

Focal inhibitory seizure with prolonged deficit in adult Sturge-Weber syndrome

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ABSTRACT – Sturge-Weber syndrome is a sporadic congenital neurocutaneous disorder often related to varying degrees of motor impairment. The phenomenon of prolonged ictal paresis is a rare seizure sign that can be due to lesions affecting the centro-parietal lobe. Focal inhibitory motor seizures can be difficult to differentiate from other clinical entities such as stroke, migraine or postictal paresis. We describe the case of a 40-year-old patient suffering from Sturge-Weber syndrome, admitted due to prolonged right-sided hemiparesis following a usual seizure. Repeated EEGs during the prolonged deficit showed only intermittent left fronto-parietal sharp waves. ^{99m}Tc HMPAO-brain SPECT performed seven days after the last seizure showed a vast area of parieto-occipital hyperperfusion in the left hemisphere. Aggressive antiepileptic therapy dramatically improved the clinical symptoms and scintigraphic images, which corroborated the diagnosis of ictal paresis. This case highlights the role of SPECT in the evaluation of Sturge-Weber syndrome, not only to investigate progressive neurological deterioration, but also exacerbation of seizures or prolonged neurological deficits. In fact, it may be possible to document ongoing epileptic activity using SPECT, despite a non-contributory EEG, which may be of help in adapting a therapeutic strategy.

Key words: Sturge-Weber syndrome, HMPAO SPECT, MRI, inhibitory seizure

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Sturge-Weber syndrome (SWS) is a sporadic congenital neurocutaneous disorder characterized by the presence of abnormal capillary venous vessels in the leptomeninges and the choroid plexus. A typical clinical sign is a portwine stain affecting the skin in the

distribution area of the ophthalmic branch of the trigeminal nerve.

Patients are usually asymptomatic during the first months of life but typically develop seizures within three years. Neurological signs such as epilepsy (which is often refractory to medical therapy), hemiparesis,



Figure 1. Repeated EEGs during prolonged deficit (10/20 system; 10 $\mu\text{V}/\text{mm}$; 20 s/epoch; high frequency filter at 70 Hz; time constant at 0.3 s; bipolar). EEG during wakefulness with eyes closed showing left fronto-parieto-temporal sharp waves with relative left centro-parietal slowing. These paroxysms were intermittent during EEGs and completely disappeared on the interictal EEG follow-up three weeks later.

intellectual impairment, and hemianopsia can be observed. The diagnosis is usually made during the first years of life, based on both clinical and radiological features.

We report the clinical, MRI and $^{99\text{m}}\text{Tc}$ -hexamethylpropylene amine oxime single-photon emission computed tomography ($^{99\text{m}}\text{Tc}$ -HMPAO SPECT) findings of an adult patient with SWS-related inhibitory seizures and prolonged neurological deficit.

Case study

A 40-year-old male Caucasian patient was admitted for unusually prolonged right-sided hemiparesis and non-fluent aphasia. These symptoms followed his regular focal seizures that typically started by upward right-sided dysesthesia, which quickly evolved into hemiparesis before usually receding after a few minutes, without loss of consciousness. This epilepsy was attributed to a traumatic event which occurred at the age of eight months and was treated by phenobarbital until he was 13 years old. In adult life, our patient experienced focal seizures approximately twice a year without any treatment. At clinical observation, we observed brachio-facial right-sided hemiparesis, right-sided hypoesthesia and moderate non-fluent aphasia. The National Institutes of Health Stroke Score (NIHSS) was 7 out of 42 and Manual Muscle Testing grading scale for the upper limb was scored at 3 out of 4

in proximal and 2 out of 4 in distal extremity. Although the aphasia regressed and neither the patient nor the health-care staff reported a usual seizure, antiepileptic therapy (levetiracetam at 1 g/d) had no effect on the hemiparesis or hypoesthesia, which remained stable without motor fluctuation. No precipitating factors were found. Repeated standard EEGs during the prolonged deficit showed only intermittent left fronto-parietal sharp waves but no sign of continuous epileptiform discharges, repetitive or periodic discharges, paroxysmal lateral epileptic discharges (PLEDs; periodic lateralized epileptiform discharges), or other seizures patterns (*figure 1*). CT showed calcifications in the left fronto-parieto-occipital lobe. The diagnosis of SWS was established by MRI, which showed a venous dilatation and a contrast enhancement in the leptomeninges (*figure 2*). Our patient never developed cutaneous port-wine stains, which may have contributed to the delayed diagnosis. Notably, the typical enlargement of the choroid plexus was absent. MRI diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR) imaging and T1 with gadolinium ruled out an ischaemic lesion or venous thrombosis. Because of persistent right-sided paresis and aphasia, $^{99\text{m}}\text{Tc}$ HMPAO-brain SPECT was performed seven days after the last documented usual seizure but during prolonged right-sided hemiparesis and showed a vast area of hyperperfusion, particularly in the parieto-occipital left hemisphere (*figure 2*).

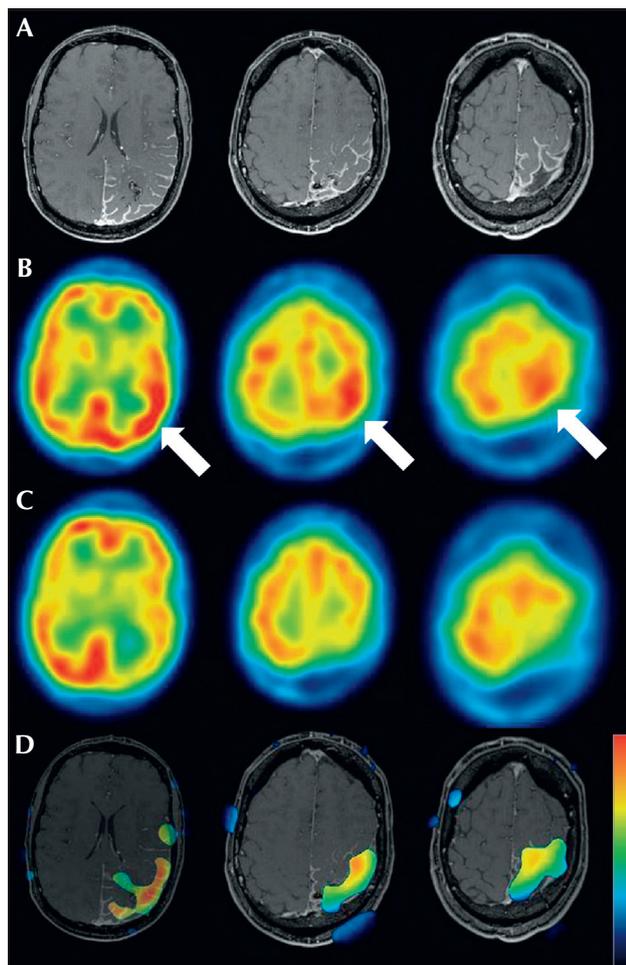


Figure 2. (A) Selected axial slices of brain MRI (T1 with gadolinium) performed two days after the last documented usual seizure, showing left parieto-occipital contrast enhancement in the leptomeninges and dilatation of veins of drainage. (B) Selected axial slices of ^{99m}Tc HMPAO SPECT performed seven days after the last documented crisis but during prolonged right-sided hemiparesis. The area of hyperperfusion involved the whole left parieto-occipital region (arrows). (C) After 29 days of aggressive antiepileptic therapy, the regions became hypoperfused. (D) Subtraction image between the two SPECT series, superposed on the MRI slices, showing an increased perfusion in the left parieto-occipital area. To perform subtraction, the two SPECT series were first normalized for injected activity and then spatially coregistered to the MRI using SPM (Wellcome Trust Center, London, UK).

On the basis of these findings, and despite a negative scalp EEG, we prescribed a more aggressive antiepileptic therapy (*i.e.* increase of levetiracetam dose to 2 g/d and introduction of clobazam at 20 mg/d), which induced complete clinical normalization in less than 48 hours. Interictal ^{99m}Tc -HMPAO SPECT was repeated 27 days after the new therapy and showed hypoperfusion in the same areas previously described (*figure 2*). Interictal EEG returned to normal.

Discussion

We describe an unusual case of prolonged ictal paresis due to SWS-related inhibitory seizures. Despite non-contributory EEGs, ^{99m}Tc -HMPAO SPECT showed extensive perfusion abnormalities, which guided our therapeutic strategy.

SWS is commonly diagnosed in paediatric patients, as its symptoms manifest in the first years of life. For our patient, because of some unusual clinical characteristics (*e.g.* absence of facial angioma, neurological deficit, or developmental delay), the correct diagnosis was reached only at the age of 40. Although MRI and CT are valuable examinations to assess the extension of leptomeningeal angiomas and calcification, they cannot be used to directly measure cerebral perfusion. On the other hand, SPECT can accurately depict blood flow changes, which are often related to the degree of cognitive, visual and motor impairment (Yu *et al.*, 2007). The analysis of the characteristics of our patient's seizure (upward right-sided dysesthesia, followed by hemiparesis and aphasia) was indicative of propagation of epileptic activity from the left parietal postcentral gyrus to temporal and probably frontal lobes.

Focal inhibitory motor seizures are difficult to differentiate from other clinical entities, such as stroke or migraine. Therefore, this rare phenomenon should be considered only after exclusion of these more common disorders. In our case, MRI ruled out a stroke or a venous thrombosis. Interictal hypoperfusion is expected in SWS, migraines, or postictal Todd's paralysis (Chiron *et al.*, 1989; Mathews *et al.*, 2008; Jiménez-Hoyuela *et al.*, 2013). Thus, the unusual hyperperfusion pattern seen using SPECT (the last documented usual seizure occurred seven days before) was decisive of the correct diagnosis. Moreover, our case fulfils some of Fisher's proposed criteria for the diagnosis of inhibitory motor seizures (Fisher, 1978), namely:

- the occurrence of a sensitive aura that precedes the epileptic seizure;
- episodes of paralysis with or without accompanying sensory phenomena in a clinical situation where a seizure, rather than another type of episode, is expected;
- efficacy of anticonvulsive therapy and failure of other therapeutic approaches;
- absence of other conditions that can account for transient attacks of focal weakness.

This ictal negative phenomenon is usually associated with EEG abnormalities, such as PLEDs or continuous epileptiform discharges, in the contralateral centroparietal area. Here, the positivity of the SPECT contrasts with the EEG findings. On EEG, only intermittent left fronto-parietal sharp waves were visible, which do not

represent usual ictal activity. Because of the lack of prolonged EEG monitoring, repeated seizures were difficult to differentiate from postictal neurological dysfunction and prolonged ictal deficit. However, the lack of motor fluctuation, the increased blood flow with SPECT, and the dramatic clinical, radiological and electrophysiological improvement after aggressive antiepileptic therapy support the hypothesis of a persistent occult epileptic activity.

Several authors have shown that ictal negative phenomenon can be due to lesions affecting the centro-parietal lobe and not necessarily SWS-related Bussi re *et al.*, 2005; Murahara *et al.*, 2013; Oono *et al.*, 2014). Moreover, the stimulation of the secondary somatosensory area (Penfield and Rasmussen, 1950) or the supplementary motor area (Penfield and Jasper, 1954) could inhibit voluntary movements or induce paralysis. In addition, L uders *et al.* (1995) postulated the existence of “negative motor areas” (NMAs) in certain dorsal or ventral premotor areas. In view of these findings, the onset of paralysis is compatible with both pre and post-central seizure, with or without SPECT abnormalities in the frontal lobe. However, it is unknown whether this inactivation effect derives from direct subcortical projections (including brainstem and/or spinal cord), from primary motor cortex relays, or from a combination of the two. Moreover, because the negative motor phenomenon is part of a complex clinical picture, there might be concurrent mechanisms including EEG discharge frequency. Several authors have shown that in negative myoclonus, a phasic discharge superimposed on fast oscillations leads to a local myoclonic jerk, whereas an oscillatory discharge of higher frequency leads to impairment in postural control (Chauvel *et al.*, 1992; Shibasaki *et al.*, 1994; Ikeda *et al.*, 2000). Thus, both the discharge frequency and the anatomical localization of the seizure can influence the clinical manifestations. In our case, the anatomical localisation of the angioma (including pre- and postcentral gyrus) and ictal semiology suggested that the seizure propagated from the left parietal postcentral gyrus to the temporal and probably frontal lobes. Unfortunately, we have not been able to highlight specific EEG discharge. Lastly, the aetiology (SWS) and its corollary, ischaemia, could have been a cause of prolonged paresis. However, the results of the MRI and SPECT, and a rapid improvement by aggressive antiepileptic therapy, were not suggestive of ischaemic lesion. The unusual seizure semiology of our patient (negative motor seizure) could be associated with the pre-existing lesion in the primary somatosensory area, which could lead to predominant activation of the inhibitory motor system (Matsumoto *et al.*, 2005).

In summary, SPECT might be a useful tool for the evaluation of SWS patients, not only to investigate progressive neurological deterioration, but also

exacerbation of seizures or prolonged neurological deficits. In fact, it may be possible to document ongoing epileptic activity, despite a non-contributory EEG, which may be of help in adapting a therapeutic strategy. □

Disclosures.

None of the authors have any conflict of interest to disclose.

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