ELECTROENCEPHALOGRAPHY AND CLINICAL PATTERNS VARIABILITY OF CHILD EPILEPTIC ENCEPHALOPATHY

Keywords: epileptic encephalopathies, West syndrome, Lennox-Gastaut syndrome, continuum epileptic encephalopathy.

Epileptic encephalopathies (EE) represent a particular form of epilepsy and are characterized by resistance to treatment, seizures with a polymorphic character, EEG patterns established in the most common forms and a great variability of clinical and electroencephalographic patterns. All these defining characteristics are the result of the involvement of multiple etiologic factors which act isolated or together, causing brain damages of different degrees, very severe in a significant proportion.

The thesis aims on one hand to emphasize the variability of certain epileptic clinical signs and of epileptic electroencephalographic patterns with focus on the phenomenon of continuum epileptic encephalopathy, and on the other hand, to clarify and establish links between etiologic factors, comorbidities and the evolution of these particular forms of epilepsy taking into account the therapeutic factor.

The thesis consists of two parts: the general part which refers to the synthesis of present data regarding epileptic encephalopathies and the special part which gives important details emphasizing the close relationship among them. The results are the outcome of a study on a group of 28 patients.

The general part includes **6** chapters. In the *first chapter* the terms commonly accepted as a definition of specific issues related to epileptic encephalopathies are specified.

The *second chapter* describes the distance covered by clinical entities constituting the EE and the place held by them in different classifications starting with 1967 and ending with that of 2001.

The *third chapter* describes the clinical features of EE forms stress being laid on their polymorphic nature, time of occurrence and their great variability.

In the *fourth chapter* are included current data on modern theories on the pathophysiology of infantile spasms, some of them (the theory of development desyncronization) are accompanied by graphics designed to support and reinforce theoretical explanations.

The *fifth chapter* describes electroencephalographic patterns characteristic to each clinical entity, their evolution according to neuropsychomotric developmental stages and variable character explained by multiple factors.

The *last chapter of the general part* deals mainly with updated panoply of modern methods of electroneurophisiology but also of the neuroimaging and their important

contribution to diagnostic accuracy and its early finding out, both of them allowing an early therapeutic intervention.

The special part (personal research), comprises **5** chapters, plus bibliography including 205 references (three belonging to the author) as well as in extenso papers presented while working on the thesis.

Chapter 7 describes in detail the group of patients who were studied, the criteria for including them in the group , characteristics of the group , the monitoring period and its periodic occurrence , the clinical forms studied using as a criterion their percentage. The equipment used for laboratory investigations (mainly serial EEG recordings) and the software used for the statistical analysis of data are also described. All the resulting data results appear in tables, such as "Pre and perinatal history, family history and personal pathology", "Age of admission to the study, types of crises, ophthalmic and imagistic investigations," "Neurological syndrome ,psychomotor development and language development "," Types of epileptic encephalopathies and comorbidities "," EEG aspects, antiepileptic treatment and seizures progress during treatment. "

Chapter 8 can be considered the "key" of the thesis, the abundance of data it provides, especially through indisputable links that confirm among various etiological factors moments when they act on the immature and vulnerable brain of the small patient, thee structural lesions and dysfunctions that they generated in the brain, all of them being essential factors in the evolution of these patients. Emphasis was laid on the combination in very significant proportions of chronic infantile encephalopathies (ECI) in its various forms and variable degrees of neuropsihomotor retardation, the most common forms of EE (West syndrome, Lennox-Gastaut and Lennox-Gastaut syndrome developed from West syndrome) as well as various types of seizures and different EEG patterns with these forms of EE. Statistics revealed in all situations significant values of p coefficient, much below 0.05. All data displayed above are exemplified by 60 charts and figures and 20 tables, the last containing statistical information.

Chapter 9, meant for discussions, resumes topics covered in previous chapters and based on identified data, tries to give some clarifying explanations. Even if the thesis title does not refer to the treatment of these particular forms, having as main characteristic resistance to treatment often discouraged by the number of AEDs that require association, we presented data on the most current treatments accepted both medicinal and non-pharmacological.

Chapter 10 contains **general conclusions** of which we expose those which refer to etiological factors, to the polymorphic and variable nature of EEG crises and issues.

1. Etiological factors recognized as having significant involvement in determining these syndromes are mostly those who work during the pre, peri and immediate postnatal periods. Different degrees of asphyxia syndromes are the outcome. They weaken the still immature brain and provide conditions for the development of severe conditions, often irreversible. We established strong correlation with statistic significance between values

of Apgar score and asphyxia syndromes .The conclusion was that these parameters are predictors for epileptic encephalopathies in general and West and Lennox-Gastaut syndromein particular.

2. Keeping in mind the etiological factors, opportunistic infections have a decisive role in determining formidable lesions in the brain, depending on the moment when they act on the embryo or fetus. Records from processing sensitive data reveal similar percentages for cytomegaloviruses and herpes viruses (26 and 23%) and lower (13%) for Toxoplasma gondii.

3. Epileptic encephalopathies comorbidities are multiple, but a very significant proportion is held by infant chronic encephalopathies in various presentations, involving severe degree of retardation in a significant percentage and different neurological syndromes (spastic and hypotonic forms in over 60%, ataxic and diskinetic). Developmental retardation may precede the onset of encephalopathy in a rate of 64%, while the decline is installed after the onset of seizures and is currently 34%. The first is more common in West syndrome, the second in Lennox-Gastaut syndrome. Significant comorbidities, not from a statistic point of view, but as determining, the neurocutaneous syndromes, the autistic syndrome, microcephaly and craniosynostosis should be taken into consideration.

4. Polymorphism of the crises is a rule in all forms of epileptic encephalopathy (both in those recognized by most epileptologists and those proposed and being on the waiting list). Even in classical West syndrome in which the infantile spasms are recognized as the only clinical manifestation, as revealed in this study, they can coexist although in generalized seizures in small proportions, not to mention focal seizures that may occur in early clinical spasm (as one can easily see from the example of the clinical case II) or as a clinical sign on onset. The same happens in Lennox-Gastaut syndrome, infantile spasms may persist in association with generalized seizures representative for SLG with an unpredictable evolution as revealed in the study on the degree of control over the seizures.

5. In the same context was noticed the variability of electroencephalographic patterns, even if some forms of epileptic encephalopathy (Ohtahara syndrome, West syndrome, Lennox-Gastaut syndrome and epileptic encephalopathy with status epilepticus in slow wave sleep) have well defined patterns. As found by analyzing the dynamics of EEG recorded tracks in Lennox Gastaut syndrome in early records the VU complex pattern was predominant with double the percentage (30%) compared with generalized periodic pseudorhytmic discharges. In time it diminished leaving space for focal abnormalities generally lesions, and finally be in equal ratio with DPP. In West syndrome, the Hypsarrhyhmic pattern, predominant (40%) at first, significantly diminishes even disappears in some records under the effect of treatment making space for the anomalies previously focused.