

Sturge–Weber syndrome and paroxysmal hemiparesis: epilepsy or ischaemia?

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Transient neurological deficits experienced by patients with Sturge–Weber syndrome can be caused by epilepsy, or may result from temporary ischaemia of the cortex underlying the vascular malformation. To show the difficulty in distinguishing seizures from ischaemic symptoms, two male children with episodes of acute unilateral weakness are presented here as well as a review of the literature. The first child presented at 2 years of age with a sudden increase in his pre-existing right hemiparesis accompanied by screaming. Ictal epileptiform activity was recorded at the moment of the attack, and subsequent seizures were controlled by adjustment of antiepileptic drug treatment. The second child presented at 4 years of age with attacks of vomiting and a coinciding increase in the pre-existing paresis of the left leg. Electroencephalogram (EEG) recording did not show ictal epileptiform activity. The origin was presumed to be vascular. Treatment with aspirin led to control of these transient ischaemic attacks. Ictal EEG is needed to differentiate between an epileptic and an ischaemic origin of transient focal deficit. Treatment with aspirin should be considered if an ischaemic origin cannot be excluded.

Sturge–Weber syndrome (SWS) is a congenital neurocutaneous disorder, typically characterized by telangiectatic venous angiomas of the leptomeninges, an ipsilateral facial angiomatous nevus involving at least the first branch of the trigeminal nerve sensory distribution, and a choroidal angioma (Gomez and Bebin 1987). At pathological examination, a paucity of normal superficial cortical veins is often found. One factor contributing to the development of cerebral damage is a lack of efficient outflow of venous blood, resulting in hypoperfusion and impaired neuronal metabolism (Maria et al. 1998b).

Epilepsy is the most common, and often presenting, symptom of SWS seen with its onset in childhood. Other neurological symptoms include learning disability*, focal deficits, such as a chronic hemiparesis and hemianopia, and stroke-like episodes which consist of transient visual field defects or unilateral weakness (Garcia et al. 1981, Maria et al. 1998a). As epilepsy is the most common symptom of SWS, ictal epileptiform activity or postictal depression of activity is usually considered causative where there are transient neurological symptoms. However, these symptoms can also be caused by temporary ischaemia of the cortex underlying the vascular malformation. Therefore, the occurrence of episodes of a transient focal deficit pose a diagnostic challenge to the clinician. Adequate differentiation between epileptic and ischaemic origins of these events is of utmost importance, as this will have consequences for therapy.

We report on two children with episodes of acute unilateral weakness which highlight the difficulty in distinguishing seizures from ischaemic symptoms. We also present a review of the literature.

*US usage: mental retardation.

Case report

CHILD 1

This male was born after an uneventful pregnancy and delivery. At birth, a port wine nevus in the first branch of the left trigeminal nerve was noticed, leading to the diagnosis of SWS. Seizures, lasting 1 minute and consisting of lowered consciousness and deviation of head and eyes to the left, occurred from the age of 5 months and were resistant to antiepileptic drugs, including vigabatrin, valproic acid, and clobazam. From the



Figure 1a: Cerebral T_2 -weighted MRI of child 1, demonstrating atrophy of left temporo-parieto-occipital region.

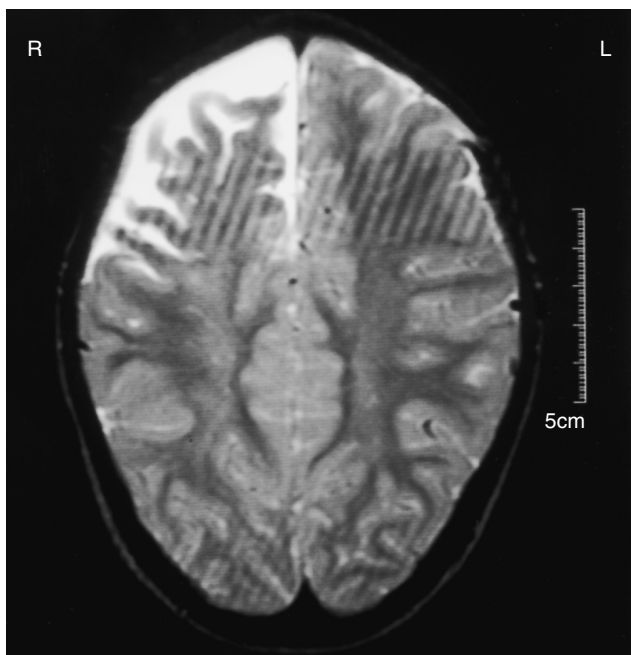


Figure 1b: Cerebral T_2 -weighted MRI of child 2, demonstrating atrophy of right frontoparietal region.

age of 1 year psychomotor development was delayed. A right hemiparesis became manifest. Cerebral magnetic resonance imaging (MRI) showed atrophy in the left temporo-parieto-occipital region (Fig. 1a). At the age of 2½ years he was admitted to the University Medical Centre, Utrecht, the Netherlands, with daily attacks of screaming (as if in pain). During attacks he grabbed for his head but was not nauseous. A coincidental sudden exacerbation of his right hemiparesis was noticed during the majority of attacks, lasting for up to several hours. An electroencephalogram (EEG) performed during an attack showed ictal epileptiform activity, consisting of spike-waves and spike activity, in the left centro-temporo-parietal region (Fig. 2a). EEGs performed before and after attacks did not show any epileptiform activity. The dose of valproic acid was increased, since which the hemiparetic attacks have not been observed during the last 2 years. Attacks of impaired consciousness, considered to be seizures, still occur with a low frequency. The child's development is now progressing.

CHILD 2

This male was born after a twin pregnancy that was complicated by hypertension and intrauterine growth retardation. No facial nevus was present at birth. The first seizures occurred at the age of 5 months and consisted of left hemiconvulsions, preceded by a sudden left hemiparesis. Cerebral computerized tomography, showing atrophy and calcifications in the left frontoparietal region, led to the diagnosis of SWS. Despite administration of several antiepileptic drugs, including carbamazepine, valproic acid, and phenytoin, cessation of seizures could not be achieved. The child was admitted to our hospital for evaluation for functional neurosurgery for epilepsy. Neurological examination revealed psychomotor delay with a mild left hypertonic hemiparesis. Cerebral MRI showed atrophy of the right frontoparietal region (Fig. 1b). Multiple lobectomy was considered. Surprisingly, following yet another change in medication, seizure frequency reduced substantially. Furthermore, psychomotor development improved. At the age of 4 years, he presented with paroxysmal events with a different semiology. Once every 1 to 3 weeks, he vomited and a sudden increase of the pre-existing paresis of the left leg occurred. Positive phenomena, e.g. tingling, were absent. The paresis recovered during the following day. An EEG performed during one of these attacks did not show ictal epileptiform activity (Fig. 2b). The underlying mechanism of these attacks was, therefore, considered to be ischaemic, and a course of aspirin (1mg/kg/day) was prescribed. Thereafter, the paroxysmal events stopped and have not occurred in the last 1½ years of follow-up.

Discussion

We present two children with apparently comparable episodes of a sudden increase in severity of a pre-existing unilateral paresis, illustrating the diagnostic problem of acute focal deficits in individuals with SWS. In the first child, the attacks were caused by focal epileptic seizures, whereas the attacks in the second child appeared to have an ischaemic origin.

Although stroke-like episodes in those with SWS have been acknowledged for many years (Garcia et al. 1981), reports are scarce and the definition of these episodes is poor. Two previous studies (Maria et al. 1998a, b) defined stroke-like episodes as the sudden onset of unilateral weakness with or without seizure activity. Unfortunately, differences in duration and accompanying features between the seizures and stroke-like

events were not analyzed. Furthermore, ancillary investigations to confirm the origin of the events were not performed.

In most cases, seizures can be distinguished from ischaemic events on clinical grounds. Positive phenomena, such as tingling, may occur in transient ischaemic attacks, but tend to arise at the same time in all affected parts of the body, whereas during focal seizures they usually spread from one part to another (Warlow et al. 2001). Accompanying features, such as eye blinking, smacking, and other automatisms, are absent during an ischaemic attack. Furthermore, consciousness is almost invariably maintained in transient ischaemic attacks, whereas it may be lowered during a seizure. However, half of the patients with

SWS have learning disabilities and, therefore, altered behaviour during the attacks may be difficult to interpret.

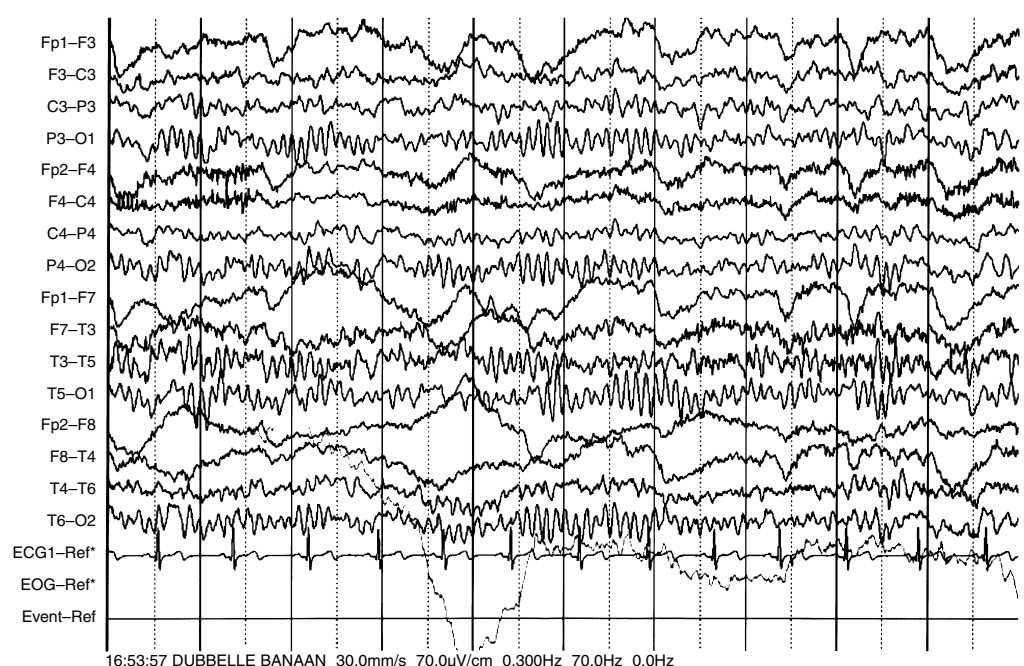
Hemiplegic migraine due to vascular phenomena around the angioma has been reported in one individual with SWS presenting with a transient hemiparesis (Dora and Balkan 2001). As demonstrated by the children in this report, differentiation by semiology may be impossible when attacks consist of sudden focal deficits without positive phenomena. In these cases, ancillary investigations should be performed.

In most people with SWS an interictal EEG is misleading, as interictal epileptiform activity may occur in those with stroke-like episodes, and may be absent in those with SWS (Jansen et

Figure 2a: Ictal EEG (double banana montage) of child 1, showing continuous epileptiform discharges in left centro-temporo-parietal region.



Figure 2b: Ictal EEG (double banana montage) of child 2, showing asymmetry of background activity. No epileptiform activity is demonstrated.



al. 2002). EEG recording during an attack is often diagnostic.

In our first patient, an EEG showed ictal epileptiform activity during an attack, which led to the diagnosis of epilepsy as the cause of his attacks. In child 2, however, EEG recordings at time of the attack did not show ictal epileptiform activity. Based on this finding, together with the clinical signs, an ischaemic cause was assumed.

Although diffusion-weighted MRI has proved useful for the evaluation of those with acute cerebral ischaemia (Roberts and Rowley 2003) as well as for patients with partial status epilepticus (Lansberg et al. 1999), its use for differentiating between ischaemic or epileptic causes of a hemiparesis is probably limited. In both acute focal cerebral ischaemia and status epilepticus, diffusion-weighted MRI demonstrates cortical hyperintensity, and corresponding hypointense areas may be found on apparent diffusion coefficient maps (Lansberg et al. 1999, Roberts and Rowley 2003). Both in individuals with partial status epilepticus and in those with transient ischaemic attacks, diffusion-weighted MRI abnormalities disappear in the subsequent days or weeks (Lansberg et al. 1999, Schulz et al. 2003).

The extent and severity of glucose asymmetry detected by 2-deoxy-2 [18F] fluoro-D-glucose positron emission tomography (FDG PET) has proved a sensitive marker for seizure severity and cognitive decline in SWS (Lee et al. 2001). With use of single photon emission computed tomography (SPECT), cerebral blood flow was found to be lower in the region of the cortex involved in the vascular malformation in patients who had experienced seizures compared with patients who had not (Pinton et al. 1997). To date, both FDG PET and SPECT scanning have not been used to differentiate between ischaemia and epilepsy in individuals with SWS, probably also because of large logistical barriers of ictal scanning.

The value of aspirin in patients with SWS and transient focal deficits has been suggested previously. In one study of 14 patients, a 65% decrease of stroke-like events was found after administration of aspirin (Maria et al. 1998b). Additionally, in a different study, Maria et al. (1998a) reported one patient who developed stroke-like episodes after discontinuation of aspirin. In the present study, the response in the second patient is in keeping with the proclaimed potential benefit of aspirin. Therefore, we suggest that treatment with aspirin should be considered for individuals with manifestations of a paroxysmal hemiparesis without ictal epileptiform activity on EEG.

Additionally, prevention of neurological deterioration after the start of aspirin treatment has been suggested (Roach et al. 1985). Persistent or progressive neurological deficits in individuals with SWS may be caused by two mechanisms (Aylett et al. 1999): the deleterious effect of recurrent seizures, and venous hypertension leading to progressive ischaemia. Local venous thrombosis has been suggested to be involved in this process (Probst 1980). When seizures occur a vicious circle may develop (Bebin and Gomez 1988). The epileptic activity increases the metabolic rate and, thus, the demand for oxygen and glucose; as blood circulation is already disturbed the demand is not fulfilled and more damage may occur, leading to progressive atrophy and calcification in the affected hemisphere, and, consequently, to an increased propensity to develop epileptic seizures (Ito et al. 1990).

Antiplatelet therapy has proved to reduce the risk of deep-vein thrombosis in high-risk patients (Hankey and Eikelboom 2003), and may also benefit people with SWS. Therefore, it would be useful to test the efficacy of aspirin in a large ran-

domized trial of individuals with SWS, even in the absence of seizures.

In conclusion, differentiation between ischaemia and epilepsy as causes of paroxysmal focal deficits in people with SWS can be difficult. Clues can be obtained from a careful targeted history of events. An attempt should be made to perform an EEG at the moment of the attack, as this is often diagnostic. If ischaemia cannot be excluded, administration of aspirin should be considered. A randomized clinical trial is warranted to investigate the value of aspirin in the prevention of neurological deterioration in individuals with SWS.

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