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Encephalopathy with status epilepticus during sleep or continuous spikes and waves during slow sleep syndrome: A multicenter, long-term follow-up study of 117 patients

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Treatment

Summary
Purpose: To retrospectively analyze the electroclinical features, etiology, treatment and prognosis of 117 patients with encephalopathy with status epilepticus during sleep (ESES) or continuous spike and waves slow sleep (CSWSS) syndrome with a long-term follow-up.
Methods: Charts of 117 patients with ESES/CSWSS syndrome followed between 1990 and 2012 were analyzed. Inclusion criteria were: (1) focal seizures or apparently generalized seizures and focal EEG epileptiform discharges; (2) further occurrence of atypical absences, and myoclonic, atonic, and/or generalized seizures; (3) cognitive impairment and/or behavior disturbances; (4) continuous spike-and-wave discharges during slow sleep in more than 85% of non-REM sleep. Patients with spike-and-wave discharges in less than 85% of slow sleep were also analyzed.
Key findings: 'Mean follow-up from onset of ESES/CSWSS was 13 years (range, 2—22 years) in the symptomatic/structural and non-idiopathic group consisting of 79 children and 10.5 years (range, 2—21 years) in the idiopathic group consisting of 38 children. The comparison of clinical findings and localization of paroxysmal EEG abnormalities (focal, multifocal, or generalized) at the different stages (before, during, and after ESES/CSWSS) and the percentage of spike-wave index during ESES/CSWSS between the symptomatic/structural and non-idiopathic and the idiopathic group was not statistically significant.

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Significance: ESES/CSWSS syndrome is an epileptic encephalopathy with similar electroclinical findings in children with a >85% spike-wave index and those with a <85% spike-wave index. In this series of patients, the most commonly used treatments were clobazam, ethosuximide, sulthiame, alone or in combination. In refractory cases, high-dose steroids were administered. *Among the AED responders, the idiopathic cases returned to normality and the structural cases returned to baseline cognitive development*.

Introduction

Electrical status epilepticus during sleep was first reported in six children in 1971 by Patry, Lyagoubi, and Tassinari (Patry et al., 1971). Subsequently, Tassinari and colleagues introduced the term encephalopathy related to electrical status epilepticus during sleep (ESES) for the phenomenon. The term continuous spikes and waves during slow sleep (CSWSS) was used as a synonym (Tassinari et al., 1985). Until further decisions are made on the name, here we will use the term ESES/CSWSS to describe the entity.

A large proportion of patients presenting with ESES/CSWSS are children with symptomatic or structural epilepsy associated with different types of brain lesions. The clinical spectrum of and guidelines for the electroencephalography (EEG) of the ESES/CSWSS syndrome have recently been published (Tassinari et al., 2009; Kramer et al., 2009; Scheltens-de Boer, 2009). The syndrome may be diagnosed when ESES/CSWSS occurs in more than 85% of non-REM sleep, however, many other authors have used different cut-off rates (Scheltens-de Boer, 2009; Buzatu et al., 2009; Sanchez Fernandez et al., 2012; Van Hirtum-Das et al., 2006) and the classification of the ILAE does not specify a cut-off value (Commission on Classification, 1989).

Patients with atypical benign partial epilepsy of childhood (ABPEC), with status of benign childhood epilepsy with centrotemporal spikes (BCECTS), with Landau—Kleffner syndrome (LKS), and with the ESES/CSWSS syndrome may have in common continuous spike-and-wave discharges on the slow-sleep EEG (Fejerman et al., 2000) and all four conditions have been reported in children with a previous diagnosis of BCECTS (Fejerman et al., 2000). The same atypical evolution associated with ESES/CSWSS has been reported in children with Panayiotopoulos syndrome and in those with childhood epilepsy with occipital paroxysms of Gastaut (Caraballo et al., 2001, 2011a).

From the clinical point of view, deterioration of one or more cognitive functions with or without motor, behavioral, and/or psychomotor decline has been described in children associated with ESES/CSWSS (Kramer et al., 2009; Boel and Casaer, 1989; De Negri, 1997; Veggiotti et al., 2002; Tassinari and Rubboli, 2006; Seri et al., 2009). Seen from a broader perspective, ESES/CSWSS 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 (Kevelam et al., in press). The syndrome may occur in children with organic brain lesions, such as unilateral polymicrogyria, hydrocephalus, and thalamic lesions (Veggiotti et al., 1998; Caraballo et al., 1999; Ben-Zeev et al., 2004).

Treatment of the ESES/CSWSS syndrome has frequently been disappointing. Classic and new AEDs have been switched to benzodiazepines and ethosuximide (Larrieu et al., 1986). An association of valproic acid and ethosuximide is still favored by different groups (Inutsuka et al., 2006; Liukkonen et al., 2010). Sulthiame has been used in isolated cases or in small series of patients with ESES/CSWSS (Kramer et al., 2009; Liukkonen et al., 2010; Wirrell et al., 2006; Fejerman et al., 2012), but is not deemed to be the drug of first choice. Levetiracetam has also been considered (Atkins and Nikanorova, 2011; Larsson et al., 2012). In refractory cases, therapeutic alternatives such as corticosteroids, gamma-globulins, and the ketogenic diet have been used (Fejerman et al., 2000; Caraballo et al., 2011b; Veggiotti et al., 2012).

The aim of this study was to describe the electroclinical features, etiology, treatment, and prognosis of 117 patients with the ESES/CSWSS syndrome with a long-term follow-up.

Methods

We conducted a retrospective, descriptive study of 117 *consecutive* patients with the ESES/CSWSS syndrome followed between 1990 and 2012. All patients 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/CSWSS period; (4) ESES/CSWSS occurring in more than 85% of the non-REM sleep, however, a lower percentage — between 85% and 30% — was also considered (Scheltens-de Boer, 2009; Tassinari et al., 2009; Kramer et al., 2009).

Other epileptic encephalopathies (e.g. Landau—Kleffner syndrome, myoclonic astatic epilepsy with cognitive deterioration, and Lennox—Gastaut syndrome) and focal epilepsies with secondary bilateral synchronies not fulfilling the criteria for the ESES/CSWSS syndrome were excluded.

In this study all patients underwent at least three prolonged sleep EEGs (more than one hour), and 55 of these 117 patients underwent all-night video-EEG in addition to the routine EEG recordings. The spike-wave index (SWI) on the non-REM sleep EEG during the ESES/CSWSS period was visually calculated based on the total number of spike-waves per unit of time or based on the information provided by the epileptologist in the clinical charts. The ranges of the index considered were: >85%, 50—85%, and 30—50%.

Brain magnetic resonance imaging (MRI) was obtained in all patients. Prolonged sleep EEGs were repeated two or more times per year. Data on school achievements and neuropsychological evaluations (Terman-Merrill or WISC III