Complex partial status epilepticus is an unrecognised feature in SESA syndrome: new insights into its pathophysiology

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ABSTRACT – We report a patient diagnosed as having subacute encephalopathy with frequent seizures in alcoholics (SESA syndrome), in which recurrent, non-convulsive seizures of frontal origin contributed significantly to the alteration of the mental state. Our case suggests that the occurrence of episodes of complex partial status epilepticus (CPSE) may contribute greatly to the origin and pathophysiology of the confusional state in this rare, epileptic entity.

Key words: subacute encephalopathy with seizures in alcoholics, SESA syndrome, alcoholism, complex partial status epilepticus, frontal non-convulsive seizure, PLEDs

In 1981, Niedermeyer et al. (1981) and Freund and Niedermeyer (1981) reported a subacute encephalopathy in chronic alcoholics characterised by confusion or lethargy, transient motor deficits, and marked electroencephalographic abnormalities such as focal slowing, spikes, and lateralised periodic epileptiform discharges (PLEDs). Partial motor and generalised tonic-clonic seizures (GTCSs) were common. They coined the term subacute encephalopathy with seizures in alcoholics (SESA syndrome) for this condition. Although a precise pathophysiology could not be established at that time, a vascular cause was proposed. Despite of the fact that focal motor and GTCSs have been the unique seizure type described in this entity for the last 25 years, we have recently demonstrated that repeated, non-convulsive seizures (complex partial seizures) may also occur (Fernández-Torre et al. 2006). We present here the clinical, neuroimaging and evolutive EEGs of another case of SESA syndrome in which recurrent complex partial seizures of frontal origin contributed significantly to alteration of the mental state.
We will discuss the pathophysiological and clinical implications of our findings so that we may better understand this rare epileptic entity.

Case report

A 55-year-old Portuguese man was admitted to our emergency unit because of several, left partial motor and secondarily GTCSs followed by right hemiparesis. Previous medical history was difficult to obtain because he did not speak Spanish. He had antecedents of chronic alcohol abuse and chronic vascular insufficiency of the lower limbs. On neurological examination, he was conscious but slightly confused and disoriented in time. Mild right weakness (MRC 4/5) of the right limbs was also observed. The cranial nerves, visual fields and sensory systems were intact. Routine laboratory tests revealed an increase in hepatic enzymes, but were otherwise unremarkable. A computed tomography (CT) scan of the head was considered to be within normal limits. Treatment with phenytoin (300 mg/24 h) was started. On the next day, despite the fact that the focal motor and GTCSs were completely controlled, he remained slightly obtunded and disoriented. An EEG was performed immediately, which supported the diagnosis of recurrent frontal complex partial seizures. In view of these findings, valproic acid (1000 mg/24 h) was added to his antiepileptic therapy. Magnetic resonance imaging (MRI) of the brain disclosed several hyperintense lesions localised in the left frontal and insular cortex (figure 1A). Moreover, 24 hours later, a cerebral 99mTc-hexamethyl-propyleneamine oxime single photon emission computed tomography (SPECT) revealed a zone of marked hyperperfusion localised on the left superior and parasagittal frontal cortex and right cerebellum (figure 1B). Smalls areas of hyperperfusion were also

Figure 1. A) MRI revealed several hyperintense lesions localized in the left frontal and insular cortex. B) Cerebral SPECT showing a notable zone of hyperperfusion localised on the left superior and parasagittal frontal cortex and right cerebellum (crossed cerebellar hyperperfusion). This examination was carried out 24 hours after the diagnosis of CPSE.
seen on the left temporal lobe. Over the following 10 days, he experienced a progressive and significant clinical improvement, and finally, he was discharged with a normal neurological examination on treatment with sodium valproate.

**Evolutive electroencephalographic studies**

On day 2, the EEG showed the occurrence of PLEDs every 1.0-1.5 seconds involving the left frontal and parasagittal region and affecting, to a lesser degree, the homologous contralateral area (figure 2A). During this recording, we captured several partial seizures arising from the left frontal lobe (figure 2B, 2C). The ictal EEG showed a focal discharge of paroxysmal, repetitive rhythmic sharp waves arising from the left superior fronto-central area and spreading rapidly over the whole of the left hemisphere. Subsequently, there was a gradual propagation of seizure activity to the contralateral side, but ictal discharges were predominating on the left hemisphere. The seizure stopped abruptly and a mild, diffuse postictal slowing and generalised decrement of background activity was observed. A few minutes later, PLEDs recurred. Neither clonic movements nor tonic postures occurred. The patient seemed to be slightly more anxious and restless, but oro-alimentary or hands automatisms were not observed. At that moment, a diagnosis of SESA syndrome and recurrent partial seizures of left frontal origin, in keeping with the diagnosis of complex partial status epilepticus (CPSE), was proposed.

On day 4, a second EEG revealed PLEDs affecting the pole of the left frontal lobe. On some occasions, these focal periodic anomalies also involved the ipsilateral temporal and the contralateral frontal area. Focal seizures were not observed. Background activity was within the normal range, but there were some periods in which a marked excess of slow waves were observed over the left hemisphere and right frontal lobe. Subsequently, his focal neurological deficit disappeared and his mental state improved noticeably, but occasionally, he still seemed to be a little confused.

On day 9, a third EEG disclosed occasional slow waves localised on the left frontal and temporal regions, but PLEDs were absent (figure 2D). At that moment, his mental state was considered to be completely normal.

![Figure 2. Evolutative electroencephalographic recordings. A] EEG revealing frontal PLEDs every 1.0-1.5 seconds. Low filter: 0.5 Hz; High filter: 30 Hz; Notch filter: 50 Hz. Vertical bar: 150 μV. Distance between solid vertical dark lines: 1 second (speed: 15 mm/second). Note that the electric field of the epileptiform discharges shows maximal electronegativity on the left frontal (Fp1, F3) and parasagittal (Fz) electrodes involving, to lesser degree, the right side. B] and C] During the first recording we also captured three partial seizures arising from the left frontal lobe. Note the occurrence of rhythmic, regular, 2-4 Hz waves showing phase reversal on the left fronto-central derivation. Low filter: 0.5 Hz; High filter: 30 Hz; Notch filter: 50 Hz. Vertical bar: 150 μV. Distance between solid vertical dark lines: 1 second (speed: 15 mm/second).](image-url)
Discussion

It is our opinion that the occurrence of CPSE in the setting of SESA syndrome is more frequent than has previously been suspected, and it is likely that recurrent complex partial seizures may contribute greatly to the confusional state seen in these patients. Although earlier, Niedermeyer et al. (1981) and Freund and Niedermeyer (1981) described only focal motor and GTCSs, it is possible that the existence of recurrent complex partial seizures were unrecognised; ictal, subclinical episodes of rhythmical spiking were observed in one of their patients. Given that the diagnosis of complex partial seizures is usually associated with the existence of an identifiable change in mental status from baseline, its recognition in a confused subject suffering from SESA syndrome may be controversial. However, the presence of an obvious ictal electroencephalographic pattern accompanied by a fluctuation in patient behaviour, as in our case, seems to be sufficient to confirm our conclusions.

Interestingly, since Niedermeyer and colleagues’ description, only a few reports have been published in the English-language literature concerning the clinical, electroencephalographic and neuroimaging features of this enigmatic condition (Otto and Kozian 2001, Rothmeier et al. 2001, Mani et al. 2003, Fernández-Torre et al. 2006). There have been some further reports on SESA in the German literature. (Homma and Niedermeyer 1993, Boroojerdi et al. 1998, Kozian and Otto 2000). However, to our knowledge, this is only the second case of SESA in which focal, non-convulsive seizures have been described (Fernández-Torre et al. 2006).

Most electroencephalographers believe that PLEDs largely represent interictal discharges. In this case, PLEDs disappeared during focal seizures. However, the patient still remained confused when PLEDs reappeared on the EEG and therefore, during this period, postictal confusion coincided with periodic anomalies. Obviously, a routine EEG recording may only include a fragment of time in which delirium and PLEDs coincide but where seizures are not detected. Under these circumstances, PLEDs can be erroneously considered to be an ictal phenomenon. Nevertheless, this is an excellent example of the hypothesis of Pohlmann et al. where PLEDs form part of a continuum between ictal and interictal states (Pohlmann-Eden et al. 1996). Furthermore, in these patients, alcohol withdrawal associated or not with certain metabolic disturbances, may trigger PLEDs in the absence of acute, destructive, cortical lesions (Chu 1980). However, it is not sensible to be excessively dogmatic because there are rare cases in which PLEDs have been considered to be part of an ictal EEG pattern (Handforth et al. 1994, Garzon et al. 2001). Interestingly, in several patients with SESA syndrome including the case described here, neuroimaging studies have revealed the presence of chronic cerebral lesions of probable vascular origin. Most of cases of SESA syndrome were published before the routine use of the MRI. Therefore, it is likely that some study results may represent false
negatives due to the lower sensitivity of CT scans than MRI for detecting acute or subacute vascular lesions. Crossed cerebellar hyperperfusion was also seen on a brain SPECT carried out 24 hours after diagnosis of CPSE. This is an interesting finding that seems to represent the inverse phenomenon to that of crossed cerebellar diaschisis, and whose mechanism probably is secondary to the activation and hypermetabolic state of the cortico- ponto-cerebellar pathways due to the occurrence of recurrent, continuous, focal cortical epileptic activity (Won et al. 1996).

It is also important to bear in mind the timing of the EEG. In our case, recurrent complex partial seizures were recorded during the first day after the onset of symptoms. Frequently in an alcoholic subject, over the subsequent few hours after the occurrence of a GTCS seizure, the presence of delirium is often thought to be consequence of a postictal state or deprivation syndrome. The case reported here demonstrates that an EEG evaluation should be carried out in all alcoholic adults who remain confused for an abnormally prolonged period of time following a GTCS. A meticulous clinical evaluation and a high level of vigilance during the first 24-48 hours after admission will be essential to diagnose this epileptic condition.

We hypothesise that those patients who develop SESA syndrome frequently have pre-existing cerebral lesions which, under some circumstances such as alcohol withdrawal, metabolic disturbances or both, became highly epileptogenic, originating PLEDs and recurrent focal seizures. While focal motor and GCTCs may be the cause of the hospital admission, complex partial status epilepticus may remain underdiagnosed, and it is likely that they play a relevant role in the pathophysiology and origin of the confusional state in this epileptic entity.

References


