Cognitive deterioration in childhood: Never forget electrical status epilepticus during slow-wave sleep

When a child shows any signs of change in cognitive/behavioral functioning (characterized by poorer attention and memory skills, loss of personal autonomy, restlessness, etc.), in the medical work-up, we should never forget the diagnostic hypothesis of electrical status epilepticus during slow-wave sleep (ESES); an electroclinical condition characterized by an electroencephalogram (EEG) picture with diffuse paroxysmal abnormalities (spike-and-waves) lasting for at least 85% of the duration of slow sleep (nonrapid eye movement [NREM] sleep). On the clinical side, in addition to the change in cognitive/behavioral functioning, which should be examined whenever possible through a neuropsychological assessment, focal or generalized epileptic seizures with heterogeneous semeiology, and motor impairment (including, inter alia, ataxia, and dyspraxia) have been described.[1,2] While for most forms of neurocognitive deterioration in childhood (e.g., those due to neurometabolic diseases), there is currently no effective treatment; in the case of ESES, effective therapy and more or less complete recovery are possible. It is mainly for this reason that the diagnostic hypothesis of ESES should never be forgotten when a child shows neurocognitive deterioration. The classic form of ESES syndrome is rare but well-known in the context of childhood epileptology. According to the International Classification of Epilepsies, ESES has been included in epileptic encephalopathies, in which by definition the relevant EEG abnormalities disrupt the neurodevelopment of the individual, leading to an often severe cognitive deterioration.[3] It should also be emphasized that in recent years in the literature, the tendency to distinguish between the term ESES, describing only the EEG findings, and the term continuous spike and wave during slow-wave sleep, which refers to the clinical picture characterized by neurocognitive deterioration related to spike-wave discharges disrupting most of NREM sleep, has been gaining ground.[4]

Today, a very important diagnostic challenge is represented, especially by the atypical variants of ESES syndrome, which are much more frequent as well as more difficult to detect than the typical forms. In particular, they are characterized by frequent EEG abnormalities that last <85% of NREM sleep duration [Figure 1 which shows an example of this type] and by heterogeneous clinical pictures that appear less severe than those reported in the typical ESES.[5-7] Especially in atypical variants of ESES, epileptic seizures may not be present and this can delay a correct diagnosis because an individual without seizures is less likely to undergo an EEG. This is a very important aspect because in ESES syndrome, a pharmacological therapy and, when needed, other interventions such as a ketogenic diet (used for drug-resistant epilepsy since the 1920s),[8] especially if timely to reduce ESES duration as much as possible, could be effective or even decisive for the cognitive long-term outcome of the individual. In this regard, we point out that the most effective drugs in this condition are represented by corticosteroids, but unfortunately drug resistance is not rare.[5-7] The timeliness of a correct diagnosis is paramount and should never be forgotten because the duration of ESES represents one of the most important variables for prognostic purposes: the longer this condition lasts, the greater the risk of an unfavorable evolution at the neuropsychiatric level.[2] It is really surprising that in 2022, a relatively easy to perform, not particularly expensive, and noninvasive examination such as the EEG during wakefulness and especially during sleep is sometimes omitted in a child who presents with a change in cognitive/behavioral functioning in the absence of clinically manifest epileptic seizures. Obviously, the electroclinical diagnosis of ESES also requires carrying out instrumental examinations aimed at understanding its etiopathogenesis, including brain magnetic resonance and genetic investigations.[5-7] However, regardless of the results of these investigations, it should be emphasized that electrophysiological as well as neuroimaging literature data suggest that involvement of the thalamus, causing a thalamocortical circuit dysfunction, could have an important role in the physiopathology of ESES.[9]

Similar considerations are also well suited to Landau–Kleffner syndrome (LKS), a condition considered nosographically close to ESES, differing due to the presence of continuous EEG abnormalities during NREM sleep limited to or clearly prevailing in the bilateral temporal regions and, clinically, of childhood-onset mixed aphasia involving both comprehension and expression (not a global cognitive regression as described

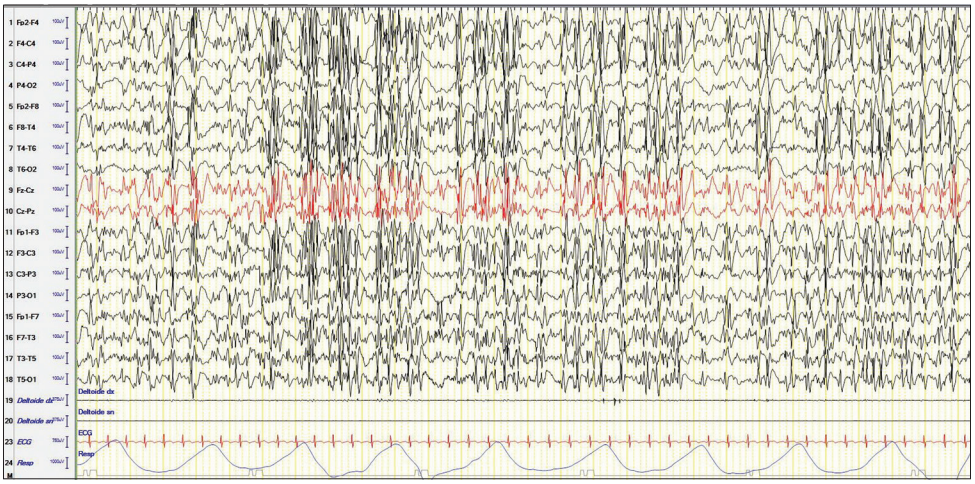

Figure 1: NREM sleep EEG in a girl aged 10 years 11 months with intellectual disability, autism, and drug-resistant epilepsy, showing very frequent diffuse paroxysmal abnormalities, but lasting <85% of NREM sleep duration. NREM: Nonrapid eye movement, EEG: Electroencephalogram

in typical ESES). In LKS, epileptic seizures are less frequent than in typical ESES, and in some cases even absent.[2,10] Furthermore, in LKS, a timely diagnosis and drug therapy are essential to obtain the best long-term outcome in terms of recovery of language.[10]

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