S.E. Aylett, K. Robinson, W.K. Chong, A.E. Martinez, V.A. Kinsler, New vascular classification of port-wine stains: improving prediction of Sturge-Weber risk, Br. J. Dermatol. 171 (2014) 861–867.
[3] M.D. Shirley, H. Tang, C.J. Gallione, J.D. Baugher, L.P. Frelin, B. Cohen, et al., Sturge-Weber syndrome and port-wine stains caused by somatic mutation in GNAQ, N. Engl. J. Med. 368 (21) (2013) 1971–1979.
[4] L. Huang, J.A. Couto, A. Pinto, S. Alexandrescu, J.R. Madsen, A.K. Greene, et al., Somatic GNAQ mutation is enriched in brain endothelial cells in sturge-weber syndrome, Pediatr. Neurol. 67 (2017) 59–63.
[5] K.N. Kanada, M.R. Merin, A. Munden, S.F. Friedlander, A prospective study of cutaneous findings in newborns in the United States: correlation with race, ethnicity, and gestational status using updated classification and nomenclature, J. Pediatr. 161 (2) (2012) 240–245.
[6] A.I. Marana Perez, M.L. Ruiz-Falco Rojas, V. Puertas Martin, J. Dominguez Carral, I. Carreras Saez, A. Duat Rodriguez, et al., Analysis of Sturge-Weber syndrome: a retrospective study of multiple associated variables Analisis del syndrome de Sturge-Weber: estudio retrospectivo de multiples variables asociadas, Neurologia 32 (6) (2017) 363–370.
[7] I. Pascual-Castroviejo, C. Diaz-Gonzalez, R.M. Garcia-Melian, I. Gonzalez-Casado, E. Munoz-Hiraldo, Sturge-Weber syndrome: study of 40 patients, Pediatr. Neurol. 9 (4) (1993) 283–288.
[8] S.A. Jagtap, G. Srinivas, A. Radhakrishnan, K.J. Harsha, A clinician's dilemma: Sturge-Weber syndrome 'without facial nevus, Ann. Indian Acad. Neurol. 16 (1) (2013) 118–120.
[9] H. Ishikawa, Y. Ii, A. Niwa, K. Matsuura, M. Maeda, H. Tomimoto, A case of 55-year-old man with first-ever generalized seizure diagnosed with Sturge-Weber syndrome type III by characteristic MRI findings, Rinsho Shinkeigaku 57 (5) (2017) 214–219.
[10] C.D. Bachur, A.M. Comi, Sturge-weber syndrome, Curr. Treat. Options Neurol. 15 (5) (2013) 607–617.
[11] E. Bosnyak, M.E. Behen, W.C. Guy, E. Asano, H.T. Chugani, C. Juhasz, Predictors of cognitive functions in children with sturge-weber syndrome: a longitudinal study, Pediatr. Neurol. 61 (2016) 38–45.
[12] A.F. Luat, M.E. Behen, H.T. Chugani, C. Juhasz, Cognitive and motor outcomes in children with unilateral Sturge-Weber syndrome: effect of age at seizure onset and side of brain involvement, Epilepsy Behav. 80 (2018) 202–207.
[13] A.M. Comi, Presentation, diagnosis, pathophysiology and treatment of the neurological features of Sturge-Weber syndrome: a longitudinal study, Neurol. 17 (2011) 179–184.
[14] J. Hu, Y. Yu, C. Juhasz, Z. Kou, Y. Xuan, Z. Latif, et al., MR susceptibility weighted imaging (SWI) complements conventional contrast enhanced T1 weighted MRI in characterizing brain abnormalities of Sturge-Weber Syndrome, J. Magn. Reson. Imag. 28 (2) (2008) 300–307.
[15] C.G. Jacoby, W.T. Yuh, A.K. Afifi, W.E. Bell, R.L. Schelper, Y. Sato, Accelerated myelination in early Sturge-Weber syndrome demonstrated by MR imaging, J. Comput. Assist. Tomogr. 11 (2) (1987) 226–231.
[16] T. Moritani, J. Kim, Y. Sato, D. Bonthius, W.R. Smoker, Abnormal hypermyelination in a neonate with Sturge-Weber syndrome demonstrated on diffusion-tensor imaging, J. Magn. Reson. Imag. 27 (3) (2008) 617–620.
[17] C. Bar, J.M. Pedespan, O. Boccara, N. Garcelon, R. Levy, D. Grevent, et al., Early magnetic resonance imaging to detect presymptomatic leptomeningeal angioma in children with suspected Sturge-Weber syndrome, Dev. Med. Child Neurol. (2019).
[18] M.H. Zweig, G. Campbell, Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine, Clin. Chem. 39 (1993) 561–577.
[19] R.A. Benedikt, D.C. Brown, R. Walker, V.N. Ghaed, M. Mitchell, C.A. Geyer, Sturge-Weber syndrome: cranial MR imaging with Gd-DTPA, AJNR Am. J. Neuroradiol. 14 (2) (1993) 409–415.

[20] L. Marti-Bonmati, F. Menor, C. Poyatos, H. Cortina, Diagnosis of Sturge-Weber syndrome: comparison of the efficacy of CT and MR imaging in 14 cases, AJR Am. J. Roentgenol. 158 (4) (1992) 867–871.
[21] T. Moritani, J. Kim, Y. Sato, D. Bonthius, W.R. Smoker, Abnormal hypermyelination in a neonate with Sturge-Weber syndrome demonstrated on diffusion-tensor imaging, J. Magn. Reson. Imag. 27 (3) (2008) 617–620.
[22] G.K. Stimac, M.A. Solomon, T.H. Newton, CT and MR of angiomatous malformations of the choroid plexus in patients with Sturge-Weber disease, AJNR Am. J. Neuroradiol. 7 (4) (1986) 623–627.
[23] P.D. Griffiths, S. Blaser, M.B. Boodram, D. Armstrong, D. Harwood-Nash, Choroid plexus size in young children with Sturge-Weber syndrome, AJNR Am. J. Neuroradiol. 17 (1) (1996) 175–180.
[24] M. Madhukar, A.K. Choudhary, D.K. Boal, M.S. Dias, M.R. Iantosca, Choroid plexus: normal size criteria on neuroimaging, Surg. Radiol. Anat. 34 (10) (2012) 887–895.
[25] E.I. Lance, A.K. Sreenivasan, T.A. Zabel, E.H. Kossoff, A.M. Comi, Aspirin use in Sturge-Weber syndrome: side effects and clinical outcomes, J. Child Neurol. 28 (2) (2013) 213–218.
[26] D. Ville, O. Enjolras, C. Chiron, O. Dulac, Prophylactic antiepileptic treatment in Sturge-Weber disease, Seizure 11 (3) (2002) 145–150.