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Sturge-Weber syndrome: a favourable surgical outcome in a case with contralateral seizure onset and myoclonic-astatic seizures

Premysl Jiruska [1,2], Petr Marusic [3], John G.R. Jefferys [1], Pavel Krsek [2], Roman Cmejla [4], Vera Sebronova [2], Vladimir Komarek [2]

[1] Neuronal Networks Group, Neuropharmacology and Neurobiology, School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, United Kingdom
[2] Department of Pediatric Neurology, 2nd Faculty of Medicine, Charles University in Prague, University Hospital Motol, Prague
[3] Department of Neurology, 2nd Faculty of Medicine, Charles University in Prague, University Hospital Motol, Prague
[4] Department of Circuit Theory, Faculty of Electrical Engineering, Czech Technical University, Prague, Czech Republic

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ABSTRACT – Sturge-Weber syndrome is a neurocutaneous disorder classically characterized by the presence of facial port-wine stain and ipsilateral leptomeningeal angiomatosis. It is often associated with refractory epilepsy which requires surgical treatment. We present a case of a patient who initially presented with partial seizures of temporo-occipital origin, ipsilateral to the pial angiomatosis. During the course of the disease, the patient developed medically refractory epilepsy with partial seizures originating predominantly from the contralateral temporo-occipital area as well as myoclonic and myoclonic-astatic seizures. Resection of the occipital and temporal lobe affected by the pial angioma resulted in favourable outcome. Bilateral dysfunction observed in Sturge-Weber syndrome may result in an increased capability of focal discharges to generate synchronous epileptiform activity leading to an increased incidence of generalised seizures, most probably via a mechanism of secondary bilateral synchrony. *[Published with video sequences]*

Key words: Sturge-Weber syndrome, myoclonic-astatic seizures, contralateral seizure onset, epilepsy surgery

Correspondence:
P. Marusic
Department of Neurology,
Charles University in Prague,
2nd Faculty of Medicine,
University Hospital Motol,
V Uvalu 84, Praha 5,
150 06, Czech Republic
<petr.marusic@fnmotol.cz>

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Sturge-Weber syndrome is characterized by facial nevus flammeus and leptomeningeal (pial) angiomatosis. Neurologically, it manifests mainly with seizures, neurological deficit (hemiparesis) and developmental delay. Epilepsy occurs in 75-80% of patients with Sturge-Weber syndrome (Arzimanoglou *et al*., 2000; Pascual-Castroviejo *et al*., 1993), commonly giving rise to partial seizures. In the majority of cases, leptomeningeal angiomatosis is unilateral and preferentially affects the occipital and parietal lobes. Despite the unilateral structural lesion, bilateral dysfunction may be observed, *e.g.* bilateral interictal epileptiform discharges or generalised seizures (Arzimanoglou *et al*., 2000; Chevrie *et al*., 1988; Rosen *et al*., 1984). Involvement of bilateral function was also demonstrated for an altered hemodynamic response and/or hypometabolism which was observed beyond the lesion and in the contralateral hemisphere (Maria *et al*., 1998; Okudaira *et al*., 1997). Contralateral and/or bilateral dysfunction in cases with a unilateral lesion may complicate or delay the decision for epilepsy surgery. In this article, we present a clinical case of Sturge-Weber syndrome, with predominantly contralateral onset of seizures and generalised seizures, which was successfully treated by resection of the unilateral lesion.

Case study

A 12-year-old boy born after an uncomplicated pregnancy. At birth, left facial nevus flammeus was identified. At eight months of age, the first seizure occurred which was characterized by versive head and eye movements to the right side, followed by clonic seizures of the right arm and leg. Neurological examination revealed mild right-sided hemiparesis and a mild deficit in cognitive functions. An MRI scan showed leptomeningeal angiomatosis in the left occipital and part of the left temporal region combined with atrophy of adjacent cortex (*figure 2A, B*). The initial EEG was characterized by the presence of epileptiform discharges in the left temporo-occipital region. From the onset, seizures were difficult to control with antiepileptic drugs. At 11 months of age, the patient underwent video-EEG monitoring which showed that all recorded seizures originated from the left temporo-occipital area. Over the following ten months, the introduction of multiple antiepileptic drugs (vigabatrin, carbamazepine, primidone, valproic acid, phenytoin and topiramate) resulted in a transient decrease in seizure frequency.

At 18 months of age, seizure frequency progressively increased to a frequency of two to six seizures per day. Seizure semiology changed with two main seizure types reported. Firstly, partial seizures characterized by a loss of contact, staring, deviation of eyes to the left, and smiling or fearful facial expressions. Secondly, and more commonly, were seizures characterized by generalised myoclonia or short tonic contractions (spasms) involving mainly both upper extremities. These seizures were sometimes bilateral and asymmetric with right side and rarely left side predominance, sometimes associated with short tonic deviation of the eyes to the right or upwards, and sometimes accompanied by head drops *(see video sequences)*. If the patient was standing, these seizures led to uncontrolled falls. Myoclonic and myoclonic-astatic seizures occurred either in isolation or accompanied partial seizures. During EEG recordings, myoclonias were associated with high-amplitude (500 μV) spike-and-wave discharges *(figure 1A and supplementary figure 1)*. These discharges were distributed bilaterally over the posterior quadrants with amplitude maximum over the right occipito-temporal area. In nine seizures, an initial bilateral synchronous discharge was followed by rhythmic theta activity in the right occipito-temporal region *(figure 1A and supplementary figure 1)*. This pattern was clinically associated with complex partial seizures. Only one seizure clearly originated electrographically from the left hemisphere *(figure 1B)*. Interictal EEG was characterized by discharges of spikes, polyspikes or sharp waves followed by slow waves *(figure 1C)*. Neuropsychological examination showed moderate cognitive delay and a mild deterioration of motor abilities. During the course of the epilepsy, cognition progressively declined and correlated with increased seizure frequency. FDG-PET showed glucose hypometabolism in the left occipital and temporal lobes combined with the inferior part of the parietal lobe *(figure 2C)*.

Surgical treatment was considered due to the refractory nature of the epilepsy and the presence of cognitive decline. However, the shift of EEG seizure onset to the contralateral side and the frequent myoclonic and myoclonic-astatic seizures raised doubts about a possible favourable outcome of surgery. After thorough consideration and consultations with other epilepsy surgery centres, multilobar (left occipital and temporal lobe and affected parts of left parietal cortex) resection at the age of two years and seven months was performed *(figure 2D)*. The postoperative period was complicated by intracerebral haemorrhage in the right parieto-occipital region and a few seizures characterized by vertical eye movements and clonic seizures of the upper right extremity. The intracerebral haemorrhage did not result in any discernable neurological consequences.

Following the surgery the patient was seizure-free for one year, after which sporadic complex partial seizures recurred. Further one-year seizure-free periods were

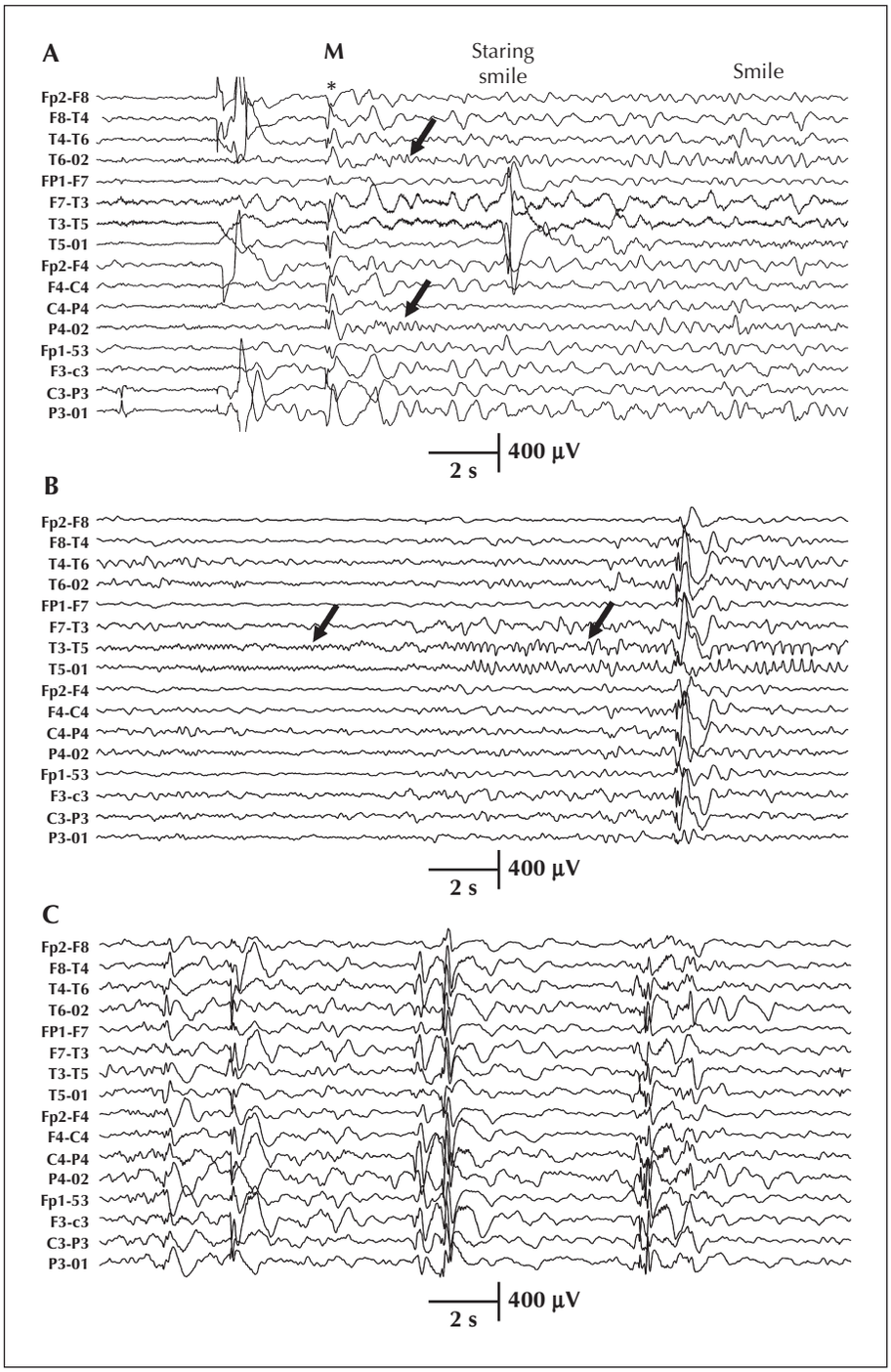

Figure 1. Seizures and interictal activity. Bipolar montage.
A) The seizure started with generalised (bilateral synchronous) high-amplitude discharge (*) accompanied by myoclonia of the upper extremities (M) and was followed by rhythmic theta (5.5 Hz) over the right occipital region (black arrows). This rhythm was associated with, and followed by, a prolonged episode of staring, eye deviation to the left and inappropriate smiling. The entire seizure evolution is presented in *supplementary figure 1*.
B) Ictal recording of rare seizure onset from the left occipital region. Low-amplitude beta activity evolving later into high-amplitude rhythmic alpha (arrows). This electrographic seizure had no correlate with behaviour.
C) Interictal EEG with bilateral synchronous discharges of spike-and-wave complexes or polyspike-and-wave complexes.

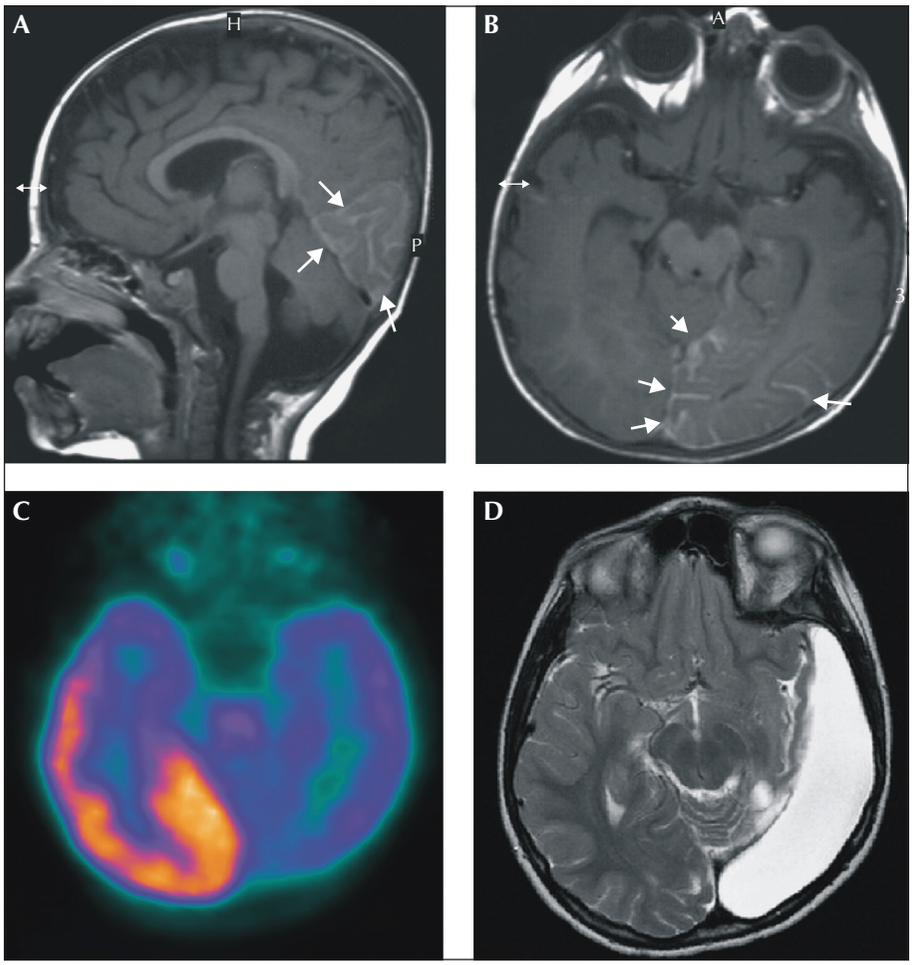

Figure 2. Structural and functional imaging.
Sagittal (**A**) and axial (**B**) T1-weighted MR images with gadolinium enhancement of leptomeningeal angiomatosis in the left occipitotemporal area (white arrows) and atrophy of adjacent cortex.
C) FDG-PET axial scan showing hypometabolism extending beyond the area of angiomatosis.
D) Postoperative MRI, axial T2-weighted image.
(Department of Radiological Techniques, Motol Hospital, Prague and PET Center, Na Homolce Hospital, Prague)

achieved after adjustments of treatment. Currently, the patient is taking vigabatrin and valproic acid. No myoclonic or myoclonic-astatic seizures have been observed since surgery. Neurological examinations revealed that mild right-sided hemiparesis and cognitive impairment persisted and that speech was delayed but continued to improve slowly. The patient was able to attend a special school and developed basic reading and writing skills. However, he also developed autistic behaviour. Postoperative MRI showed neither residual leptomeningeal angiomatosis nor presence of right parietal defect as a sequela of postoperative haemorrhage. Repeated routine EEGs did not show any epileptiform discharges.

Postoperatively, the presurgical EEG recorded during myoclonic and myoclonic-astatic seizures was analysed in more detail. A modified version of phase-coherence with an adaptive autoregressive phase method of time delay estimation was used (Kobayashi *et al*., 1992). Time delay was estimated from bipolar recordings. Signals were also averaged and scalp amplitude maps were constructed using EEGLAB (Delorme and Makeig, 2004) and Matlab (Mathworks Inc). Time delay analysis showed the presence of two types of discharge:

– discharges with a time delay >9 ms suggesting conduction through the corpus callosum *(supplementary figure 2A-C)*;

– discharges with minimal (<9 ms) interhemispheric time delay *(supplementary figure 2D-F)*.

Analysis of the temporal dynamics of bilateral synchronous discharges *(supplementary figure 2G-J)* and their averages showed initial asymmetry with negativity occurring at the onset of discharges and localisation predominantly in the left temporo-occipital region *(supplementary figure 2H)*.

Discussion

Several studies have shown that epileptiform activity in the contralateral hemisphere is a common finding in patients with Sturge-Weber syndrome (Arzimanoglou *et al.*, 2000; Fukuyama and Tsuchiya, 1979; Pascual-Castroviejo *et al.*, 1993). Fukuyama and Tsuchiya (1979) showed that both interictal discharges and ictal patterns occurred bilaterally and predominantly originated in the contralateral hemisphere in five patients with Sturge-Weber syndrome. However, none of the patients in this study underwent epilepsy surgery to reveal the prognostic significance of contralateral scalp EEG seizure onset. Arzimanoglou *et al.* (2000) demonstrated no effect of bilateral interictal abnormality on seizure outcome in patients with Sturge-Weber syndrome. The result of surgical resection in our case also suggests that the occurrence of bilateral epileptiform abnormalities with predominant contralateral seizure onset does not exclude favourable outcome. Possible explanations for the paradoxical contralateral EEG seizure onset include the following:

– the ipsilateral hemisphere is severely damaged, making it impossible for the underlying cortex to generate significant epileptic activity to be detected by scalp EEG;

– the ipsilateral seizures are undetectable by scalp EEG due to location of the seizure onset zone in interhemispheric cortex;

– the contralateral cortex has the ability to generate seizures, but has not reached a stage of complete independence. In all of these cases, resection of primary ipsilateral epileptogenic area can result in the cessation of seizures. Favourable outcome in our patient is consistent with a recent study which demonstrated that presence of contralateral seizure onset in candidates for hemispherectomy may still be associated with very good outcome (Garzon *et al.*, 2009).

Epilepsy in Sturge-Weber syndrome usually manifests with partial seizures, although an increased incidence of generalised seizures has been demonstrated in several studies. Generalised tonic-clonic seizures (Chevrie *et al.*, 1988), myoclonic-astatic seizures (Rosen *et al.*, 1984), astatic seizures (Chevrie *et al.*, 1988; Rappaport, 1988) and infantile spasms (Fukuyama and Tsuchiya, 1979) have been described in patients with Sturge-Weber syndrome. Generalised seizures usually occur during the later stages of epilepsy and, as observed in our case, are associated with bilateral synchronous epileptiform discharges on EEG and poor response to therapy (Chevrie *et al.*, 1988; Rosen *et al.*, 1984). The observation of myoclonic and myoclonic-astatic seizures reported in our patient, and also in other studies (Rosen *et al.*, 1984), can have implications for pathophysiological mechanisms. Astatic, and probably also myoclonic-astatic, seizures require bilateral synchronous epileptic discharges which have the capability to evoke the bilateral myoclonic component or to target brain-stem centres to trigger the atonic component of the seizures (Blume, 1997). The most probable mechanism of bilateral synchronization is secondary bilateral synchrony, when a unilateral epileptiform discharge spreads rapidly via the corpus callosum (or other commissures) and evokes epileptic activity in the contralateral hemisphere (Tukel and Jasper, 1952). In our case, the voltage mapping and analysis of the time delay suggested that the bilateral synchronous discharges, in fact, originated in the affected hemisphere. The absence of time delays in some of the recorded discharges may suggest that both regions behave as coupled oscillators, or that another structure with diffuse connection to both hemispheres (*e.g.* thalamus, brainstem) is involved. The main argument for secondary bilateral synchrony playing a role in the pathophysiology of myoclonic-astatic seizures and astatic seizures is their disappearance following surgery, as observed in our case and that of Rosen *et al.* (1984). Furthermore, callosotomy has been reported to prevent generalised seizures including myoclonic and atonic seizures in patients with Sturge-Weber syndrome (Rappaport, 1988).

Bilateral epileptiform activity in Sturge-Weber syndrome suggests bilateral functional involvement which extends beyond the pial angiomatosis and affected cortex (Maria *et al.*, 1998; Okudaira *et al.*, 1997). Despite the bilateral pathophysiology, resection of the pial angioma in Sturge-Weber syndrome can have a favourable outcome. □

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Legends for video sequences and supplementary figures

Supplementary figure 1

Full seizure evolution with onset from the right hemisphere. **A)** The seizure started with generalised (bilateral synchronous) high-amplitude discharge (*) accompanied by myoclonia (M) and was followed by rhythmic theta (5.5 Hz) over the right occipital region (black arrows). **B)** High-amplitude generalised rhythmic delta (2.0-2.5 Hz) was clinically associated with a prolonged episode of staring. **C)** Generalised rhythmic delta and complexes of sharp-and-slow-wave (2.5 Hz). The seizure terminated with a generalised spike-and-wave discharge, clinically associated with myoclonia (M).

Supplementary figure 2

Analysis of bilateral synchronous discharges. **A-C)** Bilateral synchronous discharges from homologous channels. Time-shift measurement using autoregressive phase-coherence revealed presence of discharges with time shift suggesting interhemispheric conduction delay. **D-F)** Analysis of another discharge demonstrating absence of interhemispheric spread. **G)** High-amplitude spike-wave discharge associated with myoclonic-astatic seizure. **H)** Corresponding voltage maps demonstrating initial negativity in occipital region preferentially on the left side. **I**, **J)** Fully developed spike-wave discharges created dipole with negative polarity in posterior and positive polarity in anterior quadrants.

Video sequence 1

Repeated bilateral asymmetric (right side predominance) or generalised myoclonic seizures, inconsistently associated with eye deviation, upwards or to the right.

Video sequence 2

Generalised or bilateral asymmetric (left side predominance) myoclonic seizure occurring at sleep.

Video sequence 3

Axial tonic seizure.

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