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Encephalopathy with status epilepticus during sleep: Unusual EEG patterns

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ABSTRACT

Purpose: To retrospectively analyze the electroclinical characteristics, etiology, treatment, and prognosis of patients with epileptic encephalopathy with status epilepticus during sleep (ESES) with unusual EEG features and to corroborate if this series of patients is part of the ESES syndrome.
Method: Charts of 17 patients with typical clinical manifestations of the ESES syndrome with focal ESES of non-REM sleep at onset and during the focal ESES phase, or bilateral synchronic and asynchronic ESES with a symmetric or asymmetric morphology, continuous or subcontinuous and sometimes multifocal paroxysms with or without slow-wave activity during slow sleep seen between 2000 and 2012 were analyzed.
Results: Mean patient follow-up from onset was 7.5 years. An idiopathic cause was found in seven patients, a structural cause in eight, and etiology was unknown in the remaining two. The median age at onset of the unusual ESES syndrome was 7 years. During the ESES phase, 15 children developed new seizure types, negative myoclonus was observed in seven patients, positive myoclonus in five, and absences in nine. Six patients had motor impairment, two had auditory verbal agnosia, and two had motor speech impairment. Attention deficit hyperactivity disorder was observed in four, aggressiveness in six, memory deficit in two, and impaired temporospatial orientation in four.

The patients with focal ESES in the frontal region showed behavioral disturbances and/or motor deterioration, and in those with temporo-occipital involvement the dominant clinical manifestations were language and/or behavioral disturbances.
Conclusion: Our patients with typical clinical manifestations of ESES syndrome but with unusual EEG patterns may be variants of this syndrome.

1. Introduction

Electrical status epilepticus during sleep was first reported in six children by Patry, Lyagoubi, and Tassinari in 1971.[1] Subsequently, Tassinari and colleagues introduced the term encephalopathy related to electrical status epilepticus during sleep (ESES) for the phenomenon.[2,3] The term continuous spikes and waves during slow sleep (CSWSS) was used as a synonym.[2] Recently, the eponym Tassinari syndrome has been proposed for this epileptic encephalopathy.[4,5] Until the terminology is further defined, here we will use the terms epileptic encephalopathy with ESES or ESES syndrome and ESES alone when referring to the EEG manifestations.

The clinical spectrum of and guidelines for the encephalography (EEG) of the ESES syndrome have recently been published.[6–8] The syndrome may be diagnosed when ESES occurs in more than 85% of non-REM sleep; however, authors have used different cut-off rates[4–8] and the classification of the ILAE does not specify the cut-off value.[9] Several authors have described isolated cases with hemi-ESES based on the distribution of epileptiform activity during sleep[10–15] and a series of patients with hemi-ESES has recently been published.[16] Patterns of focal, bilateral asynchronic, and bilateral asymmetric ESES, slow-wave activity, and multifocal spikes or spikes and waves have also been considered,[3,7] but well-described cases with these EEG features during slow sleep have not been published yet.

From the clinical point of view, deterioration of one or more cognitive functions with or without motor, behavioral, and/or

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psychomotor decline has been described in children associated with ESES.[17,18] Seen from a broader perspective, ESES may be responsible not only for acquired aphasia, but also, and often concomitantly, for other dysfunctions, such as severe behavioral disturbances, apraxia, and negative myoclonus.[2–4] Idiopathic cases and patients with benign childhood epilepsies associated with ESES syndrome have been reported.[19–21] The syndrome may occur in children with structural brain lesions, such as unilateral polymicrogyria (PMG), hydrocephalus, and thalamic lesions.[21–26]

Treatment of the ESES syndrome has frequently been disappointing, but different antiepileptic drug schemes have been proposed.[19,21,23,27–30] In refractory cases, therapeutic alternatives such as corticosteroids, gamma-globulins, the ketogenic diet, and surgery have been tried.[31,32]

The aim of this study was to describe the electroclinical characteristics, etiology, treatment, and prognosis of 17 patients with the typical clinical features of epileptic encephalopathy with ESES but with unusual EEG patterns and to evaluate if these cases are part of the ESES syndrome.

2. Methods

We conducted a retrospective, descriptive study of 17 consecutive patients with clinical features of the ESES syndrome but different EEG patterns seen between 2005 and 2012. All of them met the following inclusion criteria: (1) Onset with focal or apparently generalized seizures and focal EEG discharges; (2) Further appearance of atypical absences and myoclonic, atonic (with or without epileptic falls), and/or generalized seizures; (3) Cognitive impairment and/or behavioral disturbances related to the ESES phase; (4) Focal ESES of non-REM sleep, at onset and during the ESES phase,[2,5] or bilateral synchronic or asynchronic ESES with or without asymmetric morphology, and continuous or subcontinuous, sometimes multifocal paroxysms with or without slow-wave activity during slow sleep. Bilateral synchronic ESES differs from the generalized symmetric pattern in the sense that it is not permanently diffuse and frequently asymmetric. A spike-wave index (SWI) of minimally $\geq$60% was considered. It was evaluated in the maximum SWI during the evolution of ESES.

Focal ESES means the involvement of one or two cerebral lobes. These two patterns included in our study were constant over time. "Continuous" was defined as a permanent EEG abnormality, not interrupted by normal EEG activity, and "subcontinuous" was defined as continuous abnormal EEG activity interrupted by brief periods of normal EEG activity. The EEG abnormalities were analyzed from all charts of our series of patients by the main author.

Patients with an SWI of less 60% associated or not with unusual EEG patterns during sleep but without typical clinical manifestations of ESES syndrome were excluded. Patients with diffuse or hemi-ESES as well as those with other structural epileptic encephalopathies (e.g. myoclonic astatic epilepsy with cognitive deterioration, and Lennox–Gastaut syndrome) and focal epilepsies with secondary bilateral synchronies not fulfilling the criteria for the ESES syndrome were also excluded.

In this study all 17 patients underwent at least four prolonged (more than one hour) sleep EEGs, and nine of them underwent an all-night video-EEG in addition to the routine EEG recordings. The SWI on the non-REM sleep EEG during the ESES phase was visually calculated based on the total number of spikes and waves per unit of time or based on the information provided by the epileptologist in the clinical charts.

Brain magnetic resonance imaging (MRI) was obtained in all patients. Prolonged sleep EEGs were repeated two or more times a year. Data on school achievements and neuropsychological evaluations (Terman-Merrill or WISC III or IV) were repeatedly obtained during the follow-up of 2–9 years. In the absence of formal neuropsychological tests, the degree of cognitive changes was evaluated according to clinical judgment in four patients. The clinical data of the neuropsychological evaluations were obtained when the patients were admitted to the hospital by the same physician.

The onset and the resolution of this unusual ESES phase were defined as the time of onset of cognitive impairment and behavioral abnormalities and the time of significant functional improvement which coincided in all cases with the time of the onset and offset of the pattern on the EEG.

Biochemical controls, urine analysis, and plasma levels of the AEDs were studied. The AEDs and other treatments, such as corticosteroids, the ketogenic diet, and surgery, used before and during the ESES phase were analyzed. Efficacy of the treatment was determined based on electroclinical criteria. Response to treatment of the EEG abnormalities was graded as a normal recording, a more than 75% improvement of the SWI, a more than 50% improvement of the SWI, a more than 30% improvement of the SWI, focalization of the continuous generalized paroxysms, and no response. The percentages of improvement of the SWI were related to the baseline SWI. Clinical response was considered as the decrease of cognitive and behavioral disturbances. The clinical response was graded as complete disappearance of clinical manifestations observed during the unusual ESES phase, and clinical improvement of more than 75%, of more than 50%, or of more than 30%. It was a rough estimation of severity based on the clinical data.

This study was approved by our local ethics committee.

3. Results

3.1. General characteristics

A total of 17 children (10 boys and 7 girls) with an unusual form of the ESES syndrome were identified between March 2000 and April 2012 at the Garrahan Hospital of Buenos Aires.

The probable etiology was idiopathic in seven patients, structural in eight, and unknown in the remaining two. PMG was located in the frontotemporal lobes in three patients and in the parieto-occipital lobes in one. One patient had a bilateral thalamic lesion, one had periventricular leukomalacia, and the remaining structural case had shunted hydrocephalus. From a syndromic point of view, all these patients with structural abnormalities had cerebral palsy, and four also presented with hemiparesis, three with quadriparesis, and one with paraparesis. Mental retardation was mild in two and moderate in six; four of these children had had behavioral disturbances before the onset of the ESES.

Of 17 patients, two had a positive family history and one a positive personal history of febrile seizures.

3.2. Seizures and EEG findings before the onset of the unusual ESES

All children except two had experienced focal motor seizures before the onset of ESES. In four (23.5%) the seizures were associated with loss of consciousness. Seven (41%) had had focal seizures with secondary generalization, and three (17.6%) had had apparently generalized seizures. Atypical absences were found in five patients (29.4%). Tonic seizures were not registered. Ten patients (58.8%) only had had seizures during the sleep, two (12%) only had had seizures while awake, and five (29.4%) had had seizures during sleep and while awake.

The current median age of the patients is 11 years (range, 9–17 years). The median age at onset of focal epilepsy was 3 years (range, 1–8 years). Median time elapsed between the first focal