Continuous spike-and-wave discharges during slow sleep

Authors: Doctors Marie-Noëlle Metz-Lutz[1], Anne de Saint-Martin
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[1]Clinique Neurologique, Hôpitaux Universitaires de Strasbourg, 67091 Strasbourg Cedex, France.

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Abstract
The syndrome of continuous spike and waves discharges during slow sleep (CSWSS) is a rare form of age-related epilepsy. Onset occurs between ages 3 and 7 years, and rarely before 2 years. In the absence of brain lesions, CSWSS syndrome occurs in normally developing children. Partial or generalized seizures are rare and occur while the child is falling asleep. Cognitive functions are subsequently altered and behavioural disorders are often seen. The initial neuropsychological deficits affecting a specific cognitive function such as language, gesture or constructive abilities, attention span or behaviour control are often wrongly attributed to psychological problems. The best known cognitive deficit is aphasia. Acquired epileptic aphasia, the Landau and Kleffner syndrome, has been named after the authors who described it in 1957. EEG anomalies are always present. During wakefulness, EEG recordings show focal paroxysmal spike and wave discharges. During slow sleep, spikes and waves become generalized and continuous, occupying over 85% of sleep. There are no concomitant motor seizures, but cognitive impairments progress. With antiepileptic drugs, the EEG becomes normal and neuropsychological status improves with antiepileptic drugs. Epileptic seizures always disappear with adolescence but neuropsychological sequelae may persist. There is no specific treatment with durable effects on the seizures and neuropsychological disorders. Management of CSWSS syndrome requires teams specialized in pediatric epilepsy and neuropsychology.

Key-words
Infantile epilepsy, aphasia, cognitive disorders, EEG, child neuropsychology

Disease name and synonyms

The continuous spike-and-wave discharges during slow sleep (CSWSS) syndrome is a rare form of infantile epilepsy. It was described for the first time in 1971 under the name "electrical status epilepticus induced by sleep in children" (Patry *et al*., 1971). This clinical entity was subsequently called CSWSS, the term adopted by the Commission on Classification and Terminology of the International League against Epilepsy (ILAE, 1989).

Definition

According to ILAE, epilepsy with CSWSS covers different types of seizures, partial or general, which occur during sleep, and atypical absences during wakefulness. Tonic seizures are absent. Electroencephalogram (EEG) alterations are

continuous diffuse spikes and waves during slow sleep. The CSWSS syndrome can last several months up to several years. Despite the usually benign evolution of the epilepsy, seizures and EEG alterations regress at the beginning of adolescence whatever the effect of anti epileptic drugs. However, prognosis is guarded because of the associated neuropsychological disorders.

Differential diagnosis

At a given time in the evolution of a CSWSS syndrome, the atypical absences and the atonic seizures with falls can evoke a diagnosis of Lennox-Gastaut syndrome. However, the main characteristics of Lennox-Gastaut syndrome, *i.e.* multiple spike-and-wave discharges, spurts of rapid rhythms and tonic seizures, are absent in CSWSS syndrome.

The clinical symptoms and evolution of benign partial epilepsy with centrotemporal spikes are very similar to those of the initial phase of the CSWSS syndrome. In benign partial epilepsy, the strong activation of the focal EEG anomalies during sleep can resemble the form of continuous and diffuse spikes and waves. Although atypical absences and atonic seizures can occur in benign partial epilepsy with centrotemporal spikes, cognitive deficits are less massive and of shorter duration than in CSWSS syndrome.

Etiology

No etiology is known for the idiopathic forms, which represent two-thirds of the CSWSS syndromes.

Neuroradiological examinations do not detect a macroscopic lesion in the majority of cases. In the large series studies, neuroradiological anomalies were found in 25-30% of the patients. In such cases, psychomotor development disorders predate the first manifestations of epilepsy (Bureau, 1995). Focal anomalies of glucose metabolism in positron emission tomography (PET) have been observed during the active phase of epilepsy in a series of 9 patients with CSWSS syndrome (Maquet *et al*., 1995). In all patients, the hypermetabolic cortical regions coincide with the localization of the focus of spike-and-wave discharges recorded on the EEG during wakefulness. The motor and sensory cortical areas are not affected by the metabolic abnormalities that involve only the associated cortical areas undergoing maturation during the active period of the disease (Maquet, 1999). In addition, the specific neuropsychological deficits are in accordance with the localization of the PET-detected hypermetabolism. When the EEG becomes normal and the neuropsychological defects regress, hypometabolism is sometimes observed in the initially hypermetabolic regions (Metz-Lutz, 2001). Recent functional magnetic resonance imaging studies showed that the persisting impairment of verbal short term memory observed in the follow up of CSWSS with acquired aphasia is related to a reduced activity of the superior temporal cortex involved in phonological memory. This focal dysfunction is localised in the cortical area affected by the EEG anomalies during the active phase of CSWSS (Majerus *et al*., 2003).

Clinical description

CSWSS syndrome onset occurs between 3 and 7 years, rarely before 2 years, in children who previously have a normal neurocognitive development. However, some authors have mentioned pre-existing delayed acquisition of language or mental retardation in one-fourth of cases. Epileptic seizures occur usually rarely and are not always the first manifestation of the disease. In some cases (between 8 % to 30 %), seizures may be absent. They can be partial or generalized and most often occur while the child is falling asleep or awakening. At the same time, the family and teachers note a behavioural change associated with a sharp drop in cognitive capacities.

A review of published cases revealed a slight male predominance (Tassinari *et al*.,1992; Bureau, 1995).

Neuropsychological deficits vary in type and intensity. In all cases, they are accompanied by behavioural disorders, notably attention disorders and frequently hyperactivity. These disorders are responsible for the often severe learning difficulties of these children. Acquired aphasia is a common specific neuropsychological deficit and is also the best recognized. This clinical form was described by Landau and Kleffner in 1957 under the name of acquired aphasia with convulsive disorder. Aphasia usually manifests by verbal expression difficulties in the absence of peripheral auditory deficit and by a progressive reduction of oral expression leading to mutism within several months.

EEG characteristics

The EEG recorded during wakefulness shows slow focal spikes and waves. Sometimes there are several independent foci of spikes and waves. Anomalies occur in spurts on a basically normal EEG. During sleep, anomalies frequency increases without altering the cyclic organization of sleep, with continuous spike-and-wave activity occupying 85% of the time.

Evolution

The disease evolves irregularly with periods of aggravation during which behavioural disorders and deterioration of the intellectual capacity are

the predominant symptoms. The frequency and type of epileptic seizures vary. During the day, atypical absences may occur and atony can cause falls. The EEG then shows abundant synchronous bilateral spikes and waves associated with a slow wave focus. Sometimes, a transient focal neurological deficit is present and is associated with strong activation of the nocturnal EEG anomalies. Long term follow-up studies have shown that this fluctuation is correlated with the abundance and the diffusion of epileptic discharges.
Epilepsy disappears after several years of evolution like EEG anomalies and seizures. However, a neuropsychological deficit, which often consists of intellectual retardation, persists in more than half of the patients. In CSWSS with acquired aphasia, verbal abilities improve as EEG anomalies disappear. However, most children show long lasting impaired verbal short term memory which impedes further verbal learning ((Metz-Lutz *et al*., 1999 ; Majerus *et al*., 2003)

Clinical forms
A distinction must be made between the idiopathic forms of CSWSS syndrome, which occur in children with no prior neurological history and normal initial development, and the lesional forms, which are associated with a cerebral lesion. In the latter forms, the neuropsychological deficits that precede epilepsy are associated with a motor deficit, often hemiparesis.

Incidence
It is difficult to estimate the incidence of this disease because of the diagnostic criteria of CSWSS syndrome, which are based on the EEG recording during sleep. The behavioural disorders and the degradations of the child's intellectual capacities sometimes precede the first epileptic seizures and thus orient the child towards a paediatric psychiatrist rather than an epilepsy specialist. In such cases, the rare seizures can be considered epiphenomena and thus further delay the diagnosis of CSWSS syndrome.
From the analysis of a series of more than 12,000 cases of infantile epilepsy examined over 10 years, it was concluded that CSWSS syndrome affects approximately 0.5% of these patients (Morikawa *et al*., 1989/1992). A review of published cases indicated a slight preponderance of boys (Tassinari *et al*.,1992; Bureau, 1995).

Treatment including management
Therapeutic management
Epilepsy and cognitive disorders must both be taken into account to evaluate the severity of the disease and to guide therapeutic decisions. Management requires a pluridisciplinary team with regular clinical, neurophysiological and neuropsychological evaluation. Moreover, the treatment must be adapted to each patient. It is usually a complex therapeutic strategy combining pharmacological agents, rehabilitation and specific education.

Drug therapy
Judicious use of drugs can considerably improve the neurological and neuropsychological status of the child. The therapeutic approach remains controversial, but several broad principles have been proposed. Drug treatment aims not only at suppressing seizures but, primarily, at diminishing nocturnal EEG anomalies. The efficacy of benzodiazapines (clobazam 1 mg/kg/day or clonazepam 0.1 mg/kg/day) has been largely proven, but uncontrolled disease and behavioural side effects are not uncommon. Ethosuximide has been prescribed when atypical absences or focal atony appear. The use of corticosteroids (prednisone, 2 mg/kg/day, with gradual tapering) can sometimes be necessary for a period of about 1 year, when the disease is not controlled by conventional drugs. Some agents, such as carbamazepine or phenobarbital worsens the condition. Data on newer antiepileptics are still limited. Behavioural modifiers can be useful when the child is agitated, as is often the case. Methylphenidate, the most commonly prescribed drug, does not cause a new outbreak of seizures or EEG anomalies.

Importance of educational measures
During the active phase of the disease, affected children are often withdrawn from school because of their behavioural disorders or acquired neuropsychological defects. Individually tailored management has to be organized, sometimes within the context of an adapted educational program. Speech therapy is often essential. The rehabilitation of cognitive deficits is guided by repeated neuropsychological evaluations of the child. Psychological support, individual or familial, is also necessary.

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