Subacute Encephalopathy With Seizures in Alcoholics Syndrome: A Subtype of Nonconvulsive Status Epilepticus

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Abstract

A recent assessment of the classification of nonconvulsive status epilepticus (NCSE) has incorporated the specific electroencephalographic (EEG) patterns on a syndromic basis. Such a clinical EEG syndromic approach may enable more accurate and expedited diagnosis of particular subtypes of NCSE so as to improve therapy. Herein, we review the characteristics of subacute encephalopathy with seizures in alcoholics syndrome, a subtype of focal NCSE occurring in chronic alcoholism with specific features, including encephalopathy, lateralized periodic discharges on the EEG, chronic microvascular ischemia on neuroimaging studies, and possible recurrence when chronic antiseizure treatment is stopped.

Keywords

SESA syndrome, Alcoholics, complex partial status epilepticus, nonconvulsive status epilepticus, lateralized periodic discharges

Introduction

Neurologists have long been aware of the diversity of neurological syndromes associated with alcoholism. Traditionally, alcohol withdrawal syndrome (AWS), delirium tremens, hepatic encephalopathy, alcoholic hallucinosis, and Wernicke encephalopathy or Korsakoff psychosis are the best known. Epileptic seizures are frequent clinical features that can occur in different settings. Optimization of treatment and accurate syndromic diagnosis and classification determine the ultimate prognosis.

Alcohol withdrawal syndrome is a well-known and common condition occurring after intentional or unintentional abrupt cessation of alcohol consumption. This picture typically occurs within 24 to 48 hours of stopping alcohol, and signs and symptoms may include tremor, irritability, psychomotor agitation, disorientation, hallucinations, anxiety, and generalized tonic-clonic seizures (GTCSs).

An underrecognized clinical disorder of subacute encephalopathy with seizures in alcoholics (SESA) syndrome was first described in 1981.²,³ The SESA syndrome appears as a distinct neurological disorder in which the encephalopathy occurs in the context of focal motor or GTCSs (but often not proximate to alcohol cessation) and includes specific focal electroencephalography (EEG) abnormalities. However, SESA syndrome also occurs in patients with a history of alcohol withdrawal seizures. Awareness of this entity, its clinical findings, and EEG characteristics is essential to making an appropriate diagnosis, which in turn leads to correct and prompt treatment.

Historical Overview of SESA Syndrome

An unusual picture of a subacute encephalopathy in chronic alcoholics characterized by confusion or lethargy, transient neurological deficits, and marked EEG abnormalities was initially characterized by Niedermeyer et al² and Freund and Niedermeyer.³ The EEG findings included focal slowing, spiking, and lateralized periodic discharges (LPDs). Focal motor and GTCSs were common and convulsive status epilepticus was also reported. The patients did not fit criteria for other known neurologic complications in alcoholics, and the authors coined the term SESA syndrome to characterize this condition. Surprisingly, few cases of SESA syndrome have been reported in
Neuroimaging Findings in SESA

As pointed out by Niedermeyer et al., EEG changes in chronic alcoholic patients are not particularly striking. In contrast, in SESA syndrome, EEG abnormalities constitute one of the cornerstones of diagnosis. Focal slowing and spiking and LPDs over the temporal, central, frontal, parietal, and occipital regions were observed by Niedermeyer and associates. They proposed a diverse range of underlying pathogenic mechanisms in their patients, including vascular in 2 patients, traumatic in 1 patient, and “uncertain” in 4 patients.

Electroencephalography Abnormalities in SESA

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Neuroimaging Findings in SESA

Recently, Drake-Pérez et al. reviewed the full spectrum of neuroimaging findings in 10 published cases of SESA. Initial magnetic resonance imaging (MRI) studies revealed cortical–subcortical areas of increased T2/fluid-attenuated inversion recovery (FLAIR) signal and restricted diffusion in 6 patients. In 5 patients, the affected region included the temporal lobe. The areas of abnormal signal correlated with the origin of the LPDs on the EEG for all 6 cases. Hyperperfusion of the region was observed in 3 of the 6 patients (1 patient had increased distal flow on the magnetic resonance angiography [MRA], and the other 2 had a single-photon emission computed tomography [SPECT] revealing hyperperfusion). The other 3 patients did not have confirmatory SPECT or MRAs. Atrophy was present in 62.5% of the patients, with 2 patients showing a temporal predominance, while 3 had diffuse or unspecified atrophy. Chronic microvascular ischemic changes were described in half. Other isolated findings included hydrocephalus, Chiari I malformation, and choroid fissure cyst. Follow-up MRI in 50% of the patients showed resolution of the hyperintense lesions but revealed emerging focal atrophic changes in 75%. Residual T2 hyperintensities were seen in the right temporal lobe and in the splenium of the corpus callosum in other cases.

Kim et al. reported a high signal intensity lesion in the right thalamus associated with focal NCSE in a patient with suspected SESA. In 2 new cases, T2 FLAIR hyperintensities and diffusion restriction in the cingulate gyri, insula, and thalamus and in the right thalamus and mesial temporal lobe, respectively, were observed. To summarize, neuroimaging findings include transient cortical–subcortical T2-hyperintense areas with restricted diffusion along with atrophy and chronic multifocal vascular lesions.

Recently, Fernández-Torre et al. have described both focal hyperperfusion (SPECT) and hypermetabolism (positron emission tomography [PET]), which were strongly suggestive of an epileptic event in the clinical context. The authors concluded that cerebral SPECT and PET closely correlated with EEG can play an important role in the optimization of ASD therapy and diagnosis of SESA syndrome.

Distinguishing Between SESA and AWS

The question has been raised whether SESA is a distinct pathological condition or simply whether it represents the spectrum of CPSs, CPSE, and generalized seizures in the context of AWS or in acute intoxication in chronic alcoholic patients. However, there are significant differences between these entities, including the type of seizures, neurological symptoms, EEG abnormalities, neuroimaging features, and clinical evolution (Table 2). Thus, GTCSs, isolated or recurrent, are the most frequent type seen in AWS. In these cases, the diagnostic value of the EEG is limited and, generally, epileptiform activity is absent. Conversely, in SESA syndrome, although GTCSs or secondarily GTCSs are frequent, focal motor seizures occur in up to 40% of the cases. Moreover, frank epileptiform abnormalities on EEG constitute one of the major diagnostic criteria. Of note, when a patient has recurrence, clinical presentation, EEG, and evolution are frequently stereotyped.

Timing of the EEG is important. In some cases, recurrent CPSs were recorded during the first hours or days of...
Table 1. Summary of the Clinical, EEG, and Neuroimaging Features of All Published Patients With SESA Syndrome in the English Literature.

| Author, Year | Number of Patients/ Age/Sex | Precipitating Factor | Seizure Type | Neurological Deficit | EEG Findings | Neuroimaging | ICU Stay | AEDs |
|--------------|----------------------------|----------------------|--------------|----------------------|--------------|--------------|----------|------|
| Niedermeyer et al, 1981 | 7/41-61 (25)/4M, 3F | Alcohol withdrawal independent | SPMS, GTCS | Lethargy, hemiparesis, hemianopsia | Focal slowing, LPDs | Diffuse cortical atrophy, low density areas | No | PRM, PHT |
| Otto and Kozian, 2001 | 1/66/M | Acute alcoholic intoxication | GTCS | Wernicke aphasia | L fronto-centro-temporal LPDs | Cerebral atrophy; subcortical/periventricular hyperintensities | No | DZP, CLB |
| Rothmeier et al, 2001 | 1/60/M | Alcohol abstinence, hyponatremia | GTCS | Confusion, L homonymous hemianopsia, Wernicke aphasia | R parietooccipital LPDs | Disseminated foci of gliosis, white matter occipital lesions; enhanced signals bilaterally in the occipital white matter | No | CBZ, PHT, DZP |
| Mani et al, 2003 | 1/55/M | Acute alcoholic intoxication | SPMS, SGTCs | Confusion, inattention, R hemiparesis | L parietooccipital LPDs | Cerebral atrophy | No | CBZ |
| Fernández-Torre et al, 2006 | 1/65/M | Alcohol withdrawal, hyponatremia, hypokalemia | GTCS, CPS, focal NCSE | Confusion, disorientation, R hemiparesis | R temporal LPDs | Cerebral atrophy, R temporal hyperintense lesions, R hemisphere hyperperfusion (SPECT) | No | PHT, CZP |
| Fernández-Torre et al, 2007 | 1/55/M | Alcohol withdrawal | SPM, GTGC, focal NCSE | Confusion, disorientation, L hemiparesis, L hemianopsia | L frontal and parietal LPDs, recurrent L frontal Szs | R occipital stroke, R hemisphere transient cortical hyperintensities | No | VPA |
| Bugnicourt et al, 2008 | 1/63/M | Unknown | CPS, focal NCSE | Confusion, disorientation, L hemiparesis, L hemianopsia | L hemisphere LPDs | R occipital stroke, R hemisphere transient cortical hyperintensities | No | VPA |
| LaRoche and Shivdat-Nanhoe, 2011 | 1/61/F | Unknown | SPMS, CPS, focal NCSE | Confusion, R hemiparesis | L hemisphere LPDs, L temporal and parietal Szs | Cortical gray matter frontal, parietal and temporal hyperintensities | Yes (cEEG) | LZP, IFHT, VPA, LCM |
| Choi et al, 2014 (patient 2) | 1/54/F | Unknown | Secondarily GTCS | Drowsy, transcortical sensory aphasia, R hemiparesis | L parietooccipital LPDs + L frontotemporal rhythmic δ activities | L medial temporal, parietal and occipital T2/FLAIR/DWI/ADC hyperintensities; L middle cerebral artery hyperperfusion | No | LEV |
| Fernández-Torre and Kaplan, 2014 | 1/55/M | Alcohol withdrawal | GTCS, CPS, SPMS, focal NCSE | Stupor, L hemiparesis | R temporo-occipital LPDs | Cerebral atrophy; periventricular hypodensities | Yes | PHT, LEV |
| Fernández-Torre and Kaplan, 2014 | 1/58/M | Alcohol withdrawal | SPMS | Confusion, agitation, L hemiparesis | R temporal LPDs | Cerebral atrophy; R temporo-occipital and L parietal ischemic lesions | Yes | PHT, LEV, PPF |
| Kim et al, 2016 | 1/52/M | Alcohol withdrawal | GTCS, focal NCSE | Agitation, confusion, speech disturbances | R frontotemporal Szs, R frontotemporal LPDs | High signal intensity lesion in the R thalamus | No | CBZ |
| Drake-Pérez et al, 2016 | 1/69/M | Unknown | Secondarily GTCSs | Somnolence, L hemiparesis | R temporal LPDs | Atrophy (L medial temporal lobe), chronic white matter changes; R hippocampus enlarged, T2 hyperintensity with restricted diffusion in R insula, parietal and cingulated cortex, and posteromedial thalamus | No | LEV |

(continued)
| Author, Year   | Number of Patients/Age/Sex | Precipitating Factor | Seizure Type          | Neurological Deficit | EEG Findings                                                                 | Neuroimaging                                                                 | ICU Stay | AEDs     |
|---------------|-----------------------------|----------------------|-----------------------|----------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------|---------|----------|
| Kaplan et al, 2018 | 1/50/M                      | Unknown              | SPMS, focal NCSE     | Stupor, confusion    | Ping-pong L and R frontoparietal Szs; R frontoparietal EDs, R LPDs          | T₂ FLAIR hyperintensities and diffusion restriction in the cingulate gyri, insula, and thalami | Yes      | LEV      |
| Kaplan et al, 2018 | 1/54/M                      | Unknown              | Secondarily GTCS, focal NCSE | Disorientation, L hemiparesis | R centrotemporal EDs; R centrotemporal Szs                                    | Diffusion restriction in the R thalamic and mesial temporal lobe                  | No       | LEV, fPHT, PHT, LCM |
| Fernández-Torre et al, 2018 | 1/66/F                     | Poor compliance of ASD therapy | SPMS, secondarily GTCS, convulsive SE | Disorientation, speech disturbances | L temporo-parieto-occipital LPDs                                               | Increased T₂/FLAIR signal and restricted diffusion over the left parietooccipital region; moderate diffuse cerebral atrophy; hyperperfusion (SPECT) and hypermetabolism (PET) | No       | LEV, LCM |

Abbreviations: AEDs, antiepileptic drugs; ASD, antiseizure drug; CBZ, carbamazepine; cEEG, continuous electroencephalography; CLB, cllobazam; CPS, complex partial seizure; CZP, clonazepam; F, female; FLAIR, fluid-attenuated inversion recovery; fPHT, fosphenytoin; GTCS, generalized tonic-clonic seizure; ICU, intensive care unit; L, left; LCM, lacosamide; LEV, levetiracetam; LZP, lorazepam; LPDs, lateralized periodic discharges; M, male; NCSE, nonconvulsive status epilepticus; OXC, oxcarbazepine; PET, positron emission tomography; PHT, phenytoin; PPF, propofol; PRM, primidone; R, right; SE, status epilepticus; SGTCS, secondarily generalized tonic-clonic seizure; SPECT: single-photon emission computed tomography; SPMs: simple partial motor seizures; Szs, seizures; VPA, valproate.

¹One patient was a 25-year-old.
²First paper demonstrating the existence of complex partial seizures in SESA syndrome.
³Presumably complex partial seizures.
⁴Patient 1 of Choi et al's paper was not included because the patient had an abdominal aura and right hippocampal sclerosis suggesting a diagnosis of temporal lobe epilepsy.
symptom onset. Often, in the subsequent hours after GTCSs in alcoholic patients, a delirium is attributed to a postictal state or withdrawal syndrome. Underlying conditions along the ictal–interictal continuum, ranging from LPDs, to focal CPSE, should be considered. Both LPDs and NCSE in other settings have long been recognized as being associated with impaired cognition, focal neurologic signs, and a decreased level of consciousness, but the diagnosis of these conditions is subject to EEG sampling error, and routine 20-minute recordings might not capture them. Generally, LPDs disappear during focal CPSs and reappear after seizure resolution during which time the patient may remain confused. This dynamic represents an excellent example of the hypothesis of Pohlmann-Eden et al,20 in which LPDs form part of a continuum between ictal and interictal states. Continuous EEG appears ideal for revealing this pathophysiological electroclinical evolution. A meticulous clinical evaluation and a high level of suspicion during the first 24 to 48 hours after admission are then essential for an expedited diagnosis and optimal management.

Patients who develop SESA syndrome frequently have pre-existing cerebral lesions which, in the setting of alcohol withdrawal, acute intoxication, metabolic disturbances, or a combination, produce LPDs and recurrent focal seizures. While focal motor and GCTCs are the cause of the hospital admission, CPSs and CPSE remain underdiagnosed and hence undertreated.

Establishing a diagnosis of SESA syndrome contributes to the treatment and management. First, because we are defining what will probably be the patient’s natural history and clinical course. Second, because diagnosis points to specific ancillary tests (eg, clinical EEG [cEEG] monitoring, MRI, SPECT, PET) that will help define the pathophysiology (ictal–interictal) and which will help optimize ASD therapy. Third, because knowing that recurrences are frequent may help convince the patient of the need for strict compliance and alcohol cessation.

**Conclusions**

Subacute encephalopathy with seizures in alcoholics (SESA) syndrome should now include the spectrum of conditions that lie along an ictal–interictal continuum and that may require cEEG monitoring and ICU management. The syndrome encompasses focal NCSE in alcoholic individuals who manifest transient neurologic deficits, interictal LPDs on the EEG, and transient cortical–subcortical T2-hyperintense areas with restricted diffusion and multifocal chronic cerebrovascular abnormalities. Chronic treatment with ASDs is necessary as recurrence is common.

**Declaration of Conflicting Interests**

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**Table 2.** Differentiating AWS From SESA Syndrome.a

| Seizure type          | Alcohol Withdrawal Seizures                                                                 | SESA Syndrome                                                                 |
|-----------------------|---------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Timing                | Generalized tonic–clonic seizures Within 48-72 hours of alcohol cessation                   | Partial focal motor, complex partial and generalized tonic–clonic seizures Up to several days after alcohol cessation, not related to cessation or even associated with acute intoxication |
| Neurological examination | No focal deficits                                                                           | Hemiparesis, aphasia, neglect, hemianopsia, cortical blindness                |
| EEG                   | No focal deficits                                                                          | Focal slowing, LPDs, focal seizures                                           |
| MRI                   | Normal or diffuse slowing                                                                  | Transient cortical–subcortical T2-hyperintense areas with and restricted diffusion observed in a patient with atrophy and chronic multifocal vascular lesions. |
| SPECT                 | -                                                                                           | Focal hyperperfusion                                                          |
| PET                   | -                                                                                           | Focal hypermetabolism                                                         |
| Chronic AED treatment | No                                                                                           | Yes. Frequent recurrences if antiepileptic treatment is stopped               |

Abbreviations: AED, antiepileptic drug; EEG, electroencephalography; LPDs, lateralized periodic discharges; MRI, magnetic resonance imaging; PET, positron emission tomography; SESA, subacute encephalopathy with seizures in alcoholics; SPECT, single-photon emission computed tomography.

*aModified from LaRoche and Shivdat-Nanhoe.*

**Treatment and Response to ASDs in SESA**

Patients with SESA syndrome respond well to ASDs. In some cases, confusion is prolonged and requires intensive care unit (ICU) management.10,11,15 Several ASDs have been used, including phenytoin, valproate, benzodiazepines, and, more recently, levetiracetam and lacosamide. There are no studies that indicate which agent is most effective. Despite a good prognosis, SESA syndrome may warrant chronic treatment with ASDs and cessation of alcohol use to prevent recurrence.
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